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Editorial

Global Dermatology: Learning from the Past but Still Learning from the Best?

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Abstract

If we try to draw conclusions about events, analyse data or results (in one or a certain area) and clarify our unknown points in standard or non-standard ways, this leads to the transfer of experience from one area to another. How do we want to follow guidelines, while the most of the obligatory laws are not followed, for example? The aim of prescriptions or recommendations in medicine, for example, (or the laws of a country that do not usually apply to particular classes or castes, as well as business rules) is to give guidance on how it would be appropriate to help people or ourselves (as we have already mentioned) and the people themselves. Unfortunately, this behaviour is also characteristic of developed societies that dictate the rules and try to help ... to people, as well. If we come deeper into the system of mutual aid in medicine, it is unfortunate that sometimes the condition of this kind of "ecosystem" (or any of the ecosystems described) is worse than the best tragic-comedy. Unfortunately, the "ecosystem of medicine" is also subordinate and slaves somehow to the stronger "ecosystems" as politics and business and is dependent on them, but for evil or good, these ecosystems have glimpsed at times, no matter what are the motives, which provoke them! And they are most often ... once again personal. Although in a number of Eastern European countries, it was unthinkable to even undesirable until recently, that dermasurgery and dermatooncology to be part of modern dermatological societies, the insatiable thirst for growth of young specialists, as well as the impact of Western schools, on their formation as a kind of new hope proved to be stronger in the formation of dermatosurgery, not only all over the world, but also in particular in the Balkans and Bulgaria. These units are gradually being introduced as an indispensable part of any modern clinic, and this part guarantees the best results (in patients with dermatosurgical or dermatooncological needs). The globalisation of dermatology and dermatological science has led to the introduction and involvement of additional auxiliary units, based on a more global concept of the interdisciplinary concept that encompasses psycho-neuroendocrine dermatology which provides a good explanation for some unexplained diseases, such as vitiligo, for example.

Introduction

The advancement of dermatology as a science and introduction of novel surgical treatment techniques as well as the implication of target, non-corticosteroid innovative therapies is due to 1) (similar to the rising of each empire, in historical point of view), the conquest of new territories and the establishment of own habits in the management of patients with certain pathologies (or as in the certain “conquered new territory”) and 2) the aggressive behavior or approach of the physicians themselves (analogous to the warriors of the past, even of the present one). This approach undoubtedly helps in conquering of new units or subdivisions of specialities with a close focus of action, as well as in integrating them into the main or "our speciality" – The Dermatology.

Obviously, the phase of initial aggression or short-term aggression is a necessity for the catharsis of every individual, business lobby, politics, innovation, or a military strategy striving for progressive behaviour. Winston Churchill's quotation from 13 May 1940, in front of the Camara of the communities, postulated: "I have nothing to offer but blood, toil, tears and sweat!" [1] Isn’t Britain a great state nowadays, I would ask?

The correct application of the relevant rules and the good results in the respective "newly conquered territory" inevitably lead to the strengthening of the positions and the approval of the quality of the services to the others, no matter that someone has been affected or injured during the initial clashes, (I focus not only on the historical equivalent but on the medicine, as well). Or, to put it briefly, there is no success without collateral damage to someone or the destruction of the irrational and old-fashioned statuesque.

Often, those who unwilling to adapt to nature, medicine, science, and politics fall into oblivion, because they have lost their never-presented (false demonstrated) inspiration and have to face the reality for which they are not ready, or they no longer have the strength to fight with. Furthermore, rapid adaptation, rapid reaction, awareness and qualification turn out to be crucial weapons or additional bonuses to expand the zone of influence, even in medicine.

This is the basis of the rise of some empires before the beginning of their destruction, which is again due to the loss of control and the loss of self-consciousness of those, who determine the rules. And this loss of control (certainly, sooner or later) has its explanations, which rather affect the individual human nature or the human effigy, which should not be lost in the name of other ideas and goals- opposite to those of the group and the common goodness. We should ask ourselves - to what extent is philosophy related to medicine and to what extent we are pure and objective to ourselves as people and as clinicians? Because the last two are usually connected. If we try to draw conclusions about events, analyse data or results (in one or a certain area) and clarify our unknown points in standard or non-standard ways, this leads to the transfer of experience from one area to another from philosophy to medicine or politics, for example. Stereotypes of behaviour are repeated and analogous, as well as the predictable behaviour of most individuals. Only in the spheres where the main activities develop are different, in the framework of the so-called “theatre”. One great friend once mentioned: "Life is a cabaret!"

Namely, the philosophical point of view should not be ignored, because those who do not learn from the past are most often "absorbed in the waves of the present or the future" [2]. That's how it was in politics, business, so it is in medicine. Although the spheres of influence in these "ecosystems" are completely different, the aims of the participants in these "units" or “similar units” should be one - namely, to help people. This also determines the psychological attitude of the participants in the three to say similar "ecosystems": 1) to help people; 2) to want to help people; 3) sometimes to want to help people; 4) to want to help a little to the people and a little to themselves; or 5) more to themselves and less to the people; 6) or to do not want to help people by presumption or ... and so on to the endless. It should be noted that these attitudes are dynamic [3].

The problem is that none of these ecosystems has a presumed mandatory nature, although it is inherently pended. How do we want to follow guidelines, while the most of the obligatory laws are not followed, for example? The aim of prescriptions or recommendations in medicine, for example, (or the laws of a country that do not usually apply to particular classes or castes, as well as business rules) is to give guidance on how it would be appropriate to help people or ourselves (as we have already mentioned) and the people themselves or - how to move on in the right direction? Unfortunately, this behaviour is also characteristic of developed societies that dictate the rules and try to help ... to people, as well. If we come deeper into the system of mutual aid in medicine, it is unfortunate that sometimes the condition of this kind of "ecosystem" (or any of the ecosystems described) is worse than the best tragic-comedy.

And the reason for this is our human nature, our materiality, our indifference, and our bondage to certain models of a non-normative (at some point or permanent) pattern imposed by the society, or excuses me, from the pseudo-community. It is precisely that it leads to a refraction of the vision, the inability to be humanist, the inability to be clean when looking into the mirror, the impossibility to carry out an adequate therapy if you want to? But if we "clean up the line of behavior", if we clear our vision from the "impossible" ... and focus on the "real", then the results would inevitably be presented [4]. Or, in all likelihood, they would be better - both as humans and as healers.

Unfortunately, the "ecosystem of medicine" is also subordinate and slaves somehow to the stronger "ecosystems" as politics and business and is dependent on them, but for evil or good, these ecosystems have glimpsed at times, no matter what are the motives, which provoke them! And they are most often ... once again personal. It means that they support the thesis of the tragic-comedian point of view, which is hidden under the umbrella of many virtues such as humanity and so on [5].

Considering or guiding the slogan that only pure intentions and thoughts would lead to a successful outcome, if we observe the Hippocratic laws or at least: do not harm or, do not harm, above all, or: first of all, do not think only for yourself, or think mainly about the patients, or at least sometimes, think about the patients?! (Something that used to happened to me unfortunately, but at the moment, rarely, 😊). The person's personality, his decisions, his psychological adjustment itself, or all of them in one – aren’t they all the real prerequisite for a successful therapy? Isn’t the successful therapy determined by us? I would dare to say bravely - YES! Although these solutions are logical and easy as a spontaneous response, they are usually extremely difficult as a final act. Isn’t that... hm – propaganda?

Although in a number of Eastern European countries, it was unthinkable to even undesirable until recently, that dermatosurgery and dermatooncology to be part of modern dermatological societies, the insatiable thirst for growth of young specialists, as well as the impact of Western schools, as The German or, more precisely, the former East German school in Dresden / the Italian School in Rome, Italy / Florence, Italy) on their formation as a kind of new hope proved

to be stronger in the formation of dermatosurgery, not only all over the world, but also in particular in the Balkans and Bulgaria. These units are gradually being introduced as an indispensable part of any modern clinic, and this part guarantees the best results (in patients with dermatosurgical or dermatooncological needs) [6, 7].

The globalisation of dermatology and dermatological science has led to the introduction and involvement of additional auxiliary units, based on a more global concept of the interdisciplinary concept that encompasses psycho-neuroendocrine dermatology which provides a good explanation for some unexplained diseases, such as vitiligo, for example. For our luck, these therapies were introduced in Bulgaria as one of the first highly selective and promising methods for the treatment of major dermatological diseases due to our proximity and close cooperation with the Italian Dermatological School and Prof. Torello Lotti [8, 9].

Despite these irreplaceable and incomparable successes, including also the era of initiation of therapy with biologics for psoriasis and pyoderma gangrenosum, for example, it should be noted that in a number of current diseases, namely in melanoma patients, there are still a number of unclear points and difficulties in terms of which is the best approach in different patients' groups in order to achieve maximum satisfaction for both the physician and the patient [10].

The presence of guidelines in these patients is not always scientifically well-established, and the guidelines themselves are not obligatory, leading to the following problems in the management of these patients:

1) The necessarily of maximum knowledge of dermatologists about the available information on the treatment of skin tumours (this is not always possible due to various factors). This is hampered by the lack of precise guidelines and recommendations. Responsibility couldn't be sought, as a consequence of the variability of the management criteria.

2) The inevitable use of small doors in guidelines to provide the safeness of the physicians themselves but not initially based on maximum patient safety. Doors, used by more refined colleagues, more experienced colleagues.

The idea of creating a special edition of dermatological issue is mainly due to the idea of sharing or accepting good medical practices, which especially in Bulgaria (as well as in many other places in the world) are mediated or provided by two personalities whom I would define first as close friends, and secondly: as our teachers and mentors, as well as world's leaders in dermatology: Prof. Uwe Wollina and Prof. Torello Lotti.

Thanks to the daily and long-standing consultation with the dermatosurgical unit of Prof. Uwe Wollina in Dresden, a great number of Bulgarian patients were and are being assisted daily, and many of them are completely cured of malignant skin tumours.

The introduction of innovative therapies for vitiligo, psoriasis, atopic dermatitis and others cutaneous diseases through low-dose cytokine therapy was facilitated by the contacts and friendly attitude of another prominent person in world's dermatology – Prof. Torello Lotti.

These innovators and I would have dared to say "crusaders" in modern dermatology, are one of the motors or the main reason for:

1. Assistance in creating the special edition of dermatology in the Open Access Macedonian Journal of Medical Science to highlight the progress of good medical practice in Bulgaria, Italy and Germany.
2. The sharing of Bulgarian experience within the framework of the setting of dermatosurgical practices and the immediate results in the long term follows up.
3. Sharing innovations in some oncological and non-oncological diseases.
4. They are also the main reason for the good maintenance and work of the ecosystem, leading to satisfied and smiled patients.

I would like to express my sincere thanks, on behalf of all the participants in the specialized dermatologic issue, to another great person and friend, namely - Prof. Mirko Spiroski, who helped and support the specialized edition, despite of the emotional outbursts of some of us which was partly caused by the high summer temperatures, but also partly by the genotypic component with variable penetrance, as well as the lack of regular systemic medication's administration. They say laughter is health, and self-irony is a high degree of awareness or self-consciousness. Although unconventionally written, I hope that this editorial will make colleagues think about not only the medical but also the human aspects, which, along with the aggressiveness, should be an indispensable part of the progress in medicine. I believe that the formula of success is in balancing between these two "virtues".

It is often mentioned that there is no place in scientific journals for emotional speeches and outbursts, which is or should be correct. But as it was recently found, cytokine levels are those that define our condition such as disease and health. The levels of these small molecules make us react differently in the same situations. Furthermore, they define our emotions and decisions, our human face and nature. And this is the trail that remains behind us, and therefore, it should not be suppressed [11-13].

But we still have to ask ourselves whether we live by the rules and are the world a slave to the

rules? Are the rules a guarantee for success? I would say rather No! How should we follow the guidelines when they are not mandatory? Should only US recommendations be followed? Isn't it the right time for the creation of Independent European and National Guidelines or strict rules for diagnostic and therapeutic behaviour in melanoma patients, for example? Who defines the rules and boundaries of the correct behaviour? Aren't we? Aren't we winning more when we do not follow them? Why and by who are they created? And to whom do these rules serve?

Many questions with many question marks, but furthermore- questions that we would easily solve if we are friends! Or friends at least for a while... I would add!

Because together we are, and will always be stronger!

Thanks to all of my friends, especially to Prof. Wollina and Prof. Lotti, who helped me but also help us to become self-aware, self-defined, to be classified as good clinician! I also thank both of them, because I and all of us grew up as people or rather as humans, within our long-term cooperation. We grew up in our relationship with the people around us and the relationship between ourselves!

We have understood the right direction to which we should move on, and this ... is not a small one!

References

1. Churchill WS. Never Give In!: Winston Churchill's Speeches. A&C Black; 2013 Oct 14.

2. Lamb HH. Climate: Present, Past and Future (Routledge Revivals): Volume 1: Fundamentals and Climate Now. Routledge; 2013 Sep 5.

3. Smith G. Tagging: people-powered metadata for the social web. New Riders; 2007 Dec 27.

4. Kotter JP. Leading change. Harvard Business Press; 1996.

5. Jamieson D. Ecosystem health: some preventive medicine. Environmental Values. 1995;4(4):333-44. https://doi.org/10.3197/096327195776679411

6. Braun-falco O, de DULANTO FE, Epstein E, Bernstein G, Hanke WC. A decade of dermatologic surgery. Dermatologic Surgery. 1985;11(3):199. https://doi.org/10.1111/j.1524-4725.1985.tb02992.x

7. Pavlović MD. Widening competency gaps in the state of the art dermatology. Dermatology and Venereology. 2009:5. PMid:20400785

8. Buggiani G, Troiano M, Rossi R, Lotti T. Photodynamic therapy: off-label and alternative use in dermatological practice. Photodiagnosis and photodynamic therapy. 2008;5(2):134-8. https://doi.org/10.1016/j.pdpdt.2008.03.001 PMid:19356644

9. Nishikawa T. A history of Japanese dermatology: past, present and future. The Journal of dermatology. 2006;33(11):741-4. https://doi.org/10.1111/j.1346-8138.2006.00173.x PMid:17073987

10. Tchernev G, Chokoeva AA. New Safety Margins for Melanoma Surgery: Nice Possibility for Drinking of "Just That Cup of Coffee"? Open Access Maced J Med Sci. 2017. https://doi.org/10.3889/oamjms.2017.068

11. Kronfol Z, Remick DG. Cytokines and the brain: implications for clinical psychiatry. American Journal of Psychiatry. 2000;157(5):683-94. https://doi.org/10.1176/appi.ajp.157.5.683 PMid:10784457

12. Segerstrom SC. Personality and the immune system: Models, methods, and mechanisms. Annals of Behavioral Medicine. 2000;22(3):180-90. https://doi.org/10.1007/BF02895112 PMid:11126462

13. Danielson AM, Matheson K, Anisman H. Cytokine levels at a single time point following a reminder stimulus among women in abusive dating relationships: Relationship to emotional states. Psychoneuroendocrinology. 2011;36(1):40-50. https://doi.org/10.1016/j.psyneuen.2010.06.003 PMid:20598444

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Clinical Science

Fillers and Facial Fat Pads

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Keywords: Fillers; aesthetic medicine; facial anatomy; fat pads.

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Abstract

Fillers are used for facial sculpturing and anti-ageing treatments with increasing popularity. The optimal outcome of any filler treatment depends upon different factors: exact indication, known limitations, filler product, and filler placement. For volumizing effect and longevity of procedures, however, the interaction of fillers and facial fat pads seems to be crucial. Here, we will review the optimum filler injections for facial applications in relationship to new data and concepts concerning facial fat pads anatomy and physiology. Such a view will us enable to provide optimum results in aesthetic procedures.

Introduction

The facial ageing process is characterised loss of volume and ptosis. This is particularly visible in the two lower thirds of the face. Here, bone ligamentous structures, muscles, facial fat pads and skin contribute to the triangular frontal shape that characterises an aged face [1].

The current concept in facial rejuvenation is to gain a natural youthful appearance by three-dimensional sculpturing with a minimally invasive approach [2, 3]. The major biophysical qualities of “dermal” fillers are viscosity, elasticity and cohesivity. However, once placed into human tissue, fillers remain not inert but interact with cells and tissues [4].

Anatomy of facial fat pads

Facial fat pads can be divided into superficial and deep fat pads [5]. Recently another, the third compartment has been identified – the deepest facial fat compartment including buccal and temporal deep fat pads [6].

The superficial, subcutaneous adipose layer is separated by fibrous septae and consists of dermal white adipocytes (dWAT). In the medial and lateral face as well as parts of the periorbital region, temple and forehead the adherence to the skin are loose (Type 1 dWAT). Due to the rich, three-dimensional septal network, it can be classified as structural WAT [6-8].

The type 2 WAT is localised to eyebrows, perinasal and perioral region. Here, a tighter connection to the skin is realised by direct insertion of facial muscles and fibrous septae into the skin. The fibrous WAT is sharply demarcated from structural WAT in nasolabial, labiomandibular and submental sulci [6-8].

dWAT is a dynamic structure that is involved in the innate immune system, thermoregulation, wound healing, and hair follicle cycling. These adipocytes have been shown to transdifferentiate into myofibroblasts under certain circumstances [9].

Deep fat compartments contain subcutaneous white adipose tissue (sWAT) separated by the

superficial musculoaponeurotic system (SMAS) in the midface and the superficial temporal fascia in the temple. Boundaries of these deep fat pads are created by facial muscles and retaining ligaments. The deep fat pads are slowly renewing with an average turnover time of about ten years [10].

In some parts of the face, another deeper fat pad compartment can be found. The most prominent are the buccal fat pad localised in the Bucco temporal space and serve a metabolic function [11].

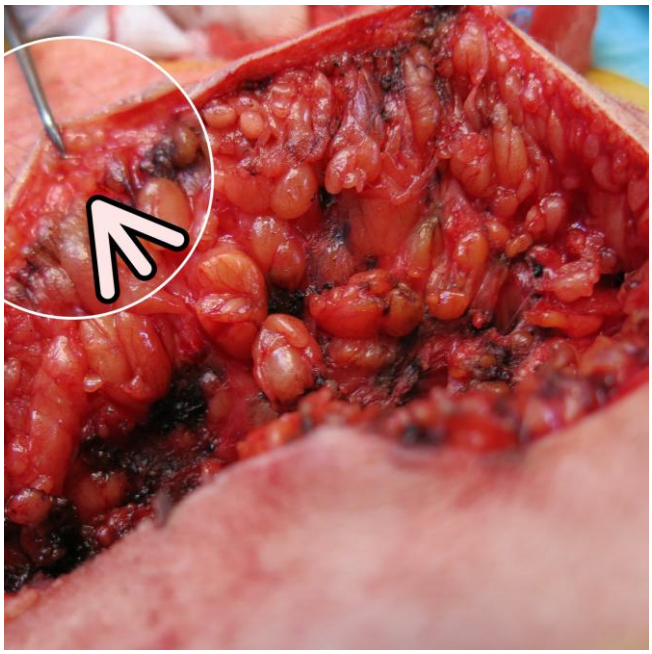

Figure 1: Abdominal subcutaneous fat with small adipocytes in the superficial layer and large adipocytes in the deep layer separated by a delicate membrane (Arrow)

Adipocytes are not uniform by size and functionality (Fig. 1). The release of chemokines from adipocytes [12] and macrophage infiltration [13] are directly related to the size of the adipocytes. Hypertrophic (large) adipocytes exhibit increased expression and secretion of pro-inflammatory cytokines, including tumour necrosis factor α (TNFα), interleukin (IL)-6, IL-8, and monocyte chemoattractant protein-1 (MCP-1) [14]. This elevation of pro-inflammatory cytokines leads to serine phosphorylation of insulin receptor substrate-1 via nuclear factor κB and Jun N-terminal kinase signalling, resulting in the development of insulin resistance [15].

A theoretical model suggests in the development of obesity, adipocyte hypertrophy and macrophage recruitment becomes a vicious cycle, that finally blocks preadipocyte recruitment and overall adipose tissue functioning and health [16]. There is also some evidence linking adipocyte size and weight loss regain [17, 18]. Additionally, Dankel et al. (2014) showed that some molecular mechanisms were significantly different in small from large adipocytes in abdominal fatty tissue. And, this difference allows the assumption that small adipocytes are the main source for endotrophin and thus control the adipose tissue development and expandability [19]. There is a strong correlation between BMP4 levels and adipocyte size, as well as insulin sensitivity in humans [20].

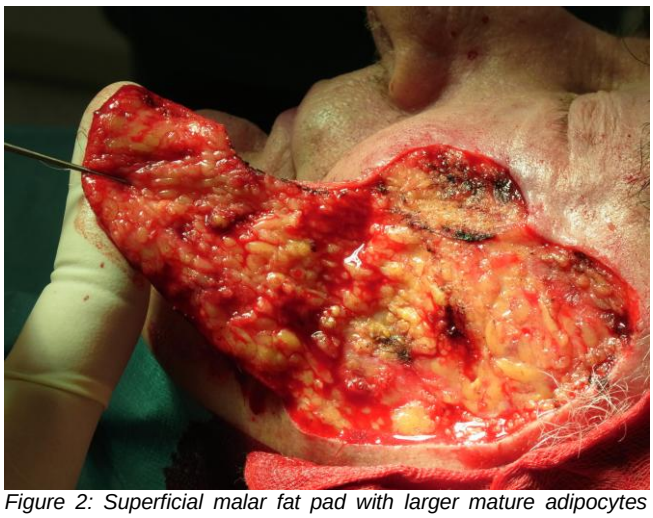

Figure 2: Superficial malar fat pad with larger mature adipocytes embedded in a fibrous network representing type 1 sWAT, also known as structural facial fat

Adipose tissue consists not only of adipocytes but extracellular matrix as well. There is an interplay between adipocytes and high-molecular weight hyaluronic acid (HA; 2000 kDa) of the extracellular matrix. HA is responsible for extracellular water binding capacity of adipose tissue. Higher water content prevents lipolysis by reduction of aquaporin-7 channels in adipocytes. The application of hyaluronidase, on the other side, can reduce fat masses and adipocyte size significantly [21, 22].

Medium molecular weight HA (50 kDa) inhibited differentiation of pre-adipocytes via major adipogenic transcription factors PPAR-γ and C/EBP-α. Also, FAS and ap2 – two target genes of PPAR-γ were also suppressed [23].

Bertossi et al. (2015) classified facial fat using transmission and scanning electron microscopy:

- Malar fat pad with large adipocytes by loose and thin collagen fibres (Type 1) (Fig. 2).
- Labial and nasal fat pads with mature adipocytes associated with a dense three-dimensional extracellular matrix (Type 2) (Fig. 3).
- Periorbital fat pads with pronounced lobules and dense basket-like extracellular matrix.
- Buccal fat pad with large mature adipocytes not completely covered by extracellular matrix fibres [8].

Mechanical stiffness of adipose tissue is inversely correlated with the average size of

adipocytes. The fibrous WAT develops the highest stiffness values. During the facial ageing process, prominent changes can be macroscopically noted in structural WAT. This leads to deformations like ptosis, wrinkles and jowls [24].

Facial fat pads and filler placement

It was Owsley and Fiala (1997) who suggested moving the malar fat pad craniolaterally to improve nasolabial folds [25]. However, surgery often is not necessary since soft tissue filler injections the malar fat pad can volumize this compartment resulting in smoothed nasolabial folds and younger appearance [26, 27].

The most versatile and popular filler nowadays is HA. Since native HA becomes rapidly decomposed by endogenous hyaluronidase, HA filler uses various cross-linking technologies to increase durability. HA fillers are of high-molecular weight [28]. Histologic investigations demonstrated filler deposits mainly within the subcutaneous tissue. Thus the term „dermal filler“ is a misnomer [29]. Activation of dermal fibroblasts has been claimed for HA fillers. Recently, this has been questioned [30]. Instead, a spatial modification of facial fat tissue and activation of adipose tissue derived stem cells has been suggested [31].

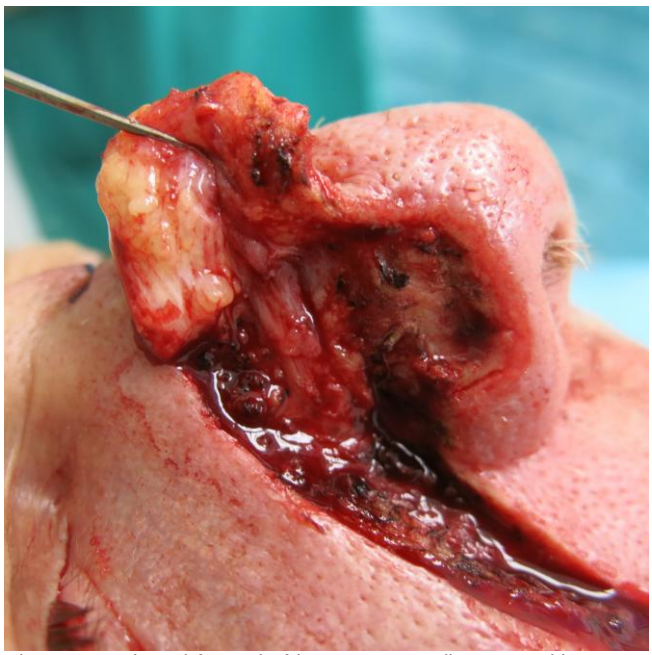

Figure 3: Perinasal fat pad of large mature adipocytes with a more densely connective tissue network representing type 2 sWAT or fibrous type fat pad

By detailed investigations – both with imaging techniques and cadaveric studies – of deep midfacial fat pads, it became evident that for volumizing one should specifically target these structures. Deep medial cheek fat pads and sup-orbicularis oculi fat pads of layer 4 of soft facial tissue are crucial in midfacial rejuvenation and are used to correct the cheek sagging which is a major aggravating factor for deep nasolabial folds [11, 24].

De Maio addressed this point and added two structural support depots of the lateral midface, i.e. zygomatic arch and zygomatic prominence, for optimal cheek rejuvenation [11].

For longevity of filler effects, however, the deep midfacial fat pads are of outmost importance (Fig. 4).

Cadaveric studies from Wan et al. (2014) argue for differences in superficial and deep facial fat pads. Indeed, they observed that the average adipocyte size of deep medial cheek fat was significantly smaller than that of nasolabial fat ($p < 0.0001$) [32]. Small adipocytes have a diameter of about 40 µm. The Smaller size is connected to alterations of fatty acid composition [33].

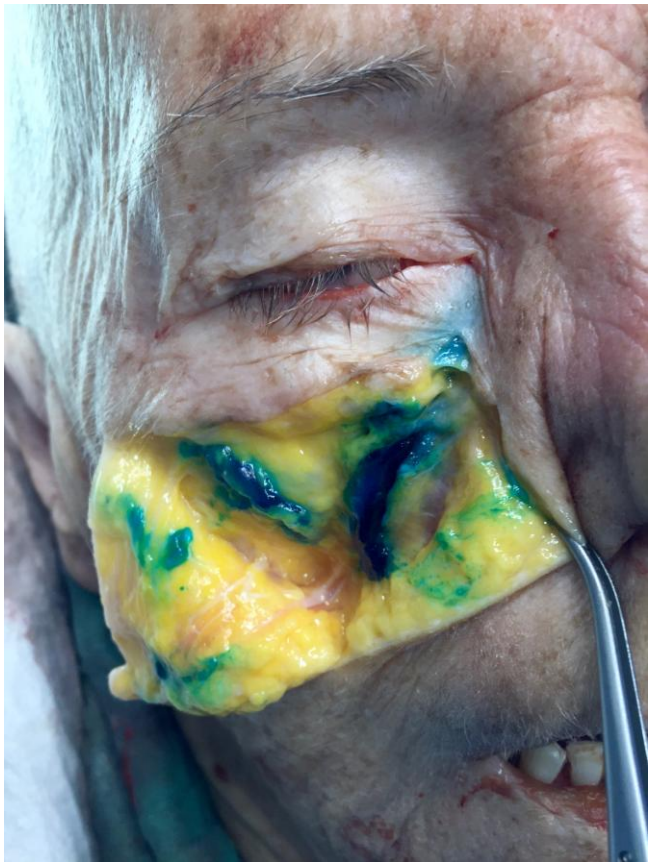

Figure 4: Filler deposition (blueish) along the suborbicularis oculi fat (SOOF) and in the deep medial fat pad

Collagen VI is one of the most abundant collagens in adipose tissue and consists of three isoforms. *COL6A3* isoform has previously been implicated in fibrosis [34]. COL6A3 mRNA expression is 2.8-fold higher in small compared to large adipocytes ($P = 0.004$) [35]. Low-molecular HA cannot only stimulate fibrosis but support assembly of

collagen IV [6]. Both factors may contribute to an improved mechanical stiffness after HA filler injections.

Hyaluronic acid and adipose tissue-derived stem cells

There is evidence that HA may support human adipose tissue derived stem cells (ASCs).

Using the in vivo model of nude mice, HA gel containing ASCs was subcutaneously injected into the subcutaneous pocket in the back. Eight weeks after injection, ASCs were well attached to and proliferated on the HA gel. By this time new adipose tissue developed. Analysis of neo-adipose tissues by PCR revealed the presence of the *Alu* gene, repetitive elements of the human genome [36].

In a vocal fold injury model of Sprague-Dawley rates, local injection of ASC (ASC group) was as effective as bone marrow-derived stem cells (BMSC group). Histological examination showed significantly increased hyaluronic acid (HA) and decreased dense collagen deposition. Real-time PCR revealed that hyaluronan synthase 1 (Has1) and Has2 were upregulated in the ASC group. Fibroblast growth factor 2 (basic), hepatocyte growth factor and Has3 were upregulated in both cell transplantation groups [37]. Interestingly, smaller scaffolds (diameter about 40 μm) produced more ADSs cells than larger ones [38].

ASCs express the HA receptor CD44 [39-41]. Proliferation among ADSs occurs almost exclusively in those who express CD44 [42].

These findings might have a consequence for facial rejuvenation with HA fillers. Injection of HA fillers deep in the facial fat pads could be a stimulator of ASC expansion and differentiation leading to adipose tissue hyperplasia. When the injected fillers become degraded, low-molecular weight HA may support the 3D-connective tissue network. Adipose tissue hyperplasia is more important for volumizing whereas stimulated extracellular connective fibre network can contribute to mechanical stiffness [6, 43].

Such a view might explain the clinical observation, which HA fillers provide a significantly longer durability in improving nasolabial folds compared to collagen fillers [44-48].

HA filler injection in more superficial fat compartments - as in lip enhancement or for perioral rejuvenation - has a more limited effect on mechanical properties, volume preservation and durability [49, 50]. The less intense stimulation of deep seated ADS may be an important underlying factor.

In conclusion, the findings discussed argue for HA fillers as stimulators of ADCs with a pronounced effect and considerable duration of beautification when injected into the deep midfacial fat pads [31]. Future direction in filler development should aim to specifically induce and control expansion and differentiation of ADCs in deep dermal fat pads, thereby aiming a durability obtained today only in case of successful adipose tissue transfer [51, 52].

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References

1. Farkas JP, Pessa JE, Hubbard B, Rohrich RJ. The science and theory behind facial ageing. Plast Reconstr Surg Glob Open. 2013;1(1). pii: e8-e15.

2. Lam SM. Volumetric rejuvenation: general concepts. Facial Plast Surg. 2015;31(1):15-21. https://doi.org/10.1055/s-0035-1544246 PMid:25763892

3. Goldman A, Wollina U. Facial rejuvenation for middle-aged women: a combined approach with minimally invasive procedures. Clin Interv Aging. 2010;5:293-239. PMid:20924438 PMCid:PMC2946856

4. Billon R, Hersant B, Meningaud JP. [Hyaluronic acid rheology: Basics and clinical applications in facial rejuvenation]. Ann Chir Plast Esthet. 2017; pii: S0294-1260(16)30210-2.

5. Rohrich RJ, Pessa JE. The fat compartments of the face: anatomy and clinical implications for cosmetic surgery. Plast Reconstr Surg. 2007;119(7):2219-2227. https://doi.org/10.1097/01.prs.0000265403.66886.54 PMid:17519724

6. Kruglikov I, Trujillo O, Kristen Q, Isac K, Zorko J, Fam M, Okonkwo K, Mian A, Thanh H, Koban K, Sclafani AP, Steinke H, Cotofana S. The facial adipose tissue: a revision. Facial Plast Surg. 2016;32(6):671-682. https://doi.org/10.1055/s-0036-1596046 PMid:28033645

7. Ghassemi A, Prescher A, Riediger D, Axer H. Anatomy of the SMAS revisited. Aesthetic Plast Surg. 2003;27(4):258-264. https://doi.org/10.1007/s00266-003-3065-3 PMid:15058546

8. Bertossi D, Conti G, Bernardi P, Benati D, Ruffoli M, Sbarbati A, Nocini P. Classification of fat pad of the third medium of the face. Aesthet Med 2015;1(3):103-109.

9. Kruglikov IL, Scherer PE. Skin aging: are adipocytes the next target? Aging (Albany NY). 2016;8(7):1457-1469. https://doi.org/10.18632/aging.100999 PMid:27434510 PMCid:PMC4993342

10. Arner P, Bernard S, Salehpour M, Possnert G, Liebl J, Steier P, Buchholz BA, Eriksson M, Arner E, Hauner H, Skurk T, Rydén M, Frayn KN, Spalding KL. Dynamics of human adipose lipid turnover in health and metabolic disease. Nature. 2011;478(7367):110-113.

https://doi.org/10.1038/nature10426 PMid:21947005 PMCid:PMC3773935

11. Cotofana S, Schenck TL, Trevidic P, Sykes J, Massry GG, Liew S, Graivier M, Dayan S, de Maio M, Fitzgerald R, Andrews JT, Remington BK. Midface: Clinical anatomy and regional approaches with injectable fillers. Plast Reconstr Surg. 2015;136(5 Suppl):219S-234S. https://doi.org/10.1097/PRS.0000000000001837 PMid:26441102

12. Skurk T, Alberti-Huber C, Herder C, Hauner H. Relationship between adipocyte size and adipokine expression and secretion. J Clin Endocrinol Metab. 2007;92(3):1023-1033. https://doi.org/10.1210/jc.2006-1055 PMid:17164304

13. Ali AT, Hochfeld WE, Myburgh R, Pepper MS. Adipocyte and adipogenesis. Eur J Cell Biol. 2013;92(6-7):229-236. https://doi.org/10.1016/j.ejcb.2013.06.001 PMid:23876739

14. Strong AL, Gimble JM, Bunnell BA. Analysis of the Pro- and Anti-Inflammatory Cytokines Secreted by Adult Stem Cells during Differentiation. Stem Cells Int. 2015;2015:412467. https://doi.org/10.1155/2015/412467 PMid:26300921 PMCid:PMC4537750

15. Choe SS, Huh JY, Hwang IJ, Kim JI, Kim JB. Adipose tissue remodeling: Its role in energy metabolism and metabolic disorders. Front Endocrinol (Lausanne). 2016;7:30. https://doi.org/10.3389/fendo.2016.00030

16. Virtue S, Vidal-Puig A. Adipose tissue expandability, lipotoxicity and the Metabolic Syndrome--an allostatic perspective. Biochim Biophys Acta. 2010;1801(3):338-349. https://doi.org/10.1016/j.bbalip.2009.12.006 PMid:20056169

17. Löfgren P, Andersson I, Adolfsson B, Leijonhufvud BM, Hertel K, Hoffstedt J, Arner P. Long-term prospective and controlled studies demonstrate adipose tissue hypercellularity and relative leptin deficiency in the postobese state. J Clin Endocrinol Metab. 2005;90(11):6207-6213. https://doi.org/10.1210/jc.2005-0596 PMid:16131581

18. MacLean PS, Higgins JA, Giles ED, Sherk VD, Jackman MR. The role for adipose tissue in weight regain after weight loss. Obes Rev. 2015;16 Suppl 1:45-54. https://doi.org/10.1111/obr.12255 PMid:25614203 PMCid:PMC4371661

19. Dankel SN, Svärd J, Matthä S, Claussnitzer M, Klöting N, Glunk V, Fandalyuk Z, Grytten E, Solsvik MH, Nielsen HJ, Busch C, Hauner H, Blüher M, Skurk T, Sagen JV, Mellgren G. COL6A3 expression in adipocytes associates with insulin resistance and depends on PPARγ and adipocyte size. Obesity (Silver Spring). 2014;22(8):1807-1813. https://doi.org/10.1002/oby.20758 PMid:24719315

20. Modica S, Straub LG, Balaz M, Sun W, Varga L, Stefanicka P, Profant M, Simon E, Neubauer H, Ukropcova B, Ukropec J, Wolfrum C. Bmp4 promotes a brown to white-like adipocyte shift. Cell Rep. 2016;16(8):2243-2258. https://doi.org/10.1016/j.celrep.2016.07.048 PMid:27524617

21. Kruglikov IL. Is the depletion of hyaluronan in hypertrophic fat tissue a key event in body-contouring procedures? Am J Cosm Surgery. 2013;30(1):244-245. https://doi.org/10.5992/AJCS-D-13-00013.1

22. Zhu Y, Creme C, Scherer PE. Hyaluronan in adipose tissue: Beyond dermal filler and therapeutic carrier. Sci Translat Med. 2016;8(323):323ps4.

23. Park BG, Lee CW, Park JW, Cui Y, Park YS, Shin WS. Enzymatic fragments of hyaluronan inhibit adipocyte differentiation in 3T3-L1 pre-adipocytes. Biochem Biophys Res Commun. 2015;467(4):623-628. https://doi.org/10.1016/j.bbrc.2015.10.104 PMid:26525853

24. Cotofana S, Fratila AA, Schenck TL, Redka-Swoboda W, Zilinsky I, Pavicic T. The anatomy of the aging face: A review. Facial Plast Surg. 2016;32(3):253-260. https://doi.org/10.1055/s-0036-1582234 PMid:27248022

25. Owsley JQ, Fiala TG. Update: lifting the malar fat pad for correction of prominent nasolabial folds. Plast Reconstr Surg. 1997;100(3):715-722. https://doi.org/10.1097/00006534-199709000-00029

26. Wollina U. Facial rejuvenation starts in the midface: three-dimensional volumetric facial rejuvenation has beneficial effects on nontreated neighboring esthetic units. J Cosmet Dermatol. 2016;15(1):82-88. https://doi.org/10.1111/jocd.12175 PMid:26304759

27. Glaser DA, Kenkel JM, Paradkar-Mitragotri D, Murphy DK, Romagnano L, Drinkwater A. Duration of effect by injection volume and facial subregion for a volumizing hyaluronic acid filler in treating midface volume deficit. Dermatol Surg. 2015;41(8):942-949. https://doi.org/10.1097/DSS.0000000000000416 PMid:26218727

28. Wollina U, Goldman A. Hyaluronic acid dermal fillers: Safety and efficacy for the treatment of wrinkels, aging skin, body sculpturing and medical conditions. Clin Med Rev Therapeutics 2011;3:107-121. https://doi.org/10.4137/CMRT.S6928

29. Arlette JP, Trotter MJ. Anatomic location of hyaluronic acid filler material injected into nasolabial fold: a histologic study. Dermatol Surg. 2008;34 Suppl 1:S56–S62. https://doi.org/10.1097/00042728-200806001-00012

30. Wollina U. Midfacial rejuvenation by hyaluronic acid fillers and subcutaneous adipose tissue--a new concept. Med Hypotheses. 2015;84(4):327-330. https://doi.org/10.1016/j.mehy.2015.01.023 PMid:25665858

31. Kruglikov IL, Wollina U. Soft tissue fillers as non-specific modulators of adipogenesis: change of the paradigm? Exp Dermatol. 2015;24(12):912-915. https://doi.org/10.1111/exd.12852 PMid:26309229

32. Wan D, Amirlak B, Giessler P, Rasko Y, Rohrich RJ, Yuan C, Lysikowski J, Delgado I, Davis K. The differing adipocyte morphologies of deep versus superficial midfacial fat compartments: a cadaveric study. Plast Reconstr Surg. 2014;133(5):615e-622e. https://doi.org/10.1097/PRS.0000000000000100 PMid:24445875

33. Sato D, Oda K, Kusunoki M, Nishina A, Takahashi K, Feng Z, Tsutsumi K, Nakamura T. PPARγ activation alters fatty acid composition in adipose triglyceride, in addition to proliferation of small adipocytes, in insulin resistant high-fat fed rats. Eur J Pharmacol. 2016;773:71-77. https://doi.org/10.1016/j.ejphar.2016.01.012 PMid:26825545

34. Khan T, Muise ES, Iyengar P, Wang ZV, Chandalia M, Abate N, Zhang BB, Bonaldo P, Chua S, Scherer PE. Metabolic dysregulation and adipose tissue fibrosis: role of collagen VI. Mol Cell Biol. 2009;29(6):1575-1591. https://doi.org/10.1128/MCB.01300-08 PMid:19114551 PMCid:PMC2648231

35. Dankel SN, Svärd J, Matthä S, Claussnitzer M, Klöting N, Glunk V, Fandalyuk Z, Grytten E, Solsvik MH, Nielsen HJ, Busch C, Hauner H, Blüher M, Skurk T, Sagen JV, Mellgren G. COL6A3 expression in adipocytes associates with insulin resistance and depends on PPARγ and adipocyte size. Obesity (Silver Spring). 2014;22(8):1807-1813. https://doi.org/10.1002/oby.20758 PMid:24719315

36. Huang SH, Lin YN, Lee SS, Chai CY, Chang HW, Lin TM, Lai CS, Lin SD. New adipose tissue formation by human adipose-derived stem cells with hyaluronic acid gel in immunodeficient mice. Int J Med Sci. 2015;12(2):154-162. https://doi.org/10.7150/ijms.9964 PMid:25589892 PMCid:PMC4293181

37. Hiwatashi N, Hirano S, Mizuta M, Tateya I, Kanemaru S, Nakamura T, Ito J. Adipose-derived stem cells versus bone marrow-derived stem cells for vocal fold regeneration. Laryngoscope. 2014;124(12):E461-E469. https://doi.org/10.1002/lary.24816 PMid:25043936

38. Brown CF, Yan J, Han TT, Marecak DM, Amsden BG, Flynn LE. Effect of decellularized adipose tissue particle size and cell density on adipose-derived stem cell proliferation and adipogenic differentiation in composite methacrylated chondroitin sulphate hydrogels. Biomed Mater. 2015;10(4):045010. https://doi.org/10.1088/1748-6041/10/4/045010 PMid:26225549

39. Zhu Y, Liu T, Song K, Fan X, Ma X, Cui Z. Adipose-derived stem cell: a better stem cell than BMSC. Cell Biochem Funct. 2008;26(6):664-675. https://doi.org/10.1002/cbf.1488 PMid:18636461

40. Ullah I, Subbarao RB, Rho GJ. Human mesenchymal stem cells - current trends and future prospective. Biosci Rep. 2015;35(2). pii: e00191. https://doi.org/10.1042/BSR20150025 PMid:25797907 PMCid:PMC4413017

41. Zhang S, Bai C, Zheng D, Gao Y, Fan Y, Li L, Guan W, Ma Y. Identification and characterization of pig adipose-derived progenitor cells. Can J Vet Res. 2016;80(4):309-317. PMid:27733786 PMCid:PMC5052883

42. Lee YH, Petkova AP, Granneman JG. Identification of an adipogenic niche for adipose tissue remodeling and restoration. Cell Metab 2013:18(3):355–367. https://doi.org/10.1016/j.cmet.2013.08.003 PMid:24011071 PMCid:PMC4185305

43. Alkhouli N, Mansfield J, Green E, Bell J, Knight B, Liversedge N, Tham JC, Welbourn R, Shore AC, Kos K, Winlove CP. The mechanical properties of human adipose tissues and their relationships to the structure and composition of the extracellular matrix. Am J Physiol Endocrinol Metab. 2013;305(12):E1427-E1435. https://doi.org/10.1152/ajpendo.00111.2013 PMid:24105412

44. Lupo MP, Smith SR, Thomas JA, Murphy DK, Beddingfield FC 3rd. Effectiveness of Juvéderm Ultra Plus dermal filler in the treatment of severe nasolabial folds. Plast Reconstr Surg. 2008;121(1):289-297. https://doi.org/10.1097/01.prs.0000294968.76862.83 PMid:18176233

45. Bauman LS, Shamban AT, Lupo MP, Monheit GD, Thomas JA, Murphy DK, Walker PS; JUVEDERM vs. ZYPLAST Nasolabial Fold Study Group. Comparison of smooth-gel hyaluronic acid dermal fillers with cross-linked bovine collagen: a multicenter, double-masked, randomized, within-subject study. Dermatol Surg. 2007;33 Suppl 2:S128-S135.

46. Lindqvist C, Tveten S, Bondevik BE, Fagrell D. A randomized, evaluator-blind, multicenter comparison of the efficacy and tolerability of Perlane versus Zyplast in the correction of nasolabial folds. Plast Reconstr Surg. 2005;115(1):282-289. PMid:15622265

47. Carruthers A, Carey W, De Lorenzi C, Remington K, Schachter D, Sapra S. Randomized, double-blind comparison of the efficacy of two hyaluronic acid derivatives, restylane perlane and hylaform, in the treatment of nasolabial folds. Dermatol Surg. 2005;31(11 Pt 2):1591-1598. https://doi.org/10.2310/6350.2005.31246 PMid:16416643

48. Narins RS, Brandt F, Leyden J, Lorenc ZP, Rubin M, Smith S. A randomized, double-blind, multicenter comparison of the efficacy and tolerability of Restylane versus Zyplast for the correction of nasolabial folds. Dermatol Surg. 2003;29(6):588-595. PMid:12786700

49. Raspaldo H, Chantrey J, Belhaouari L, Eccleston D, Saleh R, Acquilla R, Murphy DK. Lip and Perioral Enhancement: A 12-nonth prospective, randomized, controlled study. J Drugs Dermatol. 2015;14(12):1444-1452. PMid:26659938

50. Dayan S, Bruce S, Kilmer S, Dover JS, Downie JB, Taylor SC, Skorupa A, Murphy DK. Safety and effectiveness of the hyaluronic acid filler, HYC-24L, for lip and perioral augmentation. Dermatol Surg. 2015;41 (Suppl 1):S293-S301. https://doi.org/10.1097/DSS.0000000000000540 PMid:26618456

51. Wollina U, Goldman A, Berger U, Abdel-Naser MB. Esthetic and cosmetic dermatology. Dermatol Ther. 2008;21(2):118-130. https://doi.org/10.1111/j.1529-8019.2008.00179.x PMid:18394086

52. Marten TJ, Elyassnia D. Fat grafting in facial rejuvenation. Clin Plast Surg. 2015;42(2):219-252. https://doi.org/10.1016/j.cps.2014.12.003 PMid:25827566

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Clinical and Epidemiological Features of Dermatophyte Infections in Almaty, Kazakhstan

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Abstract

The cutaneous dermatomycoses are among topical issues in all countries worldwide. They are registered in 20% of the world population. Dermatophyte infections incidence frequency varies depending on a season, region, effective anti-epidemic measures management, and effective treatment methods. In Kazakhstan in 2001, dermatophyte infections ranked second in the structure of dermatologic pathology in outpatients. According to the literature data, not so many research studies on dermatophyte infections have been carried out in our country within recent years. The importance of these issues suggests a need to conduct epidemiological, clinical, microbiological studies of dermatophytosis at the present stage. A cross-sectional study was conducted, in which 195 cases of dermatophytosis were collected and investigated in the regional hospital in Almaty for the period from the beginning of January 2014 to the end of December 2014. Dermatophytoses prevalence is observed in patients within the 1 - 39 age range.

Introduction

Dermatophytoses incidence rate tends to increase around the world [6]. According to the WHO data, one in five people on the face of the earth has this pathology. In the structure of the cutaneous dermatomycoses, usually, dermatophytoses predominate [7]. The incidence of dermatophytosis, distribution, and etiological agent vary depending on the target geographical area, time of a study, a social and economic status of the population, climatic zone, age, presence of pets [8]. The relevance of this problem is primarily determined by the prevalence of this type of pathological skin lesions and by growth in the number of patients both in Kazakhstan and abroad [7]. Therefore, increase in the number of infected people in the overall population, in particular, among the population living in close contact, contributes to subsequent fungal infection dissemination. In this regard, dermatophyte infections are regarded as socially significant skin diseases and have great medical and social importance for the development of new methods of diagnosis, treatment, and prevention [9].

Investigation of the prevalence of fungal dermatitis signs will provide further insight into the epidemiological situation in the region.

Materials and Methods

A cross-sectional study has been conducted, in which 195 cases of dermatophytosis were investigated in the regional hospital in Almaty for the period from the beginning of January to the end of December 2014. Period of 2014 was characterised by the increasing incidence of cutaneous mycoses, while in 2011, 145 cases, and in 2012, even 180 cases of dermatophytosis have been recorded. In the study materials of case records over the period of 2014 were used, as well as microscopical and bacteriological examination findings for the same period. All case records of fungal infections with diagnoses according to the ICD-10 international classification were included: B 35.0 - tinea capitis et barbae, B 35.4 - tinea corporis, B 35.6 - tinea cruris, and their combinations. The study included patients 1-70 years old, men and women, diagnosed with dermatophytosis. Pregnant and breast-feeding women, patients who received systemic antimycotic drugs for 30 days before enrollment were not included in the analysis. Material for microscopical examination has been sampled from the affected areas of the patient's skin after their pre-treatment with 96% alcohol. Dermal scales were scraped with a scalpel, and crusts with epilation forceps from the periphery of the foci. The material was taken from fresh lesions. For more well-defined detection of the fungus elements, clarification of the material has been carried out using potassium hydroxide (KOH). Laboratory diagnostics of the culture-based examination was conducted regardless of the microscopy findings. The samples have been inoculated to Petri dishes with standard Sabouraud agar with 2% glucose and cultivated at the temperature of 28° for not longer than four weeks. In the absence of growth during 30 days, the results were considered negative. The grown culture served as a material for identifying the isolated dermatophyte. Statistical analysis was performed with the use of SPSS version 19. Pearson's chi-squared test was used to compare distinctions between variables.

Results

One hundred thirty-three (68.2%) of the 195 cases of dermatophytosis were men, and 62 (31.8%) were women; the ratio of men to women was 2.14: 1. The age of the youngest patient was one year, and of the oldest one was 67 years. In this study, high dermatophytosis incidence has been seen in the age group of children from 1 to 9 years old - 41.5% of the total number of the observed patients, they are followed by groups of 10-20 years (31.3%), 21-30 years (21.5%), 31-40 years (4.1%), 41-50 years (1%) and 51-70 years (0.5%).

Table 1: Age wise distribution with relation to clinical types

	Clinical types								
Group	Tinea capitis	Tinea corporis	Combi-nation of Tinea capitis and Tinea corporis	Tinea cruris	Combi-nati on of Tinea cruris and another skin disease	Combi-nati on of Tinea capitis, Tinea corporis and another skin disease	Combi-nati on of Tinea corporis and another skin disease	Combi-nati on of Tinea capitis and Tinea cruris	Total
0-9 year s	57	10	11	0	0	1	2	0	81
10-20 years	27	18	11	4	0	0	1	0	61
21-30 years	0	19	2	18	1	0	1	1	42
31-40 years	0	5	0	2	1	0	0	0	8
41-50 years	0	0	0	2	0	0	0	0	2
61-70 years	0	1	0	0	0	0	0	0	1
Total	84	53	24	26	2	1	4	1	195

χ^2 = 130.2; df = 35; P = 0.000

The highest incidence rate was recorded in autumn period (September to November) - 76 cases (39%), after that in summer (June to August) - 50 cases (26%), next in spring (March to May) - 37 cases (19%), and finally in winter (December to February) - 32 cases (16%).

Among 195 patients more than a half - 104 (53.3%) - were students of high schools or universities and colleges; 42 surveyed cases (21.5%) were children of preschool age, next 26 (13.3%) were classified as non-workers, 17 (8.7%) were employed by different organizations, housewives, military service men and pensioners - 3 (1.5%), 2 (1%), 1 (0.5%) respectively.

Table 2: Table of the contingency of etiological agents with the routes of transmission of infection

	Fungal infection transmissions								
Age group	Small pet animals - cats	Small pet animals - dogs	Cattle	Contact sports (wrest-ling)	Visiting public baths, saunas.	Sexual contact	Contact with human carriers of fungal infection	No data	Total
0-9 years	5	5	12	0	0	0	10	49	81
10-20 years	7	9	2	21	2	2	2	16	61
21-30 years	1	1	5	0	3	5	2	25	42
31-40 years	1	0	1	0	0	2	1	3	8
41-50 years	0	0	0	0	1	0	0	1	2
61-70 years	0	0	1	0	0	0	0	0	1
Total	14	15	21	21	6	9	15	94	195

χ^2 = 119.06; df = 35; P = 0.000.

One hundred sixty (82.1%) patients with superficial mycoses were among the rural population, and 35 (17.9%) were among the urban population.

The major occurring clinical form was superficial one - 140 (71.8%), it was characterised by the presence of one or more affected areas, of oval, round or irregular shape (in the form of geographical maps), with a clear boundary, pale pink colour, with raised spindle-shaped margin. Desquamation,

papules, vesicles, serosal crusts were observed on the surface of the lesion foci. The next most frequent form was infiltrative-suppurative - 29 (14.9%), that was a well-defined lesion focus, rising above the healthy skin, with evident acute inflammatory events in the form of swelling, pronounced hyperemia, and infiltration. Multiple pustules with copious purulent discharge and suppurative hemorrhagic crustings were observed on the surface. And infiltrative form was a little less frequent with 26 cases (13.3%). In a case of the infiltrative form, lesion focus was rising above the skin, had clear raised spindle-shaped margin, infiltrated, hyperaemic surface. Often the foci were running into one another forming bizarre shapes.

One hundred (51.3%) patients of 195 had skin lesions on the scalp (tinea capitis), skin lesion of upper and lower limbs and groin (pubis) (tinea cruris) were observed equally in 25 (12.8%) patients, combined skin lesion on torso, arms and legs were in 12 (6.2%) cases, isolated skin lesions on body (tinea corporis) were in 11 (5.6%) cases, combination of tinea capitis and tinea corporis was observed in 9 (4.6%) cases, skin lesions on groins with the transition to hips, facial skin lesions, combination of skin lesions on scalps and faces were observed in 6 (3.1%), 4 (2.1%) and 1 (0.5%) cases respectively.

Table 3: Dermatophyte species causing different clinical presentations

	Trichophyton Rubrum	Trichophyton Violaceum	Microsporum Ferrugineum	Micro-sporum Canis	Epider-mophyton Floccosum	No growth	Total
Tinea capitis	41	0	1	34	0	8	84
Tinea corporis	26	0	1	22	0	4	53
Combination of Tinea capitis and Tinea corporis	12	1	0	7	1	3	24
Tinea cruris	0	0	0	0	17	9	26
Combination of Tinea cruris and other skin disease	0	0	0	0	2	0	2
Combination of Tinea capitis,Tinea corporis and other skin disease	1	0	0	0	0	0	1
Combination of Tinea corporis and other skin disease	2	0	0	1	0	1	4
Combination of Tinea corporis and Tinea cruris	1	0	0	0	0	0	1
Total	83	1	2	64	20	25	195

χ^2 = 156.74; df = 35; P = 0.000.

On the basis of the diagnoses, incidence of B 35.0 skin lesions (tinea capitis et barbae) were registered in 84 (43.1%) cases, B 35.4 (tinea corporis) in 53 (27.2%) cases, B 35.6 (tinea cruris) in 26 (13.3%) cases, combination of B 35.0 and B 35.4 in 24 (12.3%) cases, B 35.4 and L 23.3 or L 20.8 in 4 (2.1%) cases, B 35.6 and L 23.8 in 2 (1.0%) cases, and combination of B 35.0 + B 35.4 + L 23.8 in 1 (0.5%) case.

Microscopy with KOH was positive in 191 (97.9%) cases, with the fungi spores detected in 106 (54.4%) cases, and mycelial filaments have been found in 85 (43.6%) cases. 4 (2.1%) cases showed a negative result. 170 (87.2%) cases of 195 cases of the bacteriological test have shown positive culture growth, in 25 (12.8%) cases growth was not observed. Among the 170 cases, Trichophyton Rubrum was the most common type of dermatophyte with 83 (42.6%) cases, further in the order of decreasing numbers follow Microsporum Canis with 64 (20.4%) cases, Epidermophyton Floccosum with 20 (10.3%) cases, Microsporum Ferrugineum with 2 (1.0%) cases, Trichophyton Violaceum with 1 (0.5%) case respectively.

Discussion

In general, our study revealed a link between the parameters of incidence. In the beginning, let us consider the dependence of the age category on the ways of transmission of infection, the localisation of skin lesions, the diagnosis, the clinical form and the type of pathogen. Contagion through immediate contact with a vehicle of disease in 66.7% of cases occurred in the age group of 1 to 9 years old. Children at the age of 1 to 9 are infected through contacts with livestock and small pet animals in 57.1% and 35.7% of the cases respectively ($\chi 2$ =119.9; df=35; P=0.000). In this age group, B 35.0 was diagnosed in 67.9% of the cases ($\chi 2$ = 130.3; df = 35; p = 0.000), isolated localization on the scalp was observed in 64% of the cases ($\chi 2$ = 155.9; df = 45; p = 0.000). Superficial clinical form prevailed being observed in 80.2% ($\chi 2$ = 29.6; df = 10; p = 0.001). Tinea capitis is one of the most common types of dermatophytosis observed more frequently in children, with various clinical manifestations and incidence worldwide. Children are particularly vulnerable to fungal infections, possibly because of poor personal hygiene and adverse environmental factors [10]. Perhaps the introduction of infection occurs due to hygiene breaches, and possibly as a result of low immune response. In this age group, the most common dermatophyte was Trichophyton Rubrum (51.9%), and Microsporum Canis is the second most common infectious agent in this age group (34.6%) ($\chi 2$ = 72.4; df = 25; p = 0.000), although, according to present knowledge, Microsporum Canis, the microsporia causative agent, prevails in Europe, especially in the Mediterranean, in the United States and South America, Japan, Israel, Kuwait, Qatar, the United Arab Emirates [4, 11, 12, 13, 14, 15]. Microsporia has become the most prevalent even in regions with the traditionally high incidence of trichophytosis. So, in Dagestan,

Uzbekistan, Tajikistan, Turkmenistan, Bashkortostan, Kazakhstan, Armenia, where formerly sporadic microsporia cases were observed, currently, it is up to 83.0 to 99.7% of all hair fungal diseases [12, 13].

Now consider a clearly visible gender dependence on other indicators. In the age group of 10 to 20 years old, there are more cases (35.4%) of introduction of fungal infection through contact sports (wrestling) ($\chi 2$ = 119.9; df = 35; p = 0.000), with localization on the scalp skin in 57.4% of cases ($\chi 2$ = 155.9; df = 45; p = 0.000). In this age group, Microsporum Canis prevails in 47.5% of cases ($\chi 2$ = 72.4; df = 25; p = 0.000). It is known that in the Russian Federation M. canis is the most often recorded microsporia causative agent [31]. It falls into the category of the widespread zoidiophilous fungi, which cause dermatophytosis in cats (especially in kittens), dogs, monkeys and other animals [16, 17].

In the age categories of 21 to 30 years old and 31 to 40 years old, the prevalence of sexual transmission of fungal infection is observed: 11.9% and 25.0% of the total number of cases in these categories respectively ($\chi 2$ = 119.9; df = 35; p = 0.000), with only public localization in the category of 21-30 years old (40.5%); in the category of 31 to 40 years old, lesions mostly often localize on the skin of upper and lower limbs (50.0%) ($\chi 2$ = 155.9; df = 45; p = 0.000). Clinical form is superficial in 50.0% and 62.5% of cases respectively for these categories ($\chi 2$ = 29.6; df = 10; p = 0.001). In this age group, among the dermatophytes the most common causative agent was Trichophyton Rubrum, 35.7% and 37.5%, respectively ($\chi 2$ = 72.4; df = 25; p = 0.000). According to some expert estimates, the share of tinea cruris accounts for 10% of the overall structure of the fungal infection with a majority of dermatophyte Trichophyton verrucosum 97.7% [18, 19, 20], the share of other tinea cruris causative agents is 12.3% with a majority of Epidermophyton Floccosum in 20-25% of cases [21, 22].

In the age groups of 41 to 50 years old and 61 to 70 years old, the incidence of fungal infections in the study is minimal: 2 and 1 cases respectively. In the age group of 41 to 50 years old, the infection disease was transmitted through use of a common bath, and in the age category of 51 to 70 years old, the infection disease was transmitted through cattle. Affected areas in patients of 41 to 50 years of age were only the pubic region with Epidermophyton Floccosum identified in 100% of cases; and in patients of 61 to 70 years of age, tinea corporis prevailed with identified Microsporum Canis. Clinical form in the category of 41 to 50 years of age is infiltrative, and patients at the age of 61 to 70 years had the surface form.

Among men, the infection was predominantly transmitted by means of contact sports (wrestling) in 15.0% of cases; among women that was contact with the infection carriers in 11.3% of cases ($\chi 2$ = 15.99; df = 7; p = 0.025). B 35.0 in conjunction with B 35.4 were diagnosed in 100% of men only. B 35.4 in conjunction with B 35.6 were diagnosed only in women ($\chi 2$ = 15.52; df = 7; p = 0.03). Clinical form in men and women is predominantly superficial 75.2% and 64.5% respectively ($\chi 2$ = 6.73; df = 72; p = 0.034). The bacteriological examination, in both men and women, Trichophyton Rubrum prevailed in 50% and 42.6% of cases respectively ($\chi 2$ = 11.78; df = 5, p = 0.038). These data differ from those of A.Karibayeva. Conducted in Almaty 2003-2007, then the main causative agent of the infection was Trichophyton violaceum [34].

The dependence of the time of year on the ways of transmission of infection, the clinical form of skin lesion and the prevalence of one or another type of causative agent of infection is also traced in this work. In winter season (December to February), contacts with human carriers were the most common channel of infection in 19.4% of cases; in spring season (March to May), both contacts with human carriers and contacts with small pet animals (cats) were 12% of cases each. In the summer season (June and July), contacts with small pet animals (dogs) were the most common channel of infection in 17.1% of cases, in 15.8% of cases that were contacted with cattle, and in 15.8% of cases that were contact sports (wrestling). And in autumn season (September to November), in 10.8% of cases contacts with cattle and contact sports (wrestling) were the most common channel of infection; these data are statistically significant ($\chi 2$ = 6.73; df = 72; p = 0.034). In contrast, in the dermatophytosis study conducted in Mali, performed multivariance analysis has shown no statistical significance regarding climatic factors and factors of transmission [23].

About clinical forms, in winter (December to February), spring (March to May) and summer (June and July) seasons, the infiltrative-suppurative form was the most common: 27.6%, 24.1% and 31.0% of cases respectively. And superficial clinical form prevailed in autumn season (September to November) with 49.3% of cases ($\chi 2$ = 26.711; df = 8; p = 0.001).

In winter season, cultures of Microsporum Canis was the most frequently identified with 38.7% of cases; in spring season, cultures of Epidermophyton Floccosum were identified in 27.0% of cases; in summer season, Trichophyton Rubrum in 68.0%, and in autumn season, Microsporum Canis in 46.1% of cases ($\chi 2$ = 60.97; df = 20, p = 0.000).

The relationship between the transmission routes of infection and the prevalence of one or another type of pathogen. Where the infection is transmitted through contacts with small pet animals,

cats and dogs, Trichophyton Rubrum prevailed in 50.0% and 46.7% of cases respectively. The same results with the highest proportion of Trichophyton Rubrum and predominance of domestic cats as infection sources have been shown in the study in the Republic of Bashkortostan, Russia [24]. Where the infection is transmitted through contacts with cattle, Trichophyton Rubrum was identified in 57.1% of cases; and where the infection is transmitted through contact sports (wrestling), Microsporum Canis was the most common causative agent in 57.1% of cases. In the case of infection when visiting public baths, saunas, and in the case of sexual contacts, the growth of Epidermophyton Floccosum was observed in 33.3% Floccosum and 77.8% of cases respectively. And where the infection was transmitted through contacts with people carriers, Microsporum Canis showed prevailing growth rate in 53.3% of cases ($\chi 2$ = 86,375; df=35; P=0).

The study has demonstrated that cultural growth with positive microscopy results with KOH was observed in 191 of 195 cases, cultural growth with negative microscopy results with KOH was observed in 3 of 4 cases ($\chi 2$ = 0.29; df = 1), i.e. there is no relationship.

In conclusion, the conducted study has demonstrated a high incidence of fungal infection in patients with the age range between 1 to 39. Trichophyton Rubrum is the most common causative agent of tinea capitis and tinea corporis; this differs from the data of the publications of colleagues from Germany and Britain, where it is indicated that Trichophyton Rubrum is rarely detected in the scalp and children it is up to 1% [32, 33]. And there is a high prevalence Epidermophyton Floccosum is the most common causative agent of tinea cruris. It is noted that small pet animals, cats, dogs are the most common transmitters of dermatophytes Trichophyton Rubrum; Epidermophyton Floccosum is transmitted when visiting public baths, saunas and by sexual contact. Statistically, the significant relationship has been shown between the studied parameters of the fungal diseases. Some study data are similar to the overall mycoses statistics data; some others do not match similar studies data acquired in other countries, this evidences the presence of special features of mycoses in this region of Kazakhstan. In-depth study of the identified relationships requires a broader sample of observations for further studies using dipper statistical methods.

References

1. Repiso B, Frieyro M, Rivas-Ruiz F, De Troya M. Condom use and number of sexual partners among male syphilis patients who report having sex with men. Actas Dermosifiliogr. 2010;101(10):847-52. https://doi.org/10.1016/j.ad.2010.06.014 PMid:21159260

2. Jebbari H, Simms I, Conti S, Marongiu A, Hughes G, Ward H, Powers C, Thomas DR, Evans B. Variations in the epidemiology of primary, secondary and early latent syphilis, England and Wales: 1999 to 2008.

3. Schnirring-Judge M, Gustaferro C, Terol C. Vesiculobullous syphilis: a case involving an unusual cutaneous manifestation of secondary syphilis. J Foot Ankle Surg. 2011;50(1):96-101. https://doi.org/10.1053/j.jfas.2010.08.015 PMid:21106408

4. Breznik V, Potočnik M, Miljković J. Papulonodular secondary syphilis in a 52-year-old non-HIV heterosexual patient. Acta Dermatovenerol Alp Panonica Adriat. 2010;19(4):27-30.

5. Furlan FC, Oliveira AP, Yoshioka MC, Enokihara MM, Michalany NS, Porro AM. Leukocytoclastic vasculitis: another condition that mimics syphilis. An Bras Dermatol. 2010;85(5):676-9. https://doi.org/10.1590/S0365-05962010000500011 PMid:21152792

6. Mullooly C, Higgins SP. Secondary syphilis: the classical triad of skin rash, mucosal ulceration and lymphadenopathy. Int J STD AIDS. 2010;21(8):537-45. https://doi.org/10.1258/ijsa.2010.010243 PMid:20975084

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Clinical Science

Scalping Surgery – Dermatologic Indications beyond Curative Primary Skin Cancer Surgery

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Keywords: Skin tumours; scalping surgery; scalp; mesh graft transplantation; dermal template.

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Abstract

Skin tumours are among the most frequent tumour types of mankind. In the case of large tumours, field cancerization, or satellitosis scalping surgery is a possible option. The procedure can also be used in a palliative setting with tumour debulking. Less common indications are multiple benign tumours of the scalp and chronic inflammatory scalp dermatoses not responding to medical treatment. We present a case series and discuss surgical modalities beyond curative surgery of primary skin cancer.

Introduction

The most common skin tumours are non-melanoma skin cancers (NMSC). A very frequent localisation is the scalp. In the case of large tumours, a scalping surgery may become necessary.

We define scalping surgery as full-thickness soft tissue removal of at least one-third of the capillitium resulting in large defects. Scalping surgery may also include removal of periosteum or outer table of the scalp. Large defects with full thickness loss of soft tissue down to the bone require complex reconstructive options. In many cases, complete defect closure can be obtained by local flaps, tissue expander or free vascularized flaps [1, 2].

Comorbidities among elderly patients often limit anaesthetic tolerance and the use of distant flaps. In such cases, a defect closure is performed by mesh graft transplantation. The graft take can be improved by a combination of a dermal matrix template. Such a technique allows also mesh graft transplantation on bony underground [3-7].

Since permanent alopecia is a consequence of scalping surgery, the procedure needs to be discussed with every single patient in detail. Nevertheless, scalping surgery has its place in primary tumour surgery, in cases of field cancerization of the scalp with multiple NMSC, palliative oncology, and in rare benign conditions. We will discuss the possible indications, outcome and limitations of such an aggressive surgical approach aside from curative surgery of primary skin tumours.

Field cancerization

A 76-year-old female patient presented in 2011 with nevoid amelanotic melanoma and satellitosis of the scalp, which was BRAF-wild type. She was treated by Mohs surgery, and the defect was closed by a rotational flap. Since resection of satellitosis was incomplete, a second surgery was planned. But on return, she already presented multiple new non-pigmented cutaneous scalp metastases. We

started with intralesional interleukin-2 (IL-2) treatment in 2011 and performed five courses until 2014. Due to the new formation of scalp satellitosis, palliative laser therapy – initially by erbium-YAG, later by pulsed 980nm diode laser – was performed as demanded. The treatment was better tolerated than IL-2 but no longer remission period could be achieved. More than 100 metastases have been observed (Fig. 1).

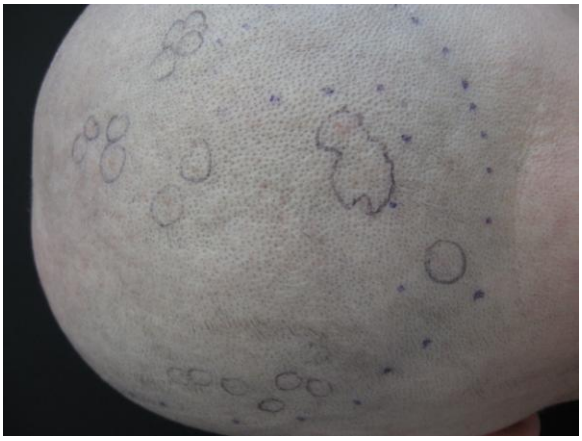

Figure 1: Satellitosis of multiple non-pigmented melanoma metastases

Repeated imaging by X-ray, magnetic resonance imaging (MRI) and positron emission computerised tomography (PET) was negative for any metastatic spread distant from the scalp. Serum level of S100 remained low. Eventually, she was treated by scalping surgery followed by meshed skin graft transplantation. During follow-up of months, no relapse occurred (Fig. 2).

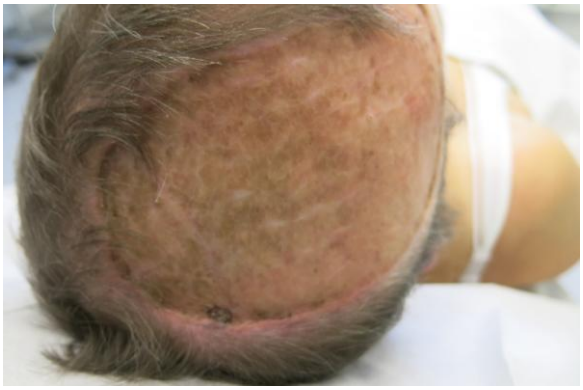

Figure 2: After scalping surgery and meshed skin graft transplantation. The marked area was removed – it was a milia-like formation, no metastasis

A 40-year-old male patients with cranial dysplasia, thoracic deformities, scoliosis, and a mandibular cyst was referred to us because of multiple basal cell carcinomas (BCCs) of the head measuring up to 4.5 cm in diameter. Some of the tumours were ulcerated (Fig. 3).

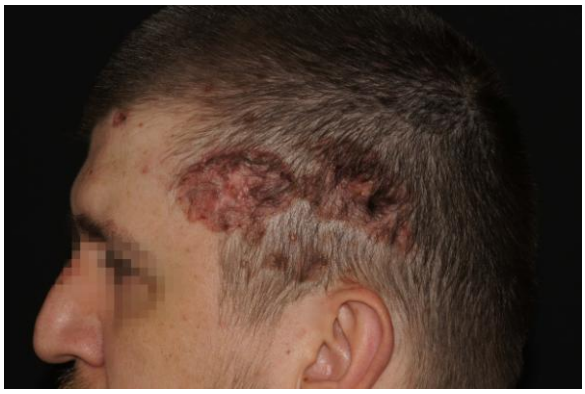

Figure 3: Gorlin-Goltz syndrome with multiple basal cell carcinomas, some ulcerated

Genetic analysis detected a heterozygous mutation c.290delA in exon 2 of the *PTCH1* gene. Our findings confirmed the diagnosis of Gorlin-Goltz syndrome. The patient had been offered serial surgery, medical treatment with hedgehog inhibitor vismodegib, and scalping surgery. He decided to have scalping surgery which was performed under general anaesthesia (Fig. 4).

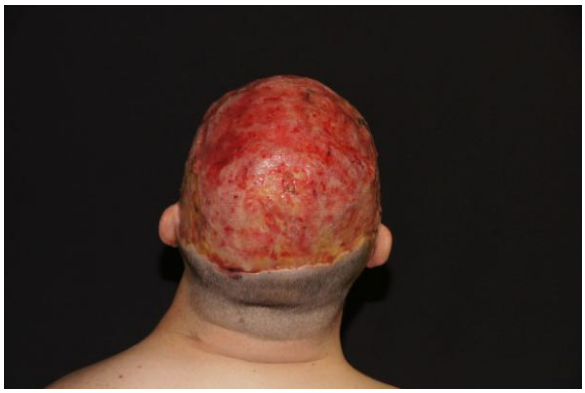

Figure 4: After scalping surgery

The full-thickness defect was closed in the second step by meshed skin graft transplantation (Fig. 5). During follow-up of 10 months, there was no relapse.

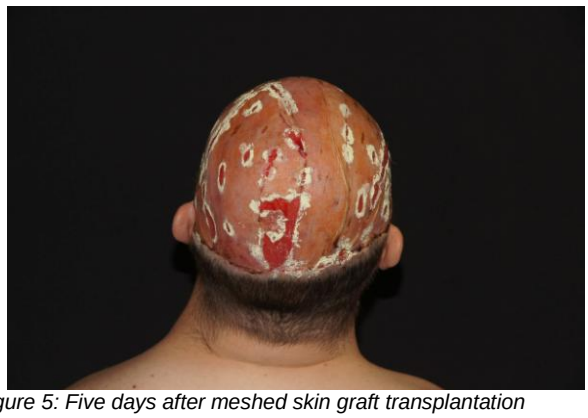

Figure 5: Five days after meshed skin graft transplantation

Debulking surgery

We performed debulking surgery in an 80-year-old male patient with a recurrent amelanotic lentigo melanoma of the scalp (Fig. 6).

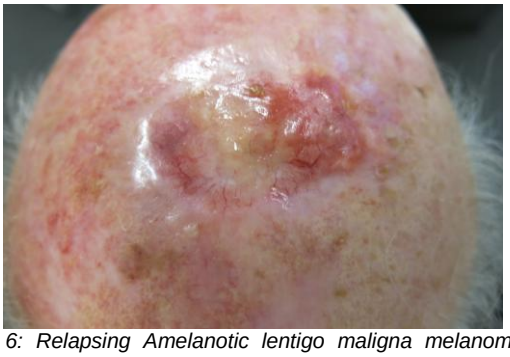

Figure 6: Relapsing Amelanotic lentigo maligna melanoma with penetration of the outer table of the scull

The tabula externa was already infiltrated by this tumour. We removed the periosteal layer and used a diamond drill for perforating the outer cortical layer of the scull to improve blood supply (Fig. 7).

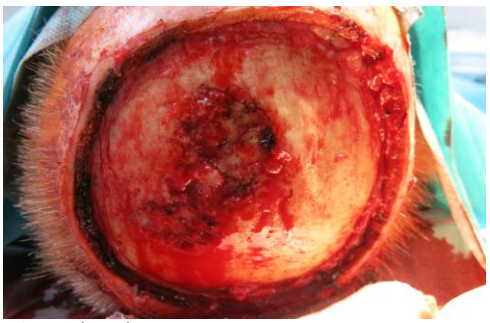

Figure 7: Operation situs

Sandwich transplantation with the elastin-collagen dermal template and meshed skin graft in the same session provided a stable defect closure until neurosurgical complete tumour resection, and skull repair was possible (Fig. 8).

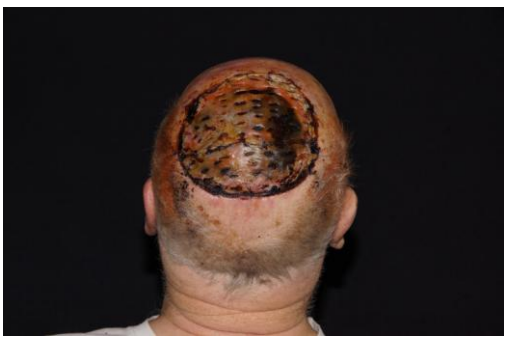

Figure 8: Stable meshed skin graft ten days after surgery

A 67-year-old male patient presented with a giant trichilemmal carcinoma of the scalp (20 x 12 x 2.4 cm), Broder grade 3 (Fig. 9).

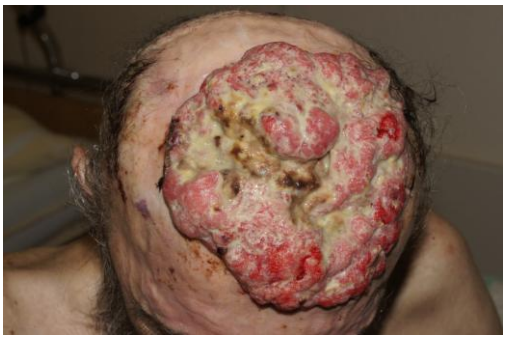

Figure 9: Giant trichilemmal carcinoma of the scalp

By cranial computerised tomography and gadolinium-enhanced vascular magnetic resonance imaging a parietal parasagittal cranial tumour invasion was detected (Fig. 10).

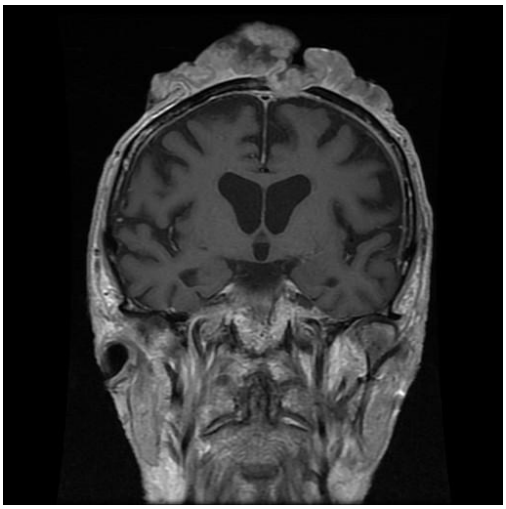

Figure 10: MRI demonstrating penetration of the scull and impression of the sagittal sinus

There was a continuous growth to the meninges on the left side with infiltration and partial closure of the medial part of the superior sagittal sinus. Together with the neurosurgeon, we decided to perform debulking surgery as a palliative treatment (Fig. 11).

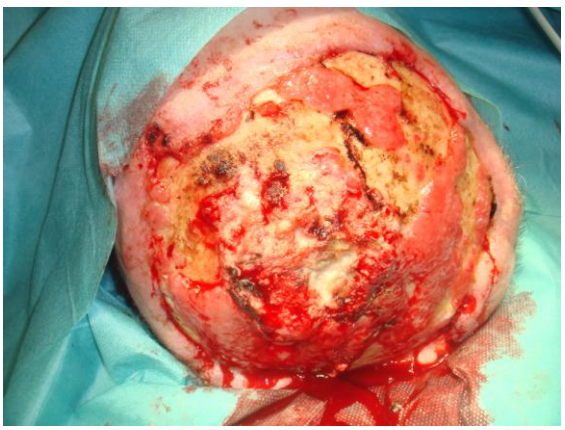

Figure 11: Operation situs

Overall survival from the first diagnosis was three years. He did not die from cancer but traffic accident one week before planned neurosurgery of the intracranial tumour residues.

Chronic inflammatory scalp dermatoses

30-year-old male patient with severe dissecting cellulitis of the scalp, who was treated in a neoadjuvant setting with anti-tumor necrosis factor-alpha treatment compound infliximab, had been subjected to scalping surgery for treatment-resistant residues (Figs. 12 & 13).

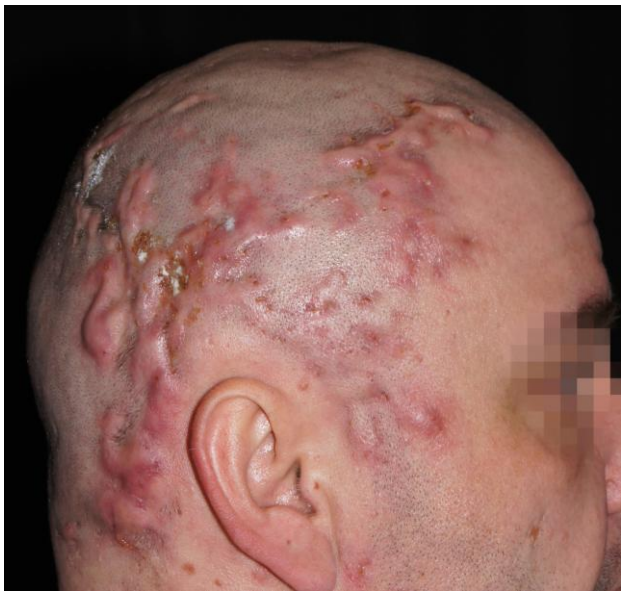

Figure 12: Dissecting folliculitis with severe inflammation and oozing lesions

He is in complete remission now for more than five years without any medical treatment.

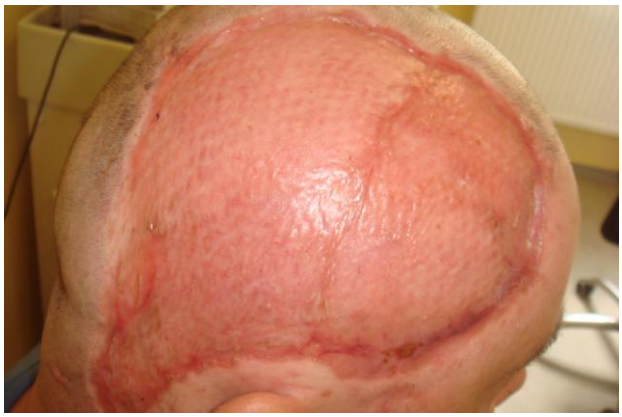

Figure 13: Two years after scalping surgery with stable meshed skin transplant take. No relapse of dissecting folliculitis.

Discussion

Scalping surgery is a niche technique with several possible indications. The advantage of the technique is its radical removal of multiple lesions, the complete change of the local immunity and the easiness of follow-up. The major drawback is the permanent hair loss in the treated area. This is an important issue to be discussed in detail with every patient before surgery.

Field cancerization is mostly used to describe the development of multiple actinic keratoses on the bald scalp. The (bald) scalp is an immunocompromised district according to the concept of Rucco [8]. In the case of only multiple superficial actinic keratoses, not responding to topical treatment, photodynamic therapy is a useful alternative [9].

We treated two patients with a related condition: A female patient with multiple cutaneous metastases of an amelanotic nevoid melanoma arising in a circumscribed area of her scalp without any metastasis to more distant sites and a male patient with Gorlin-Goltz syndrome (OMIM 109400) and multiple BCCs of the head [10].

Nevoid melanomas are melanomas that clinically and histologically resemble a nevus (only at low power magnification under the microscope), and can be divided into small cell and spitzoid types [11, 12]. The patient we present developed satellitosis without metastatic spread to more distant sites. We observed that microscopic satellitosis does not necessarily translate into the lymphovascular infiltration of the tumour [13]. In one study, the 5-year overall and disease-free survivals in patients with microscopic satellitosis were 34% and 18%, respectively, demonstrating an unfortunate prognosis [14].

Our patient had multiple treatments for numerous non-pigmented cutaneous metastases, such as 2.94 µm erbium-YAG and 980 nm pulsed dye laser, low-dose interferon alfa, and intralesional interleukin 2 [15-17]. Objective complete remissions have been achieved by intralesional interleukin-2 in up to 69% [18]. None of these treatments yielded a longer remission in the present patient. Therefore, we discussed the opportunity of scalping surgery for the area of local cutaneous metastases. The patients agreed, and so far, we did not observe any recurrence.

In Gorlin-Goltz syndrome, surgical excision allows removal BCCs with an overall chance of a cure between 94% to 98%. Surgical excision provides the advantage of three-dimensional margin control [19]. Recently, hedgehog inhibitor vismodegib was investigated for Gorlin-Goltz patients with unresectable or metastatic BCCs. In a pooled analysis of two vismodegib trials by Chang et al. (2016), 46

patients with Gorlin-Goltz syndrome were included. The investigator-rated best overall response reached 31 to 81 % in patients with unresectable BCC (n = 33) and 50 % in patients with metastatic BCC (n = 6) [20]. On the other hand, there is increasing evidence for either primary or secondary tumour resistance to hedgehog inhibitors, the transformation of BCC to squamous cell carcinoma (SCC) and increased risk of development of cutaneous SCC after vismodegib therapy [21-23]. We observed no recurrence of BCCs after scalping surgery in the treated area. Before, newly developed BCCs were noted almost every month.

In old patients, where other medical, surgical or radiological treatments and their combination is not tolerable anymore, a debulking surgery is a palliative approach to avoid tumour bleeding, secondary infection, diminish malodor and improve the quality of life of patients. Debulking surgery per se does not improve overall survival. However, in the case of possible combination with another non-surgical therapy, a positive effect on survival may be obtained.

Liao et al. (2017) treated a 92-year-old male patients with a higher multinodular mass on the scalp by this technique. The diagnosis was a cutaneous B-cell lymphoma of the parietooccipital region. Relapse-free survival was six months, and overall survival was two years [24].

We performed debulking surgery in an 82-year-old male patient with scull-penetrating amelanotic LMM and a 67-year-old male patient with scull-penetrating trichilemmal carcinoma [25]. Overall survival of the last patient was three years. The former patient was subjected to neurosurgical treatment.

Sometimes, scalping surgery is an option in patients with multiple benign scalp tumours. Sebastian and his group treated a 63-year-old man by en-bloc resection of multiple cylindromas of the scalp. After excision and granulation-stimulating local therapy, the wound was covered with meshed skin grafts from the thighs, but widespread tension blisters with ulcerations were recalcitrant to topical treatment. The defects were eventually closed with EpiDex, a tissue-engineered epidermal equivalent derived from outer root sheath keratinocytes [26].

Dissecting cellulitis of the scalp is a chronic inflammatory, oozing disorder with similarities to hidradenitis suppurative/ acne inverse. It can be recalcitrant to medical treatment. In such cases, scalping surgery with subsequent mesh graft transplantation is an option to improve patient's quality of life [27].

In the case of exposed Calvary after scalping surgery, we employed two surgical techniques – either alone or in combination. Milling the exposed outer table of the scalp bone with a rose head burr driven by a pneumatic power drill exposes diploic veins in the cancellous bone. This increases survival of free transplants [28]. The use of a dermal template has been shown to increase skin graft survival and improve the mechanical quality of the transplant after healing [3-7]. We employed the sandwich technique with a reconstituted elastin-collagen matrix covered by meshed skin graft in a single operation [6].

Despite all advantages in medical treatments and laser technology, scalping surgery is an option in the management of skin cancer patients and severe chronic inflammatory disorders.

References

1. Desai SC, Sand JP, Sharon JD, Branham G, Nussenbaum B. Scalp reconstruction: an algorithmic approach and systematic review. JAMA Facial Plast Surg. 2015;17:56-66. https://doi.org/10.1001/jamafacial.2014.889 PMid:25375669

2. Wollina U, Bayyoud Y, Krönert C, Nowak A. Giant epithelial malignancies (Basal cell carcinoma, squamous cell carcinoma): a series of 20 tumours from a single centre. J Cutan Aesthet Surg. 2012;5:12-19. https://doi.org/10.4103/0974-2077.94328 PMid:22557850 PMCid:PMC3339122

3. Johnson MB, Wong AK. Integra-based reconstruction of large scalp wounds: A case report and systematic review of the literature. Plast Reconstr Surg Glob Open. 2016;4:e1074. https://doi.org/10.1097/GOX.0000000000001074 PMid:27826471 PMCid:PMC5096526

4. Richardson MA, Lange JP, Jordan JR. Reconstruction of full-thickness scalp defects using a dermal regeneration template. JAMA Facial Plast Surg. 2016;18:62-67. https://doi.org/10.1001/jamafacial.2015.1731 PMid:26606002

5. Gironi LC, Boggio P, Colombo E. Reconstruction of scalp defects with exposed bone after surgical treatment of basal cell carcinoma: the use of a bilayer matrix wound dressing. Dermatol Ther. 2015;28:114-117. https://doi.org/10.1111/dth.12193 PMid:25546347

6. Wollina U. One-stage reconstruction of soft tissue defects with the sandwich technique: Collagen-elastin dermal template and skin graft. J Cutan Aesthet Surg. 2011;4:176-182. https://doi.org/10.4103/0974-2077.91248 PMid:22279382 PMCid:PMC3263127

7. Faulhaber J, Felcht M, Teerling G, Klemke CD, Wagner C, Goerdt S, Koenen W. Long-term results after reconstruction of full thickness scalp defects with a dermal regeneration template. J Eur Acad Dermatol Venereol. 2010;24:572-527. https://doi.org/10.1111/j.1468-3083.2009.03473.x PMid:19888947

8. Ruocco V, Ruocco E, Piccolo V, Brunetti G, Guerrera LP, Wolf R. The immunocompromised district in dermatology: A unifying pathogenic view of the regional immune dysregulation. Clin Dermatol. 2014;32:569-576. https://doi.org/10.1016/j.clindermatol.2014.04.004 PMid:25160098

9. Griffin LL, Lear JT. Photodynamic therapy and non-melanoma skin cancer. Cancers (Basel). 2016;8: pii: E98. https://doi.org/10.3390/cancers8100098 PMid:27782094 PMCid:PMC5082388

10. Edwards SL, Blessing K. Problematic pigmented lesions: approach to diagnosis. J Clin Pathol. 2000;53:409-418. https://doi.org/10.1136/jcp.53.6.409 PMCid:PMC1731214

11. Scolyer RA, Long GV, Thompson JF. Evolving concepts in melanoma classification and their relevance to multidisciplinary

melanoma patient care. Mol Oncol. 2011;5:124-136. https://doi.org/10.1016/j.molonc.2011.03.002 PMid:21482206

12. Kimsey TF, Cohen T, Patel A, Busam KJ, Brady MS. Microscopic satellitosis in patients with primary cutaneous melanoma: implications for nodal basin staging. Ann Surg Oncol. 2009;16:1176-1183. https://doi.org/10.1245/s10434-009-0350-7 PMid:19224283

13. Kaley J, Patterson JW, Chokoeva AA, Lotti T, Wollina U, Tchernev G. Are microscopic satellites in melanoma indicative of lymphovascular invasion? A preliminary case study. J Biol Regul Homeost Agents. 2015;29(1 Suppl):65-68. PMid:26016970

14. Austin E, Mamalis A, Ho D, Jagdeo J. Laser and light-based therapy for cutaneous and soft-tissue metastases of malignant melanoma: a systematic review. Arch Dermatol Res. 2017. https://doi.org/10.1007/s00403-017-1720-9 PMid:28314913

15. Boyd KU, Wehrli BM, Temple CL. Intra-lesional interleukin-2 for the treatment of in-transit melanoma. J Surg Oncol. 2011;104:711-717. https://doi.org/10.1002/jso.21968 PMid:21744347

16. Bottoni U, Clerico R, Paolino G, Corsetti P, Ambrifi M, Brachini A, Richetta A, Nisticò S, Pranteda G, Calvieri S. Melanoma and IFN alpha: potential adjuvant therapy. J Biol Regul Homeost Agents. 2014;28:271-279. PMid:25001659

17. Nouri N, Garbe C. Intralesional immunotherapy as a strategy to treat melanoma. Expert Opin Biol Ther. 2016;16:619-926. https://doi.org/10.1517/14712598.2016.1157161 PMid:26898656

18. Gorlin RJ, Goltz RW. Multiple nevoid basal-cell epithelioma, jaw cysts and bifid rib: a syndrome. N Engl J Med. 1960;262:908–912. https://doi.org/10.1056/NEJM196005052621803 PMid:13851319

19. Lo Muzio L. Nevoid basal cell carcinoma syndrome (Gorlin syndrome). Orphanet J Rare Dis. 2008;3:32. https://doi.org/10.1186/1750-1172-3-32 PMid:19032739 PMCid:PMC2607262

20. Chang AL, Arron ST, Migden MR, Solomon JA, Yoo S, Day BM, McKenna EF, Sekulic A. Safety and efficacy of vismodegib in patients with basal cell carcinoma nevus syndrome: pooled analysis of two trials. Orphanet J Rare Dis. 2016;11:120. https://doi.org/10.1186/s13023-016-0506-z PMid:27581207 PMCid:PMC5007799

21. Hansel G, Tchernev G, Chokoeva AA, Lotti T, Schönlebe J, Wollina U. Failure of vismodegib in advanced basal cell carcinoma. J Biol Regul Homeost Agents. 2015;29(1 Suppl):11-13. PMid:26016959

22. Feigenbaum L, Scott BL, Moye MS, Nijhawan RI. Development of basal cell carcinoma with squamous differentiation during vismodegib treatment. Dermatol Surg. 2016.

23. Mohan SV, Chang J, Li S, Henry AS, Wood DJ, Chang AL. Increased risk of cutaneous squamous cell carcinoma after vismodegib therapy for basal cell carcinoma. JAMA Dermatol. 2016;152:527-532. https://doi.org/10.1001/jamadermatol.2015.4330 PMid:26914338

24. Liao C, Yang M, Liu P, Zhang W. A 92-year-old man with primary cutaneous diffuse large B-cell non-Hodgkin's lymphoma manifesting as a giant scalp mass: A case report. Medicine (Baltimore). 2017;96:e6270. https://doi.org/10.1097/MD.0000000000006270 PMid:28272240 PMCid:PMC5348188

25. Wollina U, Bayyoud Y, Kittner T, Dürig E. Giant tricholemmal squamous cell carcinoma with cranial infiltration. J Clin Aesthet Dermatol. 2011;4:34-37. PMid:21532876 PMCid:PMC3084608

26. Tausche AK, Richter-Huhn G, Sebastian G. Treatment of recalcitrant wounds with autologous epidermal equivalents. After excision of multiple cylindromas of the scalp. Hautarzt. 2004;55:296-300. https://doi.org/10.1007/s00105-003-0637-8 PMid:15029438

27. Wollina U, Gemmeke A, Koch A. Dissecting cellulitis of the scalp responding to intravenous tumor necrosis factor-alpha antagonist. J Clin Aesthet Dermatol. 2012;5:36-39. PMid:22708007 PMCid:PMC3366445

28. Mühlstädt M, Thomé C, Kunte C. Rapid wound healing of scalp wounds devoid of periosteum with milling of the outer table and split-thickness skin grafting. Br J Dermatol. 2012;167:343-347. https://doi.org/10.1111/j.1365-2133.2012.10999.x PMid:22512740

ID Design 2012/DOOEL Skopje, Republic of Macedonia
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The Importance of First Aid to Burned Patients: 30 Years of Experience at the Burns Centre in Pisa

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Abstract

The first aids to burned patients are fundamental for the evolution of the disease and the success of the next medical care in a Burns Center. In our 30-years experience, we can reassume that they must be provided to limit the cause of thermal damage, to evaluate and correct eventual respiratory or cardiovascular disorders, to find out the possible damage to different organs and the primary care on cutaneous lesions.

Introduction

Burn is a tissue damage caused by the action of the heat released by a body (e.g. hot metal or stoves) or a liquid (e.g. boiling water or frying oil), a caustic agent (e.g. muriatic acid, ammonia, caustic soda), radiations (e.g. surn-burns, radiotherapy) or by a direct sources of heat (e.g. flames), which overcomes the skin's natural protection.

The entity of the tissue damage is directly proportional to the intensity of the noxae pathogens, to their time of action and the extension of the affected skin. Burn is the paradigmatic example of orthodontic dermatitis as it may affect all kind of people, without differences such as in allergic dermatitis.

When the cutaneous involvement is important (for depth and extension of the injury), by a simple dermatological disease, burn become a complex systemic disease, which involves different organs and may be deadly. The burned patient care includes a series of different treatments which follow each other in step with the progression of the burn disease.

The first aid cares to this kind of patients are fundamental, because they influence irreversibly the evolution of the disease and the success of the medical care [1, 2]. They can be chronologically divided into different stages, which start from the time of the burning accident until the patient reaches to the hospital.

First aid to burned patients

Rescue vehicles

The choice of the better rescue vehicle is the first important step in the assistance of burn patients.

In general, the possibilities of intervention in the area of the accident can be carried out by helicopter or ambulance.

Choosing the most suitable transport vehicle should be based on consideration of certain factors such as availability of the vehicle and personnel, accessibility of the nearest hospital centre, costs and others.

Even if expensive, the helicopter is the quickest means of relief. It needs in addition to medical staff, flight crew and appropriate infrastructures (e.g. landing pads, unobstructed aeroplane areas).

The main risk associated with the use of a helicopter is the lack of landing areas near the accident site or the hospital, so it is necessary to complete the journey with an ambulance. In this case, both means must be available promptly and suitably equipped with medical personnel and instruments for the patient care.

Unlike a helicopter, the ambulance is certainly less rapid in transporting the patient, but it provides a better primary care and comfort to him. Finally, it does not need any particular infrastructure to reach the headquarters of the accident or the burn centre and involves the commitment of a singular team of qualified staff.

In any case, the medical and paramedical staff, involved in the first aid of the burns victims, must have a high professional training in the treatment of burning disease and demonstrated the ability to handle emergency situations such as urgent respiratory and cardiocirculatory assistance.

Measures to carry out immediately on the side of the accident

Whereas the severity of a burn is determined by the intensity of the stimulus and the duration of its action on the skin, it is fundamental to stop it [3]. In first aid, even rescuers must be careful to not to be involved with a burn.

To avoid this, it is advisable to wear protective equipment such as gloves, masks, suits, eyeglasses, flame-retardants, etc. If the cause is an electrical current exposure, the material to be used must be insulating.

At this point, it is important to remove flaming clothing and those that are impregnated with toxic substances (e.g., Caustics). Removing jewels, belts and other accessories is also essential, as they may be overheated by the burning cause, is a further source of heat.

It is, therefore, appropriate to wipe the body of the victim with abundant sterile water, to cool the burnt area and remove any contaminants.

When the cause of burn is a caustic one, the use of a chemical antidote may be good if its application is timely. Otherwise, it may be dangerous because it may aggravate the cutaneous. Also, if there is a continuous skin solution, the late use of the chemical antidots only aggravates the burn as the substance penetrates and further damages the skin which is not primarily involved by the noxa pathogens.

In these cases, it is essential to irrigate the cutaneous lesion with sterile water to reduce the concentration of the chemical and the intensity of the burning stimulus [4].

The use of ice or a very cold source is not appropriate because, even if it inhibits the hyperthermic cause, it further damages, through ischemia, perilesional skin, which is essential for the successive repair of the wound [5].

Applying ointments or other topical remedies (potatoes, toothpaste, etc.) is not recommended as possible sources of infections.

Given the importance of an aseptic environment, it is recommended to cover the patient with sterilised blankets, particularly those that may contain the thermal dissipation of the patient's body, so as not to aggravate the hypovolemic shock condition that develops in the early stages of Burning disease. Finally, the use of blankets limits the exposure of burned areas to the environmental ventilation, thus reducing the stimulation of exposed nerve endings and the pain that characterises superficial burns.

Control of vital parameters and first medical treatments

Meanwhile, rescuers should quickly monitor the patient's vital parameters and assess any damage to the respiratory and cardiovascular systems [6].

Respiratory function evaluation is both clinical and instrumental (e.g. partial oxygen pressure assessment) (Table 1).

Table 1: Main causes of respiratory tract damage

Inhalation of irritating substances resulting in bronchospasm.
Bronchospasm due to an allergic hypersensitivity to inhaled fumes
Carbon monoxide poisoning
Damage to the respiratory centre from electrical burns
Oedema of the first airway in the case of facial and neck burns
Extensive thoracic burn that restricts its movement
Hypoxia for burns occurring in closed environments

Indirect indices of respiratory damage are evidence of burnt whiskers, burns around the mouth, pharyngeal oedema, and black-grey sputum.

Only in the hospital, the respiratory damage will be confirmed and quantified with more accurate instrumental examinations such as emogasalysis, RX chest, bronchoscopy or pulmonary scintigraphy.

The first aids to be carried out in the event of

injury to the respiratory system are aimed at:

- Ensure the patent airways (possible tracheotomy).
- Guarantee an adequate expandability of the chest cage (possible escarectomy in the case of full thickness burns that restrict the mobility of the chest cage).
- Oxygen administration.
- Eventual administration of corticosteroids.

The cardiovascular function estimation is both clinical and instrumental. Fundamental is to evaluate the blood pressure and the pulse rate (Table 2).

Table 2: Main causes of cardiovascular failures

Cardiomyopathy by hypovolemic shock
Cardiomyopathy by neurogenic shock
Cardiac arrhythmias from electrical burns

Of primary importance is to place a venous access, preferably in non-burnt surfaces.

In the case of cardiac arrhythmias, resuscitation manoeuvres or electric cardioversion should also be performed, while a fluid therapy is necessary in the case of hypovolemia.

Last but not least, a neurological and orthopaedic evaluation should be allowed due to the risk of cervical and cranial traumas.

In the suspect of a rachid trauma, the application of a cervical collar is fundamental.

In conclusion, first aids to burned patients are a crucial moment to their management, because they drive the evolution of the disease and the success of the medical treatment at the Burns Center. In our 30-years experience, we can reassume that they must be provided to limit the cause of thermal damage, to evaluate and correct eventual respiratory or cardiovascular disorders, to find out the possible damage to different organs and the primary care on cutaneous lesions.

References

1. Kattan AE, AlShomer F, Alhujayri AK et Al. Current knowledge of burn injury first aid practices and applied traditional remedies: a nationwide survey. Burns Trauma. 2016;4:37. collection 2016.

2. Hyland EJ, Harvey JG, Holland AJ. First aid for burns: too little, too late and often wrong. Med J Aust. 2014;200(2):85. https://doi.org/10.5694/mja13.11179 PMid:24484104

3. Paprottka FJ, Krezdorn N, Young K et Al. German, European or American burn guidelines - Is one superior to another? Ann Burns Fire Disasters. 2016;29(1):30-36. PMid:27857648 PMCid:PMC5108224

4. Bitter CC, Erickson TB. Management of Burn Injuries in the Wilderness: Lessons from Low-Resource Settings. Wilderness Environ Med. 2016;27(4):519-525. https://doi.org/10.1016/j.wem.2016.09.001 PMid:28029455

5. Fadeyibi IO, Ibrahim NA, Mustafa IA et Al. Practice of first aid in burn related injuries in a developing country. Burns. 2015;41(6):1322-32. https://doi.org/10.1016/j.burns.2015.02.018 PMid:25805428

6. Gloster AS, Johnson PJ. How to perform first aid. Nurs Stand. 2016 Jan 13;30(20):36-9. https://doi.org/10.7748/ns.30.20.36.s45 PMid:26758166

ID Design 2012/DOOEL Skopje, Republic of Macedonia
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Pyogenic Granuloma – A Common Benign Vascular Tumor with Variable Clinical Presentation: New Findings and Treatment Options

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Abstract

Pyogenic granuloma is a common benign vascular tumour occurring in all ages. Both skin and mucous membranes can be affected. Of pathogenetic importance are trauma, BRAF mutations and probably herpes virus type 1, Orf virus and/or human papilloma virus type 2. The tumour consists of capillary proliferations, venules and fibromyxoid stroma. The development of a lesion occurs in three stages and bleeding is a common symptom. The tumour can mimic various other vascular lesions, solid tumours, and soft tissue infections. In recent years, targeted tumour therapies have become the most common cause of drug-induced pyogenic granulomas. The backbone of treatment is surgical procedures including laser therapy. New developments in medical drug therapy include topical and systemic beta-adrenergic receptor antagonists timolol and propranolol. Drug therapy is an alternative for young children, ocular and periungual pyogenic granuloma.

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Introduction

Pyogenic granuloma (PG) – also known as lobular capillary hemangioma - is a benign vascular tumour that occurs on the skin and mucous membranes, occasional it can be found subcutaneously or intravascularly. PG can arise spontaneously, in sites of injury, or within capillary malformations [1].

PG has been associated with certain medications such as oral contraceptives, retinoids, gefitinib, cabecitabine, and afatinib [2-5]. Most tumours occur as solitary lesions, but multiple grouped or disseminated tumours have been described. Multiple disseminated tumours are an adverse cutaneous effect of melanoma treatment with selective BRAF inhibitors like vemurafenib or encorafenib [6]. Multiple periungual PGs occur with targeted oncological therapies using epidermal growth-factor receptor inhibitors or mitogen-activated protein kinase (MEK) inhibitors [7], and rituximab [8].

Histology and Pathogenesis

Histologically, PG is composed of capillaries and venules with plump endothelial cells separated into lobules by fibromyxoid stroma. The development can be classified into (i) cellular phase, (ii) capillary phase or vascular phase, and (iii) involutionary phase. Slow fibromatous regression is seen in untreated

lesions after longer time [9]. The endothelial cells in PG express CD34, ICAM-1, VCAM-1 associated with an increased microvascular density [10].

Recently, BRAF c.1799T>A mutation had been identified in endothelial cells as a major driver mutation in the pathogenesis of PG [11]. This explains the occurrence of multiple PGs in patients treated with BRAF inhibitors.

The participation of viral particles in PG pathogenesis has been discussed. Alpha-herpes viridiae type 1 is considered as a possible indirect factor stimulating angiogenesis in PG. In some patients, dermatotropic parapoxvirus (Orf) could be identified by polymerase-chain reaction (PCR). Human papilloma virus DNA could be identified in 44% of these lesions with HPV type 2 as the most common [12-15].

Clinical Presentation

PG occurs in all age groups. There is no clear predominance of a gender. PG appear as small or large, smooth or lobulated, reddish exophytic vascular nodules that can grow rapidly (Fig. 1). Larger lesions become lobulated and sometimes develop into mushroom-like, pediculated tumours (Fig. 2). PGs have a tendency to bleed profusely. Bleeding is the leading symptom for a visit to the doctor's office.

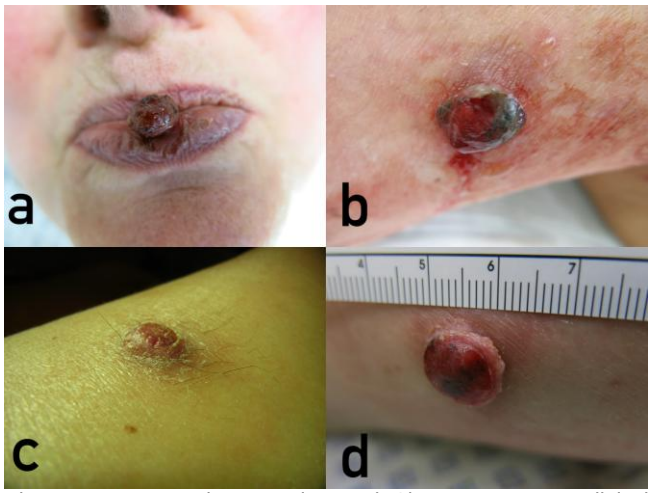

Figure 1: Pyogenic granuloma (PG) – common clinical presentations. (a) Nodular PG of the lower lip; (b) Collerette- like demarcation of a PG on the knee; (c) Flat, keratotic PG on the lower leg. (d) Marked collerette with a flat nodule on the lower arm

Hands, lower lips and gingiva are most frequently affected [1]. In one study, PG was the most common benign lesion of the lips responsible for 48% of all cases [16]. Another study from Brazil investigated gingival lesions in children and adolescents. PGs accounted for 42% of all gingival lesions [17]. Considering the nail organ, most lesions occur on the nail folds, but subungual tumours have also been observed [18].

During pregnancy, large intraoral PGs may develop [19]. Uncommon sites are vulva and penis, oesophagus, gut, and tracheobronchial tree [20-24]. Gastrointestinal PG can cause severe anaemia [25]. Extremely rare are intravascular tumours which bear the risk of thrombosis [26].

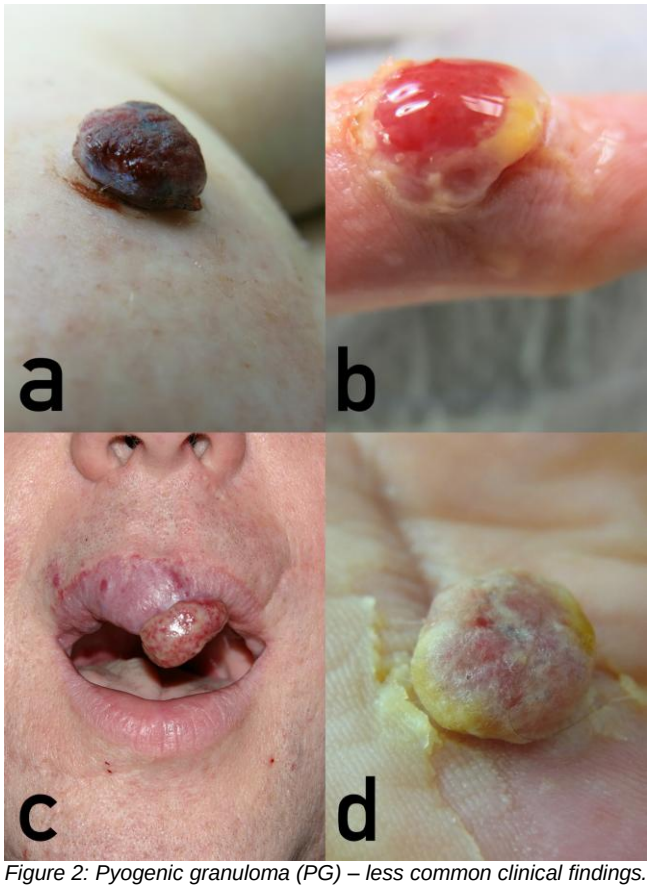

Figure 2: Pyogenic granuloma (PG) – less common clinical findings. (a) Larger mushroom-like, thrombosed PG – melanoma-like; (b) Mushroom-like PG on the finger bow with a wet surface and maceration of the surrounding skin – pyoderma-like; (c) Large pedunculated PG of the upper lip – hemangioma like; (d) Large, firm nodular PG of the palm – non-melanoma skin cancer-like

Portwine stains are at risk for secondary PG [27]. Their treatment with vascular lasers may induce PG as well [28].

Satellitosis is a very uncommon phenomenon in benign tumours. Nevertheless, satellitosis has been observed in paediatric PG [29, 30]. Deep-seated PG is a rare entity with 3.8% of all PGs diagnosed in childhood [31].

Differential diagnoses

PG can mimic other vascular tumours, including Kaposi form hemangioendothelioma,

infantile hemangiomas, vascular malformations, and Kaposi sarcoma. In so-called “Kaposi-like PG” human herpes virus type 8 could be identified. These lesions are true Kaposi sarcomas, not PG [32]. Other malignancies that can mimic PC are malignant lymphomas, basal cell carcinoma, or malignant melanoma [33-35]. In immunocompromised patients, deep soft tissue infections like phaeohyphomycosis or bartonellosis should be considered [36, 37].

Treatment

The usual treatment for PG consists of excision, the treatment with the lowest rate of recurrence [1]. Depending on the area, size and patient wishes, curettage, electrocautery, radiosurgery, cryosurgery, sclerotherapy, or laser treatment are alternative options. Among lasers, diode lasers of wave-length between 808 to 980 nm [38-40] or solid-state neodymium - yttrium aluminium garnet (Nd:YAG) lasers [41, 42], erbium-YAG and CO_2 lasers [43, 44] have all been used successfully. Erbium-YAG laser lacks coagulation, what may become a disadvantage in larger lesions. Successful photodynamic therapy (PDT) with 5-aminolevulinic acid has been reported for a single PG on a finger [45]. A possible advantage of PDT compared to laser removal has yet not proved.

In small children, topical or oral medical therapy with beta-adrenergic receptor antagonists timolol or propranolol seems to be effective [46]. Periungual PGs have been treated off-label with topical 1% propranolol cream [47]. For PG on ocular surfaces medical treatment with topical 0.5 % timolol eye drops twice daily for a minimum of 21 days, is an option [48]. The treatment, either oral or topical, warrants monitoring. Since systemic absorption can occur even after timolol eye drops, patients should be monitored for bradycardia, hypotension, hypoglycemia, and bronchoconstriction. In elderly patients, syncope and falls have been observed [49, 50].

References

1. Giblin AV, Clover AJ, Athanassopoulos A, Budny PG. Pyogenic granuloma - the quest for optimum treatment: an audit of treatment of 408 cases. J Plast Reconstr Aesthet Surg. 2007;60(9):1030-5. https://doi.org/10.1016/j.bjps.2006.10.018 PMid:17478135

2. Simmons BJ, Chen L, Hu S. Pyogenic granuloma association with isotretinoin treatment for acne. Australas J Dermatol. 2016;57(4):e144-5. https://doi.org/10.1111/ajd.12418 PMid:27885661

3. Massa A, Antunes A, Varela P. Pyogenic granuloma in a patient on gefitinib. Acta Med Port. 2016;29(6):416. https://doi.org/10.20344/amp.6343 PMid:27865223

4. Fujiwara C, Motegi SI, Sekiguchi A, Amano H, Ishikawa O. Pyogenic granuloma possibly associated with capecitabine therapy. J Dermatol. 2016. https://doi.org/10.1111/1346-8138.13691

5. Inoue A, Sawada Y, Nishio D, Nakamura M. Pyogenic granuloma caused by afatinib: Case report and review of the literature. Australas J Dermatol. 2017;58(1):61-2. https://doi.org/10.1111/ajd.12423 PMid:26603180

6. Henning B, Stieger P, Kamarachev J, Dummer R, Goldinger SM. Pyogenic granuloma in patients treated with selective BRAF inhibitors: another manifestation of paradoxical pathway activation. Melanoma Res. 2016;26(3):304-7. https://doi.org/10.1097/CMR.0000000000000248 PMid:27116335

7. Robert C, Sibaud V, Mateus C, Verschoore M, Charles C, Lanoy E, Baran R. Nail toxicities induced by systemic anticancer treatments. Lancet Oncol. 2015;16(4):e181-9. https://doi.org/10.1016/S1470-2045(14)71133-7

8. Wollina U. Multiple eruptive periungual pyogenic granulomas during anti-CD20 monoclonal antibody therapy for rheumatoid arthritis. J Dermatol Case Rep. 2010;4(3):44-6. https://doi.org/10.3315/jdcr.2010.1050 PMid:21886749 PMCid:PMC3157817

9. Marla V, Shrestha A, Goel K, Shrestha S. The histopathological spectrum of pyogenic granuloma: A case series. Case Rep Dent. 2016;2016:1323798. https://doi.org/10.1155/2016/1323798

10. Seyedmajidi M, Shafaee S, Hashemipour G, Bijani A, Ehsani H. Immunohistochemical evaluation of angiogenesis related markers in pyogenic granuloma of gingiva. Asian Pac J Cancer Prev. 2015;16(17):7513-6. https://doi.org/10.7314/APJCP.2015.16.17.7513 PMid:26625754

11. Groesser L, Peterhof E, Evert M, Landthaler M, Berneburg M, Hafner C. BRAF and RAS mutations in sporadic and secondary pyogenic granuloma. J Invest Dermatol. 2016;136(2):481-6. https://doi.org/10.1038/JID.2015.376

12. El Hayderi L, Rübben A, Nikkels AF. [The alpha-herpesviridae in dermatology: Herpes simplex virus types I and II. German version]. Hautarzt. 2017;68(3):181-6. https://doi.org/10.1007/s00105-016-3929-5 PMid:28197699

13. Biyik Ozkaya D, Taskın B, Tas B, Asıran Serdar Z, Demirkesen C, Su O, Onsun N. Poxvirus-induced angiogenesis after a thermal burn. J Dermatol. 2014;41(9):830-3. https://doi.org/10.1111/1346-8138.12589 PMid:25110123

14. Ran M, Lee M, Gong J, Lin Z, Li R. Oral acyclovir and intralesional interferon injections for treatment of giant pyogenic granuloma-like lesions in an immunocompromised patient with human Orf. JAMA Dermatol. 2015;151(9):1032-4. https://doi.org/10.1001/jamadermatol.2015.0760 PMid:25946461

15. Vázquez-Martínez OT, González-Betancourt A, Barboza-Cerda MC, González-González SE, Lugo-Trampe Á, Welsh O, Rojas-Martínez A, Martínez-Rodríguez HG, Ocampo-Candiani J, Ortiz-López R. Human papillomavirus type 2 associated with pyogenic granuloma in patients without clinical evidence of warts. Int J Dermatol. 2015;55(7):745-50. https://doi.org/10.1111/ijd.12982 PMid:26492599

16. Tobouti PL, Olegário I, de Sousa SC. Benign vascular lesions of the lips: Diagnostic approach. J Cutan Pathol. 2017;44(5):451-5. https://doi.org/10.1111/cup.12911 PMid:28111788

17. daSilva FC, Piazzetta CM, Torres-Pereira CC, Schussel JL, Amenábar JM. Gingival proliferative lesions in children and adolescents in Brazil: A 15-year-period cross-sectional study. J Indian Soc Periodontol. 2016;20(1):63-6. https://doi.org/10.4103/0972-124X.168493 PMid:27041840 PMCid:PMC4795138

18. Wollina U. Subungual telangiectatic granuloma. Dtsch Arztebl Int. 2017;114(8):136. PMid:28302264 PMCid:PMC5374259

19. Silva de Araujo Figueiredo C, Gonçalves Carvalho Rosalem C, Costa Cantanhede AL, Abreu Fonseca Thomaz ÉB, Fontoura Nogueira da Cruz MC. Systemic alterations and their oral manifestations in pregnant women. J Obstet Gynaecol Res. 2017;43(1):16-22. https://doi.org/10.1111/jog.13150 PMid:28074549

20. Abreu-Dos-Santos F, Câmara S, Reis F, Freitas T, Gaspar H, Cordeiro M. Vulvar lobular capillary hemangioma: A rare location for a frequent entity. Case Rep Obstet Gynecol. 2016;2016:3435270. https://doi.org/10.1155/2016/3435270

21. Katmeh RF, Johnson L, Kempley E, Kotecha S, Hamarneh W, Chitale S. Pyogenic granuloma of the penis: An uncommon lesion with unusual presentation. Curr Urol. 2017;9(4):216-8. https://doi.org/10.1159/000447144 PMid:28413384 PMCid:PMC5385862

22. Zhao J, Feng Q, Shi S. Pyogenic granuloma of the esophagus. Clin Gastroenterol Hepatol. 2017. https://doi.org/10.1016/j.cgh.2017.03.028

23. Romero Mascarell C, García Pagán JC, Araujo IK, Llach J, González-Suárez B. Pyogenic granuloma in the jejunum successfully removed by single-balloon enteroscopy. Rev Esp Enferm Dig. 2017;109(2):152-4. PMid:28196424

24. Qiu X, Dong Z, Zhang J, Yu J. Lobular capillary hemangioma of the tracheobronchial tree: A case report and literature review. Medicine (Baltimore). 2016;95(48):e5499. https://doi.org/10.1097/MD.0000000000005499 PMid:27902613 PMCid:PMC5134768

25. Misawa S, Sakamoto H, Kurogochi A, Kirii Y, Nakamura S, Misawa T, Yoneda S, Hirano M, Owa O, Takagi H, Ota H. Rare cause of severe anemia due to pyogenic granuloma in the jejunum. BMC Gastroenterol. 2015;15:126. https://doi.org/10.1186/s12876-015-0355-6 PMid:26444414 PMCid:PMC4596517

26. Matsuzaki K, Imamura Y, Ozawa M, Nakajima T, Ikeda A, Konishi T, Jikuya T. Intravenous lobular capillary hemangioma in the subclavian vein. Ann Thorac Surg. 2016;102(5):e427-9. https://doi.org/10.1016/j.athoracsur.2016.04.013 PMid:27772599

27. Brightman LA, Geronemus RG, Reddy KK. Laser treatment of port-wine stains. Clin Cosmet Investig Dermatol. 2015;8:27-33. PMid:25624768 PMCid:PMC4296879

28. Wollina U, Zielinski M, Knopf B, Hipler C. [Eruptive capillary hemangioma following argon laser therapy of naevus flammeus]. Hautarzt. 1989;40(4):212-4. PMid:2732049

29. Rana R, Ramachandra SS, Prasad UC, Aggarwal P, Dayakara JK. Recurrent pyogenic granuloma with a satellite lesion. Cutis. 2015;96(2):E27-30. PMid:26367761

30. Gupta V, Mridha AR, Sharma VK. Pediatric Dermatology Photoquiz: Multiple erythematous papules on the back. Recurrent pyogenic granulomas with satellitosis. Pediatr Dermatol. 2016;33(1):97-8. https://doi.org/10.1111/pde.12700 PMid:26758098

31. Putra J, Rymeski B, Merrow AC, Dasgupta R, Gupta A. Four cases of pediatric deep-seated/subcutaneous pyogenic granuloma: Review of literature and differential diagnosis. J Cutan Pathol. 2017. https://doi.org/10.1111/cup.12923 PMid:28233342

32. Ryan P, Aarons S, Murray D, Markham T, O'Sullivan S, Lyons F, Lee G, Fitzgibbon J. Human herpesvirus 8 (HHV-8) detected in two patients with Kaposi's sarcoma-like pyogenic granuloma. J Clin Pathol. 2002;55(8):619-22. https://doi.org/10.1136/jcp.55.8.619 PMid:12147659 PMCid:PMC1769721

33. Bains A, Vedant D, Shanker V, Tegta GR. Primary cutaneous anaplastic large cell lymphoma masquerading as large pyogenic granuloma. Indian Dermatol Online J. 2016;7(6):526-8. https://doi.org/10.4103/2229-5178.193896 PMid:27990392 PMCid:PMC5134171

34. Kumar P, Das A, Mondal A, Savant SS. Pyogenic granuloma-like basal cell carcinoma on the abdomen: A deceptive presentation. Indian Dermatol Online J. 2016;7(5):446-448. https://doi.org/10.4103/2229-5178.190502 PMid:27730056 PMCid:PMC5038121

35. Jafarian F, Powell J, Kokta V, Champagne M, Hatami A, McCuaig C, Marcoux D, Savard P. Malignant melanoma in childhood and adolescence: report of 13 cases. J Am Acad Dermatol. 2005;53(5):816-22. https://doi.org/10.1016/j.jaad.2005.07.013 PMid:16243130

36. Khader A, Ambooken B, Binitha MP, Francis S, Kuttiyil AK, Sureshan DN. Disseminated cutaneous due to Cladophialophora bantiana. Indian J Dermatol Venereol Leprol. 2015;81(5):491-4. https://doi.org/10.4103/0378-6323.162333 PMid:26261143

37. Bolton JG, Galeckas KJ, Satter EK. Inoculation bartonellosis in an adult: a case report. Cutis. 2010;85(1):37-42. PMid:20184210

38. Al-Mohaya MA, Al-Malik AM. Excision of oral pyogenic granuloma in a diabetic patient with 940nm diode laser. Saudi Med J. 2016;37(12):1395-1400. https://doi.org/10.15537/smj.2016.12.15941 PMid:27874157 PMCid:PMC5303780

39. Hasanoglu Erbasar GN, Senguven B, Gultekin SE, Cetiner S. Management of a recurrent pyogenic granuloma of the hard palate with diode laser: A case report. J Lasers Med Sci. 2016;7(1):56-61. https://doi.org/10.15171/jlms.2016.12 PMid:27330700 PMCid:PMC4908978

40. Wollina U. Three hundred patients treated with ultrapulsed 980 nm diode laser for skin disorders. Indian J Dermatol. 2016;61(5):540-4. https://doi.org/10.4103/0019-5154.190111 PMid:27688445 PMCid:PMC5029241

41. Au S, Fancher W, Scribner J. Treatment of pediatric pyogenic granuloma in a functionally and cosmetically sensitive area with the 1064nm Nd:Yag laser. Dermatol Online J. 2016;22(4). PMid:27617472

42. Goldman A, Rossata F, Wollina U. Versatility of the Nd-YAG laser in the treatment of facial vascular alterations. Kosmet Med 2008;29:134-7.

43. Fekrazad R, Nokhbatolfoghahaei H, Khoei F, Kalhori KA. Pyogenic granuloma: surgical treatment with Er:YAG laser. J Lasers Med Sci. 2014;5(4):199-205. PMid:25653822 PMCid:PMC4281984

44. Truschnegg A, Acham S, Kqiku L, Beham A, Jakse N. CO2 laser excision of a pyogenic granuloma associated with dental implants: A case report and review of the literature. Photomed Laser Surg. 2016;34(9):425-31. PMid:27420917

45. Liu J, Zhou BR, Yi F, Wu HJ, Zhang JA, Luo D. Pyogenic granuloma in a patient with psoriasis successfully treated by 5-aminolevulinic acid photodynamic therapy: A case report. Exp Ther Med. 2016;11(1):345-347. PMid:26889266

46. Wine Lee L, Goff KL, Lam JM, Low DW, Yan AC, Castelo-Soccio L. Treatment of pediatric pyogenic granulomas using β-adrenergic receptor antagonists. Pediatr Dermatol. 2014;31(2):203-7. https://doi.org/10.1111/pde.12217 PMid:24138457

47. Piraccini BM, Alessandrini A, Dika E, Starace M, Patrizi A, Neri I. Topical propranolol 1% cream for pyogenic granulomas of the nail: open-label study in 10 patients. J Eur Acad Dermatol Venereol. 2016;30(5):901-2. https://doi.org/10.1111/jdv.13071 PMid:25708373

48. Oke I, Alkharashi M, Petersen RA, Ashenberg A, Shah AS. Treatment of ocular pyogenic granuloma with topical timolol. JAMA Ophthalmol. 2017;135(4):383-5. https://doi.org/10.1001/jamaophthalmol.2017.0110 PMid:28301661

49. de Graaf M, Breur JM, Raphaël MF, Vos M, Breugem CC, Pasmans SG. Adverse effects of propranolol when used in the treatment of hemangiomas: a case series of 28 infants. J Am Acad Dermatol. 2011;65(2):320-7. https://doi.org/10.1016/j.jaad.2010.06.048 PMid:21601311

50. Müller ME, van der Velde N, Krulder JW, van der Cammen TJ. Syncope and falls due to timolol eye drops. BMJ. 2006;332(7547):960-1. https://doi.org/10.1136/bmj.332.7547.960 PMid:16627515 PMCid:PMC1444852

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Madelung's Disease – Case Series and Treatment by Tumescent Liposuction or Lipectomy

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Keywords: Lipomatosis; Madelung disease; adipose tissue; comorbidities; lipectomy; tumescent liposuction.

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Abstract

Madelung disease is a disfiguring disorder belonging to the heterogeneous group of lipomatosis. The aetiology is not well understood, but alcohol consumption has been regarded as of importance. The reported incidence is about 1 in 25,000 inhabitants. We reviewed our files of the last ten years and identified eight adult patients with an equal gender distribution. Their age was between 60 and 85 years of life. Comorbidities are frequent. Clinical presentation may vary. Surgical treatment is reported and discussed. Both cold steel surgery and tumescent liposuction have their place in treatment.

Introduction

Madelung's disease (MD) is a rare disorder of adipose tissue, characterised by disfiguring massive non-capsulated adipose tissue proliferations in the neck the shoulder, and the arms. It may be associated with gynecomastia or lipomastia nearly one-third of patients. The age peak is between 30 to 60 years of age with a male to female-ration of 15:1 to 30:1. The incidence is about one affected person in 25,000 inhabitants. Most cases are sporadic patients [1, 2].

The aetiology of MD is not well understood. Since 86 to > 95% of patients report chronic alcohol consumption, secondary metabolic effect may be of importance [2, 3]. Alcohol can induce abnormalities in the catecholamine-adipose tissue interactions. Adrenergic lipolysis becomes impaired and may result in excessive adipose tissue. Furthermore, a reduction of mitochondrial enzymes and increased adipose tissue lipoprotein-lipase activity have been reported [4].

Adipocytes in MD seem to be closer to brown adipocytes than to white adipocytes according to ultrastructural investigations. In culture, pre-adipocytes of MD develop large mitochondria with parallel cristae and show multi-vacuolar lipid deposits [5]. Investigations on cultured pre-adipocytes demonstrated synthesis of inner mitochondrial membrane protein UCP-1, which is a selective marker of brown adipose tissue (BAT) [6]. There are more arguments supporting MD as a disease of BAT: uncoupling protein-1 mRNA (selective BAT marker), and adipocyte fatty-acid protein-2 (a selective marker of BAT and immature adipocytes) have been observed in patients with MD in affected adipose tissue [4].

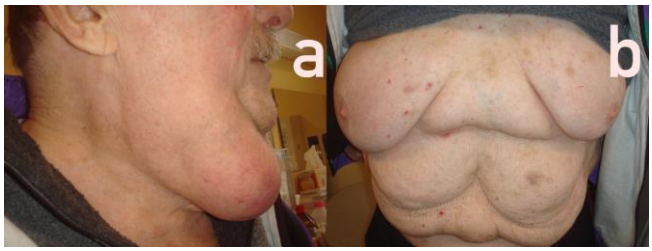

Figure 1: Madelung's disease with major disfigurement (Case 1). (a) Massive enlargement of subcutaneous adipose tissue under the chin; (b) Severe gynecomastia

Comparing affected and non-affected adipocytes of patients with MD disclosed not

differences in their surface marker profile. However, adipose tissue-derived stem cells had a higher proliferative activity. There were marked changes in the genetic profile for proliferation control, mitochondria, and hormonal regulation demonstrated by polymerase chain reaction (PCR) arrays [7].

MD patients show multiple comorbidities, such as hepatic disease (60%), metabolic syndrome (40%), chronic obstructive pulmonary disease (COPD; 23%), hypothyroidism (10%), malignant tumors of the upper airways (rarely), and chronic alcohol consumption (> 95%) [2].

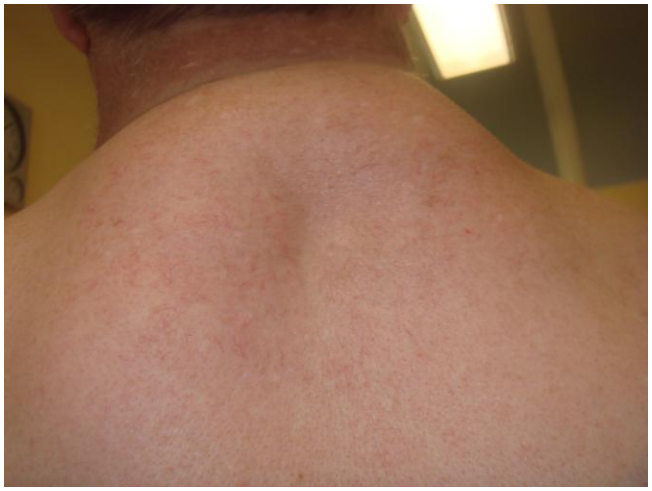

Figure 2: Moderate growth of adipose tissue of the neck in Madelung's disease with development of multiple telangiectasias (Case 2)

MD must be differentiated from Cushing syndrome and syndromic lipomatosis types of the head and neck region such as Familial Multiple Lipomatosis (FML), Encephalo-Cranio-Cutaneous Lipomatosis (ECCL), Congenital Infiltrating Lipomatosis of the Face (CIL-F), and Nasopalpebral Lipoma-Coloboma Syndrome (NLCS) [8, 9].

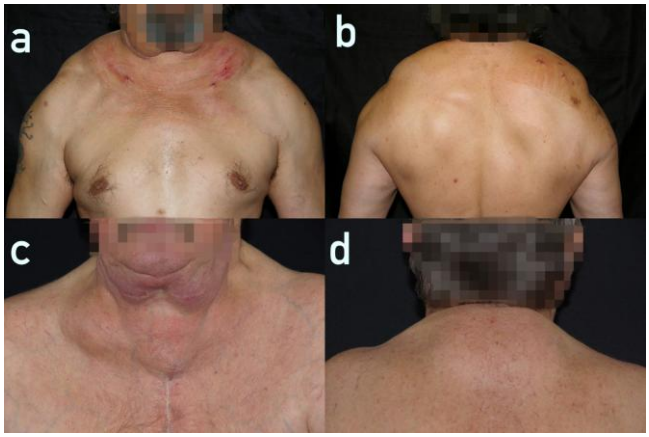

Figure 3: Improvement of Madelung's disease by tumescent liposuction (Case 3). Before treatment (a, b) and after liposuction (c, d)

Patients and Methods

We searched our files for patients with MD seen at the Department of Dermatology and Allergology during 2007 to 2017, their clinical presentation, comorbidities, and three cases of surgical treatment.

Results

We identified eight adult patients with MD, four males and four females. Most patients had significant metabolic comorbidities. Two underwent bypass surgery after myocardial infarction; two suffered from renal insufficiency. The demographics and co-morbidities are summarised in Table 1 and Figures 1 - 8.

Table 1: Demographics, clinical findings, and comorbidities in MD

Patient	Age (years)	Gender	Affected areas	Co-morbidities
1	75	Male	Neck, shoulders, gynecomastia	Hepatocellular carcinoma, alcoholic liver cirrhosis, compensated renal insufficiency
2	67	Male	Neck	Hypertension
3	68	Male	Neck, shoulders, upper arms, gynecomastia	Metabolic syndrome, myocardial infarction with bypass surgery, gonarthrosis
4	60	Female	Neck, shoulders	Cervical spine syndrome, bullous pemphigoid,
5	84	Female	Neck, upper back	myocardial infarction with bypass surgery, diabetes mellitus type II, arterial hypertension, osteoporosis
6	66	Female	Neck, shoulders, arms, lipomastia	Cervical spine syndrome
7	54	Male	Neck and upper back	Arterial hypertension, hypothyreosis, pulmonary fibrosis
8	79	Female	Neck, shoulders	Renal nephrectomy after renal cell carcinoma, chronic anaemia, chronic renal insufficiency, arterial hypertension, cholecystolithiasis, knee-TEP-surgery

Surgical treatment

Case 1 (Fig. 3)

A 68-year-old male patient presented with symmetrical progressive lipomatosis of MD-type. He suffered from impairment of neck mobility and pain sensations. Therefore, he wanted treatment for the neck region.

His medical history was positive for arterial hypertension, hyperlipidemia, bypass surgery after myocardial infarction 2013 with oral anticoagulation, and gonarthrosis of the right knee.

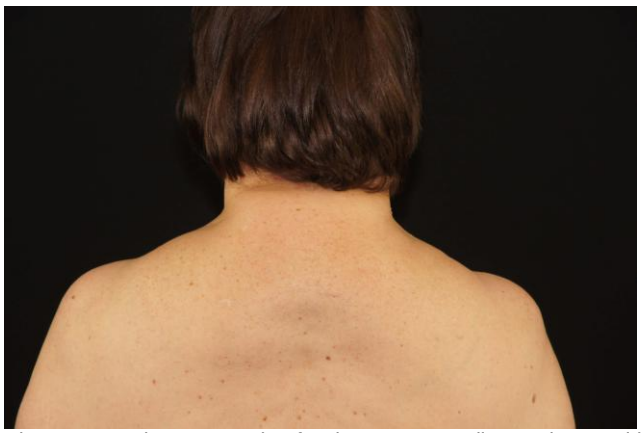

Figure 4: Moderate growth of subcutaneous adipose tissue with some telangiectasias (Case 4)

On examination, there were massive disfiguring adipose tissue deposits on neck, shoulders, arms and gynecomastia. The largest neck circumference was 50 cm.

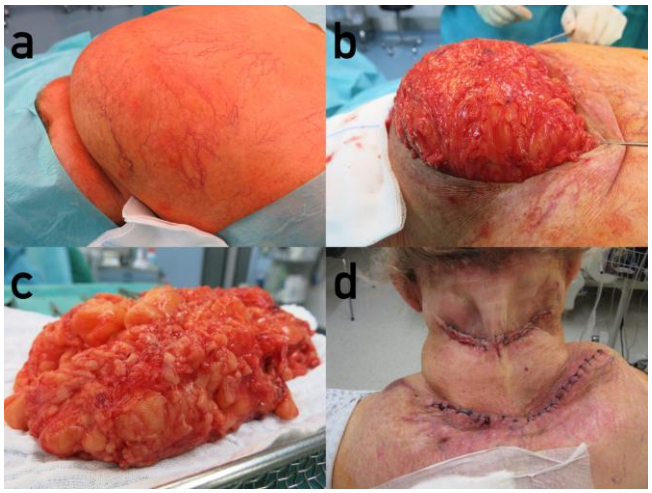

Figure 5: Massive tumor-like swelling of the neck (Case 5) with obvious telangiectasias (a). (b) Operation situs demonstrates non-encapsulated subcutaneous adipose tissue. (c) Resection specimen with massive enlarged adipocytes. (d) Two days after surgery

Laboratory investigations revealed the following pathologic parameters: GGT 3.45 µkat/l, (normal range <1), CRP 15.4 mg/l (< 5), creatinin 111µmol/l (< 90).

Histology: the Diffuse non-septal proliferation of adult enlarged mono vacuolar adipocytes with infiltration of adjacent structures.

Treatment and Course: He had a lipectomy in a plastic surgical department six years ago that relapsed. We performed two sessions of tumescent liposuction. The total amount of lipoaspiration was 600 ml. The procedures were well tolerated. After the second liposuction, he developed a symptomatic met-hemoglobinemia that was treated by intravenous injection of toluidine blue solution.

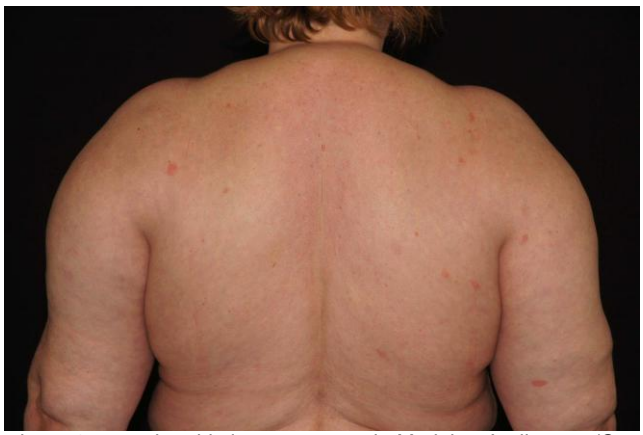

Figure 6: Pseudo-athletic appearance in Madelung's disease (Case 6)

Case 2 (Fig. 7)

A 54-year-old male patient presented with longstanding, progressive subcutaneous, symmetrical adipose tissue deposits on the neck and upper back. He had a relapse after lipectomy.

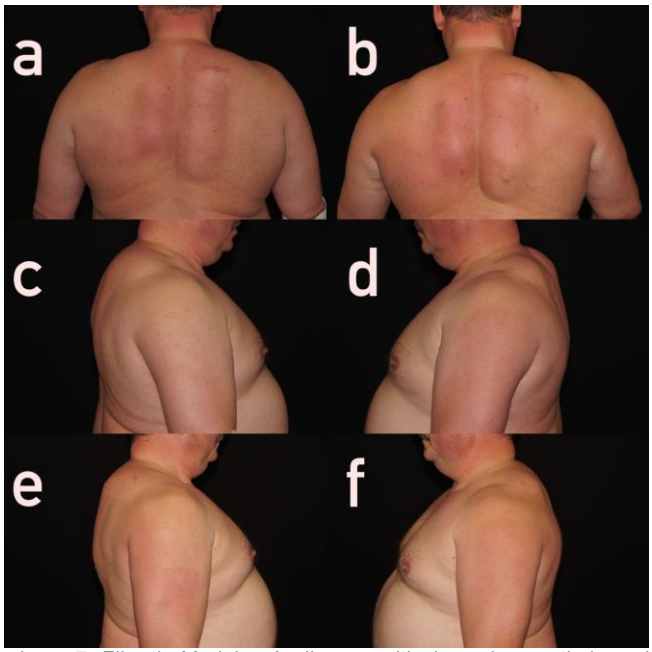

Figure 7: Fibrotic Madelung's disease with dynamic growth (a and b), relapse after lipectomy; Stepwise improvement by tumescent liposuction from (c, d) to (e, f)

Treatment and course: We treated him in 2014 by two tumescent liposuction sessions. Although the lipoaspirate was only 500 ml, he reported on significant improvement of pain sensations and mobility. After two years, he experienced a partial relapse that was treated again by tumescent liposuction with good functional results (lipoaspirate 200 ml).

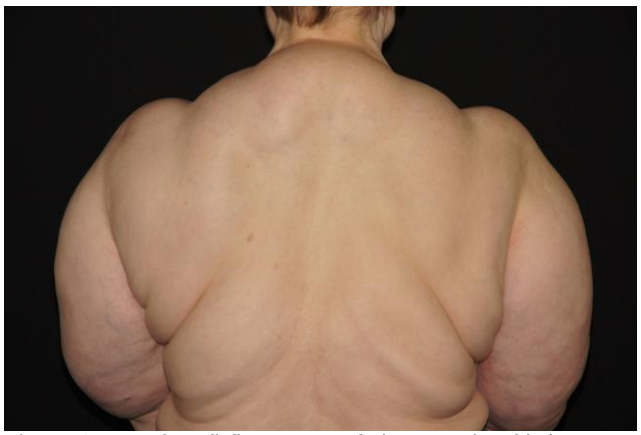

Figure 8: Massive disfigurement of the pseudo-athletic type of Madelung's disease (Case 8)

Case 3 (Fig. 5)

An 83-year-old female patient presented with large disfiguring lipoma-like subcutaneous masses of the neck region. We decided to perform combined lipectomy and dermato- lipectomy in general anaesthesia. Healing was unremarkable. The patient was satisfied by the functional and esthetic outcome. There was no relapse in the following 12 months.

Discussion

MD can lead to severe clinical complications, such as mediastinal syndrome, tracheobronchial obstruction, dysphagia, dysphonia, limited mobility of the neck, and somatic and autonomic neuropathies [6]. Such complications are an indication to surgical treatment [2, 10].

In the past, the only available treatment was open surgery [11]. Open surgery is characterised by a high rate of complications, mostly due to the severe comorbidities in MD patients. In a large series of 59 MD patients, complications by surgery (lipectomy/ dermato- lipectomy) were observed in 17.8%. However, the authors preferred surgery in advanced cases [4].

Since relapses occur frequently, less invasive techniques were developed – either as adjuvant treatment or as a substitute for extensive classical surgery such as injection lipolysis and tumescent liposuction [12-14]. Injection lipolysis, however, causes fibrosis and adhesions which prohibit the use of liposuction in the case of recurrence and possibly complicates lipectomy surgery as well. It is therefore not considered as an ideal treatment for MD [15].

Tumescent liposuction is an established technique not only for esthetic procedures but a variety of medical conditions. It offers a combination of adipose tissue removal and skin tightening [16].

Constandinidis et al. (2003) used a combined lipectomy and liposuction in 11 patients with MD. They started with lipectomy in the first place followed by liposuction in a second "course with liposuction" being done at a second session. Their mean follow-up was 2.7 years. Nine of 11 patients were satisfied with the esthetic outcome. Two relapses after 1.5 years and two years were observed [17].

In one study seven MD patients were treated by liposuction successfully. Mean follow-up of 18 months revealed a high patient satisfaction with the outcome of the procedure [18].

We report on ten adult patients with MD. The clinical presentation can vary widely concerning the areas involved and the degree of disfigurement and functional impairment. Both the clinical features of MD and the frequent occurrence of comorbidities has an impact on treatment options. In case 1, lipectomy had been performed before the patient present to our department, but there was a significant relapse. In this patient as well as in the more limited type seen in case 2, liposuction in tumescent anaesthesia was a useful and safe procedure leading to minor down-time without extensive scars. In more advanced situations, lipectomy and dermato- lipectomy may be used in the first place as demonstrated in case 3. Surgical approaches are the only treatment options with a significant improvement of MD, often with improved functionality and satisfying esthetic outcome. Although alcohol abuse is a common pathology, there is no scientific proof for reduced risk of progression and relapses if the patient stops alcohol consumption. Nevertheless, comorbidities need to be considered for an optimal long-term outcome of patients with MD.

References

1. González-García R, Rodríguez-Campo FJ, Sastre-Pérez J, Muoz-Guerra MF. Benign symmetric lipomatosis (Madelung's disease): case reports and current management. Aesthetic Plast Surg. 2004;28(2):108-12. https://doi.org/10.1007/s00266-004-3123-5 PMid:15164232

2. Brea-García B, Cameselle-Teijeiro J, Couto-González I, Taboada-Suárez A, González-Álvarez E. Madelung's disease: comorbidities, fatty mass distribution, and response to treatment of 22 patients. Aesthetic Plast Surg. 201337(2):409-16. https://doi.org/10.1007/s00266-012-9874-5

3. Pinto CI, Carvalho PJ, Correia MM. Madelung's disease: Revision of 59 surgical Cases. Aesthetic Plast Surg. 2016.

4. Plummer C, Spring PJ, Marotta R, Chin J, Taylor G, Sharpe D, Athanasou NA, Thyagarajan D, Berkovic SF. Multiple symmetrical lipomatosis--a mitochondrial disorder of brown fat. Mitochondrion. 2013;13(4):269-76. https://doi.org/10.1016/j.mito.2013.03.003 PMid:23524250

5. Zancanaro C, Sbarbati A, Morroni M, Carraro R, Cigolini M, Enzi G, Cinti S. Multiple symmetric lipomatosis. Ultrastructural

investigation of the tissue and preadipocytes in primary culture. Lab Invest. 1990;63(2):253-8. PMid:2381166

6. Enzi G, Busetto L, Sergi G, Coin A, Inelmen EM, Vindigni V, Bassetto F, Cinti S. Multiple symmetric lipomatosis: a rare disease and its possible links to brown adipose tissue. Nutr Metab Cardiovasc Dis. 2015;25(4):347-53. https://doi.org/10.1016/j.numecd.2015.01.010 PMid:25770761

7. Prantl L, Schreml J, Gehmert S, Klein S, Bai X, Zeitler K, Schreml S, Alt E, Gehmert S, Felthaus O. Transcription profile in sporadic multiple symmetric lipomatosis reveals differential expression at the level of adipose tissue-derived stem cells. Plast Reconstr Surg. 2016;137(4):1181-90. https://doi.org/10.1097/PRS.0000000000002013 PMid:27018673

8. Horev L, Lees MM, Anteby I, Gomori JM, Gunny R, Ben-Neriah Z. Oculoectodermal syndrome with coarctation of the aorta and moyamoya disease: expanding the phenotype to include vascular anomalies. Am J Med Genet A. 2011;155A(3):577-81. https://doi.org/10.1002/ajmg.a.33104 PMid:21337683

9. Tadisina KK, Mlynek KS, Hwang LK, Riazi H, Papay FA, Zins JE. Syndromic lipomatosis of the head and neck: a review of the literature. Aesthetic Plast Surg. 2015;39(3):440-8. https://doi.org/10.1007/s00266-015-0478-8 PMid:25860506

10. Sharma N, Hunter-Smith DJ, Rizzitelli A, Rozen WM. A surgical view on the treatment of Madelung's disease. Clin Obes. 2015;5(5):288-90. https://doi.org/10.1111/cob.12111 PMid:26246230

11. Brackenbury ET, Morgan WE. Surgical management of Launois-Bensaude syndrome. Thorax. 1997;52(9):834-5. PMid:9371221

12. Samdal F, Kleppe G, Tonvang G. Benign symmetric lipomatosis of the neck treated by liposuction. Case report. Scand J Plast Reconstr Surg Hand Surg. 1991;25(3):281-4. https://doi.org/10.3109/02844319109020633 PMid:1780727

13. Faga A, Valdatta LA, Thione A, Buoro M. Ultrasound assisted liposuction for the palliative treatment of Madelung's disease: a case report. Aesthetic Plast Surg. 2001;25(3):181-3. https://doi.org/10.1007/s002660010118 PMid:11426308

14. Hasegawa T, Matsukura T, Ikeda S. Mesotherapy for benign symmetric lipomatosis. Aesthetic Plast Surg. 2010;34(2):153-6. https://doi.org/10.1007/s00266-009-9374-4 PMid:19488808

15. Andou E, Komoto M, Hasegawa T, Mizuno H, Hayashi A. Surgical excision of Madelung disease using bilateral cervical lymphnode dissection technique-its effect and the influence of previous injection lipolysis. Plast Reconstr Surg Glob Open. 2015;3(4):e375. https://doi.org/10.1097/GOX.0000000000000337 PMid:25973353 PMCid:PMC4422206

16. Atiyeh B, Costagliola M, Illouz YG, Dibo S, Zgheib E, Rampillon F. Functional and therapeutic indications of liposuction: Personal experience and review of the literature. Ann Plast Surg. 2015;75(2):231-45. https://doi.org/10.1097/SAP.0000000000000055 PMid:25695452

17. Constantinidis J, Steinhart H, Zenk J, Gassner H, Iro H. Combined surgical lipectomy and liposuction in the treatment of benign symmetrical lipomatosis of the head and neck. Scand J Plast Reconstr Surg Hand Surg. 2003;37(2):90-6. https://doi.org/10.1080/02844310310005612 PMid:12755508

18. Tremp M, Wettstein R, Tchang LA, Schaefer DJ, Rieger UM, Kalbermatten DF. Power-assisted liposuction (PAL) of multiple symmetric lipomatosis (MSL)--a longitudinal study. Surg Obes Relat Dis. 2015;11(1):155-60.1997;52(9):834-5.

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Case Report

Erythema Ab Igne Successfully Treated With Mesoglycan and Bioflavonoids: A Case-Report

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Keywords: erythema ab igne; heat exposure; malignant transformation; mesoglycan; bioflavonoids.

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Abstract

Erythema ab igne is a localised, cutaneous condition consisting of reticulate hyperpigmentation, epidermal atrophy, and telangiectasias. It is caused by repetitive and prolonged exposure to moderate heat that is insufficient for producing burns. Currently, erythema ab igne is most commonly observed following repeated use of hot water bottles, infrared lamps and heating pads. If not properly treated, erythema ab igne can become chronic and even malignant. We report a case of erythema ab igne, successfully treated with systemic mesoglycan-based therapy, and local therapy with bioflavonoids.

Introduction

"Erythema ab igne" (EAI) or "erythema caloric" is a dermatosis supported by a reactive vascular impairment that develops after repeated and long-term exposure to heat [1]. The intensity of the infrared radiation responsible for this event is not sufficient for producing burns.

Erythema ab igne is a reticular, pigmented and telangiectatic dermatosis. Typically the lesions are localised in skin areas directly exposed to the heat source.

Although rare, a bullous form of erythema ab igne has been described, characterised by bullae and crusts within a localised area of reticular, brown and macular pigmentation [2]. Erythema ab igne is usually asymptomatic, but patients may report a burning sensation and pruritus.

The histopathological alterations [4] include epidermal atrophy, hyperkeratosis and parakeratosis, and aspects of lichenification. The dermis shows abundant melanophages and occasional elastic fibre alterations similar to actinic elastosis. There is also melanin and hemosiderin deposition and formation of telangiectasis, together with perivascular infiltration of polymorphonuclear cells.

Erythema ab igne is usually a chronic disease. The most significant long term risk is the malignant transformation of erythema ab igne into cutaneous squamous cell carcinomas or Merkel cell carcinomas [5-6].

The diagnosis is mainly clinical and supported by a medical history. On rare occasions, histology may be necessary.

At present, there are no effective medical therapies available.

The paramount goal of therapy is to eliminate the cause. According to some studies, treatment with topical 5-fluorouracil [8] or imiquimod may be useful in

reducing or eliminating dysplasia of the keratinocytes. A case report describes the successful of photodynamic therapy [9].

Case report

An otherwise healthy, 25-year-old female subject affected by erythema ab igne (Fig. 1), came to our Clinic with a brown reticular lesion on her legs.

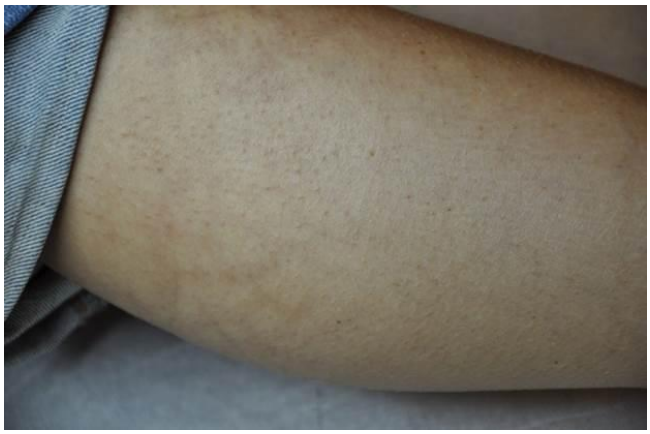

Figure 1: Woman, 25 years old, affected by erythema ab igne

The dermatosis, similar to reticular livedo, was lightly pigmented, asymptomatic, and did not change significantly with digital pressure. Otherwise, the patient did not report any subjective symptoms and enjoyed apparent good health.

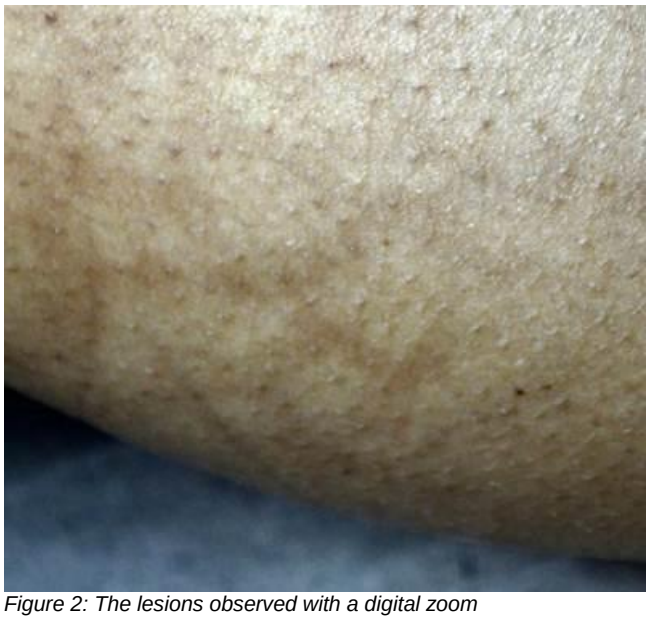

Figure 2: The lesions observed with a digital zoom

The lesions had a peculiar distribution as they were limited to the proximal right side of both legs. We studied her anamnestic history in order to understand her habits and lifestyle and clarify the nature of the lesions.

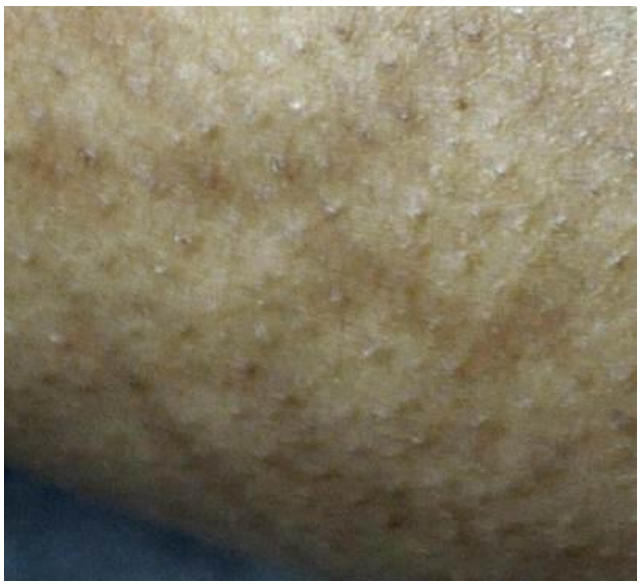

Figure 3: The lesions observed with a digital zoom

She told us she was a doughnut cook in a kiosk on the city streets. To keep warm in winter, she used a small electric heater on the floor on the right-hand side of the kiosk. After about two months of exposure to the heater, she noticed a brown, reticular dermatosis on her legs which had become increasingly darker over time. This helped us correlate the lesions with the heat source as they were visible on the right side of both legs, in the skin region directly exposed to the heater. A physical examination did not reveal any clinical signs of abnormal collagen. Routine blood tests for were negative for autoimmune diseases (ANA and antiphospholipid antibodies), diabetes, viral hepatitis or any other systemic diseases.

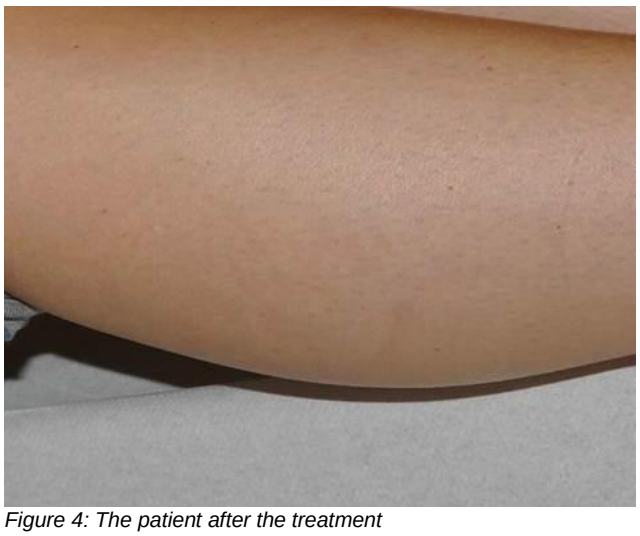

Figure 4: The patient after the treatment

We advised the patient to stop using the heater and prescribed oral mesoglycan 50 mg twice daily and a topical gel (glycosaminoglycan, flavonoids, antioxidants, saponins, etc.) with a vascular action to be applied twice daily.

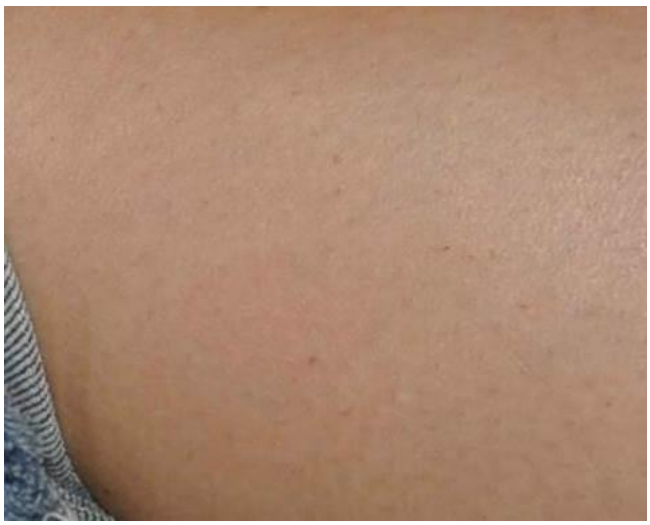

Figure 5: The patient after the treatment

At the one-month follow-up there was a partial regression of the lesion, so we reduced the dosage of mesoglycan to 50 mg/day for two months.

At the end of this period the lesions had completely healed (Fig. 4-5).

Discussion

Erythema ab igne (EAI), also known as “toasted skin syndrome” and “fire stains”, is a localised, cutaneous condition, consisting of reticulate hyperpigmentation, dusky erythema, epidermal atrophy, and telangiectasias.

Historically, it was often seen on the inner thighs and legs of women who sat in front of a stove or open fire. Nowadays erythema ab igne is a rare disease due to the general availability of central heating.

However, cases of erythema ab igne are still reported, although less frequently.

Occupational exposure to heat (such as bakers, blacksmiths, foundry workers, etc.) [10] may cause erythema ab igne. More rarely, the skin disorder has also been described on the legs of people exposed to a car heater for long periods.

In less privileged social classes we continue to observe cases deriving from repeated use of heaters, electric blankets or heated cushions.

Even exposure to infrared lamps may cause erythema ab igne, often characterised by the simultaneous damage to ocular structures (e.g. cataracts).

Some patients develop erythema ab igne using a heat source (e.g. heating pad, heated blanket or hot water bottle [11]) to relieve chronic pain. This typically occurs in patients with chronic pancreatitis [12-13] or cancer. Erythema ab igne has also been described following the use of sauna belts for abdominal obesity, and in patients using heated recliners to relieve chronic lower back pain.

One case report describes erythema ab igne following the use of a heating/cooling blanket in the intensive care unit [14].

Moreover, erythema ab igne could be associated with numerous physiotherapeutic treatments [7], which uses ultrasound and short wave diathermy to promote a rapid tissue vibration in order to generate heat and provide pain relief.

Finally, there is the “laptop dermatitis” [15-17]. Some laptops may generate significant heat when placed on the legs for long periods resulting in erythema ab igne.

The main pathogenetic aspects seem to be represented by a degeneration of the elastic fibres, by the degeneration of basal cells with release of melanin pigment, and by vascular changes. Confirming this is the higher incidence of this disease in patients with predisposing lesions, such as acrocyanosis, acrorigosis, and telangiectasias, etc.

The first sign is a transient macular erythema in a broad, reticulated pattern that blanches easily. At this stage, Erythema ab igne is very similar to reticular livedo but not limited to digital pressure or heat. Furthermore, erythema ab igne lesions are more circumscribed than livedo reticularis and have a precise local history.

With prolonged and repeated exposure, areas of reticular erythema persist and become livid and hyperpigmented. Epidermal atrophy may overlie the reticulated pigmentation. Typically, the lesions are localized in skin areas directly exposed to the heat source.

Although rare, a bullous form of erythema ab igne has also been described [3].

The histopathological alterations include epidermal atrophy, hyperkeratosis and parakeratosis, collagen fragmentation, melanin and hemosiderin deposition, the formation of telangiectasias, with perivascular infiltration of polymorphonuclear cells. The dermis shows abundant melanophages and occasional elastic fiber alterations similar to actinic elastosis (“thermal keratosis”).

If not properly treated, Erythema ab igne has an insidious course and tends to become chronic.

It also represents a precancerous lesion, which may evolve into squamous cell carcinomas [7] or Merkel cell carcinomas.

Is very important to make a correct and early

diagnosis of this dermatosis and promptly implement appropriate treatment. Unfortunately, at present, there are no effective medical therapies available.

Treatment with topical fluorouracil or imiquimod may be useful in reducing or eliminating keratinocyte dysplasia [8].

In conclusion, the Authors report a case of erythema ab igne, in which they achieved healing of the lesions via removal of the patient from the heat source and early drug therapy. Oral mesoglycan is an antithrombotic and pro-fibrinolytic drug, which has been shown to be effective in the treatment of different vascular disorders, such as atherosclerosis, venous thrombosis, inflammatory vasculitis and others. Flavonoids are a class of plant metabolites, with important antioxidant and antiinflammatory properties.

The anticoagulant action of oral mesoglycan and the vascular action of local flavonoids reduced the inflammation and luminal obliteration processes, which are the basis of erythema ab igne.

References

1. Kligman LH. Intensification of ultraviolet-induced dermal damage by infrared radiation. Arch Dermatol Res. 1982;272(3-4):229-38. https://doi.org/10.1007/BF00509050 PMid:7165330

2. Kokturk A, Kaya TI, Baz K, Yazici AC, Apa DD, Ikizoglu G. Bullous erythema ab igne. Dermatol Online J. 2003;9(3):18. PMid:12952765

3. Hirohata A, Hanafusa T, Igawa K, Inoue-Nishimoto T, Mabuchi-Kiyohara E, Nakai C, Kasugai T, Yokozeki H, Ikegami R. Bullous erythema ab igne with cutaneous reactive angiomatosis.Eur J Dermatol. 2016;26(2):191-2. PMid:27226050

4. Cavallari V, Cicciarello R, Torre V, Gagliardi ME, Albiero F, Palazzo R, Siragusa M, Schipis C. Chronic heat-induced skin lesions (erythema ab Igne): ultrastructural studies. Ultrastruct Pathol. 2001;25(2):93-7. https://doi.org/10.1080/01913120117614 PMid:11407533

5. LoPiccolo M, Crestanello J, Yoo SS, Sciubba J, Fernández C, Tausk FA. Facial erythema ab igne of rapid onset. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;105(5):e38-40. https://doi.org/10.1016/j.tripleo.2008.01.008 PMid:18442733

6. Rudolph CM, Soyer HP, Wolf P, Kerl H. Squamous epithelial carcinoma in erythema ab igne. Hautarzt. 2000 Apr;51(4):260-3. https://doi.org/10.1007/s001050051031 PMid:10810662

7. Wollina U, Helm C, Hansel G, Köstler E, Schönlebe J. Two cases of erythema ab igne, one with a squamous cell carcinoma. Giornale Italiano di Dermatologia e Venereologia. 2007;142(4):415-8.

8. Sahl W, Taira JW. Erythema ab igne: treatment with 5-fluorouracil cream. J Am Acad Dermatol. 1992; 27: 109-10. https://doi.org/10.1016/S0190-9622(08)80818-3

9. Kochs C, Hanneken S, Schulte KW, Reifenberger J. Treatment of carcinoma in situ of erythema ab igne with photodynamic therapy. Hautarzt. 2008;59(10):777-9. https://doi.org/10.1007/s00105-008-1634-8 PMid:18773179

10. Elsner P, Schliemann S. Erythema ab igne as an occupational skin disease. J Dtsch Dermatol Ges. 2014;12(7):621-2. PMid:24684647

11. Fischer J, Rein K, Erfurt-Berge C, de Zwaan M. Three cases of erythma ab igne (EAI) in patients with eating disorders. Neuropsychiatr. 2010;24(2):141-3. PMid:20605010

12. Mucklow ES, Freeman NV. Pancreatic ascites in childhood. Br J Clin Pract. 1990;44(6):248-51. PMid:2144996

13. Butler ML. Erythema ab igne, a sign of pancreatic disease. Am J Gastroenterol. 1977;67(1):77-9. PMid:851110

14. Dellavalle RP, Gillum P. Erythema ab igne following heating/cooling blanket use in the intensive care unit. Cutis. 2000;66(2):136-8. PMid:10955195

15. Arnold AW, Itin PH. Laptop computer-induced erythema ab igne in a child and review of the literature. Pediatrics. 2010;126(5):e1227-30. https://doi.org/10.1542/peds.2010-1390 PMid:20921068

16. Levinbook WS, Mallett J, Grant-Kels JM. Laptop computer--associated erythema ab igne. Cutis. 2007;80(4):319-20. PMid:18038695

17. Manoharan D. Erythema ab igne: Usual site, unusual cause. J Pharm Bioallied Sci. 2015; 7(Suppl 1): S74–S75. https://doi.org/10.4103/0975-7406.155811 PMid:26015756 PMCid:PMC4439716

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Case Report

Cutaneous Angioleiomyoma – A Rare Cause of Posterior Heel Pain: A Case Report

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Keywords: angioleiomyoma; heel pain; histology; immunohistology; surgery.

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Abstract

Heel pain is a common presentation in outpatient clinics. Here, we report a 69-year-old woman who complaint about a painful nodule on her left posterior heel. There was no history of trauma. The lesion developed during ten weeks without any bleeding or ulceration. On examination, we observed a subcutaneous firm nodule of about 1 cm in diameter. The lesion was hypoechoic in diagnostic sonography suggesting a fibromatous tumour, which was removed surgically. Histologic investigations confirmed the diagnosis of cutaneous angioleiomyoma. The occurrence of this benign tumour on the heel is quite uncommon but obvious a possible cause for heel pain. During follow-up, no recurrence was observed.

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Introduction

Cutaneous angioleiomyoma (ALM) is a benign smooth-muscle tumour. It occurs in several subtypes, i.e. venous, cavernous, solid, and lipomatous AL. The tumours can develop a variable degree of hyalinization or calcification. The vascular subtypes show a predilection for the lower limbs [1-3].

These tumours represent as painful well-circumscribed nodules in about 50% of cases. AL can occur at any age but reach a peak incidence between the 4th and 6th decade of life. Women are almost as double as much affected as men [4].

The following case report points to AL as a rare possible cause for heel pain.

Case Report

A 69-year-old woman presented with a painful nodule on her left posterior heel. She did not remember any trauma. The lesion developed during ten weeks without any bleeding or ulceration. Her medical history was unremarkable so far. She had no medications.

On examination, we observed a firm subcutaneous nodule covered by a callus reaction of skin on the left posterior heel of approximately 1 cm in diameter (Fig. 1a). Sonographic examination described a 10 x 7 x 5 mm large subcutaneous, well circumscribed, hypoechoic lesion closely related but not attached to the Achilles tendon.

Figure 1: Cutaneous angioleiomyoma on the left heel. (a) Clinical presentation as a firm subcutaneous nodule covered by epidermal callus formation (left). (b) Surgical specimen of a well-circumscribed tumour with a smooth surface (middle). (c) After wound closure (right)

We performed surgery under local anaesthesia to remove the lesion completely and obtain a histopathologically confirmed diagnosis. During surgery, we observed a well circumscribed firm tumour of about 1 cm in diameter with a smooth pseudocapsular surface (Fig. 1b). The tumour was not attached to deeper structures but skin.

The wound was sutured, and the subsequent healing process was uneventful (Fig. 1c).

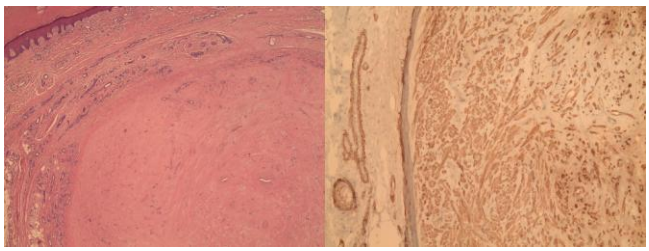

Figure 2: Histological examination of cutaneous angioleiomyoma. (a) A nodular hyalinized tumor of dermis and upper subcutaneous tissue with a pseudo capsule covered by hyperplastic, compact, orthokeratotic epidermis (hematoxylin-eosin, x 4) (left); (b) The tumor consisted of actin-positive spindle cells with uniform oval nuclei without atypia or increased mitotic activity (immunoperoxidase stain with monoclonal actin-antibody, x 10) (right)

Histologic examination revealed a nodular hyalinized tumour of the dermis and upper subcutaneous tissue covered by hyperplastic, compact, orthokeratotic epidermis. The tumour consisted of actin-positive spindle cells with uniform oval nuclei without atypia or increased mitotic activity. The vascular component was CD34-positive with thickened vessel walls. There was no expression of S100 (Fig. 2).

The diagnosis of AL, the venous type with hyalinization, was made. During follow-up of 12 months, no recurrence occurred.

Discussion

Our patient presented with posterior heel pain. Heel pain is not uncommon in outpatient clinics. Several differential diagnoses have to be considered. Plantar fasciitis is the most common cause, with medial plantar heel pain after long periods of rest. A calcaneal stress fracture is progressively worsening during activity. Nerve entrapment, heel pad syndrome, neuromas, plantar warts, Achilles tendinopathy, Haglund deformity of the calcaneus, tarsal tunnel syndrome or sinus tarsi syndrome are other possible pathologies causing heel pain as well [5].

AL has rarely been described on the heel [6-9]. Since the tumours may be painful AL is an important differential diagnosis in heel pain, independent from the level of calcification.

AL is a benign tumour of smooth muscle origin. Diagnostic sonography demonstrates a well circumscribed hypoechoic nodule. AL has a characteristic histopathology that confirms the clinically suspected diagnosis [4]. In contrast to sporadic infantile or solitary adult myofibroblastomas somatic mutations of platelet-derived growth factor-receptor B are absent among AL's [10]. Treatment of choice is surgery, and the patient will become pain-free. In the case of complete excision, relapses are very uncommon [11].

The rare occurrence of AL on the heel and its clinical presentation as chronic heel pain prompted us to report this case. AL is a rare but possible cause of heel pain – in the present case of posterior heel pain. Complete pain-free remission is achieved by surgical removal of the benign tumour

References

1. Kacerovska D, Michal M, Kreuzberg B, Mukensnabl P, Kazakov DV. Acral calcified vascular leiomyoma of the skin: a rare clinicopathological variant of cutaneous vascular leiomyomas: report of 3 cases. J Am Acad Dermatol. 2008; 59:1000-1004. https://doi.org/10.1016/j.jaad.2008.07.008 PMid:19022102

2. Upreti S, Morine A, Ng D, Bigby SM. Lipomatous variant of angiomyofibroblastoma: a case report and review of the literature. J Cutan Pathol. 2015;42:222-226. https://doi.org/10.1111/cup.12450 PMid:25407897

3. Díaz-Flores L, Gutiérrez R, Alvarez-Argüelles H, González-Gómez M, García Mdel P, Díaz-Flores L Jr. Ultrastructure and histogenesis of the acral calcified angioleiomyoma. Ultrastruct Pathol. 2016;40:24-32. https://doi.org/10.3109/01913123.2015.1120839 PMid:26691377

4. Zhang JZ, Zhou J, Zhang ZC. Subcutaneous angioleiomyoma: clinical and sonographic features with histopathologic correlation. J Ultrasound Med. 2016;35:1669-1673. https://doi.org/10.7863/ultra.15.06056 PMid:27371376

5. Tu P, Bytomski JR. Diagnosis of heel pain. Am Fam Physician. 2011;84:909-916. PMid:22010770

6. Pastore RL, Ianiro G. Cutaneous angioleiomyoma. J Am Podiatr Med Assoc. 1999;89:145-147. https://doi.org/10.7547/87507315-89-3-145 PMid:10095339

7. Murata H, Matsui T, Horie N, Sakabe T, Konishi E, Kubo T. Angioleiomyoma with calcification of the heel: report of two cases. Foot Ankle Int. 2007;28:1021-1025. https://doi.org/10.3113/FAI.2007.1021 PMid:17880879

8. Cheung MH, Lui TH. Plantar heel pain due to vascular leiomyoma (angioleiomyoma). Foot Ankle Spec. 2012;5:321-523. https://doi.org/10.1177/1938640012457677 PMid:22935412

9. Szolomayer LK, Talusan PG, Chan WF, Lindskog DM. Leiomyoma of the foot and ankle: A case series. Foot Ankle Spec. 2016;pii: 1938640016670243. [Epub ahead of print]. PMid:27654461

10. Agaimy A, Bieg M, Michal M, Geddert H, Märkl B, Seitz J, Moskalev EA, Schlesner M, Metzler M, Hartmann A, Wiemann S, Michal M, Mentzel T, Haller F. Recurrent somatic PDGFRB mutations in sporadic infantile/solitary adult myofibromas but not in angioleiomyomas and myopericytomas. Am J Surg Pathol. 2017;41(2):195-203. https://doi.org/10.1097/PAS.0000000000000752 PMid:27776010

11. Scapinelli R, Iacobellis C, Taglialavoro G, Blandamura S, Baggio ME. Vascular leiomyoma of the limbs. Chir Organi Mov. 2001;86:143-152. PMid:12025046

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Case Report

Fibroepithelioma of Pinkus (FeP) Located in the Left Lower Quadrant of the Abdomen - Case Report and Review of the Literature

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Abstract

BACKGROUND: Fibroepithelioma of Pinkus (FeP) is an uncommon and controversial skin lesion, sharing features of both basal cell carcinoma (BCC) and trichoepithelioma. In this article, we present a case of FeP and synthesise current concepts on the etiopathogenesis, diagnosis and treatment of this uncommon tumour.

CASE REPORT: We report the case of an 88-year-old male patient presenting to the dermatology clinic for a sharply demarcated, pink, exophytic cutaneous tumour situated in the left inguinal region. The histopathological examination performed after complete surgical excision of the lesion revealed a diagnosis of FeP. A systematic review of the literature was conducted. The terms `fibroepithelioma` and `Pinkus` have been searched in bibliographical databases, including PubMed and Google Scholar, without time limitation up to February 15th, 2017. Seventy-nine articles that fulfilled all the required conditions were identified. Relevant citations and additional articles identified from references have been assessed. The systematic review included a total number of 452 cases of FeP.

CONCLUSION: Even though FeP is considered a relatively rare tumour, its true incidence rate might be higher than previously believed. The clinical aspects of the lesion described in this paper and its location in the left lower quadrant of the abdomen are classic features of FeP. Histopathologic examination revealed features of both BCC and trichoepithelioma. Further epidemiological studies are required to clarify whether patients with FEP should be screened for the occurrence of other malignancies.

Introduction

Fibroepithelioma of Pinkus (FeP) is an uncommon and controversial skin lesion, sharing features of both basal cell carcinoma (BCC) and trichoepithelioma. While some authors differentiate trichoblastoma from trichoepithelioma, the World Health Organization classifies the terms synonymously [1]. In the present paper, we will use the term trichoepithelioma.

FeP was described for the first time by Hermann Pinkus in 1953, who regarded this skin lesion as a variant of BCC [2], a theory that continued for many years [3, 4]. Recent research has highlighted the fact that BCC and trichoepithelioma have the same origin; that is, the epithelial stem cells of the hair follicle [5, 6]. Such a concept has led to the proposal that FeP might be a trichoblastic tumour intermediate between trichoepithelioma and BCC [7]. The clinical presentation of FeP is that of a flesh-coloured, well-demarcated, sessile, dome-shaped papule or

pedunculated tumour frequently often located in the lumbosacral area. The clinical differential diagnosis includes benign tumours such as intradermal nevus, fibroma, acrochordon, and seborrheic keratosis [8], as well as a variety of cutaneous neoplasms, including basal cell carcinoma and amelanotic melanoma. The pathogenesis of FeP is still a matter of debate. As is the case with conventional BCC, theories include mutations in the tumour suppressor gene P53 and the PATCHED gene, inducing inhibitory signals in the Hedgehog pathway [7]. There are several reports on the dermatoscopic, reflectance confocal microscopic, and histopathologic features of FeP. The treatment of choice is complete surgical excision. Other surgical techniques, such as cryosurgery, electrodesiccation and Mohs micrographic surgery have also been performed successfully [7].

In this article, we present a case of FeP and summarise current concepts on the etiopathogenesis, diagnosis and treatment of this uncommon tumour.

Case Report

An 88-year-old male presented to the dermatology clinic for evaluation, diagnosis and treatment of a skin tumour that had been slowly growing for the preceding five years in the left inguinal region. There were no complaints regarding pain or itching of the skin lesion. The patient's medical history revealed several cardiovascular risk factors: an elevated blood pressure and non-insulin dependent diabetes mellitus type 2 but was otherwise unremarkable. Clinical examination revealed a sharply demarcated, pink, exophytic cutaneous tumour with a lobulated, cerebriform surface, measuring approximately 5 x 3.6 cm situated in the left lower quadrant of the abdomen (Fig. 1a). Paraclinical Diagnostic tests were unremarkable. Abdominal ultrasound, chest x-ray and ultrasound of the axillary and inguinal lymph node groups showed no evidence of disease progression or other abnormal findings. In the light of the history of tumour growth and clinical differential diagnosis, the lesion was surgically excised with wide margins under local anaesthesia, thus creating an elliptical defect (Fig. 1b), followed by the primary closure (Fig. 1c) and by the application of antiseptic dressings. Postoperatively, the patient was well and was discharged with a set of follow-up instructions. Histopathologic examination of the excised cutaneous tumour showed a polypoid tumoral proliferation with superficial ulcerated areas (Fig. 2b). Focal solid cribriform areas (Fig. 2a), tumour islands and long anastomosing strands and columns of basaloid cells with scant cytoplasm, hyperchromatic nuclei and moderate cytologic atypia could be seen projecting downwards from the epidermis into the papillary dermis. Relatively frequent mitoses could be seen along with abundant fibro hyaline tumoral stroma. Based on the clinical and microscopic features, a final diagnosis of fibroepithelioma of Pinkus was made. The pathology report confirmed its complete excision, with tumour-free surgical resection margins.

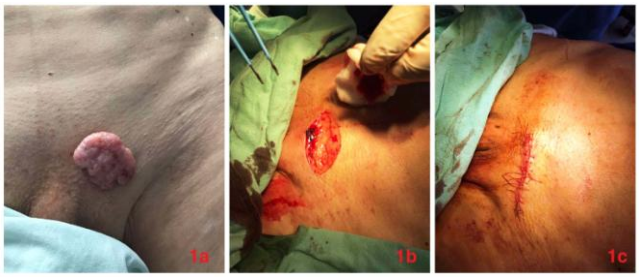

Figure 1: 1a) Cutaneous tumour in the left inguinal region; 1b) Elliptic surgical defect after haemostasis, ready for reconstruction; 1c) Primary closure of the defect with interrupted non-absorbable sutures

Discussion

FeP was first described as a distinct clinicopathologic entity by Hermann Pinkus in 1953 [2]. In a retrospective study that included over 900 epitheliomas, he described four cases with unique clinical and microscopic features, emphasising their importance in enhancing the understanding of epitheliomas in general [2].

While FeP is considered a relatively rare tumour, it is probably underreported. It can be easily confused with other benign skin tumours that may not be treated or biopsied [9]. After a thorough literature review, we identified 79 articles reporting a total number of 452 FeP cases. FeP usually appears in the fourth to fifth decades of life [10], although two cases of FeP in children have been reported [11, 12]. In the largest clinical study, Bowen et al. (2005) observed a slightly higher prevalence rate in women: 54% of 114 patients [13].

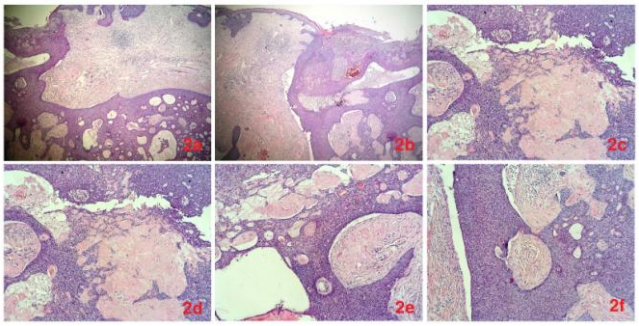

Figure 2: Several histopathologic images from the tumour, showing branching cords of basaloid epithelium, some narrow (2a - lower left, 2c and 2d - centre, and figure 2e - upper left) and some more broad (2b and 2f), within a cellular fibrotic stroma

After almost 65 years since the first description of FeP, its classification and pathogenesis are still matters of debate. The following alternatives were taken into consideration: a premalignant tumour, a fenestrated trichoepithelioma subtype, or an indolent BCC subtype. The first reports described FeP as a BCC subtype. Due to its indolent, long-term course, and histological particularities it was further classified as a premalignant tumour - a precursor of BCC. In 2005, Bowen et al. argued that FeP is a trichoepithelioma rather than a BCC subtype, based upon their histopathological and immunohistochemical studies of 75 FePs [13]. The same year Ackerman et al. provided criteria for the histopathologic differentiation of FeP from trichoblastoma (trichoepithelioma) and classified `the fibroepithelial tumour of Pinkus as a trichoblastic (Basal-cell) carcinoma` [4], reflecting the controversial nature of the problem.

It is well known that BCC can spread directly into the dermis, by perifollicular or perineural extension. However, BCC might also spread via eccrine ducts. In 1994, Stern et al. hypothesised that eccrine ducts might serve as the starting point of FeP development, based on the immunohistochemistry of 9 tumours that stained positively for carcinoembryonic antigen (CEA) [14]. This glycoprotein is usually found in eccrine sweat glands as well as gastrointestinal tumours and fetal tissues. In 2007 Stern and Haupt provided another argument that supports this theory: FeP lesions have been found in glabrous skin areas that lack hair follicles [15]. In 2007, Kurokawa et al. also supported the hypothesis, proposing that FeP may originate from intraepidermal eccrine ducts and afterwards proliferate into the dermis [16]. An important observation is that BCC might replace a FeP or develop independently by the eccrine ductal spread.[14]

Further contributing to the debate regarding the true origin of this tumour, it has been shown that both Merkel cells and androgen receptors are found in FeP.

In a study of 76 adnexal tumours of skin Wollina and Schrepel (2006) reported that trichoepitheliomas had an increased proliferative activity but not an increased number of MC (17). In basal cell carcinomas and trichofolliculomas, however, MC was found near proliferating tumour cells. Androgen receptors are expressed in BCCs, but only exceptionally in trichoepitheliomas [7]. Katona et al. (2007) observed that 10 out of 13 FeP, as well as 8 out of 11 BCCs, stained positively for androgen receptors [7]; only 2 out of 15 trichoepitheliomas expressed androgen receptors [7]. These results support the theory that FeP is an indolent BCC subtype. Merkel cells are a feature of benign follicular tumours, and it is well known that moderate hyperplasia of Merkel cells is present in chronic sun-damaged skin and hypertrophic actinic keratoses [18]. Merkel cells are found in trichoepitheliomas but are absent in BCCs [7]. This supports the theory that FeP may be a fenestrated trichoepithelioma subtype.

To provide more clarity in this debate, Sellheyer et al. (2012) used a stem cell marker, PHLDA1 (TDAG51), which is expressed in the basal cell layer during embryogenesis and is present in trichoepitheliomas, but not BCCs. The results were consistent with a mixed histological pattern, showing an anastomosing network of thin cellular strands positive for PHLDA1 and basaloid nests with negative results for this marker [3]. The authors concluded that FeP is a premalignant lesion with a specific type of epidermal hyperplasia that stains positively for PHLDA-1 and has the capability of developing multifocal BCCs [3].

Previous literature reports have linked FeP with several risk factors:

Genetic factors: Some authors theorise that, like BCC, mutations in p53 and PATCHED-1 genes may also be responsible for the development of FeP [7, 19] and that both tumours originate in the follicular germinative cells. Others suggest that FeP might be a premalignant lesion that progresses to BCC by acquiring additional genetic mutations [20] or that it might develop from seborrheic keratosis, based on some histopathologic similarities [4]. Also, FePs have been identified in continuity with both BCC and seborrheic keratosis [4].

Radiotherapy: There is a frequent occurrence of FeP in patients with a history of radiotherapy. Hartschuch et al. observed hyperplasia of Merkel cells in chronic radiation dermatitis, as well as their presence in FePs and trichoepitheliomas, though they are absent in BCCs. The researchers further suggested that Merkel cells might be responsible for the benign biological behaviour of the tumours that have them [18]. Although previous irradiation might constitute the initial carcinogenic factor in some cases, this is not invariably the case, and the evolution and prognosis of the tumours are the same when compared to those due to other triggering factors [21]. ***Sun-exposure:*** It was observed that unlike BCCs, FeP has a predilection for sun-protected skin, is often located in the dorsal, lumbar and sacral regions. Bowen et al. showed that only 5% of tumours develop in anatomic sites that receive significant amounts of solar elastosis [13].

Association with other neoplasms: Some authors have suggested that FeP might be a reactive process (22) associated with other neoplasms, including breast cancer [23, 24], extramammary Paget's disease [25], gastrointestinal neuroendocrine tumours [26] or BCCs and Gorlin-Goltz syndrome [27]. Longo et al. (2016) investigated whether FeP is an expression of a more complex gastrointestinal syndrome and observed that in 9 of the 49 cases it was associated with gastrointestinal tumours [26]. The expression of CEA in both FeP and gastrointestinal tumours could suggest a common pathogenesis [14].

Further epidemiological studies are required to clarify whether or not these associations are coincidental and whether patients with FEP should be screened for the occurrence of other malignancies [26]

Chronic inflammation: There has been a case report of malignant degeneration in a chronic lower limb ulcer with the histological image of a FeP [28]. Clinically, most FePs appear in individuals between 40 and 60 years old, with a history of BCC [19], of solitary or multiple slow-growing papules or plaques. Typically, the lesions appear as flesh-coloured, pink, red, grey or even brown [29, 30], firm, sessile or pedunculated papules with a broad base. As previously noted, and in contrast to most BCCs, FeP develops mainly in sun-protected areas such as the lower back, inguinal, and crural areas, or the extremities. Atypical clinical forms of FeP may present as multiple lesions with different presentations [30]; these include ulcerated lesions or tumours arising in atypical locations such as the head, axillae, torso, umbilicus [31], plantar region [14, 32], or even on mucocutaneous junctions [33].

FeP is considered to be either a rare tumour or an underdiagnosed one because of its non-specific clinical appearance. Therefore, it can easily be mistaken for a wide variety of skin lesions such as acrochordons, intradermal or compound nevi, sebaceous nevi, seborrheic keratoses, fibromas, lipomas, cysts, and even amelanotic melanomas [10, 30, 34, 35].

Regarding diagnostic methods, the dermoscopy of FeP is not specific, as there are mixed features of BCC and trichoepithelioma, consisting of polymorphous vessels - mainly short arborizing and dotted types, gray-brown and gray-blue areas and dots, and shiny white streaks (also known as crystalline structures) [8, 36], secondary to fibrosis. Some structures similar to BCC or seborrheic keratosis may be present, such as ulceration, large ovoid nests, and milia-like cysts. Recently, Kornreich et al. reported an additional dermoscopic feature of FeP; namely, a white network, which could be more specific for FeP [37]. The white network is the manifestation of elongated hyperplastic, anastomosing epithelial strands [37]. This finding, together with additional BCC-related dermoscopic features, may facilitate the diagnosis of FeP [37].

The main reflectance confocal microscopy findings of FeP include a fenestrated pattern corresponding to the fibrous stroma and the presence of bright cells in pigmented lesions [38].

The histopathological features of FeP are distinctive, characterised by long, anastomosing strands of basaloid cells, embedded in a fibrous stroma, that project downwards from the epidermis and extend into the papillary dermis, giving the tumour a honeycomb or sponge-like appearance [22]. The cells from the edge of the strands are columnar and arranged in a palisade. Sometimes, follicular germ-like structures can be identified within the tumour [4]. FeP usually has a distinct interface with the normal, underlying dermis [13], but sometimes tumour cells may extend into the reticular dermis [4].

FeP is typically treated by complete surgical excision, with generally excellent results [10]. Other possible treatment options include cryosurgery, electrodesiccation, or Mohs micrographic surgery [7]. In contrast to the treatment of some BCCs, topical Imiquimod 5% has been proven to be ineffective in the treatment of FeP [36]. Overall, FeP is a not-aggressive tumour with no metastatic potential and good prognosis after complete surgical excision [39].

In conclusion, the tumour presented in our case report appeared in a male in his eighties, which stands in contrast to epidemiological studies in which the majority of FePs appear to occur in women in the fourth to fifth decades of life. Nevertheless, the clinical features of the lesion and its location in the left lower quadrant of the abdomen are classical presenting features of FeP. The systematic review performed in this paper includes a total number of 452 FePs that have been reported in the medical literature. Even though FeP is considered a relatively rare tumour, its true incidence rate might be higher than suggested in published studies. Outside of dermatology, FeP is a relatively unknown tumour in the medical field, and, as indicated by our review, it can be easily confused with other benign or even malignant tumours.

The histopathologic findings appear to support Ackerman's theory that FeP is a 'trichoblastic (basal-cell) carcinoma' [4], sharing both features of BCC and trichoepithelioma. To further sustain this argument, the history of our patient's tumour evolution raises the hypothesis that a lesion originating as a trichoblastoma may have acquired additional genetic mutations over time, progressing to the premalignant lesion described in our histopathology report.

There is no known history of radiotherapy in our patient, and the abdominal ultrasound, chest x-ray and ultrasound studies of the axillary and inguinal lymph node groups showed no evidence of disease progression or other malignancies. Further epidemiological studies will be required to clarify whether or not these associations are merely hypothetical or fortuitous, or if patients with FeP should be carefully screened for the occurrence of other malignancies.

References

1. Hurt MA, Cribier B, Kaddu S, Schulz T, Kutzner H, Hartschuh W. Chapter 3—appendageal tumors. In: LeBoit PE, Burg G, Weedon D, Sarasin A, editors. World Health Organization classification of tumors: pathology and genetics of skin tumors. Lyon: IARC, 2006: p. 152–153.

2. Pinkus H. Premalignant fibroepithelial tumors of skin. AMA Arch Derm Syphilol. 1953; 67(6):598-615. https://doi.org/10.1001/archderm.1953.01540060060009 PMid:13050184

3. Sellheyer K, Nelson P, Kutzner H. Fibroepithelioma of Pinkus is a true basal cell carcinoma developing in association with a newly identified tumour-specific type of epidermal hyperplasia. Br J Dermatol. 2012; 166(1):88-97. https://doi.org/10.1111/j.1365-2133.2011.10612.x PMid:21910710

4. Ackerman AB, Gottlieb GJ. Fibroepithelial tumor of pinkus is trichoblastic (Basal-cell) carcinoma. Am J Dermatopathol. 2005; 27(2):155-9. https://doi.org/10.1097/01.dad.0000154395.14971.71

5. Cotsarelis G. Epithelial stem cells: a folliculocentric view. J Invest Dermatol. 2006; 126(7):1459-68. https://doi.org/10.1038/sj.jid.5700376 PMid:16778814

6. Peterson SC, Eberl M, Vagnozzi AN, Belkadi A, Veniaminova NA, Verhaegen ME, Bichakjian CK, Ward NL, Dlugosz AA, Wong SY. Basal cell carcinoma preferentially arises from stem cells within hair follicle and mechanosensory niches. Cell Stem Cell. 2015; 16(4):400-12. https://doi.org/10.1016/j.stem.2015.02.006 PMid:25842978 PMCid:PMC4387376

7. Katona TM, Ravis SM, Perkins SM, Moores WB, Billings SD. Expression of androgen receptor by fibroepithelioma of Pinkus: evidence supporting classification as a basal cell carcinoma variant? Am J Dermatopathol. 2007; 29(1):7-12. https://doi.org/10.1097/01.dad.0000245201.59762.d2 PMid:17284955

8. Reggiani C, Zalaudek I, Piana S, Longo C, Argenziano G, Lallas A, Pellacani G, Moscarella E. Fibroepithelioma of Pinkus: case reports and review of the literature. Dermatology. 2013; 226(3):207-11. https://doi.org/10.1159/000348707 PMid:23711617

9. Zalaudek I, Ferrara G, Broganelli P, Moscarella E, Mordente I, Giacomel J, Argenziano G. Dermoscopy patterns of fibroepithelioma of pinkus. Arch Dermatol. 2006; 142(10):1318-22. https://doi.org/10.1001/archderm.142.10.1318 PMid:17043187

10. Cohen PR, Tschen JA. Fibroepithelioma of Pinkus presenting as a sessile thigh nodule. Skinmed. 2003; 2(6):385-7. https://doi.org/10.1111/j.1540-9740.2003.02491.x

11. Pan Z, Huynh N, Sarma DP. Fibroepithelioma of pinkus in a 9-year-old boy: a case report. Cases J. 2008; 1(1):21. https://doi.org/10.1186/1757-1626-1-21 PMid:18588684 PMCid:PMC2474574

12. Scalvenzi M, Francia MG, Falleti J, Balato A. Basal cell carcinoma with fibroepithelioma-like histology in a healthy child: report and review of the literature. Pediatr Dermatol. 2008; 25(3):359-63. https://doi.org/10.1111/j.1525-1470.2008.00683.x PMid:18577044

13. Bowen AR, LeBoit PE. Fibroepithelioma of pinkus is a fenestrated trichoblastoma. Am J Dermatopathol. 2005; 27(2):149-54. https://doi.org/10.1097/01.dad.0000138051.71415.fe

14. Stern JB, Haupt HM, Smith RR. Fibroepithelioma of Pinkus. Eccrine duct spread of basal cell carcinoma. Am J Dermatopathol. 1994; 16(6):585-7. https://doi.org/10.1097/00000372-199412000-00002 PMid:7864295

15. Stern JB, Haupt HM. Basal cell carcinoma of the sole: implications for fibroepithelioma of pinkus. Am J Dermatopathol. 2007; 29(5):494. https://doi.org/10.1097/DAD.0b013e3181462889 PMid:17890926

16. Kurokawa I, Yokoyama T, Nishimura K, Hakamada A, Isoda K, Yamanaka K, Tsubura A, Mizutani H. Pinkus tumor may originate from intraepidermal eccrine ducts and proliferate in the dermis. Oncol Rep. 2007; 17(1):49-54. https://doi.org/10.3892/or.17.1.49

17. Wollina U, Schrepel U. Merkel cells in adnexal neoplasias of skin. Čes-slov Derm. 2006;81(4):206-9.

18. Hartschuh W, Schulz T. Merkel cell hyperplasia in chronic radiation-damaged skin: its possible relationship to fibroepithelioma of Pinkus. J Cutan Pathol. 1997; 24(8):477-83. https://doi.org/10.1111/j.1600-0560.1997.tb01321.x PMid:9331893

19. Tarallo M, Cigna E, Fino P, Lo Torto F, Corrias F, Scuderi N. Fibroepithelioma of Pinkus: variant of basal cell carcinoma or trichoblastoma? Case report. G Chir. 2011; 32(6-7):326-8. PMid:21771402

20. Misago N, Suzuki Y, Miura Y, Narisawa Y. Giant polypoid basal cell carcinoma with features of fibroepithelioma of Pinkus and extensive cornification. Eur J Dermatol. 2004; 14(4):272-5. PMid:15319165

21. Cahuzac P, Hermier C, Thivolet J. [Premalignant fibroepithelial tumors of Pinkus and previous irradiation: report of a survey of 20 patients]. Ann Dermatol Venereol. 1982; 109(4):355-7. PMid:7125488

22. Haddock ES, Cohen PR. Fibroepithelioma of Pinkus Revisited. Dermatol Ther (Heidelb). 2016; 6(3):347-62. https://doi.org/10.1007/s13555-016-0123-8 PMid:27329375 PMCid:PMC4972729

23. Bryant J. Fibroepithelioma of Pinkus overlying breast cancer. Arch Dermatol. 1985; 121(3):310. https://doi.org/10.1001/archderm.1985.01660030030013 PMid:2983617

24. Sandbank M, Bashan D. Multiple trichoepithelioma and breast carcinoma. Simultaneous appearance of epithelioma adenoides cysticum and infiltrating lobular carcinoma of the breast. Arch Dermatol. 1978; 114(8):1230. https://doi.org/10.1001/archderm.1978.01640200082026 PMid:677927

25. Warner TF, Burgess H, Mohs FE. Extramammary Paget's disease in fibroepithelioma of Pinkus. J Cutan Pathol. 1982; 9(5):340-4. https://doi.org/10.1111/j.1600-0560.1982.tb01070.x PMid:6292274

26. Longo C, Pellacani G, Tomasi A, Mandel VD, Ponti G. Fibroepithelioma of Pinkus: Solitary tumor or sign of a complex gastrointestinal syndrome. Mol Clin Oncol. 2016; 4(5):797-800. https://doi.org/10.3892/mco.2016.794

27. Gorlin RJ, Goltz RW. Multiple nevoid basal-cell epithelioma, jaw cysts and bifid rib. A syndrome. N Engl J Med. 1960; 262:908-12. https://doi.org/10.1056/NEJM196005052621803 PMid:13851319

28. Ebner H, Niebauer G. Malignant degeneration of an ulcus cruris under the histological image of a fibroepithelioma Pinkus. Z Haut Geschlechtskr. 1967; 42(12):417-21. PMid:5590296

29. Strauss RM, Edwards S, Stables GI. Pigmented fibroepithelioma of Pinkus. Br J Dermatol. 2004; 150(6):1208-9. https://doi.org/10.1111/j.1365-2133.2004.06018.x PMid:15214913

30. Sehli Attafi S, Jones M, Fazaa B, Zermani R, Rommany SR. Pinkus tumour: an unusual case. Pathologica. 2013; 105(4):140-1. PMid:24466765

31. Inskip M, Longo C, Haddad A. Two adjacent individual fibroepithelioma of Pinkus of the umbilicus-one pink, one pigmented-a case report and review of the literature. Dermatol Pract Concept. 2016; 6(2):17-20. https://doi.org/10.5826/dpc.0602a04 PMid:27222767 PMCid:PMC4866622

32. Lin TC, Lee TL, Lin TY, Wu PY. An infrequent case of neoplasm with fibroepithelioma of pinkus and hidradenomatous features arising at the umbilicus: a rare finding. Am J Dermatopathol. 2011; 33(7):750-2. https://doi.org/10.1097/DAD.0b013e31820978cf PMid:21885941

33. Karatas D, Erten S. Pinkus tumor at the nostril floor. J Craniofac Surg. 2014; 25(4):e317-8. https://doi.org/10.1097/SCS.0000000000000582 PMid:24978450

34. Gellin GA, Bender B. Giant premalignant fibroepithelioma. Arch Dermatol. 1966; 94(1):70-3. https://doi.org/10.1001/archderm.1966.01600250076015

35. Jones CC, Ansari SJ, Tschen JA. Cystic fibroepithelioma of pinkus. J Cutan Pathol. 1991; 18(3):220-2. https://doi.org/10.1111/j.1600-0560.1991.tb00157.x PMid:1918510

36. Zalaudek I, Leinweber B, Ferrara G, Soyer HP, Ruocco E,

Argenziano G. Dermoscopy of fibroepithelioma of pinkus. J Am Acad Dermatol. 2005; 52(1):168-9. https://doi.org/10.1016/j.jaad.2004.06.033 PMid:15627105

37. Kornreich DA, Lee JB. White network in fibroepithelioma of Pinkus. JAAD Case Rep. 2016; 2(5):400-02. https://doi.org/10.1016/j.jdcr.2016.07.011 PMid:27766301 PMCid:PMC5065638

38. Longo C, Soyer HP, Pepe P, Casari A, Wurm EM, Guitera P, Pellacani G. In vivo confocal microscopic pattern of fibroepithelioma of pinkus. Arch Dermatol. 2012; 148(4):556. https://doi.org/10.1001/archdermatol.2011.945 PMid:22508888

39. Su MW, Fromer E, Fung MA. Fibroepithelioma of pinkus. Dermatol Online J. 2006; 12(5):2. PMid:16962017

ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2017 Jul 25; 5(4):445-447.
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Case Report

Secondary Syphilis Presenting As Palmoplantar Psoriasis

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Keywords: secondary syphilis; great imitator; palmoplantar psoriasis; diagnosis; treatment.

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Abstract

In a recent past, the incidence of syphilis has increased in various geographical regions. The authors describe a case of secondary syphilis mimicking palmoplantar psoriasis.

Introduction

Recent data underline how syphilis infection has re-emerged as a major public health problem in the last years. Most of the syphilis cases occur in men having sex with men and in HIV-positive patients [1-3]. Multiple partners and non-protected intercourses are frequently reported.

If the primary infection is not properly diagnosed and treated, after 4-10 weeks, the disease evolves in secondary syphilis, characterised by systemic manifestations. Secondary syphilis, also known as the “great imitator”, can present itself in a variety of ways, mimicking, both clinically and histologically, several diseases and making its diagnosis a challenge for clinicians [4-6].

Case report

A 45-years old, homosexual, Caucasian man has been presenting numerous palmoplantar pustular lesions (1-3 cm in diameter), surrounded by a keratotic rim, on an erythematous basis (Fig. 1A-B). The lesions were asymptomatic. They were present by 3-4 months and had shown a rapid extension. At first, they were localised on his palms and, afterwards, also on his sole (Fig. 2).

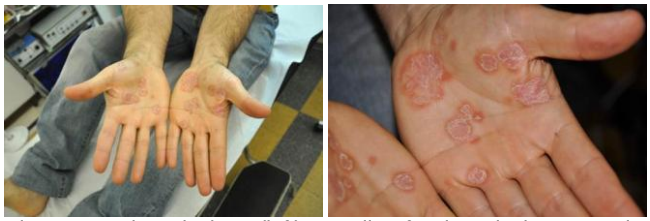

*Figure 1: Palmar lesions (left); Details of palmar lesions: papular lesions (1-3 cm in diameter), surrounded by a keratotic rim (**Biett’s** collar), on an erythematous basis (right)*

History for drug assumption was negative, and he didn't report any contact with local irritants. The patient didn't refer any revealing pathology, except for a mild form of diabetes mellitus. He showed familiarity for psoriasis and diabetes.

Before referring to us, the patient had been evaluated by a colleague dermatologist, who made the diagnosis of palmoplantar psoriasis and prescribed to him a systemic therapy with colchicine. Due to the occurrence of diarrhoea as a side effect, the patient stopped the treatment and started a new therapy with systemic glucocorticoids, which didn't provide any beneficial effects.

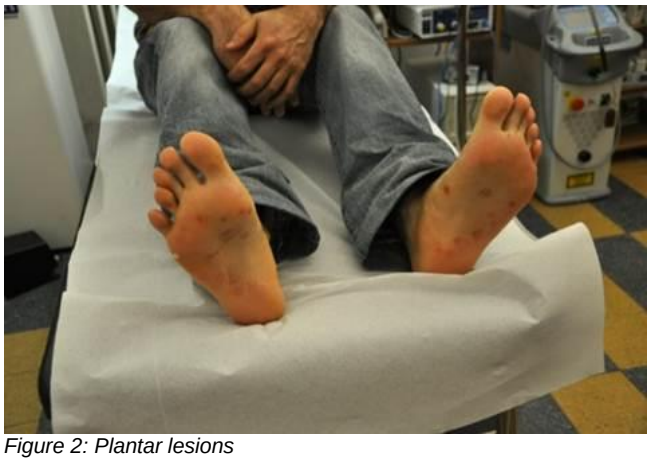

Figure 2: Plantar lesions

During the clinical evaluation, we didn't detect psoriatic lesions in other skin areas, neither on the fingers nor in nails. A diffuse lymph-adenopathy was described. The patient had no disturbance of deep sensation, of tendon and oculomotor reflexes. A rheumatologic evaluation showed no apparent joint involvement.

As a result of the clinical and anamnestic valuation, we advised the patient to perform routine blood tests and specific tests for syphilis (RWt, RWI, VDRL, TPHA, FTA-ABS-IgG, FTA-ABS-IgM). Even if European and American guidelines recommend one treponemal test and one non-treponemal test for the diagnosis of syphilis, accordingly to the experience of our laboratory, we performed all the specific to tests to rule out the possibility of a false result.

The routine blood tests were insignificant except for a neutrophilic leucocytosis and an increased VES. Instead, the second ones were positive, confirming our suspect of syphilis (RWt +++, RWI ++, VDRL ++, TPHA ++ 1:2560, FTA-ABS-IgG+ +, FTA-ABS-IgM ++).

We prescribed to the patient diaminocillina therapy (2400000 U.I./week) for four weeks. Moreover, we advised the patient to abstain from sexual activity and to suggest serological tests to his partners. No antiretroviral therapy was prescribed.

The patient has been monitored for the duration of treatment. The antibiotic treatment improved quickly the clinical conditions. Serological tests, one month after that, showed the improvement of the disease.

Discussion

Syphilis is a well-known infectious disease, caused by Treponema pallidum subspecies pallidum, a spirochete bacterium. Usually, the infection is transmitted through sexual contact with an infected partner [7]. In the last years, the incidence of the disease has rapidly increased maybe for changes in sexual activities, increase of HIV-prevalence and immigration phenomenon [8, 9].

After a long replication time at the site of inoculation, characterised by local mucocutaneous manifestations (primary syphilis), T. pallidum rapidly disseminates, through the blood, in the other parts of the body, giving systemic manifestations (secondary syphilis). Secondary syphilis usually starts 4-10 weeks after the primary infection and lasts for several weeks. Because of the variety of clinical manifestation in this stage, secondary syphilis is known as the great imitator and represents one of the more important problems in dermatologic diagnosis [10].

At this stage, patients may be asymptomatic, even if non-specific flu-like symptoms (e.g. fever, headache, malaise) have often been reported. About 75% of patients develop a diffuse and symmetric macular or maculopapular rash [11]. Other typical clinical manifestations include lichenoid, papulopustular, psoriasiform, vesicular or corymbiform lesions [12, 13]. Condylomata lata is another typical presentation of secondary syphilis. It consists of flat eroded papules, usually localised in the genital areas, even if extragenital occurrences have been described [14, 15]. More rarely, lue malignant (nodular-ulcerative syphilis) has been described. It is characterised by erythematous-violaceous or reddish papules and nodules, which evolve into well-defined round or oval, necrotic ulcerated plaques. Lesions are usually multiple, irregularly distributed on the scalp, face, trunk, and extremities [16, 17]. A rapid manifestation, characterised by large papules and plaques covered by a dark crust, has rarely been described too [18].

Finally, secondary syphilis may be characterised by common but less specific alterations, such as pigmentary disorders or alopecia [19, 20]. About 30% of patients have oral lesions, such as maculopapular lesions, ulcerations, leukoplakia like plaques or condyloma lata [21]. Although rare, extra mucocutaneous manifestations of syphilis are

numerous and may interest different districts, such as liver, stomach, neurological and vascular systems [22, 23].

In this report, we have described an unusual case of secondary syphilis characterised by palmoplantar, pustular lesions, surrounded by a keratotic rim, on an erythematous basis. Due to the clinical manifestations and to the familiarity for psoriasis, at first, the case was wrongly diagnosed as pustular palmoplantar psoriasis [24, 25].

The failure of the common antipsoriatic treatments, and a complete examination of the patient, which showed us particular features, such as the presence of Biett's collar and diffuse lymphadenopathy, suggested us the diagnosis of syphilis. The serological tests for syphilis (RWt, RWI, VDRL, TPHA, FTA-ABS-IgG, FTA-ABS-IgM) were highly positive, confirming our diagnosis.

In conclusion, despite being an uncommon disease, the incidence of syphilis has increased in the last years. If not properly treated in the initial stage, the disease tends to evolve in secondary one, which is characterised by a systemic involvement. Secondary syphilis can present in a variety of ways, making its diagnosis extremely difficult. As the re-emerging of syphilis as a major public health problem, we recommend keeping the disease in the list of the differential diagnosis.

References

1. Angus J, Langan SM, Stanway A, Leach IH, Littlewood SM, English JS. The many faces of secondary syphilis: a re-emergence of an old disease. Clin Exp Dermatol. 2006;31(5):741-5. https://doi.org/10.1111/j.1365-2230.2006.02163.x PMid:16901332

2. Konstantopoulou M, Andrady U, Lord MG, Macfarlane AW. Papulosquamous dermatitis. Syphilis: a forgotten disease? Dermatol Online J. 2006 Dec 10;12(7):27. PMid:17459313

3. Mattei PL, Beachkofsky TM, Gilson RT, Wisco OJ. Syphilis: a reemerging infection. Am Fam Physician. 2012 Sep 1;86(5):433-40. PMid:22963062

4. Arfan-ul-Bari, Mehmood T, Khan B, Malik N, Malik KZ, Sukhera AM. Secondary syphilis presenting as vertigo. J Coll Physicians Surg Pak. 2006 Nov;16(11):727-8. PMid:17052426

5. Schnirring-Judge M, Gustaferro C, Terol C. Vesiculobullous syphilis: a case involving an unusual cutaneous manifestation of secondary syphilis. J Foot Ankle Surg. 2011 Jan- Feb;50(1):96-101. https://doi.org/10.1053/j.jfas.2010.08.015 PMid:21106408

6. Chiang MC, Chiang FC, Chang YT, Chen TL, Fung CP. Erythema multiforme caused by Treponema pallidum in a young patient with human immunodeficiency virus infection. J Clin Microbiol. 2010 Jul;48(7):2640-2. Epub 2010 May 26. https://doi.org/10.1128/JCM.00075-10 PMid:20504989 PMCid:PMC2897489

7. Cohen SE, Klausner JD, Engelman J, Philip S. Syphilis in the Modern Era An Update for Physicians. Infect Dis Clin N Am. 2013;27:705-722. https://doi.org/10.1016/j.idc.2013.08.005 PMid:24275265

8. Public Health England. Sexually transmitted infections and chlamydia screening in England, 2014. Health protection agency report. Vol. 9, No. 22, 2015.

9. Clark LL, Hunt DJ. Incidence of syphilis, active component, U.S. Armed Forces, 1 January 2010 through 31 August 2015. MSMR. 2015 Sep;22(9):8-16.

10. Angus J, Langan SM, Stanway A, Leach IH, Littlewood SM, English JS. The many faces of secondary syphilis: a re-emergence of an old disease. Clin Exp Dermatol. 2006 Sep;31(5):741-5. https://doi.org/10.1111/j.1365-2230.2006.02163.x PMid:16901332

11. Dourmishev LA, Dourmishev AL. Syphilis: uncommon presentations in adults. Clinics in Dermatology. 2005; 23 (6): 555–564. https://doi.org/10.1016/j.clindermatol.2005.01.015 PMid:16325063

12. Jeerapaet P, Ackerman AB Histologic patterns of secondary syphilis. Arch Dermatol 1973; 107 (3) : 373 – 377. https://doi.org/10.1001/archderm.1973.01620180027008 PMid:4348110

13. Baughn RE, Musher DM. Secondary Syphilitic Lesions. CLINICAL MICROBIOLOGY REVIEWS. 2005 Jan; 18 (1): 205–216. https://doi.org/10.1128/CMR.18.1.205-216.2005 PMid:15653827 PMCid:PMC544174

14. Rosen T, Hwong H. Pedal interdigital condylomata lata: a rare sign of secondary syphilis. Sex Transm Dis 2001;28:184-6. https://doi.org/10.1097/00007435-200103000-00011 PMid:11289202

15. Ikeda E, Goto A, Suzaki R, Sawada M, Dekio I, Ishizaki S, Fujibayashi M, Takahashi H, Tanaka M. Condyloma lata on the ankle: an unusual location. Dermatol Pract Concept 2016;6(2):9. https://doi.org/10.5826/dpc.0602a09 PMid:27222772 PMCid:PMC4866627

16. Martins Ortigosa Y, Bendazzoli PS, Barbosa AM, Martins Ortigosa LC. Early malignant syphilis. An Bras Dermatol. 2016;91(5 Supl 1):S148-50. https://doi.org/10.1590/abd1806-4841.20164491 PMid:28300925 PMCid:PMC5325024

17. Kumar B, Muralidhar S. Malignant syphilis: a review. AIDS Patient Care STDs 1998; 12 (12) : 921–925. https://doi.org/10.1089/apc.1998.12.921 PMid:11362063

18. Krase IZ, Cavanaugh K, Curiel-Lewandrowski C. A case of rupioid syphilis. JAAD Case Reports 2016;2:141-3. https://doi.org/10.1016/j.jdcr.2016.01.006 PMid:27051856 PMCid:PMC4810282

19. Bi MY, Cohen PR, Robinson FW, Gray JM. Alopecia syphilitica-report of a patient with secondary syphilis presenting as moth-eaten alopecia and a review of its common mimickers. Dermatol Online J. 2009 Oct 15;15(10):6. PMid:19951624

20. Swanson J, Welch J. The Great Imitator Strikes Again: Syphilis Presenting as "Tongue Changing Colors". Case Reports in Emergency Medicine. 2016. Article ID 1607583.

21. Guimarães TF, Lobo Novi CF, Bertolini Bottino C, D'Acri AM, Barbosa Lima R, Carlos Martins J. Gastric syphilis - Case report. An Bras Dermatol. 2016;91(5):670-2. https://doi.org/10.1590/abd1806-4841.20164174 PMid:27828649 PMCid:PMC5087234

22. Chadwick JA, MacNab A, Sarma J, Ray S, Kadir I, Muldoon EG. Secondary syphilis presenting with aortitis and coronary ostial occlusion. Sex Transm Infect. 2016;92(2):108-9. https://doi.org/10.1136/sextrans-2015-052247 PMid:26670911

23. Lynn WA, Lightman S. Syphilis and HIV: A dangerous combination. Lancet Infect Dis. 2004;4:456–66. https://doi.org/10.1016/S1473-3099(04)01061-8

24. Meier M, Sheth PB. Clinical spectrum and severity of psoriasis. Curr Probl Dermatol. 2009;38:1-20. https://doi.org/10.1159/000232301 PMid:19710547

25. Farley E, Masrour S, McKey J, Menter A. Palmoplantar psoriasis: a phenotypical and clinical review with introduction of a new quality-of-life assessment tool. J Am Acad Dermatol. 2009;60(6):1024-31. https://doi.org/10.1016/j.jaad.2008.11.910 PMid:19467374

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Case Report

Interdigital Melanoma of the Foot Affecting Two Neighbouring Interdigital Spaces – Second Case Report

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Keywords: Melanoma; acrolentiginous melanoma; Mohs surgery; interdigital spaces; staging.

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Abstract

Melanoma affecting two interdigital spaces has been recently described by our group for the first time in medical literature. Here we present a second patient with acrolentiginous melanoma of the sole affecting the 1st and 2nd interdigital space. The tumour was removed by delayed Mohs surgery. Due to the extension of the melanoma, digit II and III had to be removed. Staging excluded metastatic spread. The tumour was classified as pT4bN0M0.

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Introduction

Acrolentiginous melanoma (ALM) is an uncommon subtype in Caucasians. It is considered as a tumour with an unfavourable prognosis, mainly because of delayed diagnosis. In the German population, ALM patients are significantly older than the average of melanoma patients and the most common localisation is plantar [1]. Subungual ALM often is diagnosed in an advanced stage that needs functional amputation [2]. The preferred site of metastasis in ALM is bone [3].

In the case of primary misdiagnosis of ALM, the prognosis becomes even worse due to the delay of appropriate treatment [4, 5].

Recently, the first case of ALM involving two neighbouring interdigital spaces has been reported by Tchernev et al. (2017) [6]. Here, we report another case of this unusual presentation of ALM.

Case report

A 90-year-old female patient presented with a slow-growing lesion of the left foot pad which was easily bleeding for a couple of weeks. Her medical history was positive for diabetes mellitus type 2, pulmonary hypertension, arterial hypertension and hyperlipidemia. In 2009, she was diagnosed with colon cancer, and a hemicolectomy had been performed. She had a cataract surgery on her left eye in 2010.

On examination, we observed a 15 x 10 mm large, partially ulcerated tumour on the plantar skin with the involvement of interdigital spaces II and III and digits II and III (Fig. 1a). We performed diagnostic biopsies. Histologic examination revealed a largely amelanotic ALM with numerous MART-1 and Ki67-positive cells (Fig. 2).

We decided to perform complete surgical

removal by delayed Mohs technique (Fig. 1b-d). Histologic examination of the specimen confirmed the diagnosis of ALM, tumour thickness, Clark level. The first Mohs session was successful in removing the tumour but margins were positive for melanoma in situ component. The histologic investigation revealed a tumour thickness of 6.8 mm with Clark's level V.

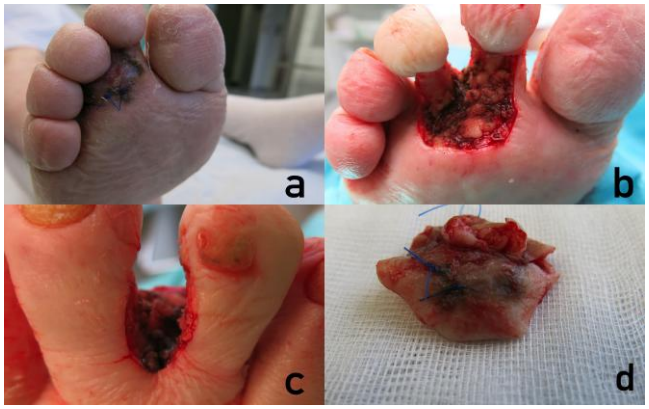

Figure 1: Amelanotic acrolentiginous melanoma involving two interdigital spaces. (a) Clinical presentation; (b) and (c) After first Mohs session; (d) Surgical specimen

In a second session, we achieved a complete resection with free margins, but digits II and III had to be sacrificed. After careful hemostasis, the wound was sutured (Fig. 3). Antibiotic prophylaxis with oral ciprofloxacin has been performed. A forefoot offloading shoe was prescribed to ensure undisturbed complete wound healing.

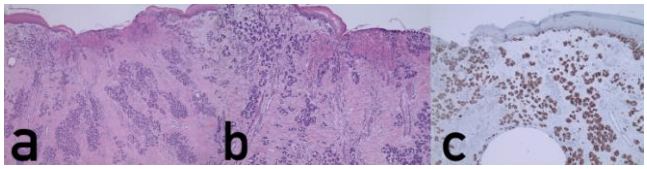

Figure 2: Histopathology of amelanotic acrolentiginous melanoma. (a) Overview and (b) detail of an amelanotic epitheloid cell proliferation in the mid dermis and increased number of melanocytic cells in the basal cell layer of the epidermis (Hematoxylin-eosin x 2 and x 4, respectively). Immunoperoxidase stain for MART-1 demonstrating numerous positive tumour cells (x4)

Staging with diagnostic ultrasound of lymph nodes and abdomen, and X-ray of lungs and the right foot did not show any signs of metastatic spread.

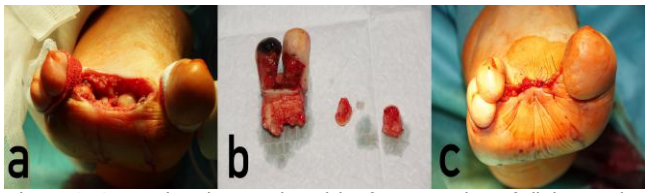

Figure 3: Second Mohs session. (a) After resection of digit II and II; (b) Resection specimen; (c) After suturing

Laboratory investigations: S100 0.113 µg/l (normal range < 0.125), lactate dehydrogenase 4.49 µkat/l (2.25-3.55), uric acid 397 µmol/l (140-340), creatinine 90 µmol/l (< 80), cholesterol 7.12 mmol/l (< 5.2), HbA1C 56 mmol/ml (20-42), neutrophils 0.20 Gpt/l (1.8-7.6), monocytes 5.90 Gpt/l (0-1.0).

Due to the patient's age, we decided to run a wait and see the strategy.

Discussion

In Germany, the number of annually documented melanoma cases increased by 53.2% between 2002 and 2011 with a statistically significant positive trend in the proportion of thin melanomas (stage UICC I). The overall 5-year relative survival for melanoma was estimated between 83.4% and 89.4% [7,8].

ALM is an uncommon tumour type with an unfavourable prognosis [9]. Ulceration was present in 38.6% of ALM, and average tumour thickness reached 3.5 mm in a study from Barcelona [10]. Patients with ALM are usually older that the non-ALM melanoma patients and the tumour size are larger at the time of diagnosis [11]. Also, ALM show distinct features of mutations. Comprehensive genomic and transcriptomic analysis of 34 ALM patients demonstrated the absence of UV-derived mutation signatures. PAK1 copy gains and somatic TERT mutations or germline events were detected in 41% of patients [12].

We present a peculiar, rare presentation of ALM of the foot pad with the involvement of two neighboring interdigital spaces that have been reported before only once [6]. We consider such a clinical presentation as a sign of an advanced tumour stage.

The treatment of choice is complete surgical excision. In the case of thick ALM, a safety margin of 2 cm is recommended to decrease the risk of local recurrence, while disease-free survival and melanoma-specific survival were not improved [13]. To achieve a complete tumour resection amputation is not always preventable – as shown in our patient [2].

References

1. Haenssle HA, Hoffmann S, Buhl T, Emmert S, Schön MP, Bertsch HP, Rosenberger A. Assessment of melanoma histotypes and associated patient-related factors: basis for a predictive statistical model. J Dtsch Dermatol Ges. 2015;13(1):37-45. https://doi.org/10.1111/ddg.12561

2. Guarneri C, Bevelacqua V, Semkova K, Tchernev G, Tempel S, Wollina U. Subungual acrolentiginous amelanotic melanoma treated with amputation of the distal and middle phalanges. Wien Med Wochenschr. 2013;163(15-16):368-371. https://doi.org/10.1007/s10354-013-0194-4 PMid:23591855

3. Schoenewolf NL, Belloni B, Simcock M, Tonolla S, Vogt P, Scherrer E, Holzmann D, Dummer R. Clinical implications of

distinct metastasizing preferences of different melanoma subtypes. Eur J Dermatol. 2014;24(2):236-241. PMid:24721680

4. Wollina U, Tchernev G, Chokoeva AA, Lotti T. Melanoma of the heel - a case series of a rare melanoma subtype. J Biol Regul Homeost Agents. 2015;29(1 Suppl):69-73. PMid:26016971

5. Sondermann W, Zimmer L, Schadendorf D, Roesch A, Klode J, Dissemond J. Initial misdiagnosis of melanoma located on the foot is associated with poorer prognosis. Medicine (Baltimore). 2016;95(29):e4332. https://doi.org/10.1097/MD.0000000000004332 PMid:27442685 PMCid:PMC5265802

6. Tchernev G, Lozev I, Pidakev I, Mangarov H, Grigorov Y, Cardoso JC, Popchristova E, Patterson JW, Lotti T, Pehlivanov G, Voicu C, Clatici VG, Wollina U. Interdigital melanoma affecting two neighboring interdigital spaces. First description in the medical literature. Wiener Med Wochenschr, 2017(in press). https://doi.org/10.1007/s10354-017-0558-2

7. Schoffer O, Schülein S, Arand G, Arnholdt H, Baaske D, Bargou RC, Becker N, Beckmann MW, Bodack Y, Böhme B, Bozkurt T, Breitsprecher R, Buchali A, Burger E, Burger U, Dommisch K, Elsner G, Fernschild K, Flintzer U, Funke U, Gerken M, Göbel H, Grobe N, Gumpp V, Heinzerling L, Kempfer LR, Kiani A, Klinkhammer-Schalke M, Klöcking S, Kreibich U, Knabner K, Kuhn P, Lutze S, Mäder U, Maisel T, Maschke J, Middeke M, Neubauer A, Niedostatek A, Opazo-Saez A, Peters C, Schell B, Schenkirsch G, Schmalenberg H, Schmidt P, Schneider C, Schubotz B, Seide A, Strecker P, Taubenheim S, Wackes M, Weiß S, Welke C, Werner C, Wittekind C, Wulff J, Zettl H, Klug SJ. Tumour stage distribution and survival of malignant melanoma in Germany 2002-2011. BMC Cancer. 2016;16(1):936. https://doi.org/10.1186/s12885-016-2963-0 PMid:27919243 PMCid:PMC5139127

8. Hiripi E, Gondos A, Emrich K, Holleczek B, Katalinic A, Luttmann S, Sirri E, Brenner H; GEKID Cancer Survival Working Group. Survival from common and rare cancers in Germany in the early 21st century. Ann Oncol. 2012;23(2):472-479. https://doi.org/10.1093/annonc/mdr131 PMid:21597096

9. Goydos JS, Shoen SL. Acral lentiginous melanoma. Cancer Treat Res. 2016;167:321-329. https://doi.org/10.1007/978-3-319-22539-5_14 PMid:26601870

10. Carrera C, Gual A, Díaz A, Puig-Butillé JA, Noguès S, Vilalta A, Conill C, Rull R, Vilana R, Arguis P, Vidal-Sicart S, Alós L, Palou J, Castel T, Malvehy J, Puig S. Prognostic role of the histological subtype of melanoma on the hands and feet in Caucasians. Melanoma Res. 2017. https://doi.org/10.1097/CMR.0000000000000340 PMid:28296711

11. Wada M, Ito T, Tsuji G, Nakahara T, Hagihara A, Furue M, Uchi H. Acral lentiginous melanoma versus other melanoma: A single-center analysis in Japan. J Dermatol. 2017. https://doi.org/10.1111/1346-8138.13834

12. Liang WS, Hendricks W, Kiefer J, Schmidt J, Sekar S, Carpten J, Craig DW, Adkins J, Cuyugan L, Manojlovic Z, Halperin RF, Helland A, Nasser S, Legendre C, Hurley LH, Sivaprakasam K, Johnson DB, Crandall H, Busam KJ, Zismann V, Deluca V, Lee J, Sekulic A, Ariyan CE, Sosman J, Trent J. Integrated genomic analyses reveal frequent TERT aberrations in acral melanoma. Genome Res. 2017;27(4):524-532. https://doi.org/10.1101/gr.213348.116 PMid:28373299

13. Lee KT, Kim EJ, Lee DY, Kim JH, Jang KT, Mun GH. Surgical excision margin for primary acral melanoma. J Surg Oncol. 2016;114(8):933-939. https://doi.org/10.1002/jso.24442 PMid:27642170

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Case Report

Hereditary Lymphedema of the Leg – A Case Report

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Keywords: Primary lymphedema; Secondary lymphedema; Complex decongestive therapy; Immunocompromised district; Erysipelas; Fibrosis; Elephantiasis nostra.

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Abstract

Primary of hereditary lymphedema is a rare but progressive disease. It is yet not curable. We present a 48-year-old male patient with hereditary lymphedema of his left leg, that was realised by minor trauma (able twist) when he was seven years old. He had never been treated for lymphedema but experienced multiple erysipelas during his life. After diagnostic procedures to exclude other causes of leg swelling, the diagnosis of hereditary lymphedema of the leg, stage III was confirmed. We initialized complex decongestive therapy. During two weeks of intensive treatment, the circumference of the left leg could be reduced by 10 cm. This case illustrates the "natural course" hereditary lymphedema. But it raises the hope that even after decades of ignorance, the patients benefits from complex decongestive treatment. Therapeutic nihilism is unnecessary and poses lymphedema patients to risks of infection and secondary malignancies like Stewart-Trewes syndrome.

Introduction

Primary or congenital lymphedema is a rare disorder. It occurs 1 in 100 000 persons affecting in < 90 % of cases the lower limbs [1]. Primary lymphedema may be present at birth or sometimes develop year's later - also called lymphedema tardum. Secondary lymphedema is seen more often after an injury to lymphatic vessels and lymph nodes – a common problem in certain cancer treatment protocols like in breast or endometrial cancer [2, 3].

Primary lymphedema is a progressive, not-curable disease. Subcutaneous enlargement of fibro-adipous tissue leads to progressive limb swelling, loss of functionality, mobility and quality of life. Lymphedematous skin is an immunocompromised district predisposing to infection and tumours [4].

Case report

A 48-year-old male patient presented with a swelling of his left leg. He had a medical history of multiple erysipelas of the same leg and an ankle twist when he was 7-year-old. Despite antibiosis, he had never had diagnostics or treatments before.

On examination, we observed men without any signs of cardiopulmonary decompensation. He had neither inguinal lymphadenopathy nor a total involvement of the oedema. There were no sensorimotoric deficiencies.

There was a collum-like pasty oedema of his left leg, pressable on the upper leg but impressable on the lower leg. The distal lower leg was further characterised by fibrosis, pachydermia, and hyperkeratosis left leg. There was a dewlap-like disfiguration of soft tissue in the ankle region (Fig. 1a). Foot and toes were edematous with a positive Stemmer sign. The interdigital skin was macerated.

Routine laboratory was unremarkable.

Imaging: Color Duplex sonography demonstrated normal venous and arterial blood flow without any signs of recent or previous thrombosis.

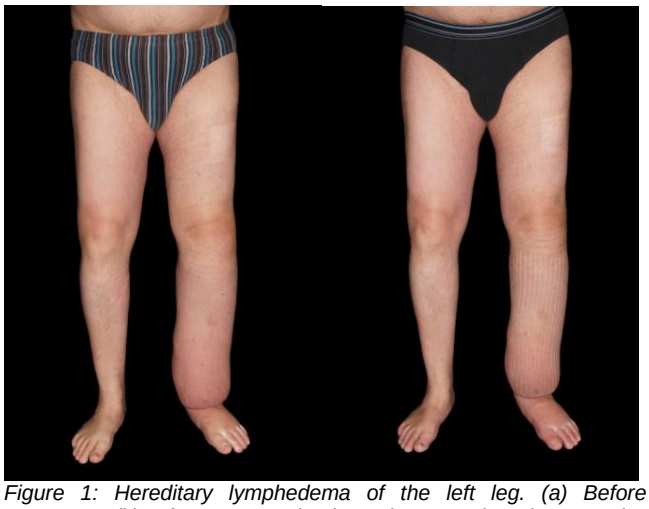

Figure 1: Hereditary lymphedema of the left leg. (a) Before treatment, (b) After two weeks intensive complex decongestive treatment

X-ray of feet disclosed degenerative changes of the proximal joint of digitus I on both feet and edematous soft tissue changes (Fig. 2a, b). Abdominal ultrasound remained unremarkable.

We diagnosed hereditary lymphedema of the left leg, stage III.

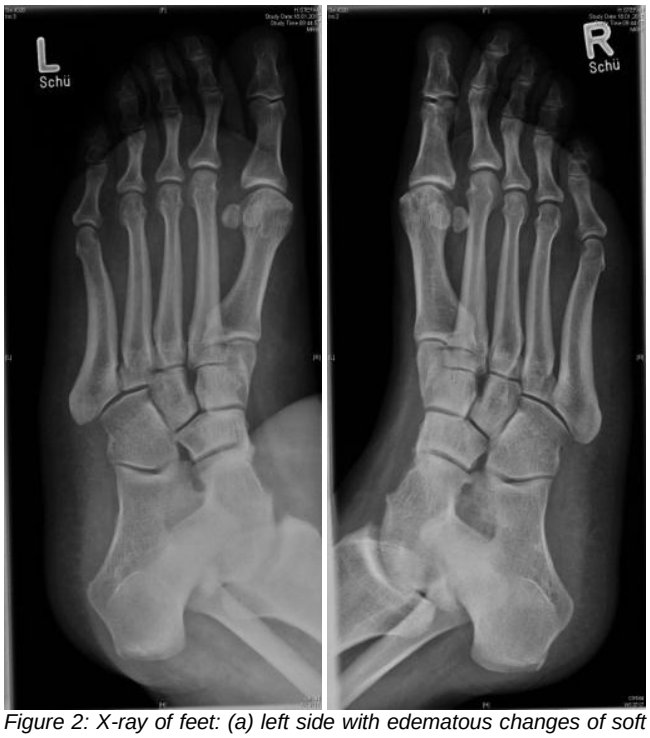

Figure 2: X-ray of feet: (a) left side with edematous changes of soft tissue, (b) right side. Arthrosis of Dig. I proximal joints on both sides

Treatment and course: We started with manual decongestive therapy (manual lymph drainage for the left leg combined with padded short stretch bandages and manual mobilisation of the left ankle. Topical interdigital treatment consisted of nystatin zinc-oil. During 15 days of inpatient complex decongestive therapy, there was a reduction of leg circumferences of 10 cm (Fig. 1b). Outpatient treatment was continued. Bandaging was replaced by flat knitted socks for the upper leg (compression class II) and flat knitted socks for lower leg and foot (compression class III).

Discussion

The patient suffered from an ankle twist at the age of seven. After that a persistent swelling oft he left leg developed. The trauma caused an overload for his lymphatic vessels. Usually, no lymphedema develops, but in the case of a predisposition with congenital malformation of lymphatic vessels, any trauma may realise the genetic disposition. His course was characterised by ignorance of lymphedema and absence of any treatment. This predisposed him to an increased risk of streptococcal soft tissue infections (erysipelas). The possible enters forte for germs is the intertriginous dermatitis of the interdigital space.

In primary (congenital) lymphedema germline mutations of at least 20 different genes have been identified which are enoding for protein interacting with vascular endothelial growth factor (VEGF) receptor-3 or with other tyrosin kinases. These mutations act on RAS/MAPK or PI3/AKT signal transduction [5].

There is yeat no cure for hereditary lymphedema. Complex decongestive therapy is considered the major approach. However, sufficient muscular-joint interactions are important for decongestion as well [6].

Our case report demonstrates that (a) therapeutic nihilism is contra productive and (b) even in longstanding lymphedema complex decongestive therapy is an effective treatment [7]. Surgical treatments include liposuction, lymphodemous anastomosis, vascularized lymph node transfer, and combined/multiple approaches. These methods are limited to a minority of patients [8].

Debulking soft tissue resection can become necessary in case of major fibrosis according to elephantiasis nostras with formation of immature lacune-like lymphatic vessels and massive fibrosis [9]

References

1. Schook CC, Mulliken JB, Fishman SJ, Grant FD, Zurakowski D, Greene AK. Primary lymphedema: clinical features and management in 138 pediatric patients. Plast Reconstr Surg. 2011;127:2419–2431. https://doi.org/10.1097/PRS.0b013e318213a218 PMid:21617474

2. Soran A, Ozmen T, McGuire KP, Diego EJ, McAuliffe PF, Bonaventura M, et al. The importance of detection of subclinical lymphedema for the prevention of breast cancer-related clinical lymphedema after axillary lymph node dissection; a prospective observational study. Lymphat Res Biol. 2014;12:289-294. https://doi.org/10.1089/lrb.2014.0035 PMid:25495384

3. Lindqvist E, Wedin M, Fredrikson M, Kjølhede P. Lymphedema after treatment for endometrial cancer - A review of prevalence and risk factors. Eur J Obstet Gynecol Reprod Biol. 2017;211:112-121. https://doi.org/10.1016/j.ejogrb.2017.02.021 PMid:28242470

4. Ruocco E, Puca RV, Brunetti G, Schwartz RA, Ruocco V. Lymphedematous areas: privileged sites for tumors, infections, and immune disorders. Int J Dermatol. 2007;46:662. https://doi.org/10.1111/j.1365-4632.2007.03244.x PMid:17550576

5. Brouillard P, Boon L, Vikkula M. Genetics of lymphatic anomalies. J Clin Invest. 2014;124:898-904. https://doi.org/10.1172/JCI71614 PMid:24590274 PMCid:PMC3938256

6. Cohen MD. Complete decongestive physical therapy in a patient with secondary lymphedema due to orthopedic trauma and surgery of the lower extremity. Phys Ther. 2011;91:1618-1626. https://doi.org/10.2522/ptj.20100101 PMid:21868611

7. Heinig B, Wollina U. Complex decongestive therapy. Hautarzt. 2015;66:810-818. https://doi.org/10.1007/s00105-015-3674-1 PMid:26315101

8. Carl HM, Walia G, Bello R, Clarke-Pearson E, Hassanein AH, Cho B, Pedreira R, Sacks JM. Systematic review of the surgical treatment of extremity lymphedema. J Reconstr Microsurg. 2017; doi: 10.1055/s-0037-1599100. https://doi.org/10.1055/s-0037-1599100

9. Wollina U, Heinig B, Schönlebe J, Nowak A. Debulking surgery for elephantiasis nostras with large ectatic podoplanin-negative lymphatic vessels in patients with lipo-lymphedema. Eplasty. 2014;14:e11. PMid:24741382 PMCid:PMC3944717

ID Design 2012/DOOEL Skopje, Republic of Macedonia
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Case Report

A Case of "Inflammatory Linear Verrucous Epidermal Nevus" (ILVEN) Treated with CO_2 Laser Ablation

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Keywords: inflammatory linear verrucous epidermal nevus; ILVEN; malignant transformation; frustrating treatments; CO_2 laser.

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Abstract

The "inflammatory linear verrucous epidermal nevus" is a rare disease, consisting of hyperplasia of the normal components of the epidermis. Its clinical features include erythematous and hyperkeratosic, warty, sometimes psoriasiform or lichenoid patches with a typical linear arrangement. At present, there are no effective medical therapies available. Currently, the best therapeutic results are obtained with surgical excision or the latest laser therapy. The Authors present a 9-years old girl with an inflammatory linear verrucous epidermal nevus on her neck, successfully treated with CO_2 Laser ablation.

Introduction

The "inflammatory linear verrucous epidermal nevus" (ILVEN) is a rare hamartomatous lesion consisting of hyperplasia of the normal components of the epidermis. Children are more commonly affected, and it predominates in females [1].

Clinically, it is characterised by erythematous and hyperkeratosic, warty lesions, in a linear arrangement which follows the lines of Blaschko.

Typically, the lesions are pruritic and unilateral. They usually occur on a limb following the lines of Blaschko, more rarely on the trunk, in a curvilinear pattern, or in different areas [2, 3].

Case report

An otherwise healthy 9-years old girl showed up to our clinic for a curvilinear, erythematous, warty-like eruption on her neck. The lesion was pruritic and rough to the touch. It was present by less than one year and showed a rapid growth. The past medical and familial histories were insignificant. In the patient's family, no one had a similar lesion or other skin diseases.

The patient did not refer previous treatments of the lesion, except for 10-days of corticosteroids topical application without any beneficial effects.

During the clinical evaluation, no other lesions were observed in any other part of the body.

Routine blood tests showed no involvement of other body regions, a sign of systemic infection or inflammation.

Due to the rapid growth of the lesions, the proven ineffectiveness and invasiveness of medical treatment and other physical therapies, as well as the aesthetic and functional complications of surgery (Table1), accordingly with the patient and her parents, we decided to remove the lesion with a CO_2 laser.

Table 1: CO_2 laser vs. surgical excision

	CO_2 laser	Surgical excision
Controindications	-	+
Pre-operative treatment	-	+
Anaesthesia	-/+	+
Procedure time	Quick	Slow
Complications/side effects	Poor	Possible
Post operative treatment	-	+
Time of wound healing	Days	Weeks

Before starting the treatment, we made an incisional biopsy which confirmed the diagnosis of ILVEN. The histology showed acanthosis, papillomatosis, parakeratotic hyperkeratosis and an inflammatory infiltrate in the upper dermis.

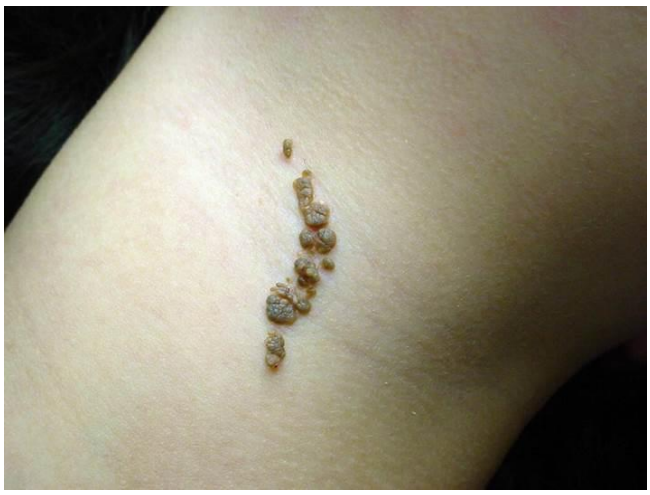

Figure 1: A 9 years-old girl, with an ILVEN on her neck

We used the 10,600-nm CO2 pulsed laser at a frequency of 10 Hz and a level of 1.0-1.5 (Fig. 2).

By the hamartoma's size, we decided to remove the lesion in a singular session. The operation has been performed without anaesthesia and did not require any patient-preparation.

The laser application was rapid and well tolerated by the young patient (Fig. 3).

At the end of the laser treatment, no specific medication was necessary except for the local application of antibiotic ointment for about a week.

No side effects or complications (e.g. scar, pigment modification) were observed in the follow-up the treatment (after one week, one month and three months).

A long-term follow-up (24 months) did not show any signs of recurrence.

Discussion

First described by Unna in 1896 [4], the inflammatory linear verrucous epidermal nevus (ILVEN) is as congenital malformations or hamartomas derived from embryonic ectoderm. It is a rare disease, more common in female [5]. Even if familial cases have been reported, ILVEN is usually sporadic. It usually appears at birth or within the first five years of life, although an adult onset has been described too [6].

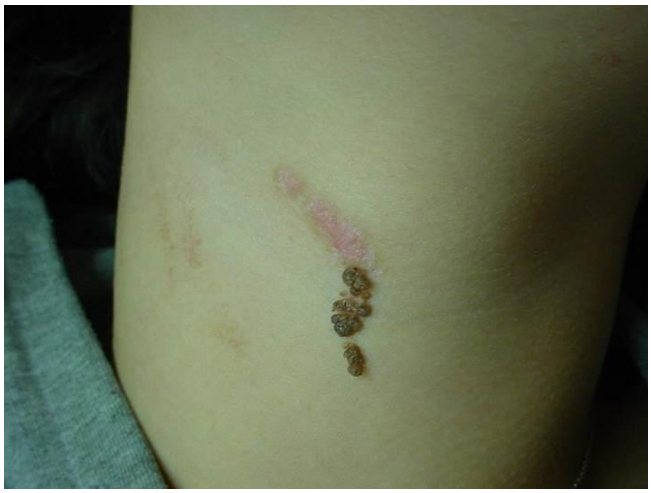

Figure 2: The patient during CO_2 laser ablation

Clinically, it presents with pruritic, erythematous and verrucous papules, in a linear distribution following Blaschko's lines. Usually, they are unilateral and localised to the left side of the body [7]. Extremities, especially the limb, are the more common localisation. The length of the nevus is highly variable, and in some cases it can involve the entire limb, causing nails alterations, such as subungual hyperkeratosis and local inflammation. More rarely, ILVEN has been described on the trunk with typical curvilinear transverse bands, which follow the Blaschko lines, sometimes stopping at the midline [8]. Different localisations, like genital or mucosal, are extremely rare [9-11].

Occasionally, as in the "Child Syndrome" ("Congenital naevus Hemidysplasia with inflammatory and Limb Defects"), the epidermal inflammatory hamartoma may be associated with skeletal-articular defects and visceral hypoplasias, which usually occur ipsilateral [12].

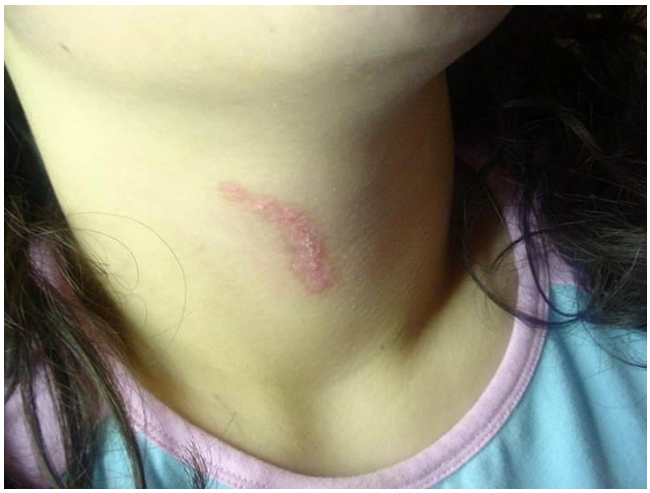

Figure 3: The patient immediately after the laser treatment

More rarely, the "epidermal nevus syndrome" has been described. It is characterised by complex developmental abnormalities of skin, eyes, nervous system, skeletal, urogenital and cardiovascular systems [13, 14].

The clinical course and prognosis are varied, depending on the individual characteristic and the possible association with more important organs alterations.

The inflammatory epidermal hamartoma is usually a chronic and progressive disease characterised by periodic inflammatory breakthroughs associated with increased pruritic symptoms, and rarely with microbial superinfection, eczema, or even necrosis. In the long term, the disease can stabilise and may even show spontaneous regression. On the other hand, even if extremely rare, ILVEN has seen to be associated with malignant transformation, such as basal or squamous cell carcinoma and keratoacanthoma [15-17].

The diagnosis of ILVEN is mainly clinical, supported by the medical history and histological examination. The histology is characterised by epidermal hyperplasia of normal components, with acanthosis, papillomatosis, hyperkeratosis and parakeratosis. Diffuse or perivascular inflammatory reactions have been reported in the papillary dermis [18].

If a more complex syndrome is suspected, it is recommended to exclude the involvement of other body parts with specific diagnostic exams (e.g. fundus examination, skeletal X-rays, ultrasounds, abdominal CT).

The treatment of NEVIL is very complex and often frustrating.

At present, there are no effective medical therapies available. Topical corticosteroids, dithranol and retinoids are beneficial in a small percentage of patients [9, 19, 20]. Topical vitamin D analogues, 5-FU and calcineurin inhibitors may be considered as therapeutic options [21, 22].

Currently, the best therapeutic results are obtained with the physical modalities, like surgical excision, cryotherapy, photodynamic and laser therapy. Among these, the last one seems to be the better therapeutic option, because of the low risk of complication and recurrences, and for the excellent aesthetical results [23-27].

In conclusion, due to the ineffectiveness of conventional drug therapies based on steroids and retinoids, and pending the outcome of case-control studies on the effects of new drugs such as derivatives of vitamin D, 5-FU or calcineurin inhibitors, we can state that the most effective therapeutic approach is represented by surgical exeresis and CO_2 laser therapy.

In particular, based on our clinical experience, laser therapy seems to be the best treatment. In fact, compared to surgery, laser therapy has no contraindications and requires no special patient-preparation, such as anaesthesia is not always necessary. The laser action is faster, less invasive and less destructive than surgery. Side effects are practically absent and, even more importantly, there is no contact therapy or any related complications. The laser lesions showed rapid re-epithelisation and the aesthetic and functional results were excellent. Our patient and her parents were very satisfied not only with the effectiveness of the operation but also with the speed of the treatment, the tolerability and absence of any special pre- or post-operative treatments or precautions except for short-term local antibiotic therapy.

References

1. Kosann MK. Inflammatory linear verrucous epidermal nevus. Dermatol Online J. 2003;9:15. PMid:14594588

2. Mazereeuw-Hautier J, Marty C, Bonafé JL. Familial inflammatory linear verrucous epidermal naevus in a father and daughter. Clin Exp Dermatol. 2008;33:679–80. https://doi.org/10.1111/j.1365-2230.2007.02666.x PMid:18801106

3. Nag F, Ghosh A, Surana TV, Biswas S, Gangopadhyay A, Chatterjee G. Inflammatory linear verrucous epidermal nevus in perineum and vulva: A report of two rare cases. Indian J Dermatol. 2013;58:158. https://doi.org/10.4103/0019-5154.108078 PMid:23716825 PMCid:PMC3657235

4. Unna PG. The histopathology of the diseases of the skin. New York: MacMillan, 1876: p.1148.

5. Morag C, Metzker A. Inflammatory linear verrucous epidermal nevus: Report of seven new cases and review of the literature. Pediatr Dermatol. 1985;3:15–8. https://doi.org/10.1111/j.1525-1470.1985.tb00479.x PMid:3906609

6. Goldman K, Don PC. Adult onset of inflammatory linear verrucous epidermal nevus in a mother and her daughter. Dermatology. 1994;189:170–2. https://doi.org/10.1159/000246825 PMid:8075448

7. Gon AS, Minelli L, Franzon PG. A case for diagnosis. Ann Bras

Dermatol. 2010;85:729–31. https://doi.org/10.1590/S0365-05962010000500024

8. Miteva LG, Dourmishev AL, Schwartz RA. Inflammatory linear verrucous epidermal nevus. Cutis. 2001;68(5):327-30. PMid:11766117

9. Debabrata Bandyopadhyay, Abanti Saha. Genital/Perigenital Inflammatory Linear Verrucous Epidermal Nevus: A Case Series. Indian J Dermatol. 2015; 60(6): 592–595. https://doi.org/10.4103/0019-5154.169132 PMid:26677274 PMCid:PMC4681199

10. Kumar CA, Yeluri G, Raghav N. Inflammatory linear verrucous epidermal nevus syndrome with its polymorphic presentation - A rare case report. Contemp Clin Dent. 2012; 3(1): 119–122. https://doi.org/10.4103/0976-237X.94562 PMid:22557913 PMCid:PMC3341748

11. Tesi D, Ficarra G. Oral linear epidermal nevus: a review of the literature and report of two new cases. Head Neck Pathol. 2010; 4(2):139-43. https://doi.org/10.1007/s12105-010-0165-7 PMid:20512640 PMCid:PMC2878623

12. Moss C, Burn J. CHILD+ILVEN=PEN or PENCIL. J Med Genet. 1990;27:390–1. https://doi.org/10.1136/jmg.27.6.390 PMid:2359103 PMCid:PMC1017139

13. Cabanillas M, Aneiros A, Monteagudo B, Santos-García D, Suárez-Amor O, Ramírez-Santos A. Epidermal nevus syndrome associated with polyostotic fibrous dysplasia, CNS lipoma and aplasia cutis. Dermatol Online J. 2009;15:7. PMid:19951625

14. Booth TN, Rollins NK. MR imaging of the spine in epidermal nevus syndrome. Am J Neuroradiol. 2002;23:1607–10. PMid:12372757

15. Horn MS, Sausker WF, Pierson DL. Basal cell epithelioma arising in a linear epidermal nevus. Arch Dermatol. 1981;117:247. https://doi.org/10.1001/archderm.1981.01650040063028 PMid:7212753

16. Jones EW, Heyl T. Nevus sebaceous. A report of 140 cases with special regard to the development of secondary malignant tumors. Br J Dermatol. 1970;82:99–117. https://doi.org/10.1111/j.1365-2133.1970.tb15000.x PMid:5435080

17. Ichikawa T, Saiki M, Kaneko M, Saida T. Squamous cell carcinoma arising in a verrucous epidermal nevus. Dermatology. 1996;193:135–8. https://doi.org/10.1159/000246229 PMid:8884151

18. Su WP. Histopathologic varieties of epidermal nevus. Am J Dermatopathol. 1982;4:161–70. https://doi.org/10.1097/00000372-198204000-00011

19. Rulo HF, van de Kerkhof PC.Treatment of inflammatory linear verrucous epidermal nevus. Dermatologica. 1991;182(2):112-4. https://doi.org/10.1159/000247756

20. Kim JJ, Chang MW, Shwayder T. Topical tretinoin and 5-fluorouracil in the treatment of linear verrucous epidermal nevus. J Am Acad Dermatol. 2000;43(1 Pt 1):129-32. https://doi.org/10.1067/mjd.2000.105563 PMid:10863239

21. Böhm M, Luger TA, Traupe H. Successful treatment of inflammatory linear verrucous epidermal naevus with topical natural vitamin D3 (calcitriol). Br J Dermatol. 2003;148(4):824-5. https://doi.org/10.1046/j.1365-2133.2003.05194.x PMid:12752150

22. Mutasim DF. Successful treatment of inflammatory linear verrucous epidermal nevus with tacrolimus and fluocinonide. J Cutan Med Surg. 2006 Jan-Feb;10(1):45-7. https://doi.org/10.1007/7140.2006.00004 PMid:17241573

23. Fox BJ, Lapins NA. Comparison of treatment modalities for epidermal nevus: a case report and review. J Dermatol Surg Oncol. 1983 Nov;9(11):879-85. https://doi.org/10.1111/j.1524-4725.1983.tb01035.x PMid:6630702

24. Parera E, Gallardo F, Toll A, Gil I, Sánchez-Schmidt J, Pujol R. Inflammatory linear verrucous epidermal nevus successfully treated with methyl-aminolevulinate photodynamic therapy. Dermatol Surg. 2010;36:253–6. https://doi.org/10.1111/j.1524-4725.2009.01401.x PMid:20402956

25. Ulkur E, Celikoz B, Yuksel F, Karagoz H. Carbon dioxide laser therapy for an inflammatory linear verrucous epidermal nevus: a case report. Aesthetic Plast Surg. 2004;28(6):428-30. https://doi.org/10.1007/s00266-004-0024-6 PMid:15583849

26. Michel JL, Has C, Has V. Resurfacing CO2 laser treatment of linear verrucous epidermal nevus. Eur J Dermatol. 2001;11(5):436-9. PMid:11525951

27. Conti R, Bruscino N, Campolmi P, Bonan P, Cannarozzo G, Moretti S. Inflammatory linear verrucous epidermal nevus: why a combined laser therapy. J Cosmet Laser Ther. 2013;15(4):242-5. https://doi.org/10.3109/14764172.2013.807115 PMid:23692514

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Case Report

Very Rare Amelanotic Lentigo Maligna Melanoma with Skull Roof Invasion

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Keywords: Melanoma; amelanotic lentigo malignant melanoma; relapses; surgery; skull invasion; follow-up.

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Abstract

BACKGROUND: Lentigo malignant melanoma is a melanoma subtype of chronic sun-damaged skin in elderly Caucasians. Amelanotic variants of lentigo malignant are extremely rare.

CASE PRESENTATION: This is a case report of an 80-year-old male patient who presented with a non-pigmented exophytic tumour of his bald head. After complete surgical excision under the suspicion of squamous cell carcinoma, three-dimensional histologic examination confirmed an amelanotic lentigo malignant melanoma with a tumour thickness of 1.76 mm, resected R0. Five years later he developed the first relapse, the other year a satellite metastasis was surgically removed. One year later, this patient had developed a large relapsing lentigo malignant melanoma with skull roof invasion. There was no evidence of distant metastatic spread. Amelanotic lentigo malignant melanoma is a very rare tumour.

CONCLUSIONS: Serial excision or slow Mohs and Mohs micrographic surgery are the treatments of choice especially in the head and neck area. These tumours may be locally very aggressive as it is shown by skull invasion in the present case.

Introduction

Lentigo malignant melanoma (LMM) is a melanoma subtype that develops on chronic sun-damaged skin mostly in elderly patients (age >70 years). Its precursor, lentigo maligna or Hutchinson's melanotic freckle is a melanoma in situ on average with a remarkable slow growth rate. In 2% to 20% of patients lentigo maligna will further progress to invasive melanoma. Lentigo maligna and LMM may have similar clinical presentation, what challenges their differential diagnosis [1].

LMM accounts for 4% to 15% of all melanomas. The propensity to lentigines is higher in LMM versus superficial spreading melanoma (SSM), while high nevus counts are a stronger indicator for SSM. In addition, SSM is stronger associated to non-melanoma skin cancer compared to SSM. Sunburns don't seem to be not an independent risk factor for LMM [2]. A recent study from the Netherlands analysed age-standardized incidence rate for LMM between 1989 to 2013. The incidence rate increased from 0.24 to 1.19 [3].

On histopathologic examination LMM is characterised by the atypical junctional growth of melanocytic cells, pagetoid growth not only in interfollicular but follicular skin, cellular atypia, and increased proliferative activity. The affected skin shows marked epidermal atrophy, solar elastosis and dermal inflammatory infiltrate. LMM radial growth may regress, a feature that may notoriously lead to false negative surgical margins. Therefore, diagnosis of LMM is not an easy one especially in the interpretation of resection margins. To assist LMM diagnosis, various immunostains are used with monoclonal antibodies against S100, HMB-45 (against Pmel 17), soluble adenylyl cyclase (antibody R21), microphthalmia transcription factor or MART-1 (protein melan-A) [1, 4].

Dermoscopy may aid melanoma diagnosis, but studies so far have considered pigmented LMM only [5, 6]. Confocal microscopy could be a tool for the definition of tumour margins before surgery, but the technique is yet no standard procedure [7].

Case report

A 73-year-old male patient presented with a firm tumour on his bald head with a diameter of approximately 2 cm. The reason for the first presentation was frequent bleeding.

He had a medical history of prostate cancer (Gleason score 7) and subsequent radiotherapy, squamous cell cancer of the right hand, arterial hypertension, hyperlipidemia, chronic ischemic heart disease with four by-passes and pace maker implantation.

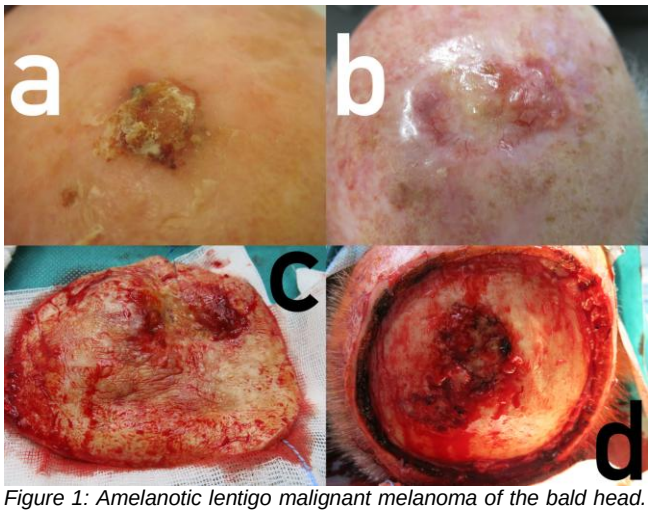

Figure 1: Amelanotic lentigo malignant melanoma of the bald head. (a) Initial presentation of the primary tumour resembling squamous cell carcinoma; (b) Relapse on the borders of the transplant, telangiectasias but again no pigmentation at all; (c) Surgical specimen; (d) Defect before closure with skull roof invasion located centrally

On examination, we observed a skin coloured exophytic nodule, covered by scales (Fig. 1a). Under the working diagnosis of a squamous cell carcinoma, the tumour was removed by standard excision followed by three-dimensional histology.

Histologic examination confirmed a lentigo malignant melanoma (LMM) with a tumour thickness of 1.76 mm and Clark level IV. The tumour cells were positive for S100 with coexpression of MART-1 and HMB45. They were negative for CD10 and CD68.

The surgical margins were free. The staging was performed by imaging techniques. No metastases were observed. This lead to the final diagnosis of LMM (pT2b N0 M0). Healing was unremarkable.

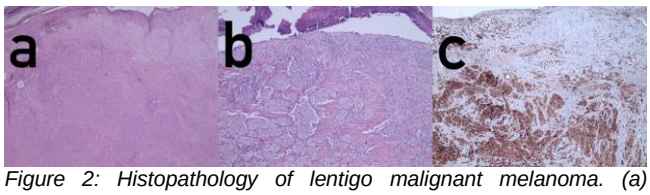

Figure 2: Histopathology of lentigo malignant melanoma. (a) Overview (hematoxylin-eosin x 2); (b) detail (hematoxylin-eosin x 4); (c) immunoperoxidase staining for S100 (x4)

Five years later, he presented with an amelanotic relapse of his LMM, which was surgically removed by slow Mohs again. Tumour thickness was 3.00 mm (rpT3a). Tumour staging was unremarkable, no metastases.

One year later, he returned with another skin coloured nodule of the bald head which was removed by slow Mohs surgery. The defect was closed by sandwich transplantation using dermal equivalent (Matriderm) and meshed skin graft [8]. Histologic examination revealed a satellite metastasis of his LMM. Healing was uneventful. The tumour was now staged as rpT3a pN2c cM0, stage IIIb.

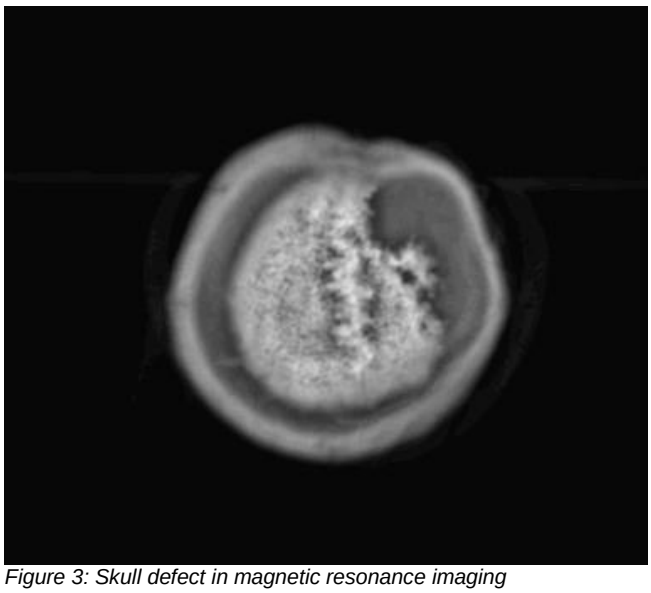

Figure 3: Skull defect in magnetic resonance imaging

Almost exactly one year later, he presented with a firm tumour proliferation around the skin transplant with some telangiectasias but without pigmentation (Fig. 1b). A skin biopsy was taken. Histologically, there was a proliferation of atypical melanocytes singly and in nests along the basal layer of the epidermis and epitheloid nests in the adjacent dermis. The atypical cells were small with prominent nuclei. These findings confirmed LMM (Fig. 2). Staging demonstrated a tabula externa defect (Fig. 3). Surgery was planned a tumour debulking. The patient was treated surgically as a tumour by wide excision with 2 cm safety margins (Fig. 1c), after decortication the tabula externa was partially removed by a diamond drill. During surgery, it became obvious that the tumour had already infiltrated the skull roof in an area of about 4 x 2.5 cm (Fig. 1d). The defect was

closed by sandwich transplantation (Fig. 4) and the patient was presented to the tumour board for either neurosurgery and radiotherapy. Since the tabula interna was still intact as demonstrated by cranial computerised tomography, he was referred to the neurosurgery and plastic surgery department for tumour removal and skull repair. Staging did not provide any hint for the further metastatic spread.

Discussion

In our department, LMM is seen in 12% of female and 11% of male melanoma patients. Amelanotic melanoma comprises only two percent of all melanoma subtypes. Amelanotic LMM is an unusual rare tumour type with less than 25 cases reported worldwide (9-15). The clinical suspicion for amelanotic LMM is extremely low. Dermoscopy is not sensitive enough to detect this melanoma subtype [5, 6].

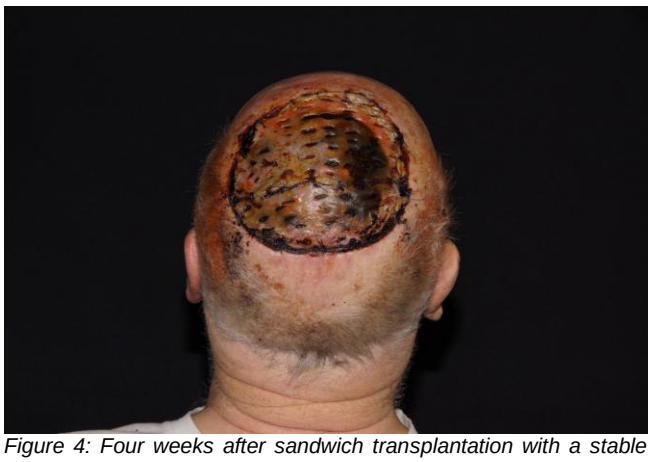

Figure 4: Four weeks after sandwich transplantation with a stable graft

Major differential diagnoses are actinic keratosis and squamous cell carcinoma (SCC). Diagnosis can only be confirmed by histopathological examination.

Due to the growth characteristics of LMM with recurrent regression, the assessment of free surgical margins is not an easy task. The medical history of our patient demonstrated that even with slow Mohs, experienced dermatopathologist and dermasurgeon, recurrence is possible [5].

The present case is exceptional for several reasons: (i) it is an amelanotic LMM; (ii) recurrence was only locally; (iii) it invaded and destroyed the roof of the skull; and (iv) it remained locally over a period of 7 years. We could not find any other case with such a locally aggressive behaviour but without the further metastatic spread. The occurrence of a relapse five years after the first diagnosis is quite characteristic. Most LMM relapse between 3 to 5 years [16].

Treatment of LMM consists of surgery with wide excision, staged excision or Mohs surgery. Nevertheless, a higher recurrence rate has been reported for LMM, depending on histopathological methods for tumour margin examination, safety margins, and length of follow-up. With an average safety margin of 5 mm, only 56% of tumours could be cleared, while a safety margin of 15 mm achieved a 97% complete clearance rate (17Felton et al. 2016). Therefore, a 5-mm safety margin is inadequate for LMM. However, 15 mm is not always possible like in the face. A better choice is Mohs surgery or staged excision [17]. With staged excision, the recurrence rate within a mean of 11.5 years was 5.9 % [18]. By staged excision or slow Mohs technique, formalin-fixed tissue specimen are used that offer a better quality of tissue sections than frozen sections do. In a retrospective study comparing serial excision (slow Mohs) with Mohs micrographic technique on frozen sections, the recurrence rate was 7.3% and 33.0%, respectively [19]. On average, recurrence rates of 8% to 20% have been reported with standard surgery compared to 4% to 5 % by Mohs surgery [20].

Topical treatment with ingenol mebutate, imiquimod or cryotherapy is not recommended due to the ill-defined tumour borders and the microscopic growth pattern along the hair follicles deep downwards. Also, the progression of lentigo maligna into LMM has been reported after topical treatment [21]. Relapse rate after topical therapy or cryosurgery ranges from 20% to 100% after five years [20].

For patients who refuse surgery or could not be operated for medical reasons, a radiotherapy is a therapeutic option. An 88% complete clearance rate has been reported for lentigo maligna and early LMM using 100 to 160 Gy fractioned Grenz rays [22].

Debulking surgery is an established method to reduce tumour load in advanced melanoma [23]. In metastatic melanoma, debulking surgery may be necessary in emergency situations in case of heavily bleeding or obstructing tumour growth for instance [24].

Skull roof invasion by melanoma is very rare. It can occasionally be seen in patients with squamous cell carcinoma of the skin, basal cell carcinoma and rare neoplastic adnexal tumours of skin [25-30]. Research on PubMed with “lentigo maligna melanoma” and “skull roof invasion” provided not a single hit.

The management of skull invasion warrants interdisciplinary cooperation. Therefore, the patient had been presented to the interdisciplinary tumour board.

References

1. Juhász ML, Marmur ES. Reviewing challenges in the diagnosis and treatment of lentigo maligna and lentigo-maligna melanoma. Rare Cancers Ther. 2015;3:133-145. https://doi.org/10.1007/s40487-015-0012-9 PMid:27182482 PMCid:PMC4837936

2. Kvaskoff M, Siskind V, Green AC. Risk factors for lentigo maligna melanoma compared with superficial spreading melanoma: a case-control study in Australia. Arch Dermatol. 2012;148(2):164-170. https://doi.org/10.1001/archdermatol.2011.291 PMid:22004881

3. Greveling K, Wakkee M, Nijsten T, van den Bos RR, Hollestein LM. Epidemiology of lentigo maligna and lentigo maligna melanoma in the Netherlands, 1989-2013. J Invest Dermatol. 2016;136(10):1955-1960. https://doi.org/10.1016/j.jid.2016.06.014 PMid:27349862

4. Christensen KN, Hochwalt PC, Hocker TL, Roenigk RK, Brewer JD, Baum CL, Otley CC, Arpey CJ. Comparison of MITF and Melan-A immunohistochemistry during Mohs surgery for lentigo maligna-type melanoma in situ and lentigo maligna melanoma. Dermatol Surg. 2016;42(2):167-175. https://doi.org/10.1097/DSS.0000000000000600 PMid:26771682

5. Jaimes N, Marghoob AA, Rabinovitz H, Braun RP, Cameron A, Rosendahl C, Canning G, Keir J. Clinical and dermoscopic characteristics of melanomas on nonfacial chronically sun-damaged skin. J Am Acad Dermatol. 2015;72(6):1027-1035. https://doi.org/10.1016/j.jaad.2015.02.1117 PMid:25824275

6. Bollea-Garlatti LA, Galimberti GN, Galimberti RL. Lentigo maligna: keys to dermoscopic diagnosis. Actas Dermosifiliogr. 2016;107(6):489-497. https://doi.org/10.1016/j.ad.2016.01.001 PMid:26875792

7. Guitera P, Moloney FJ, Menzies SW, Stretch JR, Quinn MJ, Hong A, Fogarty G, Scolyer RA. Improving management and patient care in lentigo maligna by mapping with in vivo confocal microscopy. JAMA Dermatol. 2013;149(6):692-698. https://doi.org/10.1001/jamadermatol.2013.2301 PMid:23553208

8. Wollina U. One-stage reconstruction of soft tissue defects with the sandwich technique: Collagen-elastin dermal template and skin grafts. J Cutan Aesthet Surg. 2011;4(3):176-182. https://doi.org/10.4103/0974-2077.91248 PMid:22279382 PMCid:PMC3263127

9. Kaufmann R, Nikelski K, Weber L, Sterry W. Amelanotic lentigo maligna melanoma. J Am Acad Dermatol. 1995;32(2 Pt 2):339-342. https://doi.org/10.1016/0190-9622(95)90399-2

10. Cliff S, Otter M, Holden CA. Amelanotic lentigo maligna melanoma of the face: a case report and review of the literature. Clin Exp Dermatol. 1997;22(4):177-179. https://doi.org/10.1111/j.1365-2230.1997.tb01056.x PMid:9499607

11. Allan SJ, Dicker AJ, Tidman MJ, McLaren KM, Hunter JA. Amelanotic lentigo maligna and amelanotic lentigo maligna melanoma: a report of three cases mimicking intraepidermal squamous carcinoma. J Eur Acad Dermatol Venereol. 1998;11(1):78-81. https://doi.org/10.1111/j.1468-3083.1998.tb00961.x PMid:9731974

12. Conrad N, Jackson B, Goldberg L. Amelanotic lentigo maligna melanoma: a unique case presentation. Dermatol Surg. 1999;25(5):408-411. https://doi.org/10.1046/j.1524-4725.1999.08271.x PMid:10469082

13. Rocamora V, Puig L, Romaní J, de Moragas JM. Amelanotic lentigo maligna melanoma: report of a case and review of the literature. Cutis. 1999;64(1):53-56. PMid:10431675

14. Abdulla FR, Kerns MJ, Mutasim DF. Amelanotic lentigo maligna: a report of three cases and review of the literature. J Am Acad Dermatol. 2010;62(5):857-860. https://doi.org/10.1016/j.jaad.2009.06.017 PMid:19766347

15. Perera E, Mellick N, Teng P, Beardmore G. A clinically invisible melanoma. Australas J Dermatol. 2014;55(3):e58-e59. https://doi.org/10.1111/ajd.12022 PMid:23425084

16. Bub JL, Berg D, Slee A, Odland PB. Management of lentigo maligna and lentigo maligna melanoma with staged excision: a 5 year follow up. Arch Dermatol. 2004;140(5):552–558. https://doi.org/10.1001/archderm.140.5.552 PMid:15148099

17. Felton S, Taylor RS, Srivastava D. Excision margins for melanoma in situ on the head and neck. Dermatol Surg. 2016;42(3):327-334. https://doi.org/10.1097/DSS.0000000000000648 PMid:26866286

18. Wilson JB, Walling HW, Scupham RK, Bean AK, Ceilley RI, Goetz KE. Staged excision for lentigo maligna and lentigo maligna melanoma: analysis of surgical margins and long-term recurrence in 68 cases from a single practice. J Clin Aesthet Dermatol. 2016;9(6):25-30. PMid:27386048 PMCid:PMC4928453

19. Walling HW, Scupham RK, Bean AK, Ceilley RI. Staged excision versus Mohs micrographic surgery for lentigo maligna and lentigo maligna melanoma. J Am Acad Dermatol. 2007;57(4):659-664. https://doi.org/10.1016/j.jaad.2007.02.011 PMid:17870430

20. McKenna JK, Florell SR, Goldman GD, Bowen GM. Lentigo maligna/lentigo maligna melanoma: current state of diagnosis and treatment. Dermatol Surg. 2006;32(4):493-504. https://doi.org/10.1097/00042728-200604000-00003

21. Tio D, van der Woude J, Prinsen CA, Jansma EP, Hoekzema R, van Montfrans C. A systematic review on the role of imiquimod in lentigo maligna and lentigo maligna melanoma: need for standardization of treatment schedule and outcome measures. J Eur Acad Dermatol Venereol. 2017;31(4):616-24. PMid:27987308.

22. Hedblad MA, Mallbris L. Grenz ray treatment of lentigo maligna and early lentigo maligna melanoma. J Am Acad Dermatol. 2012;67(1):60-68. https://doi.org/10.1016/j.jaad.2011.06.029 PMid:22030019

23. Gajdos C, McCarter MD. Debulking surgery in advanced melanoma. Expert Rev Anticancer Ther. 2011;11(11):1703-1712. https://doi.org/10.1586/era.11.98 PMid:22050019

24. Mantas D, Tsaparas P, Charalampoudis P, Gogas H, Kouraklis G. Emergency surgery for metastatic melanoma. Int J Surg Oncol. 2014;2014:987170. https://doi.org/10.1155/2014/987170

25. Guitera P, Moloney FJ, Menzies SW, Stretch JR, Quinn MJ, Hong A, Fogarty G, Scolyer RA. Improving management and patient care in lentigo maligna by mapping with in vivo confocal microscopy. JAMA Dermatol. 2013;149(6):692-698. https://doi.org/10.1001/jamadermatol.2013.2301 PMid:23553208

26. Wollina U, Tchernev G. Advanced basal cell carcinoma. Wien Med Wochenschr. 2013;163(15-16):347-353. https://doi.org/10.1007/s10354-013-0193-5 PMid:23589318

27. Wollina U, Bayyoud Y, Krönert C, Nowak A. Giant epithelial malignancies (Basal cell carcinoma, squamous cell carcinoma): a series of 20 tumors from a single center. J Cutan Aesthet Surg. 2012;5(1):12-19. https://doi.org/10.4103/0974-2077.94328 PMid:22557850 PMCid:PMC3339122

28. Wollina U, Bayyoud Y, Kittner T, Dürig E. Giant tricholemmal squamous cell carcinoma with cranial infiltration. J Clin Aesthet Dermatol. 2011;4(4):34-37. PMid:21532876 PMCid:PMC3084608

29. Soma PF, Chibbaro S, Makiese O, Marsella M, Diemidio P, Fricia M, Passanisi M, Catania V, Siragò P, Ventura F. Aggressive scalp carcinoma with intracranial extension: a multidisciplinary experience of 25 patients with long-term follow-up. J Clin Neurosci. 2008;15(9):988-992. https://doi.org/10.1016/j.jocn.2007.09.014 PMid:18653348

30. Abo Sedira M, Amin AA, Rifaat MA, El-Sebai HI, El-Badawy MA, Aboul Kassem HA. Locally advanced tumors of the scalp: the Egyptian National Cancer Institute experience. J Egypt Natl Canc Inst. 2006;18(3):250-257. PMid:17671535

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Case Report

Pustular Palmoplantar Psoriasis Successfully Treated with Nb-UVB Monochromatic Excimer Light: A Case-Report

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Keywords: psoriasis; palmoplantar; monochromatic excimer light; UVB; treatment.

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Abstract

Barber's palmoplantar pustulosis (PPP) is a form of localised pustular psoriasis, affecting the palmar and plantar surfaces. It is a chronic disease, with a deep impact on the patients' quality of life. The Authors discuss a case of Baber Psoriasis successfully treated with monochromatic excimer light.

Introduction

Pustular palmoplantar psoriasis is a peculiar form of localised pustular psoriasis occurring on palmar and plantar surfaces of the skin (type Barber or Barber-Königsbeck). It is a chronic and stubborn pathology, difficult to manage and with the tendency to recur over time [1]. In contrast to plaque-type psoriasis, pustular psoriasis shows homozygous or compound heterozygous interleukin-36 (IL36RN) gene mutations leading to aberrations in IL-36R antagonist function [2]. The immunological peculiarities of pustular psoriasis contribute to the less favourable outcome of this psoriasis type with tumor-necrosis factor-alfa antagonists. Narrow-band ultraviolet-B phototherapy (308-311 nm) has been recognised as a valid therapeutic option for the disease, leading to quick remissions and low recurrence rates. In recent years, devices able to deliver the radiation only to affected areas of the skin have been developed, with the major advantages of sparing unaffected areas of the body surface and being more compliant for the patients [3].

Case Presentation

An otherwise healthy male subject, 38 years old, affected by a pustule palmar psoriasis (Fig. 1), showed up to our Clinic presenting, on his palms, numerous small flat pustules (2-3 mm in diameter), whitish to yellowish in colour, on an erythematous basis. He lamented a slight, continuous, burning sensation. He reported the appearance of these lesions about two months before, at first on his left palm, and then rapidly spreading to involve also the

right palm. He also described how new pustules appeared in a few hours, while the older ones were creating a yellowish crust which was falling spontaneously.

History for drug assumption was negative, and he didn't report any contact with local irritants. The patient didn't refer any revealing pathology, and he showed no familiarity for psoriasis or other skin diseases.

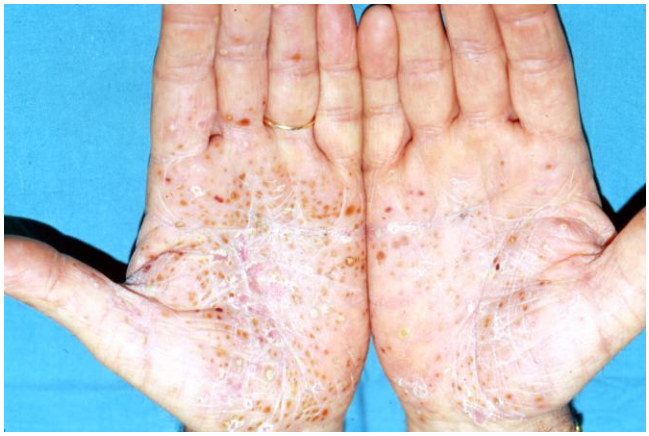

Figure 1: Our patient affected by pustular psoriasis on his palms

During the clinical evaluation, no other lesions were observed in any other part of the body, apart from small, hurting fissurations on the flexural surfaces of the wrists, while fingers were not affected. Nails showed no sign of psoriatic lesions. A rheumatologic evaluation showed no apparent joint involvement. Routine blood testing for inflammation and infections was negative.

A punch biopsy performed on a pustular area showed subcorneal unilocular pustulosis and a neutrophilic infiltration with neutrophilic exocytosis, configuring the classical aspect of "spongiform pustule of Kogoj". Moreover, the cultural test showed sterile pustules, confirming the initial diagnosis of palmoplantar psoriasis (Barber's palmoplantar psoriasis). Narrowband UVB (308-311 nm) is considered by dermatologists worldwide an efficient treatment for psoriasis [1]. For this reason (and according to our positive personal experience), after having discussed with the patient about the therapeutic possibilities, and after having received his informed consent, we decided to perform a focused narrowband UVB treatment, using a monochromatic excimer light device developed to deliver a 308 nm radiation only to the affected areas, thus sparing the unaffected surrounding skin. The device emits UVB light with the wavelength of 308 nm, with a power density of 50 mW/cm^2 at a distance of 15 cm from the skin, and a maximum radiation area of 512 cm^2.

The therapeutic procedure schedules two sessions in a week for the first four weeks of treatment, and then one session in a week for the rest of the treatment. During the first session, we estimated the MED (Minimal Erythema Dose) of the patient in an uninjured part of the body (flexural part of the forearm), to be able to set the first dose of radiation, corresponding to the MED decreased by 10%. During the following sessions, we proceeded increasing the dose gradually depending on the clinical response. Regarding time (seconds of irradiation), our patient needed 15 seconds of illumination for the first session (0.75 J/cm^2); the duration of the following treatments was increased by 5 seconds (0.25 J/cm^2) each time.

At week 6 (10 treatments), the clinical picture was substantially improved, showing a clear reduction of inflammation, erythema, desquamation, and the complete disappearance of pustules. We decided to interrupt the treatment at week twelve (16 total sessions) since we evaluated the complete resolution of the disease (Fig. 2).

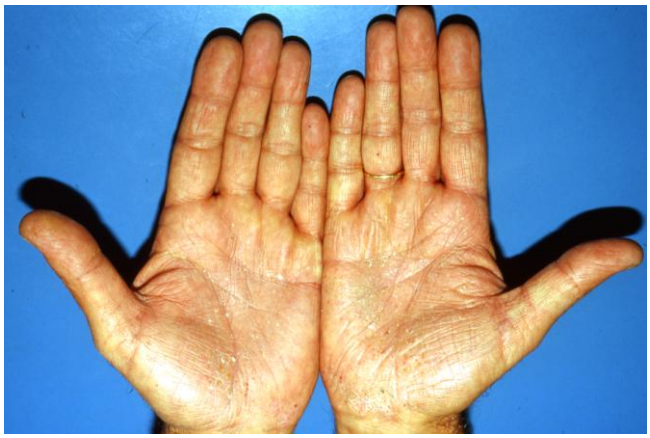

Figure 2: The same patient after the treatment with excimer light

During the entire treatment time, no side effects or adverse events were noted. Only a slight, transient erythema appeared after each of the first four sessions, however leading to no harms or discomfort for the patient. Since treatment discontinuation, we are monitoring the subject to evaluate the possible recurrence of psoriasis. However, after 12 weeks without any treatment, no lesions are present to date.

Discussion

Psoriasis is a chronic inflammatory disease involving the skin, and sometimes affecting joints, bones, tendons, ligaments, nails, and mucosal membranes [1]. About 3% of the Italian population is affected by psoriasis, and this percentage reflects the worldwide prevalence of the disease [4].

Psoriasis has many clinical variants, the most common of which is the vulgar type (plaque-type), guttate, inverse, mucosal, sebopsoriasis, pustular,

arthropathic, erythrodermic. Pustular psoriasis can be divided into two major clinical variants, localised and generalised, both characterised by the same elementary lesion, a sterile, non-follicular, superficial pustule, but differentiated, among the others, by the degree of body surface involvement. Its histopathology is characterised by the "spongiform pustule of Kogoj", that is a suppuration pustule located in the upper part of spinosus layer and filled with neutrophils [5].

By the localisation of the lesions, and depending on their different evolution, two main variants of localised pustular psoriasis may be distinguished, namely the Barber's palmoplantar pustulosis (PPP) and the Hallopeau's continuous acrodermatitis. PPP is the most common one, and it is characterised by the outbreak of little pustules on an erythematous and scaly basis, located on the palms of the hands and the soles of the feet. Pustules arise by rushes in a few hours, are 1 to 5 mm in diameter, and are surrounded by an erythematous ring. Usually, they are asymptomatic, but they can cause a burning sensation. They are flat-topped, whitish to yellowish with the tendency to become darker until they dry in a couple of days, leaving a crust and a brownish hyperpigmentation. Rushes are rapidly arising in the acute phase of the disease so that it is possible to observe in lesions in several stages of maturation. Going ahead with the disease, inflammation and erythema may spread to the fingers and the wrists, and painful rhagadiform lesions may appear.

PPP mainly occurs in middle-aged persons, more often females, even if we can't rule out a more premature exordium in child's age. Even if in around half of the patients, the disease can start with unilateral lesions, it is any way inclined to be symmetrically present on the extremities. The presence (contemporary or diachronic) in the same subject of pustular lesions together with lesions peculiar of other forms of psoriasis is not unusual, even if the real incidence of this association is still discussed [6, 7].

PPP can be associated with osteoarthritis, in a multifocal recurrent chronic form (CRMO) [8] or the sternocostoclavicular hyperostosis (SCCH), in this last case configuring the so-called SAPHO (Synovitis, Acne, Pustulosis, Hyperostosis, Osteomyelitis) syndrome [9].

The diagnosis of PPP is essentially clinical, possibly held up by laboratory studies; though these may be usually insignificant (there is the possibility of a transitory neutrophilic leucocytosis). Histopathology of the lesions shows different aspects according to the stage of the disease. In the initial phase, intraepidermal vesicles containing mononuclear cells may be seen, caused by focal spongiosis. With the evolution of the lesion, neutrophils can be seen inside the vesicles, leading to the development of the typical subcorneal pustules in the latter phase. Usually, a cultural test of the pustulosis gives a negative result (sterile pustules). Many therapeutic options are nowadays available for PPP; however, none of them can be addressed to as the gold standard treatment [10].

Topical high potency corticosteroids, alone or in association with salicylic acid or vitamin D analogues, are still considered the best treatment for PPP [11]. This approach is effective in a large percentage of patients, yet doesn't seem to possess the capability for a long-term control of the disease doesn't prevent the recurrences, and the event of tachyphylaxis and side effects are major contraindications for its continuous use [12]. Better results can be obtained with systemic corticosteroids [13] and with oral acitretin [14], but the possible side effects, and the worsening of psoriasis that can be experienced early after their interruption makes them desirable only for particularly selected cases. Oral colchicine [15] leads to good results, but its use is limited by side effects like diarrhoea and nausea. Systemic cyclosporine A has proven efficacy in the control of the disease [16], but quick relapses after its interruption and the well-known collateral effects connected by the intrinsic characteristics of the drug (arterial hypertension, renal insufficiency, nausea and tiredness) limit its use [17]. A few studies quest for the possibility to recur to local administration of methotrexate-based gel [18], but the experience is still anecdotic.

In recent years, the new biological therapies (monoclonal antibodies, receptor fusion proteins and similar) have been developed to manage psoriasis in its inner mechanisms of immune regulation. In the clinical experiences with these new generation drugs, there are some reports of PPP successfully treated with efalizumab, alefacept, infliximab, adalimumab, and etanercept [10]. However, the legal (i.e. FDA and EMA-approved use of biologics in psoriasis) and scientific limitations (i.e. guidelines) for the use of biologics, together with the major possible medical involvements connected to this category of therapeutic agents, make of them a treatment dedicated to a few well-chosen patients and it is off-label.

Among the physical therapies, PUVA therapy, probably in association with oral retinoids (RePUVA) [19] has been used for pustular psoriasis.

The efficacy of UVB light in psoriasis has been largely demonstrated (10, 11, 19) so that nowadays UVB treatment may be considered the first-line treatment in many forms of psoriasis. UVB treatments can be safely used in pregnant women and children, and are related to less erythema in respect of UVA, no phototoxic effects and no epidermal thickening after long-term irradiation. No statistical differences have been shown between PUVA and UVB regarding success rates [19].

However, during the last years focused phototherapy with narrowband UVB (307-311 nm) showed a similar efficacy, but without a risk of secondary skin cancer development [21-24]. This therapeutical approach considers that psoriasis patients undergoing phototherapy usually receive high cumulative doses of radiation during their lives, thus leading to secondary cutaneous disorders, like photoaging, teleangectasias, excessive tanning, etc. On the contrary, a phototherapic device capable of delivering the UV-radiation only to affected areas could lower all these collateral effects dramatically decreasing the total dose of radiation. Moreover, the treatment may be tailored to each affected area with different doses of UV.

The monochromatic excimer light (MEL) device delivers a UVB wavelength at 308 nm only to the lesional skin, and seems particularly effective for variants of psoriasis were the involvement of the skin is lower than 20-25% of the total body surface. Its high potency (up to 4.5 J/cm^2) and subsequently the need for short time of irradiation, together with the possibility to schedule just 1 session per week, makes MEL mostly appreciated to a large part of patients, thus increasing treatment compliance, which is particularly useful when we have to deal with long-lasting therapeutic protocols. Finally, the possibility to focus the radiations on skin lesions reduces the risks of acute and chronic side effects in the uninvolved safe skin.

In conclusion, our experience scores another point in favour of focused narrowband UVB treatments for localised psoriasis, showing once more its efficacy, relative rapidity of action and safety. Moreover, in our opinion, the efficacy of MEL on localised pustular psoriasis, a challenging clinical picture, which management is often difficult both for the patient and the dermatologist, makes it one of the best weapons we have to fight, and win, against this disease.

References

1. Meier M, Sheth PB. Clinical spectrum and severity of psoriasis. Curr Probl Dermatol. 2009;38:1-20. https://doi.org/10.1159/000232301 PMid:19710547

2. Mavilia L, Mori M, Rossi R, Campolmi P, Puglisi Guerra A, Lotti T. 308 nm monochromatic excimer light in dermatology: personal experience and review of the literature. G Ital Dermatol Venereol. 2008;143:329-337. PMid:18833074

3. Tauber M, Bal E, Pei XY, Madrange M, Khelil A, Sahel H, Zenati A, Makrelouf M, Boubridaa K, Chiali A, Smahi N, Otsmane F, Bouajar B, Marrakchi S, Turki H, Bourrat E, Viguier M, Hamel Y, Bachelez H, Smahi A. IL36RN mutations affect protein expression and function: A basis for genotype-phenotype correlation in pustular diseases. J Invest Dermatol. 2016;136:1811-1819. https://doi.org/10.1016/j.jid.2016.04.038 PMid:27220475

4. Naldi L. Epidemiology of psoriasis. Curr Drug Targets Inflamm Allergy. 2004;3(2):121-8. https://doi.org/10.2174/1568010043343958 PMid:15180464

5. Farley E, Masrour S, McKey J, Menter A. Palmoplantar psoriasis: a phenotypical and clinical review with introduction of a new quality-of-life assessment tool. J Am Acad Dermatol. 2009;60:1024-1031. https://doi.org/10.1016/j.jaad.2008.11.910 PMid:19467374

6. Yamamoto T. Extra-palmoplantar lesions associated with palmoplantar pustulosis. J Eur Acad Dermatol Venereol. 2009;23:1227-1232. https://doi.org/10.1111/j.1468-3083.2009.03296.x PMid:19453807

7. Brunasso AMG, Massone C. Can we really separate palmoplantar pustulosis from psoriasis? J Eur Acad Dermatol Venereol. 2010;24:619-621. https://doi.org/10.1111/j.1468-3083.2010.03648.x PMid:20337817

8. Stam MA, Bloem JL, De Schepper AM. Chronic recurrent multifocal osteomyelitis associated to psoriasis. JBR-BTR. 2007;90:212-213. PMid:17696102

9. Sallés M, Olivé A, Perez-Andres R, Holgado S, Mateo L, Riera E, Tena X. The SAPHO syndrome: a clinical and imaging study. Clin Rheumatol. 2011;30:245-249. https://doi.org/10.1007/s10067-010-1560-x PMid:20878342

10. Benjegerdes KE, Hyde K, Kivelevitch D, Mansouri B. Pustular psoriasis: pathophysiology and current treatment perspectives. Psoriasis: Targets Therapy 2016; 6:131-144. https://doi.org/10.2147/PTT.S98954

11. Marsland AM, Chalmers RJ, Hollis S, Leonardi-Bee J, Griffiths CE. Interventions for chronic palmoplantar pustulosis. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD001433. PMid:16437433

12. Laws PM, Young HS. Topical treatment of psoriasis. Expert Opin Pharmacother. 2010;11:1999-2009. https://doi.org/10.1517/14656566.2010.492778 PMid:20569091

13. Tempark T, Phatarakijnirund V, Chatproedprai S, Watcharasindhu S, Supornsilchai V, Wananukul S. Exogenous Cushing's syndrome due to topical corticosteroid application: case report and review literature. Endocrine. 2010;38:328-334. https://doi.org/10.1007/s12020-010-9393-6 PMid:20972726

14. Lee CS, Li K. A review of acitretin for the treatment of psoriasis. Expert Opin Drug Saf. 2009;8:769-79. https://doi.org/10.1517/14740330903393732

15. Stefanaki C, Kontochristopoulos G, Kedikoglou S, Hatziolou E, Zakopoulou N. Subcorneal pustular dermatosis associated with palmo-plantar pustular psoriasis: response to colchicine therapy. J Dermatol. 2004;31:946-948. https://doi.org/10.1111/j.1346-8138.2004.tb00634.x PMid:15729873

16. Adişen E, Tekin O, Gülekon A, Gürer MA. A retrospective analysis of treatment responses of palmoplantar psoriasis in 114 patients. J Eur Acad Dermatol Venereol. 2009;23:814-819. https://doi.org/10.1111/j.1468-3083.2009.03197.x PMid:19470063

17. Erkko P, Granlund H, Remitz A, Rosen K, Mobacken H, Lindelöf B, Reitamo S. Double- blind placebo-controlled study of long-term low-dose cyclosporin in the treatment of palmoplantar pustulosis. Br J Dermatol. 1998;139:997-1004. https://doi.org/10.1046/j.1365-2133.1998.02555.x PMid:9990362

18. Kumar B, Sandhu K, Kaur I. Topical 0.25% methotrexate gel in a hydrogel base for palmoplantar psoriasis. J Dermatol. 2004;31:798-801. https://doi.org/10.1111/j.1346-8138.2004.tb00602.x PMid:15672706

19. Redon E, Bursztejn AC, Loos C, Barbaud A, Schmutz JL. A retrospective efficacy and safety study of UVB-TL01 phototherapy and PUVA therapy in palmoplantar psoriasis. Ann Dermatol Venereol 2010;137:597-603. https://doi.org/10.1016/j.annder.2010.06.016 PMid:20932438

20. Han L, Somani AK, Huang Q, Fang X, Jin Y, Xiang LH, Zheng ZZ. Evaluation of 308-nm monochromatic excimer light in the treatment of psoriasis vulgaris and palmoplantar psoriasis. Photodermatol Photoimmunol Photomed. 2008;24:231-236. https://doi.org/10.1111/j.1600-0781.2008.00364.x PMid:18811863

21. Bianchi B, Campolmi P, Mavilia L, Danesi A, Rossi R, Cappugi P. Monochromatic excimer light (308 nm): an immunohistochemical study of cutaneous T cells and apoptosis-related molecules in psoriasis. J Eur Acad Dermatol Venereol. 2003;17:408-413.

https://doi.org/10.1046/j.1468-3083.2003.00758.x PMid:12834450

22. Nisticò SP, Saraceno R, Stefanescu S, Chimenti S. A 308-nm monochromatic excimer light in the treatment of palmoplantar psoriasis. J Eur Acad Dermatol Venereol. 2006;20:523-526. https://doi.org/10.1111/j.1468-3083.2006.01503.x PMid:16684278

23. Wollina U, Koch A, Scheibe A, Seme B, Streit I, Schmidt WD. Targeted 307 nm UVB- phototherapy in psoriasis. A pilot study comparing a 307 nm excimer light with topical dithranol. Skin Res Technol. 2012;18:212-218. https://doi.org/10.1111/j.1600-0846.2011.00556.x PMid:22092772

24. Wollina U, Koch A, Scheibe A, Seme B, Streit I, Schmidt WD. Targeted 307 nm UVB- excimer light vs. topical dithranol in psoriasis. J Eur Acad Dermatol Venereol. 2012;26:122-3. https://doi.org/10.1111/j.1468-3083.2010.03972.x PMid:21251088

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Case Report

Subungual Nail Pigmentation and Malalignment of the Great Toe Nail in a Cancer Patient - A Diagnostic Challenge

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Keywords: Nail apparatus; subungual pigmentation; cancer; melanoma; hematoma.

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Abstract

Subungual pigmentation may have a variety of underlying pathologies, but clinicians should consider malignancies such as subungual melanoma or metastasis, even if they are not common. A delayed diagnosis can dramatically worsen the prognosis. Therefore, histologic examination is highly recommended. We present a 75-year-old female cancer patient presenting with subungual blackish pigmentation of the great toe nail for several years suspicious of a subungual melanoma even by dermoscopy. Nail avulsion and histological investigations excluded melanoma. The final diagnosis was subungual hematoma with growth malalignment of the great toe nail.

Introduction

Subungual pigmentation has a variable underlying pathology. The most common cause is subungual hematoma followed by infections of the nail apparatus. Vascular diseases including tumours and malformations represent important differential diagnoses [1].

It is most important not to overlook malignancies. Subungual metastases are uncommon. They most frequently occur in patients with primary malignant tumours of the lung (41%), genitourinary tract (17%), or breast (9%) [2].

Subungual melanoma is part of the acrolentiginous subtype with a worse prognosis due to diagnostic delay [3]. Subungual melanoma is the most common type in Asians, where melanoma is uncommon, while it is rare in Caucasians, where melanoma is raising [4]. Hutchinson's sign, i.e. the periungual extension of brown-black pigmentation from melanonychia onto the nail folds, is an important clinical indicator of subungual melanoma. Nevertheless, it is neither highly specific nor sensitive enough to confirm or exclude subungual melanoma [5, 6].

Case report

A 75-year-old female patient was referred to our department with a subungual hyperpigmentation of the right great toe nail suspicious of subungual

melanoma. She did not remember any recent trauma. The pigmentation had been there for a couple of years.

Her medical history was remarkable for a malignant mixed Mullerian tumour of the uterus T2, N1, L1, V0, R0 (FIGO Stage IIIc) surgically removed followed by brachytherapy three years ago. Afterwards, she developed a secondary lymphedema stage II of the legs. She suffered from arterial hypertension and rheumatoid arthritis.

On examination, we observed a dark blackish subungual pigmentation of the proximal lateral part of the right great toenail (Fig. 1). The nail plate was thickened in the lateral part and yellowish separated by Beau's line from the proximal part. There was a deviation of the long axis of the nail plate laterally, i.e. growth malalignment of the great toenail, not obvious on the contralateral foot. Stemmer's sign was positive on the toes due to chronic lymphedema of the legs. Dermoscopy was performed, but melanoma suspicion remained. The pigmentation was not homogeneous, globules were missing, and the distal margins were blurred.

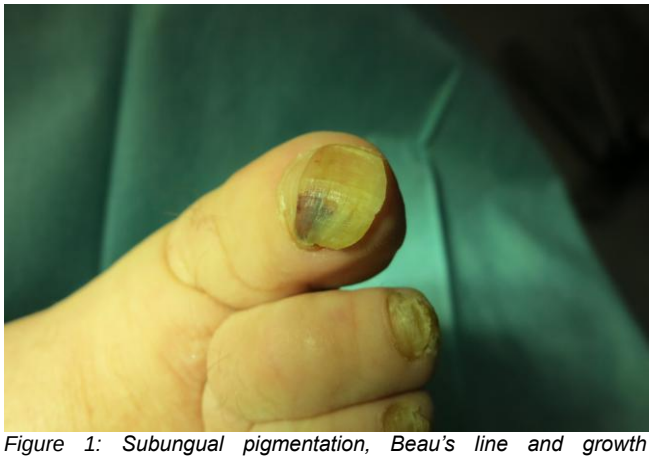

Figure 1: Subungual pigmentation, Beau's line and growth malalignment of the great toe nail associated with lymphedema

Diagnostic ultrasound excluded lymph node enlargement of the groins.

We performed a nail avulsion for diagnostic purposes. After Oberst's regional anaesthesia with 1% prilocaine, the nail elevator was introduced beneath the distal margin of the nail plate. The nail plate was separated from the hyponychium and the nail bed towards the proximal nail matrix. We performed a cut of the proximal nail fold and prepared laterally on each side two skin flaps to ensure a complete examination of the matrix. After that, the complete nail plate and nail matrix were removed (Fig. 2). By the naked eye, the bottom of the nail plate seemed almost free of pigment. The nail bed was completely free of pigmentation. Therefore, nail bed biopsy was omitted. The matrix zone was coagulated by bipolar pincer. The proximal flaps were sutured. A disinfectant ointment was applied, and the great toenail was covered by a sterile dressing. Wound healing was unremarkable.

Histologic evaluation of the nail plate excluded a pigmentary tumour but confirmed hematoma. Prussian blue stain for iron was positive.

Eventually, the following diagnosis was confirmed: Subungual hematoma of the great toenail in the case of malalignment of the great toe nail and rheumatoid arthritis.

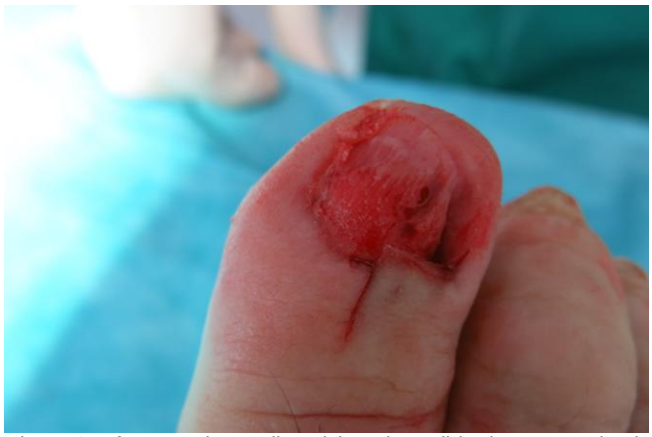

Figure 2: After complete nail avulsion, the nail bed was completely free of hyperpigmentation

Discussion

A subungual hematoma is common. It is an important differential diagnosis of subungual melanoma. The ABCD rule for melanoma has a low sensitivity and specificity for this melanoma subtype [3]. Dermoscopy may be helpful, but in cases of thickened nail plates, its value remains limited [7]. On the other hand, subungual melanoma may also imitate subungual hematoma [8]. Subungual melanoma has a poor prognosis due to delayed diagnosis. Therefore, every unclear subungual pigmentation needs a histologic evaluation [1].

In the present case, the patient suffered from secondary lymphedema after treatment of a malignant mixed Mullerian tumour of the uterus and rheumatoid arthritis. Lymphedema and rheumatoid arthritis may have contributed to the yellowish colour of the nail plate causing a yellow nail syndrome [9, 10].

Growth malalignment is either a congenital disease caused by desynchronization of growth between the nail and the adherent end-phalanx of the hallux resulting in temporarily larger nail plates, which are gliding laterally, to fit into the underlying bony space [11, 12]. Acquired growth malalignment of the great toe nail can also be a consequence of trauma [13].

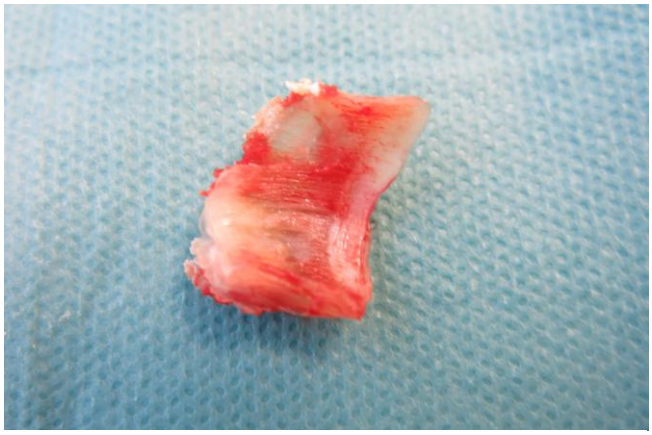

Figure 3: The removed nail (bottom view) with remarkable thickening of the nail plate but without marked pigmentation

The patient had worked in a brewery where she used to move the beer boxes with her feet causing repeated trauma to the nail apparatus of the great toe nail. In consequence, Beau's line may have evolved [14]. The secondary changes of the nail plate were responsible for the limited benefit of dermoscopy to confirm hematoma. If dermoscopy had been suspicious for subungual hematoma, we would have performed a punch biopsy only. But in this case, we decided to perform nail avulsion.

In conclusion, the subungual hematoma is a possible imitator for subungual melanoma. In any case of suspicious subungual pigmentation, diagnosis needs to be confirmed by histology without unnecessary delay [1].

References

1. Wollina U, Nenoff P, Haroske G, Haenssle HA. The diagnosis and treatment of nail disorders. Dtsch Arztebl Int. 2016;113:509-518. PMid:27545710

2. Cohen PR. Metastatic tumors to the nail unit: subungual metastases. Dermatol Surg. 2001;27:280-293. https://doi.org/10.1097/00042728-200103000-00014

3. Tronnier M, Semkova K, Wollina U, Tchernev G. Malignant melanoma: epidemiologic aspects, diagnostic and therapeutic approach. Wien Med Wochenschr. 2013;163:354-358. https://doi.org/10.1007/s10354-013-0207-3 PMid:23715934

4. Kim SY, Yun SJ. Cutaneous melanoma in Asians. Chonnam Med J. 2016;52:185-193. https://doi.org/10.4068/cmj.2016.52.3.185 PMid:27689028 PMCid:PMC5040767

5. Baran R, Kechijian P. Hutchinson's sign: a reappraisal. J Am Acad Dermatol. 1996;34:87-90. https://doi.org/10.1016/S0190-9622(96)90839-7

6. Tchernev G, Chokoeva AA, Wollina U, Lotti T. Persistent subungual and periungual hematoma versus melanoma: to cut it or to leave it? Dermatol Ther. 2016;29:150-151. https://doi.org/10.1111/dth.12293 PMid:26333508

7. Mun JH, Kim GW, Jwa SW, Song M, Kim HS, Ko HC, Kim BS, Kim MB. Dermoscopy of subungual haemorrhage: its usefulness in differential diagnosis from nail-unit melanoma. Br J Dermatol. 2013;168:1224-1229. https://doi.org/10.1111/bjd.12209 PMid:23302009

8. Deinlein T, Hofmann-Wellenhof R, Zalaudek I. Acral melanoma mimicking subungual hematoma. J Am Acad Dermatol. 2016;75:e181-e183. https://doi.org/10.1016/j.jaad.2016.02.1222 PMid:27745646

9. Chaniotakis I, Bonitsis N, Stergiopoulou C, Kiorpelidou D, Bassukas ID. Dizygotic twins with congenital malalignment of the great toenails: reappraisal of the pathogenesis. J Am Acad Dermatol. 2007;57:711-715. https://doi.org/10.1016/j.jaad.2007.05.033 PMid:17692994

10. Kaatz M, Wenzel H-C, Trebing D, Barta U, Wollina U. Yellow-Nail-Syndrom. Med Welt. 1997;48:501-503.

11. Mishra AK, George AA, George L. Yellow nail syndrome in rheumatoid arthritis: an aetiology beyond thiol drugs. Oxf Med Case Reports. 2016;2016:37-40. https://doi.org/10.1093/omcr/omw013 PMid:26989491 PMCid:PMC4794558

12. Decker A, Scher RK, Avarbock A. Acquired congenital malalignment of the great toenails. Skin Appendage Disord. 2016;1:147–149. https://doi.org/10.1159/000441391 PMid:27171597 PMCid:PMC4857820

13. Wollina U, Wollina K. Growth malalignment of the great toenails - A cause of chronic relapsing paronychia in infants. Z Hautkrankh. 1995;70:35-37.

14. Braswell MA, Daniel CR 3rd, Brodell RT. Beau lines, onychomadesis, and retronychia: A unifying hypothesis. J Am Acad Dermatol. 2015;73:849-855. https://doi.org/10.1016/j.jaad.2015.08.003 PMid:26475537

ID Design 2012/DOOEL Skopje, Republic of Macedonia
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Case Report

A Primary Cutaneous Nocardiosis of the Hand

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Keywords: Actinomycetes; Nocardiosis; Hand; Antibiosis; Sabauroud agar; Primary cutaneous infection.

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Abstract

BACKGROUND: Nocardiosis is caused by an aerobic actinomycete, most commonly introduced through the respiratory tract. The *Nocardiae* are gram-positive, partially acid-fast bacteria. Primary cutaneous nocardiosis infections are rare and caused by the traumatic introduction of organisms percutaneously. The manifestation is usually an opportunistic infection. Cutaneous involvement may develop as one of four types: mycetoma, lymphocutaneous infection, superficial skin infection, or systemic disease with cutaneous involvement. Diagnosis and evaluation of appropriate specimens are principally by culture.

CASE PRESENTATION: A 55-year-old female patient with diabetes type II presented with chronic skin lesions on the hand. Otherwise, her medical history was unremarkable. There were no signs of systemic disease. Direct examination of swabs demonstrated gramme bacteria and culture on Sabouraud agar was positive for *Nocardia spp*. The specimen of nocardiae was not identified. The patient was treated during nine months with sulfamethoxazole plus trimethoprim. There was an important clinical improvement of the cutaneous aspect of the lesions in hand. Some scars and fibrosis remained after nocardiosis.

CONCLUSIONS: Primary cutaneous nocardiosis of the hand is a rare condition. The clinical diagnosis is difficult, and culture is mandatory.

Introduction

The genus *Nocardia* has widely distributed a group of bacteria found in soil, organic matter, fresh and salt water. *Nocardia* and *Rhodococcus* belong to the family *Nocardiaceae* of the suborder of so-called aerobic actinomycetes that includes *Mycobacterium*, *Corynebacterium*, *Gordona*, and *Tsukamurella*. *Nocardia* includes more than 50 different species, but *N. asteroids complex* is responsible for most of the human infections [1]

Nocardia is aerobic, filamentous gram-positive, atypical acid-fast bacteria that can cause localised or systemic infections mostly in immunocompromised patients, i.e. post-transplantation, in renal insufficiency, chronic lung disease, human immunodeficiency, cancer and lymphoma or HIV/AIDS. Infections occur either by inhalation or direct skin inoculation [1]

Primary cutaneous nocardiosis, however, is a rare disease characterised by nodules, subcutaneous abscess formation, ulcerations, pyoderma or cellulitis. In contrast to systemic nocardiosis, mostly immunocompetent patients get affected. The most frequently isolated species is *N. brasilensis. N asteroides* and *Nocardia otitidiscaviarum* and some other species have only occasionally been isolated [1, 2]

The major differential diagnoses of primary cutaneous nocardiosis are bacterial soft tissue infections caused by *Staphylococcus aureus* or *Streptococci spp.*, but nocardiosis tends to be more indolent. An untreated infection can develop into lymphocutaneous nocardiosis with sporotrichosis and ulceroglandular tularemia as important differential diagnoses. Nocardia bacteriemia is uncommon [3, 4]

Case Report

A 55-year-old female patient from Brazil presented with a chronic skin lesion on the hand. She suffered from diabetes mellitus type II but had no other risk factors in her medical history.

On examination, we observed an erythematous lesion on her right hand with plaque-like thickening and superimposed partly ulcerated nodules (Fig. 1 a, b). The lesion was moderately painful. There was no lymphadenopathy. Ultrasound investigations remained unremarkable.

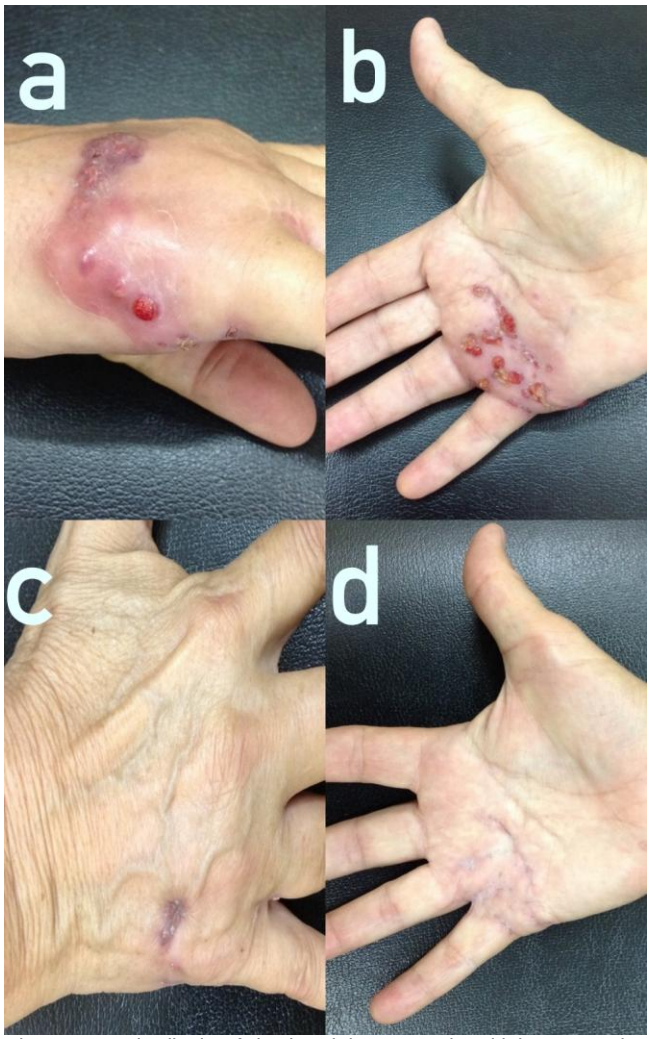

Figure 1: Nodardiosis of the hand (Mycetoma). Initial presentation with inflammatory plaques and nodules of the hand partially ulcerated (a, b). Complete remission with scarring after nine months of antibiosis (c, d)

Direct microbiological examination demonstrated gram-positive bacteria. After ten day-culture on Sabouraud dextrose agar at 35 degrees, Celsius colonies with a chalky appearance and purple or white colour could be identified. The texture was smooth or heaped. Microscopy of the colonies revealed gram-positive branching filaments of 0.8 µm diameter characteristic for *Nocardia spp* (Fig. 2). Unfortunately, molecular techniques for *Nocardiae spp* were not available.

A biopsy was taken for histology which found pustules and fragments of granulation tissue were seen with neutrophilic infiltration. Granulomatous alterations were absent. Intense neutrophilic infiltrates with a pustule and abscess formation is characteristic for cutaneous infection by *Nocardia spp.* The diagnosis of primary cutaneous nocardiosis was confirmed.

The patient was treated during nine months with 160 mg trimethoprim- 800 mg sulfamethoxazole twice daily. There was an important clinical improvement of the cutaneous aspect of the lesions in hand. Some scars and fibrosis remained after nocardiosis (Fig. 1 c, d).

Figure 2: Nocardia spp. on Sabauroud agar. Upper part – view from above, lower part – view from below

Discussion

Nocardia species are Gram-positive, weakly acid-fast with Kinyoun stain, and non-acid-fast with the Ziehl-Neelsen stain, and develop branching filaments only in aerobic culture. *Nocardia spp.* can be grown on Sabouraud agar, which is a selective medium for these bacteria. Colony morphology and

smell are other characteristics used for their identification [1, 5].

In a specialized laboratory analysis, 16S rDNA, multilocus sequence typing (MLST) using housekeeping genes for genotyping, or matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) is employed for species identification [6-9]. Unfortunately, molecular assays were not available in our case.

In Brazil, pulmonary disease is the most common nocardiosis [7]. *N. farcinica* and *N. asiatica* have been isolated from rare cases of primary cutaneous nocardiosis in Brazil [8]. Cutaneous involvement may develop as one of four types: superficial skin infection, mycetoma, lymphocutaneous infection, or systemic disease with cutaneous involvement [1]. Our patient can be classified into the first group. We treated the patient successfully with trimethoprim-sulfamethoxazole what is the most commonly used sulfonamide preparation. Some species are often resistant to this combined drug [8, 10]. Therefore, we can exclude *N. otitidiscaviarum*, *N. nova* and *N. farcinica* as responsible species for the primary cutaneous nocardiosis we observed.

Primary cutaneous nocardiosis of the hand, as in our patient, raises possible differential diagnoses, like staphylococcal or streptococcal soft tissue infections, ulceroglandular tularemia, or sporotrichosis [1]. Epitheloid cell sarcoma is another important differential diagnosis confirmed by histopathology [11]. In the case of mycetoma of the hand, the differential diagnosis confirmed by culture could be either eumycetoma or actinomycetoma. *Nocardia spp., Actinomadura spp.,* and *Streptomyces spp.* cause actinomycetoma, while eumycetoma is due to infection with *Madurella mycetomatis, Leptosphaeriae spp.,* and related species [12]. Mycetoma of the hand can lead to severe soft tissue and bone destruction [12]. In patients with the immunocompromising disease, primary cutaneous nocardiosis of the hand my lead to severe complications such as cellulitis-like nocardiosis [13], sporotrichoid nocardiosis [14] or necrotizing nocardiosis – an emergency [15].

In conclusion, nocardiosis should be considered even in immunocompetent patients with rather indolent infections of the hands. Rapid identification *Nocardia spp.*, early and sufficient antibiotic treatment ensure a good prognosis.

References

1. Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ Jr. Clinical and laboratory features of the Nocardia spp. Based on current molecular taxonomy. Clin Microbiol Rev. 2006;19:259-282. https://doi.org/10.1128/CMR.19.2.259-282.2006 PMid:16614249 PMCid:PMC1471991

2. Smego RA Jr, Gallis HA. The clinical spectrum of Nocardia brasiliensis infections in the United States. Rev Infect Dis. 1984;6:164-180. https://doi.org/10.1093/clinids/6.2.164

3. Kim YK, Sung H, Jung J, Yu SN, Lee JY, Kim SH, et al. Impact of immune status on the clinical characteristics and treatment outcomes of nocardiosis. Diagn Microbiol Infect Dis. 2016;85:482-487. https://doi.org/10.1016/j.diagmicrobio.2016.05.004 PMid:27241370

4. Chen B, Tang J, Lu Z, Wang N, Gao X, Wang F. Primary cutaneous nocardiosis in a patient with nephrotic syndrome: A case report and review of the literature. Medicine (Baltimore). 2016;95:e2490. https://doi.org/10.1097/MD.0000000000002490 PMid:26817885 PMCid:PMC4998259

5. Magalhães GM, Oliveira SC, Soares AC, Machado-Pinto J, de Resende MA. Mycetoma caused by Nocardia caviae in the first Brazilian patient. Int J Dermatol. 2010;49:56-58. https://doi.org/10.1111/j.1365-4632.2009.04263.x PMid:20465613

6. Du P, Hou X, Xie Y, Xu S, Li L, Zhang J, et al. Genotyping of Nocardia farcinica with multilocus sequence typing. Eur J Clin Microbiol Infect Dis. 2016;35:771-778. https://doi.org/10.1007/s10096-016-2596-x PMid:26972429

7. Baio PV, Ramos JN, dos Santos LS, Soriano MF, Ladeira EM, Souza MC, et al. Molecular identification of nocardia isolates from clinical samples and an overview of human nocardiosis in Brazil. PLoS Negl Trop Dis. 2013;7:e2573. https://doi.org/10.1371/journal.pntd.0002573 PMid:24340116 PMCid:PMC3854972

8. Condas LA, Ribeiro MG, Muro MD, de Vargas AP, Matsuzawa T, Yazawa K, et al. Molecular identification and antimicrobial resistance pattern of seven clinical isolates of Nocardia spp. In Brazil. Rev Inst Med Trop Sao Paulo. 2015;57:251-256. https://doi.org/10.1590/S0036-46652015000300012 PMid:26200967 PMCid:PMC4544251

9. Girard V, Mailler S, Polsinelli S, Jacob D, Saccomani MC, Celliere B, et al. Routine identification of Nocardia species by MALDI-TOF mass spectrometry. Diagn Microbiol Infect Dis. 2017;87:7-10. https://doi.org/10.1016/j.diagmicrobio.2016.09.024 PMid:27802877

10. Hashemi-Shahraki A, Heidarieh P, Bostanabad SZ, Hashemzadeh M, Feizabadi MM, Schraufnagel D, et al. Genetic diversity and antimicrobial susceptibility of Nocardia species among patients with nocardiosis. Sci Rep. 2015;5:17862. https://doi.org/10.1038/srep17862 PMid:26638771 PMCid:PMC4671095

11. Wollina U, Schönlebe J, Haroske G, Unger L, Kittner T, Tchernev G, Chokoeva AA, Lotti T. Nodular epitheloid sarcoma of the upper limb. A case report and review of the literature. J Biol Regul Homeost Agents. 2015;29(Suppl):23-26. PMid:26016962

12. Omer RF, Seif El Din N, Abdel Rahim FA, Fahal AH. Hand mycetoma: The Mycetoma Research Centre experience and literature review. PLoS Negl Trop Dis. 2016;10:e0004886. https://doi.org/10.1371/journal.pntd.0004886 PMid:27483367 PMCid:PMC4970814

13. Asgeirsson H, Sigurdardottir B. Nocardiosis in immunocompromised host presenting as cellulitis. Laeknabladid. 2010;96:423-425. PMid:20519773

14. Wang AW, D'Cruz M, Leung M. Primary cutaneous nocardiosis of the hand: a case report and literature review. Hand Surg. 2002;7:155-157. https://doi.org/10.1142/S0218810402000868 PMid:12365059

15. Ricci JA, Weil AA, Eberlin KR. Necrotizing cutaneous nocardiosis of the hand: A case report and review of the literature. J Hand Microsurg. 2015;7:224-227. https://doi.org/10.1007/s12593-015-0173-7 PMid:26078549 PMCid:PMC4461627

ID Design 2012/DOOEL Skopje, Republic of Macedonia
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Case Report

A Misleading Anamnesis: Learning To Suspect

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Abstract

Leishmaniasis represents a complex, globally widespread opportunistic infection ranging from the visceral form, also called *kala-azar*, to the mucocutaneous and cutaneous disease. It is endemic in the Mediterranian Basin, *Leishmania infantum* being demonstrated as the main causative agent of autochthonous cases in Sicily, Italy. The long-term use of systemic antipsoriatic agents, including biotechnological drugs, may cause a higher susceptibility to opportunistic infections, so physicians maintain a high level of suspicion with treated patients. However, some skin tumours, because of the rare occurrence and/or the atypical clinical features, may mimic another kind of disease thus leading to a delay in diagnosis and treatment. An exemplary case is reported herein.

Case report

A 57-year-old Caucasian man, who was a farmer affected by psoriasis and treated with cyclosporine A periodically in the last two years, presented for the first time to our Unit with a one-year history of an asymptomatic, approximately round, well-demarcated lesion on the second finger of the left hand, reported as the possible consequence of a previous trauma or insect bite. In anamnesis, the patient revealed that indeed he had subsequently noticed a small bump, gradually increasing in size and elevating, but never experiencing pain in the affected area. Apart from psoriasis, medical history was also notable for the chronic obstructive pulmonary disease.

The lesion was initially treated with topical gentamycin/betamethasone cream for about one month, and then the patient commenced oral amoxicillin/clavulanate (2g/day) for two months. Because of the lack of any improvement, together with the further ulceration of the nodule, and having cutaneous leishmaniasis in mind as suspect diagnosis, general physician empirically prescribed rifampicin (600 mg/day for two months) and then oral itraconazole (200 mg/day for one month) with no significant changes of the clinical picture. He also proposed possible intralesional therapy with meglumine antimoniate, but the patient sought dermatological consultation.

Cutaneous examination revealed a firm, flesh-coloured, slightly erythematous eroded nodule, measuring 9 mm in diameter, located on the medial surface of the medial phalange, close to the interphalangeal joint. The skin surrounding the tumour was normal, except for xerosis with light scaling (Fig.1 and 2).

An x-ray film of the hand in two projections showed no evidence of bone abnormality. A biopsy specimen was obtained: hematoxylin-eosin staining revealed an ulcerated surface epithelium with hyperkeratosis and acanthosis and nests of non-pigmented atypical epithelioid cells at the dermo-epidermal junction; also, nests and trabeculae of neoplastic cells extended down to the reticular dermis.

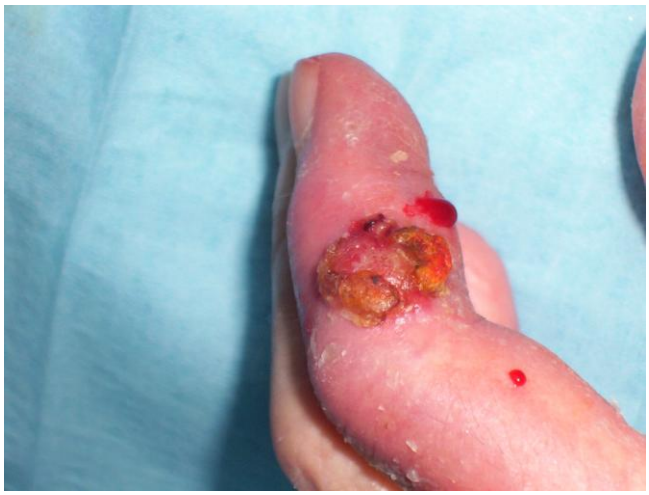

Figure 1: Ulcerated amelanotic nodule of the second finger, left hand

Frequent mitotic activity was present, with poor intra- or perilesional inflammation and no vascular involvement (Fig. 3 and 4); immunohistochemical staining, revealing strong S-100 and HMB-45 protein expression (Fig. 5), confirmed the diagnosis of amelanotic melanoma.

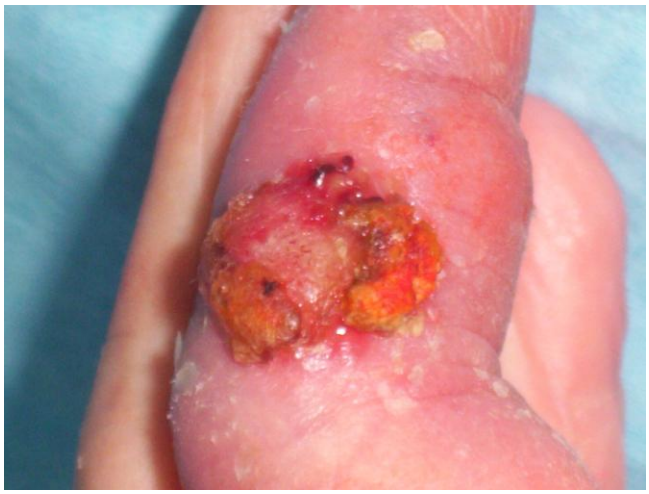

Figure 2: Particular of the lesion

Surgical excision of the neoplasm was requested, and the patient decided to continue the diagnostic and therapeutic procedure at another centre.

Discussion

Malignant melanoma (MM) is one of the most aggressive malignant neoplasms with a steadily increasing incidence in the last 30 years as well as mortality, despite the advances in treatment [1, 2]. When localised at acral body sites, it is much more frequent in dark-skinned and Oriental populations [3]. Typically, the clinical hallmark of cutaneous MM is the presence of pigment, varying from black to blue, to the shades of brown, tan, pink and white, within lesions with irregular contours on clinical examination [4].

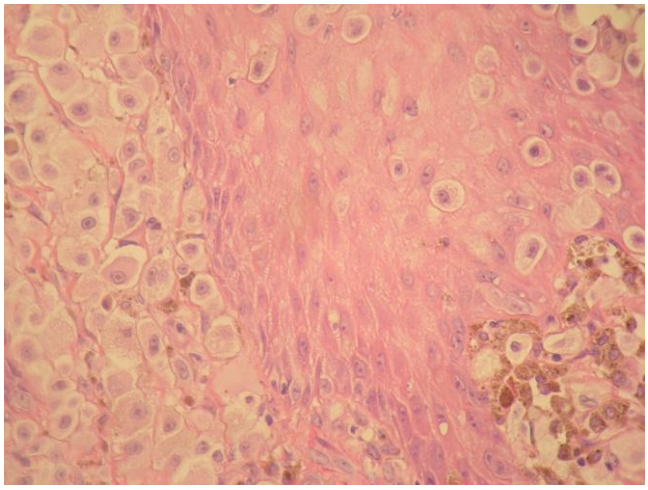

Figure 3: Histological view, H&E stain, original magnification x100 (detailed in the text)

On the contrary, amelanotic melanoma shows little or no pigment on visual inspection. Although the incidence of amelanotic melanoma among MM is low (2% to 8% of cases), the digits (and the subunguals) seem to be an area of predilection, a rate of about 25% of MM being amelanotic at these sites [5, 6]. In dermatologic consultation, the skilled eye of the specialized observer as well as dermoscopy, if applicable, are the unique instruments to make an often difficult diagnosis [7, 8], whereas radiographic studies of the part are useful to exclude bone lesions [9].

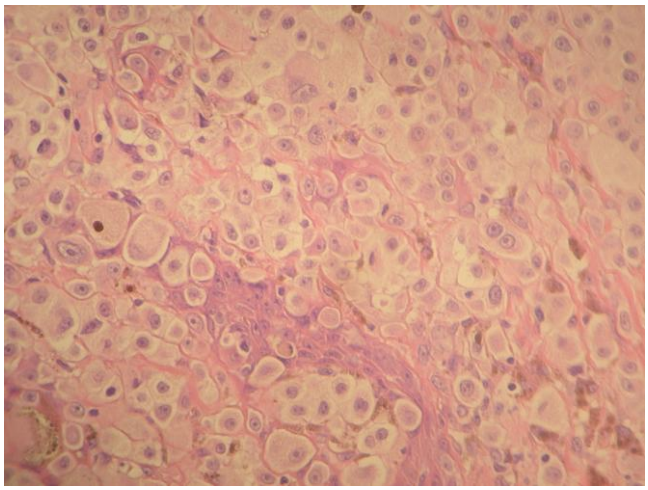

Figure 4: Histological view, H&E stain, original magnification x100 (detailed in the text)

In facts, there is still no evidence that amelanotic melanomas behave more aggressively than their pigmented counterpart, but the lack of pigmentation obviously adds further difficulties to an

already hard diagnosis. As in all types of MM, there is a direct relationship between increasing tumour thickness and decreasing survival time. Due to its atypical presentation, with consequent late detection, amelanotic melanoma is often diagnosed at a late stage of the disease with a worsened prognosis [4, 10].

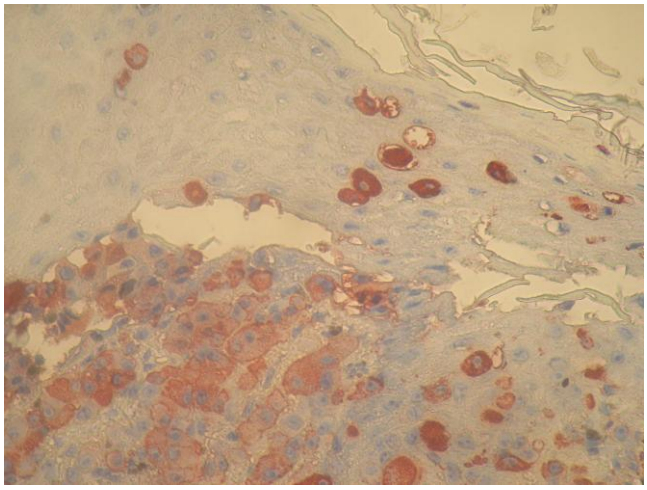

Figure 5: Immunohistochemical staining (HMB-45)

About our case, the confounding anamnesis represented an additional misleading, as the patient came from a rural area endemic for cutaneous leishmaniasis [11, 12] and the clinical picture of the condition was also evocative [13].

Also, immunosuppression in patients treated for the chronic autoimmune disease could theoretically facilitate the occurring of opportunistic infections [14]. This concern has to be dramatically stressed nowadays with the growing use of biotechnological drugs [15].

In conclusion, we presented the case with the aim of underlining the importance for physicians of performing incisional biopsies in the presence of clinically featureless cutaneous lesions. In particular, although asymptomatic, clearly growing amelanotic papules and nodules, with no of diagnostic criteria at imaging (e.g., Dermoscopy or x-ray) and with ulceration, should be histologically evaluated to exclude malignant melanoma at a first stage. Local or systemic prolonged medical treatments should be avoided in the absence of immediate improvement.

References

1. Thompson JT, Scolyer RA, Kefford RF. Cutaneous melanoma. Lancet. 2005;365(9460):687-701. https://doi.org/10.1016/S0140-6736(05)70937-5

2. Bevelacqua V, Bevelacqua Y, Candido S, Skarmoutsou E, Amoroso A, Guarneri C, Strazzanti A, Gangemi P, Mazzarino MC, D'Amico F, McCubrey JA, Libra M, Malaponte G. Nectin like-5 overexpression correlates with the malignant phenotype in cutaneous Melanoma. Oncotarget. 2012;3(8):882-92. https://doi.org/10.18632/oncotarget.594 PMCid:PMC3478464

3. Russo A, Ficili B, Candido S, Pezzino FM, Guarneri C, Biondi A, Travali S, McCubrey JA, Spandidos DA, Libra M. Emerging targeted therapies for melanoma treatment (review). Int J Oncol. 2014;45(2):516-24. https://doi.org/10.3892/ijo.2014.2481

4. Wada M, Ito T, Tsuji G, Nakahara T, Hagihara A, Furue M, Uchi H. Acral lentiginous melanoma versus other melanoma: A single-center analysis in Japan. J Dermatol. 2017. https://doi.org/10.1111/1346-8138.13834

5. Guarneri C, Valenti G. Question: can you identify this condition? Can Fam Physician. 2008;54(12):1697, 1698.

6. Kato T, Suetake T, Sugiyama Y, Tabata N, Tagami H. Epidemiology and prognosis of subungual melanoma in 34 Japanese patients. Br J Dermatol. 1996;134:383-387. https://doi.org/10.1111/j.1365-2133.1996.tb16218.x PMid:8731657

7. McClain SE, Mayo KB, Shada AL, Smolkin ME, Patterson JW, Slingluff CL Jr. Amelanotic melanomas presenting as red skin lesions: a diagnostic challenge with potentially lethal consequences. Int J Dermatol. 2012;51(4):420-6. https://doi.org/10.1111/j.1365-4632.2011.05066.x PMid:22435430 PMCid:PMC4465919

8. Guarneri C, Cannavò SP, Bevelacqua V, Urso C. A false diabetic foot ulcer. J Am Geriatr Soc. 2011;59(10):1964-6. https://doi.org/10.1111/j.1532-5415.2011.03610_3.x PMid:22091511

9. Guarneri C, Guarneri F, Risitano G, Lentini M, Vaccaro M. Solitary asymptomatic nodule of the great toe. Int J Dermatol. 2005;44(3):245-7. https://doi.org/10.1111/j.1365-4632.2004.02475.x PMid:15807738

10. Koch SE, Lange JR. Amelanotic melanoma: the great masquerader. J Am Acad Dermatol. 2000;42(5 Pt 1):731-4. https://doi.org/10.1067/mjd.2000.103981 PMid:10775846

11. Guarneri C, Guarneri F. Symmetrical cutaneous leishmaniasis. Acta Derm Venereol. 2005;85(3):281-2. https://doi.org/10.1080/00015550510026596

12. Alvar J, Velez ID, Bern C, herrero M, Desieux P. WHO Leishmaniasis Control Team: leishmaniasis worldwide and global estimates of its incidence. PLoS ONE. 2012;7:e35671. https://doi.org/10.1371/journal.pone.0035671 PMid:22693548 PMCid:PMC3365071

13. Guarneri C, Tchernev G, Bevelacqua V, Lotti T, Nunnari G. The unwelcome trio: HIV plus cutaneous and visceral leishmaniasis. Dermatol Ther. 2016;29(2):88-91. https://doi.org/10.1111/dth.12303 PMid:26555699

14. Ali T, Bronze MS, Kaitha S, Mahmood S, Ftaisi A, Stone J. Clinical use of anti-TNF therapy and increased risk of infections. Drug Health Patient Saf. 2013; 5:79-99. https://doi.org/10.2147/DHPS.S28801 PMid:23569399 PMCid:PMC3615849

15. Piaserico S, Conti A, Lo Console F, De Simone C, Prestinari F, Mazzotta A, Gualdi G, Guarneri C, Borsari S, Cassano N. Efficacy and safety of systemic treatments for psoriasis in elderly patients. Acta Derm Venereol. 2014;94(3):293-7. https://doi.org/10.2340/00015555-1719 PMid:24158307

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Case Report

Rapid Evolving Unilateral Indurated Oozing Facial Plaques in a Patient with Head-and-Neck Cancer: Peripheral T-Cell Lymphoma Not Otherwise Specified (NOS)

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Keywords: Peripheral T-cell lymphoma – not otherwise specified; Chemotherapy; R-CHOP; Facial plaques and nodules; Herpes; Bexarotene; Differential diagnosis.

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Abstract

BACKGROUND: The sudden development of facial plaques and nodules may be an alarming clinical sign for underlying malignancies. Nevertheless, a broad range of inflammatory and infectious diseases must be considered as well in the differential diagnosis.

CASE REPORT: We report on a 53-year-old male patient with a left-sided cheek infiltration with oozing but no lymphadenopathy. He had a medical history of head-and-neck cancer. The primary differential diagnosis was herpes zoster with secondary impetiginization or pyoderma facial. About eight weeks later, the patient presented with progressive formation of nodules and plaques on the face and isotretinoin was stopped. Skin biopsy suggested mycosis fungoid and an oral treatment with bexarotene was started. After limited response for another eight weeks, he returned later with massive facial swelling, nodules and impetiginization. Another skin biopsy was performed to exclude diagnostic error or investigate possible disease progression. Microscopic evaluation and multiplex-polymerase chain reaction confirmed the diagnosis of peripheral T-cell lymphoma, not otherwise specified (PTL-NOS), stage Ia (T1 N0 M0). Imaging techniques excluded metastatic spread. By interdisciplinary tumour board, R-CHOP (rituximab, cyclophosphamide, hydroxyl-doxorubicin, vincristine, and prednisolone) was recommended and initiated by hemato-oncologists.

CONCLUSIONS: PLT-NOS confirmed in the present patient has a poor prognosis with a 5-year survival rate of less than 20%.

Introduction

Sudden development of indurated facial plaques refers to a broader range of benign but also serious life threatening diseases. Various inflammatory disorders are warranting consideration in the differential diagnosis.

Pyoderma facial or rosacea fulminant is characterised by erythematous indurated and painful plaques, sometimes oozing. It can develop unilaterally but is a rare diagnosis in males in contrast to females [1]. Sweet syndrome is a rare neutrophilic disease with rapid onset, fever, neutrophilic leukocytosis and painful cutaneous plaques, which may involve the face [2].

Well's syndrome or eosinophilic cellulitis is a rare disorder characterised by flame figures of eosinophils in dermal tissue. Pruritic cellulitis-like plaques may masquerade as bacterial facial infection [3]. Granuloma faciale is an uncommon, chronic inflammatory disorder initially described as eosinophilic granuloma, responding to corticosteroids, and shares the apple jelly phenomenon on diascopy with sarcoidosis [4].

Histiocytic diseases may affect the facial skin. Benign cutaneous Rosai-Dorfman disease - a rare, non-Langerhans cell histiocytosis, affects the facial skin in about 11% of cases with erythematous plaques [5]. Disseminated xanthogranuloma typically involves periorbital skin [6].

Among infectious disorders, cutaneous leishmaniasis is emerging in non-epidemic areas. The disease is caused by vector-borne protozoal cutaneous infection by several species of *Leishmania* transmitted by sandflies [7, 8].

In the case of immunosuppression, bacterial papillomatosis and severe facial soft tissue infections may develop [9]. Invasive zygomycosis is another potentially fatal infection [10]. Malignancies need to be taken into consideration in any atypical case of facial nodular plaque-type affection, as the following case report illustrates.

Case presentation

A 53-year-old male patient was admitted to our hospital in July 2016 because of a left sided cheek infiltration with oozing. We observed an oozing indurated nodular plaque of about 6 x 8 cm (Fig. 1A) but no lymphadenopathy. The primary differential diagnosis was herpes zoster with secondary impetiginization or pyoderma facial.

The patient was treated initially with oral acyclovir 5 x 800 mg /d plus 100 mg prednisolone/d (with tapering the dose) for seven days. Oozing diminished but infiltrates were still present.

After that isotretinoin therapy was initiated. Topical treatment consisted of disinfectant washings and fusidinic acid ointment. The marked lymphedema could be explained by a history of head-and-neck cancer (T2 N2 M0 G2 V1 R0) the year before with surgery, neck dissection and radiotherapy.

The patient returned in September 2016 (Fig. 1B). Since there was progress with nodules and lid oedema, isotretinoin was stopped, and a skin biopsy was performed. The working diagnosis was mycosis fungoides. Based on the cutaneous T-cell lymphoma (CTCL) diagnosis the patient was discussed in the interdisciplinary tumour board. Radiotherapy was impossible due to the previous radiotherapy of head-and-neck cancer. Therefore, oral treatment with 525 mg/ d bexarotene was started. There was progress in December leading to a cessation of bexarotene (Fig. 1C).

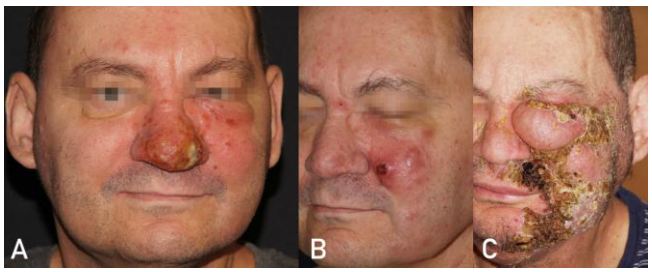

Figure 1: Peripheral T-cell lymphoma, not otherwise specified. (A) Initial presentation resembling herpes infection; (B) Worsening with an aspect of mycosis fungoides; (C) Further progression with massive lid oedema and secondary impetiginization

Another skin biopsy was performed. There was a dense inflammatory infiltrate in dermis and subcutis, but no interface dermatitis and no epidermal infiltration. Hair follicles were partly destroyed. The infiltrate consisted mostly of medium-sized polymorphous cells with notched nuclei and numerous mitoses. Some small lymphocytic cells and individual plasma cells and mast cells were intermingled (Fig. 2).

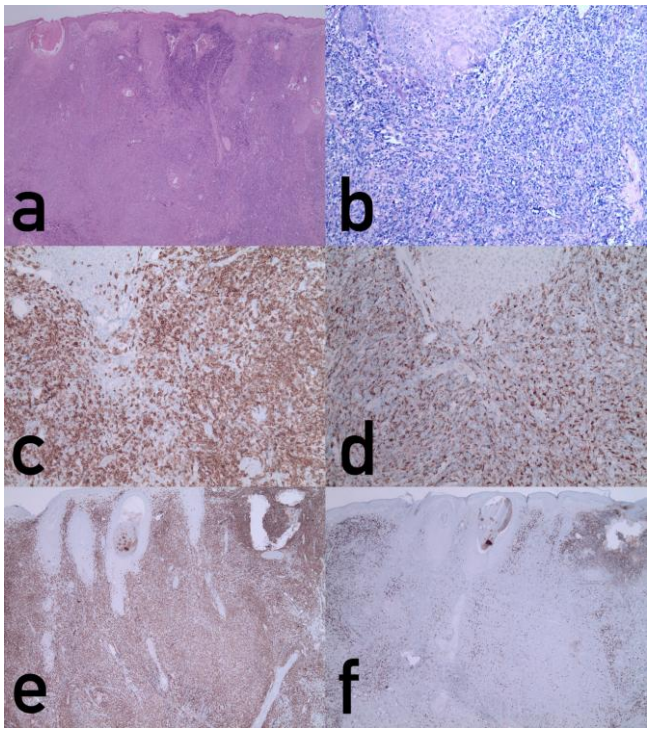

Figure 2: Histologic investigations. (a) Dense dermal infiltrate (hematoxylin-eosin x 4); (b) Detail – mononuclear cells with cellular atypia and atypical mitoses (hematoxylin-eosin x 10); (c) Strong expression of CD3 (immunoperoxidase x 10); (d) CD8 expression (immunoperoxidase x 10); (e) Beta-F1 expression (immunoperoxidase x 4; (f) Ki67 for proliferating cells (immunoperoxidase x 4)

Immunohistological findings are summarised in Table 1. After DNA extraction multiplex-polymerase chain reaction (PCR) had been performed to investigate clonality of cells (Institute of Pathology, University of Kiel, Germany) (Table 2). Monoclonality only could be demonstrated for T-cells, not B-cells.

Table 1: Immunohistological findings

Marker	Reactivity
CD1a	+ (for single cells only)
CD3	+++
CD4	(+)
CD5	+
CD7	+++
CD8	+++
CD10	-
CD20	+ (focally in the surrounding tissue by small lymphocytes)
CD30	-
CD56	-
CD68	+ (for single histiocytes only)
Bcl-6	-
Beta-F1 (T-cell receptor beta chain)	+++
Cyclin-D1	-
Ki67	++ (up to 60% of medium-sized cells)
PD1	+
Perforin	-

Imaging with diagnostic ultrasound and thoracic X-ray excluded metastatic spread. However, a parotic adenoma was identified. Laboratory investigations revealed an increased ratio of

CD3+CD4+/ CD3+CD8+ of 3.56 (normal range: 1.0-2.3).

The diagnosis of peripheral T-cell lymphoma, not otherwise specified (PTL-NOS), stage Ia (T1 N0 M0), was confirmed.

Table 2: Multiplex-PCR (bp – base pair; negative means polyclonality instead of monoclonality)

Beta-chain T-cell receptor gene		monoclonality
	A-multiplex PCR	247 & 248 bp
	B-multiplex PCR	253 & 261 bp
	C-multiplex PCR	193 & 303 bp
Gamma-chain T-cell receptor gene		
	va-multiplex PCR	negative
	vb-multiplex PCR	negative
Immunoglobulin heavy chain gene		
	F1-multiplex PCR	negative
	F2-multiplex PCR	negative
	F3-multiplex PCR	negative

By interdisciplinary tumour board, R-CHOP (rituximab, cyclophosphamide, hydroxyl-doxorubicin, vincristine, and prednisolone) was recommended and initiated in January by hemato-oncologists. The treatment is continued.

Discussion

Peripheral T-cell lymphoma (PTL) NOS is a rare but aggressive malignancy. The initial stages often resemble non-malignant plaque-type or nodular dermatoses as in the present case. These primary lesions may become infected and imitate an infectious disease [11].

In the differential diagnosis, other lymphomas need to be considered. The most common CTCL – mycosis fungoides - was the first suspicion. The aggressive course and the missing epidermotropism of atypical cells argued against. Because of the dominance of CD8+ lymphocytes in the second biopsy, primary cutaneous CD8-positive aggressive epidermotropic T-cell lymphoma (CD8+ AECTCL) had to be considered. AECTL is characterised by rapidly evolving erosive or necrotic plaques and nodules. Epidermotropic infiltrates of CD8+ atypical lymphocytes are the hallmark of CD8+ AECTCL, which exhibits a poor prognosis [12]. Again, in the present case, there was no epidermotropism at all, confirming the diagnosis of PTL-NOS.

PTL-NOS may present with single nodules or nodular plaques but tends to disseminate rapidly. Responses to radio- and chemotherapy a short-lived. Our patient has achieved a partial remission during R-CHOP therapy [Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Vincristine (Oncovin®), and Prednisolone].

Negative prognostic factors for PTL-NOS are age > 60, Eastern Cooperative Oncology Group (ECOG) performance status of ≥ 2, lactate dehydrogenase levels at normal values or above, and involvement of the bone marrow are independent predictors of decreased survival [13]. Prognosis is poor even with stem cell transplantation and systemic chemotherapy and radiotherapy with a 5-year survival rate of less than 20% [14].

In conclusion, sudden development of facial plaques and nodules can be a red flag of unknown malignancy. Even if routine laboratory tests are unremarkable and lymphadenopathy is absent, an aggressive lymphoma-like PTL-NOS in this case, may be present. Repeated skin biopsies are needed to confirm or exclude diagnosis. PTL-NOS, however, has a poor prognosis not improved substantially by systemic treatment.

References

1. Carter A, Viswanathan K, Shulman K. Sudden appearance of indurated erythematous plaques on a man's face. Case Rep Dermatol Med. 2016;2016:5192689. https://doi.org/10.1155/2016/5192689

2. Khan U, Rizvi H, Ali F, Lebovic D. Sweet syndrome: a painful reality. BMJ Case Rep. 2016;2016.

3. Gallard C, Law-Ping-Man S, Darrieux L, et al. Wells syndrome mimicking facial cellulitis: Three cases. Ann Dermatol Venereol. 2016 Nov 10. pii: S0151-9638(16)31089-4.

4. Ravikiran SP, Jaiswal AK, Syrti C, et al. Granuloma faciale: An unusual diascopic finding. Indian Dermatol Online J. 2016;7:174-176. https://doi.org/10.4103/2229-5178.182358 PMid:27294051 PMCid:PMC4886588

5. Al-Khateeb TH. Cutaneous Rosai-Dorfman disease of the face: A comprehensive literature review and case report. J Oral Maxillofac Surg. 2016;74:528-540. https://doi.org/10.1016/j.joms.2015.09.017 PMid:26455470

6. Klingner M, Hansel G, Schönlebe J, Wollina U. Disseminated necrobiotic xanthogranuloma. Hautarzt. 2016;67:902-906. https://doi.org/10.1007/s00105-016-3839-6 PMid:27380383

7. Wollina U, Koch A, Schönlebe J, et al. Non-healing facial lesions: cutaneous old world leishmaniasis in Dresden. J Biol Regul Homeost Agents. 2015;29(Suppl):99-102. PMid:26016983

8. Guarneri C, Wollina U, Chokoeva A, et al. A strange infiltrative plaque on the face. Braz J Infect Dis. 2016;20:214-215. https://doi.org/10.1016/j.bjid.2015.11.005 PMid:26748228

9. Markowicz M, Käser S, Müller A, et al. Bacillary angiomatosis presenting with facial tumor and multiple abscesses: A case report. Medicine (Baltimore). 2016;95:e4155. https://doi.org/10.1097/MD.0000000000004155 PMid:27428207 PMCid:PMC4956801

10. Abdel-Naser MB, Yousef N, el-Fakar NZ, et al. Invasive zygomycosis with a fatal outcome. Arch Dermatol. 2005;141:1211-1213. https://doi.org/10.1001/archderm.141.10.1211 PMid:16230557

11. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. Blood. 2005;105:3768-3785. https://doi.org/10.1182/blood-2004-09-3502 PMid:15692063

12. Kempf W, Rozati S, Kerl K, et al. Cutaneous peripheral T-cell lymphomas, unspecified/NOS and rare subtypes: a heterogeneous group of challenging cutaneous lymphomas. G Ital Dermatol Venereol. 2012;147:553-562. PMid:23149701

13. Gallamini A, Stelitano C, Calvi R, et al. Peripheral T-cell lymphoma unspecified (PTCL-U): a new prognostic model from a retrospective multicentric clinical study. Blood. 2004;103:2474-2479. https://doi.org/10.1182/blood-2003-09-3080 PMid:14645001

14. Rodriguez-Abreu D, Filho VB, Zucca E. Peripheral T-cell lymphomas, unspecified (or not otherwise specified): a review. Hematol Oncol. 2008;26:8-20. https://doi.org/10.1002/hon.836 PMid:18050364

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Case Report

Subungual Squamous Cell Carcinoma Associated with Long Standing Onychomycosis: Aggressive Surgical Approach with a Favourable Outcome

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Keywords: Subungual squamous cell carcinoma; nail neoplasms; HPV; viral wart; surgery; onychomycosis.

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Abstract

BACKGROUND: Tumours of the nail bed are rare. Squamous cell carcinoma is the most frequent among them. Chronic infection, chemical or physical trauma/microtrauma, genetic disorders such as congenital ectodermal dysplasia, radiation, tar, arsenic or exposure to minerals, sun exposure, immunosuppression, and previous HPV infection have all been discussed as etiologic factors. The diagnosis is often delayed because of the variety of clinical manifestations, often resembling benign or common infectious processes. Rapidly growing ulcerative lesions should also be considered as potential malignancy. Furthermore, a lack of antifungal or antibacterial treatment response is the most indicative symptom, always requiring subungual biopsy. Early diagnosis is of great importance for therapeutic effectiveness.

CASE PRESENTATION: We present a case of subungual squamous cell carcinoma, associated with long-lasting onychomycosis in a 76-year-old female patient, treated with amputation of the distal phalanx and the distal part of the proximal phalanx.

CONCLUSION: Although there are no available data in the literature to confirm or reject the contribution of the chronic nail infection to the malignant process, we emphasise the importance of this co-existence regarding the possible disguising of the malignant process. An early biopsy of a chronic persistent nail lesion may be preventive and beneficial regarding avoiding more aggressive treatments and achieving a favourable prognosis.

Introduction

Subungual squamous cell carcinoma (SSCC) is a rare malignancy, with few reported cases affecting the toe reported in the medical literature [1]. The aetiology of these lesions is poorly understood, and although this location is associated with low risk for metastasis, cases with inguinal lymph node metastasis after amputation of the affected toe have also been described [1]. The diagnosis is often delayed because of the variety of clinical manifestations, often resembling benign or common infectious processes [2]. For that reason, the real incidence of this tumour is difficult to determine [2, 3]. Although a standardised therapeutic approach does not currently exist, early diagnosis is essential for treatment effectiveness [3].

Case report

We present a 76-year-old Caucasian female patient who presented to the dermatology unit with a 3-year history of chronic, persistent ulceration on the left great toenail (Figure 1a). The diagnosis of onychomycosis was made three years ago, based on the clinical manifestation of yellowish discoloration of the nail, dystrophy of the nail, confirmed by direct

microscopy with KOH. No trauma was remembered by the patient, nor was there a history of viral warts. Arterial hypertension and arrhythmia were reported as comorbidities, well controlled with medications (Enalapril 10 mg 1-0-0, metoprolol 12.5 mg 1-0-0, and torasemid 20 mg 0-1-1). The initial symptoms were treated as an ordinary fungal infection with systemic administration of itraconazole and topical application of 40% urea cream, without significant effectiveness during the following year. Because of the lack of improvement, the nail bed was biopsied, and the diagnosis of SSCC was confirmed by histological examination (Figures 2a to d).

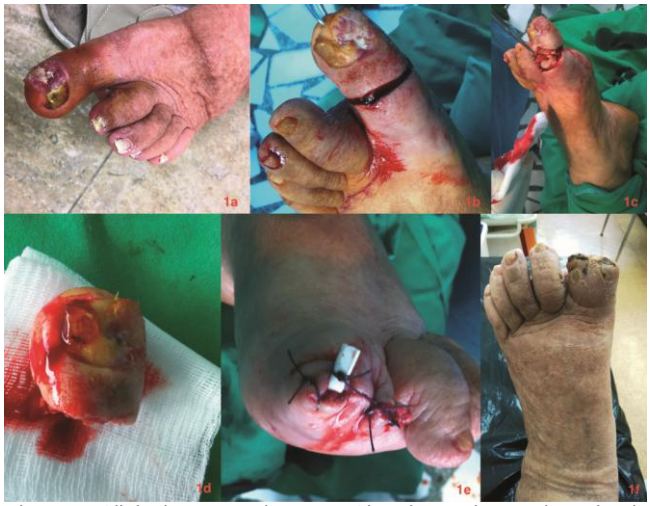

Figure 1: Clinical presentation: 1a - Chronic persistent ulceration in the left toe; 1b – Intraoperative findings. Skin incision; 1c – Disarticulation of the interphalangeal joint; 1d - The resected phalanx; 1e – Disarticulation completed - single layer suture and drainage; 1f – Clinical findings on the 16th postoperative day

Radiographic findings revealed cancer-mediated osteolysis. The patient underwent amputation of the distal phalanx of the left great toe and the distal part of the proximal phalanx (Figures 1a to d). Histopathological evaluation revealed low grade (moderately differentiated) invasive squamous cell carcinoma with vertical growth phase, multifocal superficial epidermal ulceration and non-invasive intraepidermal tumour component with histological degree – G2 and pathological staging – pT2NxMxV0L0R0. Image screening and laboratory testing did not show any evidence of disease progression or dissemination. At 17 months-follow-up the patient showed no signs of relapse.

Discussion

Disorders of the nail and nail bed are most frequently benign, and fungal infections account for approximately 50 % of them [3]. The remainder includes benign solid or cystic lesions and malignant neoplasms [3]. These conditions frequently resemble one another clinically, making the early and correct diagnosis of nail disorders a challenge [1,3]. Subungual tumours are rare [2]. SSCC is the most frequent among all of the histological variants, in contrast to basal cell carcinoma, which almost never affects this location [2]. Bowen's disease of the nail apparatus is an important differential diagnosis [4]. Nevertheless, SSCC is a rare entity compared to SCC in other locations [3]. It can arise either from the nail bed, nail matrix, nail groove, or lateral folds [3, 5]. SSCC often affects a single digit, with the thumb and the great toe being most frequently involved [1-3]. Multiple finger involvement has also been described [5]. The incidence is higher in men between the fifth and seventh decades of life [1, 2, 6, 7]. The rare occurrence and indolent natural history of SSCC, along with the higher prevalence of other benign conditions affecting the ungual apparatus, often mislead the physician with a subsequent delay in the correct diagnosis and therapy, potentially leading to disease progression [2].

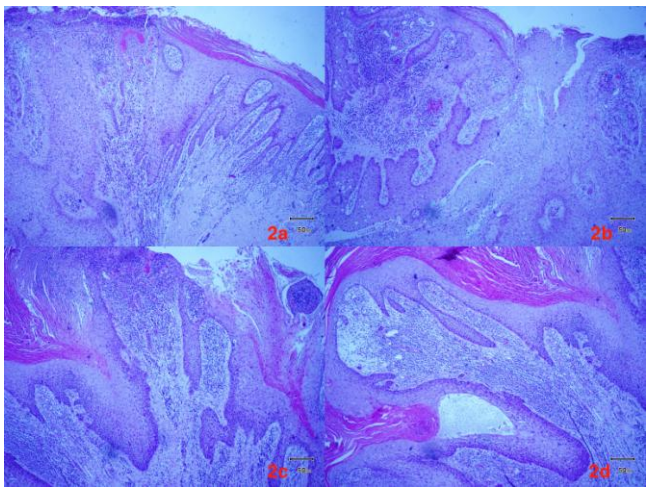

Figure 2: Histopathological findings (H-E staining, magnification 40x): 2a- Atypical keratinocytes extend from the epidermis into the dermis. Focal epidermal ulceration; 2b: Atypical cells have enlarged hyperchromatic nuclei with mitotic activity. Variable depth of dermal invasion. The stromal background consists of lymphocytes, plasma cells, and neutrophils; 2c: Epidermal papillomatosis and finger-like epidermal hyperplasia; 2d: Hyperkeratosis and keratin pearl formation. The non-specific inflammatory infiltrates with lymphocytes and plasma cells.

Chronic infection, chemical or physical trauma/microtrauma, genetic disorders such as congenital ectodermal dysplasia, radiation, tar, arsenic or exposure to minerals, sun exposure, immunosuppression, and previous HPV infection have all been discussed as etiologic factors that may contribute to malignant transformation [2]. HPV DNA has been recovered from 60% to 90% of cases of SSCC, and it has been stated that >60% are related to HPV 16 [2]. Although viral warts of the hands are also implicated as possible triggering factors for the development of SSCC, chronic HPV infection remains probably the most important factor, with or without the clinical presentation of conventional warts, which are rarely seen in patients with SSCC [2, 3].

In contrast to other locations, SSCC can cause very mild subjective symptoms, while at the same time presenting a variety of clinical manifestations [3]. Nonspecific ulcerative lesions or not significant swelling under the distal lateral edge of the nail can sometimes be the only presentations of the disease [3, 5]. Subungual, pigmented SCC presenting as grey longitudinal melanonychia has also been reported [6]. Late symptoms usually associated with an advanced process, including nodular lesions of the nail, bleeding, ulceration, or a large exophytic mass, are highly suggestive of malignancy [5, 6]. In particular, in any rapidly growing ulcerative lesion, a potential malignancy should be considered, especially SSCC [7]. Also, a lack of response to antifungal or antibacterial therapy is strongly suggestive of malignancy, virtually always requiring a subungual biopsy [6, 7].

Early diagnosis is of great importance for therapeutic effectiveness and to reduce the risk of recurrence or metastasis [8]. Although there is no standardised treatment for SSCC, wide local excision and simple excision are usually effective in early stages [1, 2, 8, 9]. The therapy of choice depends on the extent of the tumour and the presence or absence of underlying bone involvement [9, 10]. While lesions without bone involvement can be locally excised, amputation of the distal phalanx is usually the recommended treatment option for patients with bone infiltration [6]. Radiation therapy has also been reported as effective, depending on the tumour size and depth of invasion [9]. Possible bone involvement can be detected via imaging procedures [2, 6]. Exploratory nail plate removal and subsequent biopsy are advised in all patients with chronic nail conditions that fail to respond to conventional treatment for common infections [2]. Because of the high recurrence rate of SSCC, long-term follow-up is mandatory [2]

In conclusion, although chronic inflammation has been suggested as an etiological factor in SCC, it is still unclear whether chronic inflammation and in that case - persistent onychomycosis could trigger a malignant transformation of the nail bed, or such association is just an occasional finding. While there are no available data in the literature to confirm or reject the contribution of the chronic subungual or periungual infection to the malignant transformation, we emphasise the importance of this co-existence regarding the possible disguising of the malignant process.

References

1. Kelly KJ, Kalani AD, Storrs S, Montenegro G, Fan C, Lee MH, Wallack MK. Subungual squamous cell carcinoma of the toe: working toward a standardised therapeutic approach. J Surg Educ. 2008;65: 297-301. https://doi.org/10.1016/j.jsurg.2008.05.013 PMid:18707664

2. Batalla A, Feal C, Rosón E, Posada C. Subungual squamous cell carcinoma: a case series. Indian J Dermatol. 2014; 59: 352-354. https://doi.org/10.4103/0019-5154.135480 PMid:25071252 PMCid:PMC4103269

3. Bui-Mansfield LT, Pulcini JP, Rose S. Subungual squamous cell carcinoma of the finger. AJR Am J Roentgenol. 2005; 185: 174–175. https://doi.org/10.2214/ajr.185.1.01850174 PMid:15972419

4. Wollina U. Bowen's disease of the nail apparatus: a series of 8 patients and a literature review. Wien Med Wochenschr. 2015; 165: 401-405. https://doi.org/10.1007/s10354-015-0383-4 PMid:26376982

5. Meesiri S. Subungual squamous cell carcinoma masquerading as chronic common infection. J Med Assoc Thai. 2010; 93: 248–251. PMid:20302009

6. Gatica-Torres M, Arguello-Guerra L, Manuel Ruiz-Matta J, Dominguez-Cherit J. Subungual pigmented squamous cell carcinoma presenting as a grey longitudinal melanonychia in a young patient. BMJ Case Rep. 2016: pii: bcr2016215390. https://doi.org/10.1136/bcr-2016-215390

7. Wessendorf U, Bruch-Gerharz D, Homey B, Schulte KW. Subungual squamous cell carcinoma. An important differential diagnosis of subungual tumors. Hautarzt. 2009; 60: 282-283. https://doi.org/10.1007/s00105-009-1742-0 PMid:19296058

8. Kaksi SA, Ozdemir M, Balevi A, Cakir A, Tavh Y. Early diagnosis of subungual squamous cell carcinoma of the hallux. Dermatol Online J. 2015: pii: 13030/qt428217hj.

9. Wong KY, Ching DL, Gateley D. Subungual squamous cell carcinoma. BMJ Case Rep. 2015: pii: bcr2014207565, 2015. https://doi.org/10.1136/bcr-2014-207565

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Case Report

Hoigne Syndrome Caused by Intralesional Meglumine Antimoniate

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Keywords: Hoigne syndrome; adverse drug reaction; injection; meglumine antimoniate; leishmaniasis.

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Abstract

Hoigne syndrome (HS) is the term coined to describe an acute, non-allergic, psychiatrically based reaction occurring with a wide list of medications, mainly antibiotics. Since its first description by Hoigne and Schoch in 1959, few cases have been reported in medical literature and, although antimicrobials are commonly used, very rarely in dermatology. The authors describe the first case occurred after intralesional administration of meglumine antimoniate and briefly discuss the pathogenetic hypotheses on this atypical adverse drug reaction.

Introduction

Hoigne syndrome (HS) is the term coined to describe an acute, non-allergic, psychiatrically based reaction [1] occurring with a wide list of medications, mainly antibiotics (thus the other terms used as “pseudoanaphylactic reaction to procaine penicillin” [2], “acute psychotic syndrome after penicillin” [3] or “antibiomania [4]).

Since its first description by Hoigne and Schoch [5] in 1959 few cases have been reported in medical literature and, although antimicrobials are commonly used, very rarely in dermatology. No reports of HS with the use of antiparasitic drugs have also been found.

A 56-year-old woman sought attention because of an erythematous-infiltrative slowly progressing lesion of the medium dorsal third of the right forearm present for the last four months. At he beginning of the disease, the patient noticed a small red, itchy papule, which he treated as a mosquito bite using betamethasone/fusidic acid cream, with no significant improvement. A complete clinical evaluation showed the patient in good health, with a history of cutaneous superficial spreading melanoma seven years ago.

A 3 mm punch-biopsy was performed for diagnostic assessment and histologically stained with haematoxylin and eosin. Microscopic examination revealed a granulomatous dermic infiltrate, consisting of lymphocytes, histiocytes and multinuclear giant cells, being coherent with the clinical suspect of cutaneous leishmaniasis. Touch imprint from the biopsy specimen and microscopic examination (Giemsa stain) confirmed the diagnosis through the evidence of Leishmania amastigotes. Therapeutic regimen with N-methylglucamine antimoniate, 1 ml twice a week was proposed and the drug administered intralesionally at our clinic.

Immediately after the fourth injection of the drug, the patient presented confusion, disorganised

thinking, visual and auditory hallucinations. She also reported exaggerating anxiety and psychomotor agitation.

We provided laboratory tests including thyroid levels and toxicology, electrocardiogram together with neurological and psychiatric evaluation, all resulting within normal limits. A computer tomography of the brain was also unremarkable. In the further two days, the patient referred sleep disturbances with underlying anxiety and fear.

Antimonials were withdrawal, and a significant improvement of these symptoms was seen in the following days. The patient denied any previous similar manifestations to drugs as well as the personal and familial history of allergic/anaphylactic diseases in the past. He refused any further drug administration, including replacement with oral itraconazole, and the cutaneous disease remained unchanged.

HS is a sort of acute pseudoallergic reaction having psychiatric symptoms, disturbances of perceptions and intense anxiety as main clinical features, occurring with the administration, especially infusion, of a series of drugs, varying from anaesthetics to intralesional steroids and oral antibiotics.

Neurological signs and symptoms may present at a different degree, most cases including panic, fear of death, alteration of consciousness, hallucinations, accompanied by tachycardia, tachypnea, hypertension and numbness in the extremities [7].

Usually, the withdrawal of the offending drug leads to the rapid attenuation of symptoms, with excellent prognosis [1,3,5]. As many different drugs, with different pharmacodynamics and ways of administration, have been reported to cause acute psychiatric reactions, the complete improvement of the condition occurs in minutes to days [4,7,8].

The exact mechanism by some drugs may induce these effects remains largely unexplained and more than 200 pharmacological agents have been claimed as causative.

Local anaesthetics (lidocaine, procaine, cocaine) have been involved in the majority of case reports and suspected to be responsible for the development of limbic kindling through the facilitation of excitatory N-methyl-D-aspartate receptors [6,9] and a reduction in the inhibitory activity of gamma-aminobutyric acid (GABA) transmission [6,10]. This theory, however, requires previous sensitization to the anaesthetic that is not met in all cases of HS described in the medical literature [11].

Alternatively, it was speculated that drug microcrystals injection might cause microembolization of small vessels of the brain and/or lungs [12]. In fact, an embolism is a well-known biological phenomenon representing a possible complication of a variety of conditions [13,14], which can also involve any organ or apparatus with drug administration as well as it occurs locally with Nicolau syndrome [15] at the cutaneous level. Depending upon the size of these particles and their solubility in the blood, they can reach the diverse systems thus explaining such reactions [16]. Lastly, some authors postulated that the inhibition of the hepatic cytochrome P450 (CYP) isoenzymes, subclass CYP3A4, may play a role in the induction of neurological [17] and psychiatric [8] disorders.

Mediterranian basin is an endemic region for several parasitoses [18, 19]. Among these, cutaneous leishmaniasis is relatively frequent, mostly due to *Leishmania infantum* , carried by the female sandflies of *Phlebotomus perniciosus* [20].

Several drug therapies are effective in the treatment of cutaneous leishmaniasis [19] and antimonials have been widely used in localized forms [21]. In our experience intralesional meglumine antimoniate (Glucantime®) is useful and manageable, through the selective inhibition of enzymes involved in parasite anaerobic metabolism, with rapid clinical response and little discomfort for the patient [22].

To the best of our knowledge this is the first report of HS in course of antiparasitic drugs.

References

1. Araszkiewic A, Rybakowski JK. Hoigne's syndrome: a procaine induced limbic kindling. Med Hypoth. 1994;42:261-4. https://doi.org/10.1016/0306-9877(94)90128-7

2. Galpin JE, Chow AE, Yoshikawa TT, Guze LB. Pseudoanaphylactic reactions from inadvertent infusion of procaine penicillin G. Ann Intern med. 1975;81:358-61. https://doi.org/10.7326/0003-4819-81-3-358

3. Utley PM, Lucas JB, Billings TE. Acute psychotic reactions to aqueous procaine penicillin. South med J. 1966;59:1271-4. https://doi.org/10.1097/00007611-196611000-00005 PMid:5954416

4. Przybylo HJ, Przybylo JH, Todd Davis A, Cotè CJ. Acute psychosis after anaesthesia: the case of antibiomania. Pediatr Anaesth. 2005;15:703-5. https://doi.org/10.1111/j.1460-9592.2004.01525.x PMid:16029408

5. Hoigne R, Schoch K. Anaphylaktischer schock nd akute nichtallergische reaktionen nach procain-penicillin. Schweitz Med Wochenschr. 1959;89:1350-6. PMid:14402529

6. Araszkiewicz A, Rybakowski JK. Hoigne's syndrome, kindling, and panic disorder. Depress Anxiety. 1996-1997;4(3):139-43. https://doi.org/10.1002/(SICI)1520-6394(1996)4:3<139::AID-DA7>3.0.CO;2-B

7. Baran R. Proximal nail fold intralesional steroid injection responsible for Hoigne syndrome. J Eur Acad Dermatol Venereol. 2014;28:1563-5. https://doi.org/10.1111/jdv.12283 PMid:24164703

8. Rallis E, Moussatou V, Saltos L. Clarythromycin-induced Hoigne syndrome in a patient treated for rosacea. J Eur Acad Dermatol

Venereol. 2009;23:1092-115. https://doi.org/10.1111/j.1468-3083.2008.03085.x PMid:19207666

9. Mori N, Wada JA. Bidirectional transfer between kindling induced by excitatory amino acids and electrical stimulation. Brain Res. 1987;425:45-8. https://doi.org/10.1016/0006-8993(87)90481-1

10. Nutt E, Cowen P, Batts C, Smith D, Green A. Rejected administration of subconvulsant doses of GABA antagonist drugs. I. Effect on seizures threshold (kindling). Psychopharmacology. 1982;76:84-9. https://doi.org/10.1007/BF00430762 PMid:6281839

11. Thompson TM, Theobald JL. Hoigne syndrome: a little-known adverse effect of lidocaine. Am J Emerg med. 2016;34:679.e3-679.e4. https://doi.org/10.1016/j.ajem.2015.06.058 PMid:26175337

12. Mehrabian S, Raycheva MR, Petrova EP, Tsankov NK, Traykov LD. Neurosyphilis presenting with dementia, chronic chorioretinitis and adverse reactions to treatment: a case report. Cases J. 2009;2:8334. https://doi.org/10.4076/1757-1626-2-8334 PMid:19918420 PMCid:PMC2769430

13. Chu HJ, Lee CW, Yeh SJ, Tsai LK, Tang SC, Jeng JS. Cerebral Lipiodol Embolism in Hepatocellular Carcinoma Patients Treated with Transarterial Embolization/Chemoembolization. PLoS One. 2015;10(6):e0129367. https://doi.org/10.1371/journal.pone.0129367 PMid:26107693 PMCid:PMC4481105

14. Bevelacqua V, Bevelacqua Y, Candido S, Skarmoutsou E, Amoroso A, Guarneri C, Strazzanti A, Gangemi P, Mazzarino MC, D'Amico F, McCubrey JA, Libra M, Malaponte G. Nectin like-5 overexpression correlates with the malignant phenotype in cutaneous Melanoma. Oncotarget. 2012;3(8):882-92. https://doi.org/10.18632/oncotarget.594 PMid:22929570 PMCid:PMC3478464

15. Guarneri C, Polimeni G. Nicolau syndrome following etanercept administration. Am J Clin Dermatol. 2010;11 Suppl 1:51-2. https://doi.org/10.2165/1153426-S0-000000000-00000 PMid:20586511

16. Bredt J. Akute nicht-allergische reaktionen bei anwendung von depot-penicillin. Dtsch Med Wochenschr. 1965;90:1559. https://doi.org/10.1055/s-0028-1113375 PMid:14344427

17. Guarneri C, Polimeni G. Sclerosing lymphangitis of the penis after coadministration of tadalafil and fluconazole. Clin Exp Dermatol. 2009;34(7):e225-6. https://doi.org/10.1111/j.1365-2230.2008.03068.x PMid:19508584

18. Guarneri F, Puglese A, Giudice E, Guarneri C, Giannetto S, Guarneri B. Trombiculiasis: clinical contribution. Int J Dermatol. 2005;15(6):495-6.

19. Guarneri C, Tchernev G, Bevelacqua V, Lotti T, Nunnari G. The unwelcome trio: HIV plus cutaneous and visceral leishmaniasis. Dermatol Ther. 2016;29(2):88-91. https://doi.org/10.1111/dth.12303 PMid:26555699

20. Guarneri C, Wollina U, Chokoeva A, Lotti TM, Tchernev G. A strange infiltrative plaque on the face. Braz J Infect Dis. 2016;20(2):214-5. https://doi.org/10.1016/j.bjid.2015.11.005 PMid:26748228

21. Guarneri C, Guarneri F. Symmetrical cutaneous leishmaniasis. Acta Derm Venereol. 2005;85(3):281-2. https://doi.org/10.1080/00015550510026596

22. Barrett MP, Croft SL. Management of trypanosomiasis and leishmaniasis. Brit Med Bull. 2012;104:175-96. https://doi.org/10.1093/bmb/lds031 PMid:23137768 PMCid:PMC3530408

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Case Report

Trichorhinophalangeal Syndrome

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Keywords: Trichorhinophalangeal syndrome; congenital; skeletal abnormalities; radiological imaging; differential diagnosis.

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Abstract

Trichorhinophalangeal syndrome (TRPS) is the collective name of three rare congenital conditions characterised by craniofacial and skeletal abnormalities. The three known types of TRPS have different modalities of genetic transmission: namely, TRPS I and III are inherited as an autosomal dominant disease, while the cases of TRPS II are essentially sporadic.The diagnosis of the different types of TRPS is based on clinical and radiological findings, eventually integrated by genetic analysis, particularly useful in some cases with the non-classical clinical presentation. Alopecia and structural abnormalities of the nose and the hands should be considered as clinical hallmarks, whereas endocrine disorders, renal alterations, ureteral reflux, heart pathology and bone dysplasia have been documented, in the setting of a multisystem involvement.

Introduction

Trichorhinophalangeal syndrome (TRPS) is the collective name of three rare congenital conditions characterised by craniofacial and skeletal abnormalities. The three known types of TRPS have different modalities of genetic transmission: namely, TRPS I and III are inherited as an autosomal dominant disease, while the cases of TRPS II are essentially sporadic.The diagnosis of the different types of TRPS is based on clinical and radiological findings, eventually integrated by genetic analysis, particularly useful in some cases with the non-classical clinical presentation. Alopecia and structural abnormalities of the nose and the hands should be considered as clinical hallmarks, whereas endocrine disorders, renal alterations, ureteral reflux, heart pathology and bone dysplasia have been documented, in the setting of a multisystem involvement. Pigmentation disorders have never been reported in TRPS patients.

Herein is described a case of skin discoloration occurring in a boy affected by TRPS: it was only a fortuitous association?

Case report

A 16-year-old boy presented to our department with a complaint of an asymptomatic dirt-like hyperpigmentation of the upper chest and abdomen, which had been present for about six months (Fig. 1). The condition became progressively more evident after holidays at the seaside, despite the routinary hygiene and the application of various emollients and oils.

The patient was apparently health, although his hairs were referred as slowly growing and being, in fact, thin and sparse. General physical examination was notable for *pectus excavatum* (Fig. 1), short and

stubby hands with lateral deviations and deformations of the interphalangeal joints (Fig. 2). About these, he presented the report of a previous x-ray examination, showing cone-shaped epiphyses of the second to the fifth middle phalanges of both hands and bilateral brachymetacarpalia of the metacarpal IV. The short stature had also been strictly checked by his paediatrician, as well as the flat feet, the arched palate and the hypoplastic mandible.

Biochemical and endocrinological investigations failed to demonstrate abnormal pituitary gland, related to the GH-IGF-1, hypothalamic-pituitary-thyroid, -adrenal and -gonadal axis, and prolactin secretion.

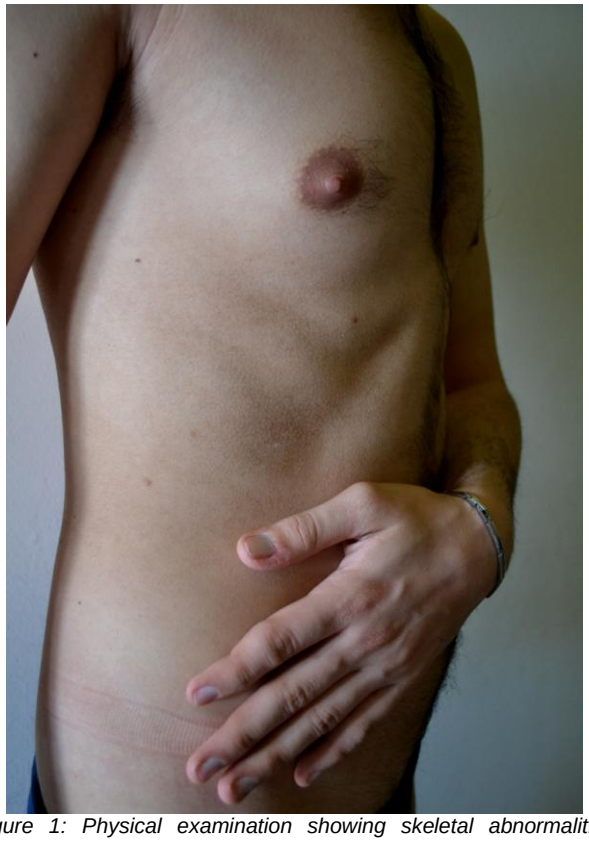

Figure 1: Physical examination showing skeletal abnormalities (pectus excavatum and left hand) and darkening of the skin of the lateral thorax

On mother repeated interviewing, it emerges that other two members of the family (the father and the sister of the patient) presented similar skull features, having both triangular face, bulbous pear-shaped nose, elongated philtrum, thin upper lip, horizontal groove on the chin and protruding ears. In particular, the sister, who was 20, was previous diagnosed with TRPS type I in 2008 through cytogenetic analysis. About the cutaneous concern, anamnesis was not significant for possible underlying diseases (diabetes, obesity or supplementations/medications assumption) and only the sister manifested similar hyperpigmentation of the umbilicus and axillae. He also denied local trauma, eczema or excessive use of cosmetics before.

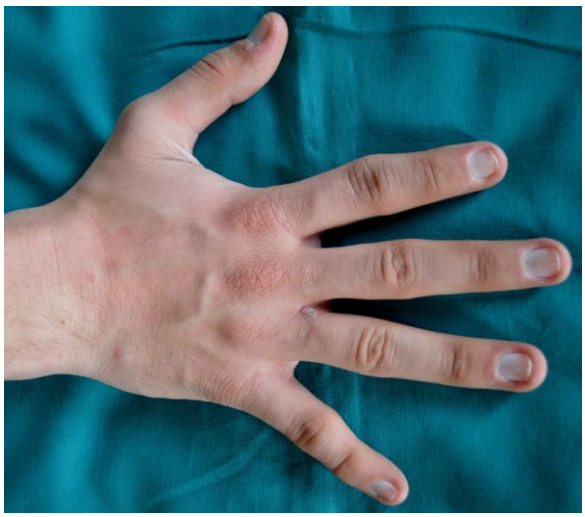

Figure 2: Particular of the hand: note the lateral deviations and deformations of the interphalangeal joints

On physical examination, abnormal brown to dark discoloration of the lateral part of the thorax was apparent (Fig. 3). Dermoscopy of the lesions showed large polygonal plate-like brown scales arranged together giving an irregular mosaic pattern (Fig. 4).

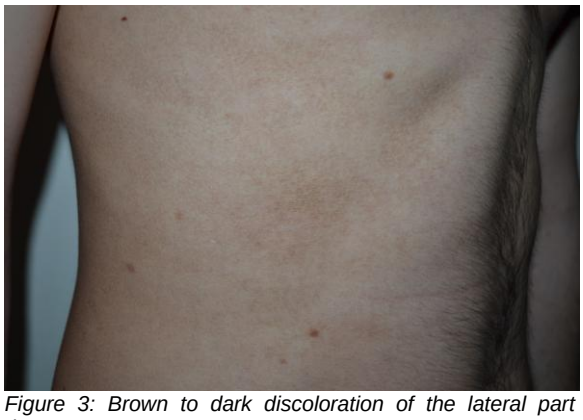

Figure 3: Brown to dark discoloration of the lateral part of the thorax.

Tentative rubbing with 70% isopropyl alcohol lead to the partial removal of the hyperpigmented patch (Fig. 5), and the patient refused any further diagnostic procedure (e.g. punch biopsy).

Discussion

Trichorhinophalangeal syndrome type I is a malformation syndrome characterised by craniofacial and skeletal abnormalities [1]. Inherited in an autosomal dominant manner with high penetrance and variable expressivity, TRPS have sparse and slow-growing hair, pear-shaped nose, elongated philtrum, thin upper lip, protruding ears and bone deformities, including cone-shaped epiphyses of the phalanges, hip malformations and short stature as typical clinical features [2].

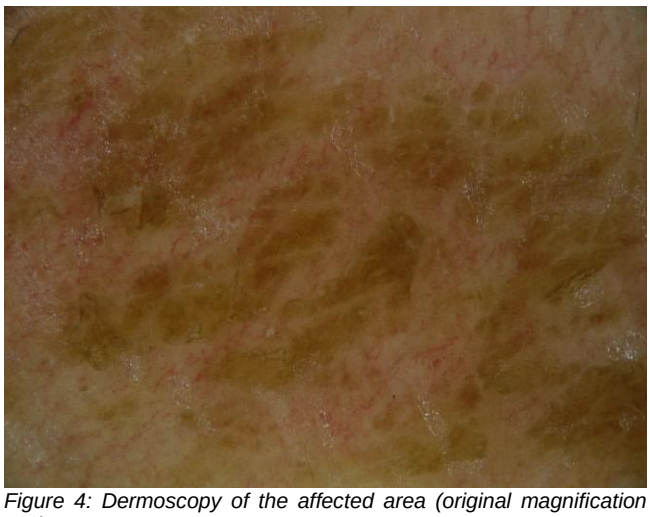

Figure 4: Dermoscopy of the affected area (original magnification x60)

Although there is a great variability in the clinical findings with considerable overlap, even among subjects of the same family, three subgroups of TRPS can be distinguished: TRPS I, associated with alterations of chromosome 8 band q24.1, TRPS II caused by a larger deletion, involving the TRPS 1 and EXT 1 (hereditary multiple exostoses) genes (8q24.11-q24.13), and TRPS III which results from missense mutations in exon 6 of TRPS1 [3].

Short stature is usual in TRPS type I [4]. Winged scapulae, multiple cartilaginous exostoses, redundant skin, and mental retardation are distinctive characteristics of TRPS type II, while severe brachydactyly, due to short metacarpals, and severe short stature are typical of TRPS type III [1, 5].

The diagnosis of the different types of TRPS is based on clinical and radiological findings, eventually integrated by genetic analysis, particularly useful in some cases with non-classical clinical presentation; other syndromes that include alopecia and structural abnormalities of the nose and the hands should be considered in differential diagnosis (Larsen's syndrome, oral-facial-digital syndrome, Coffin-Siris syndrome, alopecia-onycho- dysplasia-hypohidrosis-deafness syndrome, trichoonychodental dysplasia, Clouston's syndrome, Ellis-van Creveld syndrome) [1, 2, 6, 7].

TRPS may be associated with endocrine disorders, renal alterations, ureteral reflux, heart pathology and bone dysplasia: thus, a follow-up has to be set up in order to make an early diagnosis of a possible multisystemic involvement, a Perthes-like disease (dysplasia of the hip in >70% of the cases) [9], because of the frequent evolution in avascular necrosis of the femoral head (Legg-Perthes-Calvé disease) [9], or the appearance of exostoses because of a possible, although rare, sarcomatous degeneration [2]. Radvanyi et al. also showed that the TRPS1 gene is overexpressed in more than 90% of breast cancers [10].

Apart from the above mentioned cutaneous involvement, no other skin abnormalities have been reported in TRPS. In particular, no pigmentation disorders have been noted, according to with the updated literature.

With regard to our case, dermatological findings should not strictly considered in the field of pigmentation disorders, since Terra Firma Forme Dermatosis (TFFD), or Duncan 'dirty' disease, implies Incomplete maturation of keratin squames, combined with retention of melanin and build-up and compaction of scales, sebum and dirt through inadequate cleansing [11]. In facts, TFFD is an idiopathic benign condition that may represent an exasperating skin defect, as it involves exposed areas in psychologically more fragile patient categories (mainly children and adolescents) with the features of 'dirt' and giving the picture of poor body hygiene [12]. Atopy seems to be a predisposing condition [13].

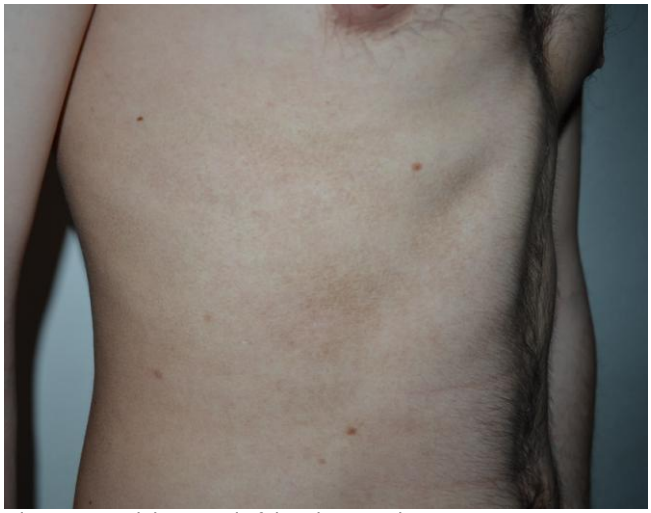

Figure 5: Partial removal of the pigmentation

By excluding other dirty-appearing disorders, and using some ancillary tools (e.g. dermoscopy), the diagnosis is easy [13], thus avoiding inappropriate exams and unnecessary treatments [11, 12].

The occurrence of some cases presenting 'topographic' disease (Unal E et al., unpublished data) and the anecdotal association with genetic diseases (Guarneri C et al., unpublished data) may suggest the possibility of a 'syndromic' phenotype, as in this case, and it is worthy of attention in future cases of these conditions.

However, in clinical practice, TFFD is more frequent than the only 44 cases reported in literature lead to expect [14].

In conclusion, TRPS is a group of rare congenital conditions characterised by craniofacial and skeletal abnormalities, Type I and III being more frequent and inherited as an autosomal dominant

character. As the diagnosis is based on clinical and radiological findings, eventually integrated with genetic analysis, the role of a dermatologist is pivotal, through recognising the typical hallmarks and managing the further in-depth analyses.

Specialist's should also be aware of unexpected clinical signs, thus eventually expanding the phenotype of the disease and/or characterising new variants.

References

1. Vaccaro M, Guarneri C, Blandino A. Trichorhinophalangeal syndrome. J Am Acad Dermatol. 2005;53:858-60. https://doi.org/10.1016/j.jaad.2005.06.003 PMid:16243138

2. Maas S, Shaw A, Bikker H, Hennekam RCM. Trichorhinophalangeal Syndrome. 2017 Apr 20. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017.

3. Seitz CS, Lüdecke HJ, Wagner N, Bröcker EB, Hamm H. Trichorhinophalangeal syndrome type I: clinical and molecular characterization of 3 members of a family and 1 sporadic case. Arch Dermatol. 2001;137(11):1437-42. https://doi.org/10.1001/archderm.137.11.1437 PMid:11708946

4. Hazan F, Korkmaz HA, Yararbaş K, Wuyts W, Tükün A. Trichorhinophalangeal syndrome type II presenting with short stature in a child. Arch Argent Pediatr. 2016;114(6):e403-e407. PMid:27869420

5. Unglaub F, Hahn P, Spies CK. Type I Trichorhinophalangeal Syndrome - Rare, but Catchy. Handchir Mikrochir Plast Chir. 2017;49(1):58-59. PMid:28423447

6. Carrington P R, Chen H, Altick J A. Trichorhinophalangeal syndrome, type I. J Am Acad Dermatol. 1994;31:331-336. https://doi.org/10.1016/S0190-9622(94)70166-0

7. Vaccaro M, Guarneri F, Barbuzza O, Gaeta M, Guarneri C. A familial case of trichorhinophalangeal syndrome type I. Pediatr Dermatol. 2009;26(2):171-5. https://doi.org/10.1111/j.1525-1470.2009.00905.x PMid:19419465

8. McGuire KJ, Westacott S, MacEwen GD. Trichorhinophalangeal syndrome: evolution of Perthes-like changes in the hips. Orthopedics. 2000;23(8):855-6. PMid:10952053

9. Minguella I, Ubierna M, Escola J, Roca A, Prats J, Pintos-Morel G. Trichorhinophalangeal syndrome, type I, with avascular necrosis of the femoral head. Acta Paediatr. 1993;82:329-30. https://doi.org/10.1111/j.1651-2227.1993.tb12676.x PMid:8495099

10. Radvanyi L, Singh-Sandhu D, Gallichan S et al. The gene associated with trichorhinophalangeal syndrome in humans is overexpressed in breast cancer. Proc Natl Acad Sci USA. 2005;102:11005-10. https://doi.org/10.1073/pnas.0500904102 PMid:16043716 PMCid:PMC1182410

11. Duncan WC, Tschen JA, Knox JM. Terra firma-forme dermatosis. Arch Dermatol. 1987;123(5):567-9. https://doi.org/10.1001/archderm.1987.01660290031009 PMid:3579334

12. Guarneri C, Guarneri F, Cannavò SP. Terra firma-forme dermatosis. Int J Dermatol. 2008; 47(5):482-4. https://doi.org/10.1111/j.1365-4632.2008.03516.x PMid:18412867

13. Solak B, Erdem T. Terra firma-forme dermatosis: wipe first. Int J Dermatol. 2015;54(12):e548-9. https://doi.org/10.1111/ijd.12938 PMid:26341247

14. Unal E, Guarneri C, Chokoeva AA, Wollina U, Tchernev G. Terra firma-forme dermatosis. Wien Med Wochenschr. 2017;167(3-4):66-69. https://doi.org/10.1007/s10354-016-0519-1 PMid:27770322

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Case Report

Erythema Ab Igne Caused By Laptop Computer

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Keywords: Erythema ab igne; modern technologies; panniculitis; cancer; differential diagnosis.

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Abstract

Erythema ab igne (EAI) represents the stereotype of a modern technology induced disease. Originally produced by repeated exposure of the skin to a heat source, more often because of habits related to the job or personal activities, this condition now tends to occur more frequently, being associated with a variety of modern instruments. The aim of our report is to discuss this strange medical condition with a focus on clinical features, possible confounding differential diagnoses and recommendations for prevention.

Introduction

Erythema ab igne (EAI) represents the stereotype of a modern technology induced disease.

Originally produced by repeated exposure of the skin to temperatures close to the burn threshold (43-47°C) [1], and being unchanged in its pathogenesis – based on the superficial injury on the dermal vascular plexus – the occurrence of EAI has been associated with a wide variety of 'new' warming sources, thus also involving a wider range of age of affected patients [2, 3]. In facts, due to its infrequency, EAI still constitutes a clinical conundrum, diagnostically misinterpreted and hard to be solved in the absence of suspected anamnestic data.

The aim of our report is to discuss this strange medical condition with a focus on clinical features, possible confounding differential diagnoses and recommendations for prevention.

Case report

A 32-year-old Caucasian woman, who was a secretary in a legal office, presented with skin changes of the left thigh. The lesion had appeared at some undetermined moment and got worse progressively in the last three months, always being only mildly pruritic.

Physical examination disclosed a well-defined erythematous-violaceous, reticulated macular rash limited to the anterior part of the medium third of the left thigh (Fig. 1).

The patient was referred to our department by a rheumatologist with the suspect of vasculitis. Thus she had just received a diagnostic laboratory work-up, including tests for ANA and ANCA, all resulting within normal limits.

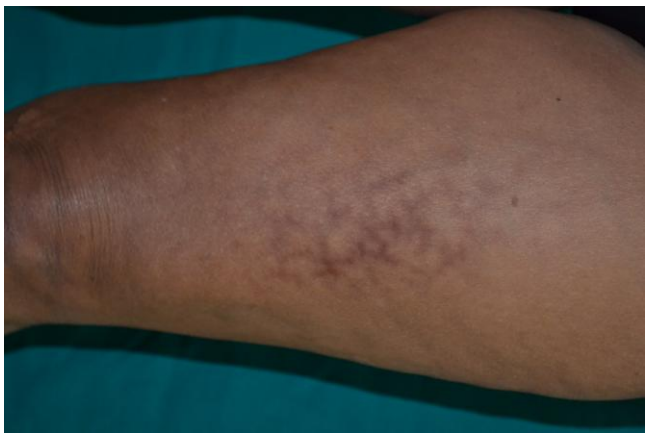

Figure 1: Erythematous, violaceous, reticulated rash on the left thigh

On repeated anamnesis, the patient reported that she had been assigned to its actual job exactly four months before; in particular, due to her role of barrister assistant, she was used to having laptop on thighs during most of her work time. Checking patient's laptop, we noted that the lesional area was exactly in contact with the ventilation fan (fig.2).

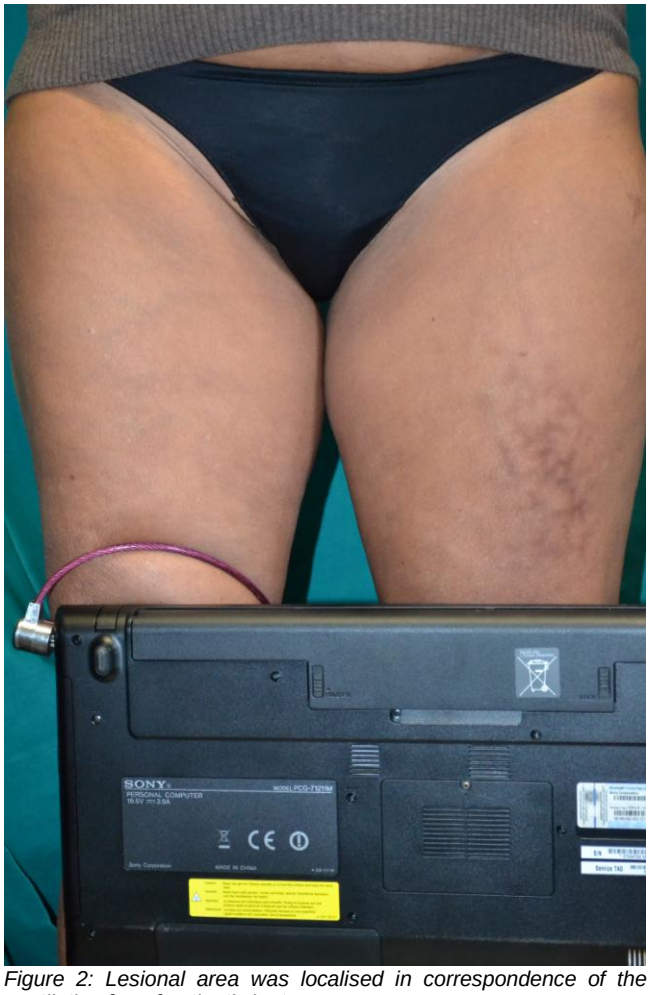

Figure 2: Lesional area was localised in correspondence of the ventilation fan of patient's laptop

Since the history of persistent skin exposure to the localised heat source, a diagnosis of erythema ab igne was made and proposed the use of a protective lap pad to create an efficient barrier between the user and the personal computer together with a favourable work surface.

Given the absence of significant symptoms, no pharmacological therapy was prescribed.

Discussion

Erythema ab igne is an initially transient, and then chronic cutaneous condition, caused by direct exposure of the skin to a heat source, more often because of habits related to the job or personal activities [4].

Originally also known as "hot water bottle rash", typical of the pretibial area in subjects used to expose to space heaters [1], this condition now tends to occur more frequently, being associated with a variety of modern instruments including heating pillows [5], space heaters [6], electric blankets [7], heated car seats and backs [8], portable personal computers [9] and smartphones [2, 10].

Pathogenesis has not been fully understood. Long term and/or repeated heat exposure can determine, in general, superficial damage to the vascular structures, with vasodilatation and deposition of hemosiderin [1, 2]; other changes include changes in dermal elastic fibres, epidermal atrophy and melanin accumulation in the dermis [2, 11].

Depending on the frequency, temperature and time of exposure, we expect different degrees and onset of the condition [12].

Typical manifestations consist of transient-to-persistent, reticulated, initially erythematous or, later hyper-/hypopigmented patches, sometimes characterised by superficial changes (atrophy, xerosis, telangiectasia, bullae). The eruption is mainly asymptomatic, although warming in the acute phase and itch chronically have been anecdotally reported [1, 10, 13].

Diagnosis is based on the supportive history and the clinical picture, whereas histologic changes are non-specific [14], thus skin biopsy has to be considered only in limited cases. Differential diagnosis of EAI should include livedo vasculitis (the idiopathic as well as the symptomatic form in collagenosis) [4], panniculitis [15, 16], and side effects of some drugs (amantadine and memantine) [4]. As suggested by some authors, EAI may also mimic infectious diseases when anamnesis is not clear as well as original culture practices and conditions of the exotic patients [17].

Early awareness [1, 5, 12] of the disease and

preventive measures [18] usually lead to a favourable prognosis. Chronic cases have been treated with topical retinoids and 5-fluorouracil, Nd-YAG, ruby and alexandrite lasers [2, 5, 19] plus antihistamines and/or FANS symptomatically. Monitoring of long-standing EAI is mandatory, whereas hyperkeratosis and ulceration have to be considered as a sign of premalignant changes at the epithelial level [20].

Finally, chronic pain and persistent systemic symptoms in EAI have to be carefully checked as a possible sign of occult internal malignancies. A total of 11 cases have been reviewed in a recent paper by Bunick and Ibrahim [21], with gastrointestinal (colorectal, pancreatic, gastric) cancer being the most represented tumour; lung, renal breast and hematologic malignancies have also been reported thus underlines the importance of complete assessment of this otherwise benign condition [21, 22].

References

1. Hernandez AC, Arbedol SB, Montalvo SM, Marugàn LT. Erythema ab igne. Reumatol Clin. 2016;12:233-4. https://doi.org/10.1016/j.reuma.2015.08.009 PMid:26654294

2. Salgado F, Handler MZ, Schwartz RA. Erythema ab igne: new technology rebounding upon its users? Int J Dermatol. 2017; Mar 30. https://doi.org/10.1111/ijd.13609

3. Guarneri F, Guarneri C, Cannavò SP. An unusual case of cell phone dermatitis. Contact Dermatitis. 2010;62(2):117. https://doi.org/10.1111/j.1600-0536.2009.01674.x PMid:20136896

4. Elsner P. Erythema ab igne as an occupational skin disease. J Dtsch Dermatol Ges. 2014; 12(7):621-2. PMid:24684647

5. Fareedy SB, Rettew A, Karmacharya P, Jehangir A, Shaikh B, Pathak R. erythema ab igne secondary to repeated heating pad use: an image case. J Community Hosp Intern Med Perspect. 2015;5(4):28335. https://doi.org/10.3402/jchimp.v5.28335 PMid:26333862 PMCid:PMC4558291

6. Morrison M, Cotton J, LaFond A. Reticulated erythematous patch on a teenager foot. J Fam Pract. 2014;63:537-9. PMid:25353026

7. Leal-lobato MM, Blasco-Morente G. electric blanket induced erythema ab igne. Semergen. 2015;41:456-7. https://doi.org/10.1016/j.semerg.2014.12.008 PMid:25662480

8. Brodell D, Mostow EN. Automobile seat heater-induced erythema ab igne. Arch Dermatol. 2012;148:264-5. https://doi.org/10.1001/archdermatol.2011.1158 PMid:22351837

9. Brazzelli V, Grassi S, Barruscotti S, Croci G, Borroni G. Erythema ab igne induced by laptop computer: an emerging disease among adolescents? G Ital Dermatol Venereol. 2015[epub ahead of print].

10. Kesty K, Feldman SR. Erythema ab igne: evolving technology, evolving presentation. Dermatol Online J. 2014;20:19.

11. Soholm Secher LL, Vind-Kezunovic D, Zachariae CO. Side-effects to the use of laptop computers: erythema ab igne. Dermatol reports. 2010;2:e11. https://doi.org/10.4081/dr.2010.e11 PMid:25386248 PMCid:PMC4211471

12. Turan E, Yesilova Y, Ucmak D, Celik OI. Thermal pillow: an unusual causative agent of erythema ab igne. Turk J Pediatr. 2013;55:648-50. PMid:24577987

13. Milchak M, Smucker J, Chung CG, Seiverling EV. Erythema ab igne due to heating pad use: a case report and review of clinical presentation, prevention and complications. Case Rep Med. 2016;2016:1862480. https://doi.org/10.1155/2016/1862480 PMid:26880929 PMCid:PMC4735926

14. Miller K, Hunt R, Chu J, Meehan S, Stein J. Erythema ab igne. Dermatol Online J. 2014;20:11.

15. Borgia F, De Pasquale L, Cacace C, Meo P, Guarneri C, Cannavò SP. Subcutaneous fat necrosis of the newborn: be aware of hypercalcemia. J Paediatr Child Health. 2006;42(5):316-8. https://doi.org/10.1111/j.1440-1754.2006.00862.x PMid:16712567

16. Cannavò SP, Borgia F, Vaccaro M, Guarneri F, magliolo E, Guarneri B. Pretibial myxoedema associated with Hashimoto's thyroiditis. J Eur Acad Dermatol Venereol. 2002;16(6):625-7. https://doi.org/10.1046/j.1468-3083.2002.00532.x PMid:12482050

17. Treister-Goltzman Y, Peleg R. Images in clinical tropical medicine. Erythema ab igne. A J Trop Med Hyg. 2015;92(3):476. https://doi.org/10.4269/ajtmh.14-0474 PMid:25740953 PMCid:PMC4350531

18. Riahi RR, Cohen PR. Practical solutions to prevent laptop computer-induced erythema ab igne. Int j Dermatol. 2014;53:e389-e409. https://doi.org/10.1111/ijd.12407 PMid:24961574

19. Kim HW, Kim EJ, Park HC, Ko JY, Ro YS, Kim JE. Erythema ab igne successfully treated with low fluenced 1064-nm Q-switched neodymium-doped yttrium aluminium garnet laser. J Cosmet Laser ther. 2014;16:147-8. https://doi.org/10.3109/14764172.2013.854623 PMid:24131068

20. Sigmon JR, Cantrell J, Teague D, Sangueza O, Sheehan DJ. Poorly differentiated carcinoma arising in the setting of erythema ab igne. Am J Dermatopathol. 2013;35:676-8. https://doi.org/10.1097/DAD.0b013e3182871648 PMid:23872874

21. Bunick CG, King BA, Ibrahim O. When erythema ab igne warrants an evaluation for internal malignancy. Int J Dermatol. 2014;53:e347-e366. https://doi.org/10.1111/ijd.12329 PMid:24601874

22. Ashby M. Erythema ab igne in cancer patients. J R Soc Med. 1985;78:925-7. https://doi.org/10.1177/014107688507801110 PMid:4067962 PMCid:PMC1290002

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Case Report

A Case of Alopecia Areata in a Patient with Turner Syndrome

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Keywords: alopecia areata; Turner syndrome; autoimmunity; corticosteroids; cyclosporine A.

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Abstract

The Authors report a case of alopecia areata totalis in a woman with Turner syndrome.

Introduction

Alopecia areata (AA) is an inflammatory non-scarring form of hair loss, which may involve all the follicular units of the body. It is a common disease, with an incidence of 1-2% [1].

AA may affect people of both sex and all age, even if it is more commonly described in under 30-years old patients [2]. Often, it is associated with different inflammatory or autoimmune diseases, like atopic eczema, Hashimoto's thyroiditis, Graves' disease, Celiac disease, vitiligo, psoriasis and others [1].

AA is an autoimmune disease, characterised by a T-cell mediated immune response that targets hair follicles. The clinical manifestations are numerous, ranging from mild lesions, characterised by round or oval patches of hair loss, to the total hair loss, such as in the universal form [3].

Case report

A 28-year-old woman affected by AA, showed up to our Clinic presenting a widespread non-scarring alopecia, which was localised in the scalp and face area. The skin was white-pink in colour and normal-trophic. Black dots and exclamations points were no detected. Only a few vellus-like hairs were present in the midline of the scalp (Fig.1).The patient did not report any subjective symptoms and enjoyed apparent good health.

She reported the appearance of the disease about 26 months ago. Initially, the hair loss was limited to the left temporal side, and consisted in two round little (diameter less than 2 cm), well defined, areas. After few weeks, the hair loss rapidly spread, involving the entire scalp. By five months, the patient also observed the loss of her eyelashes and eyebrows.

The woman told us to be affected by Turner syndrome, Hashimoto's thyroiditis and celiac disease. Her medical treatment consisted of oral levothyroxine

and oestrogen replacement. No other diseases had been reported. She had no familiarity for AA or other autoimmune diseases.

The patient reported previous treatment of alopecia with oral supplements and topical minoxidil 2% 1 ml twice a day for six months. Due to the lack of clinical improvement, she was treated with low dose of topical corticosteroids (hydrocortisone once a day) for three weeks and PUVA therapy, which has been performed twice a week for a total of 20 sessions, both without beneficial results.

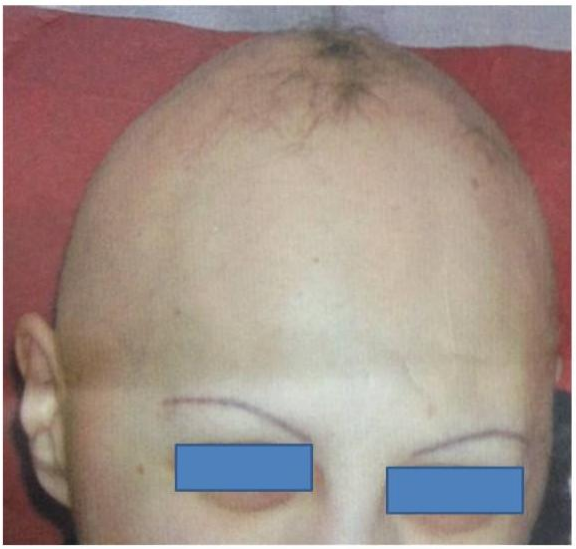

Figure 1: Alopecia areata in a woman with Turner syndrome

During the clinical evaluation, the woman showed characteristic features of Turner syndrome, such as short stature (150 cm), short and squat neck, poor breast development and stubby little hands. She had ears and lower eyelids bigger than normal, enophthalmos, reduced upper lip and a small chin. On the other hand, no other skin lesions were observed. Nails were smaller than normal. A routine laboratory test, including thyroid function tests, were normal.

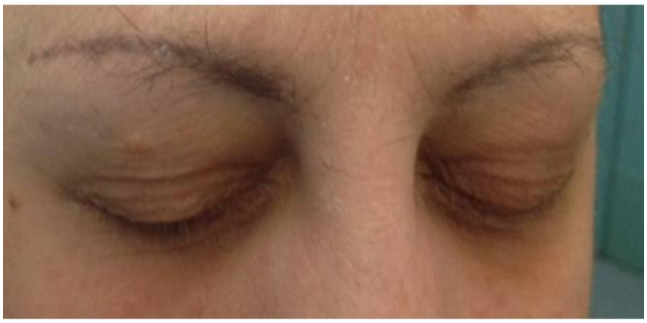

Figure 2: Eyelashes and eyebrows re-growth after cyclosporine A therapy

Due to the long duration of the hair disease, we applied intralesional triamcitolone acetonide once a week for two months. Surprisingly, even if localised, we observed a re-growth of the hair. Since hair growth responded to corticosteroids, we switched to oral methylprednisolone 32 mg/die for ten days, followed by 16 mg/die for ten days and, eventually 8 mg/die for another ten days. The clinical response was quite good: the patient showed new hair in the frontal area of the scalp.

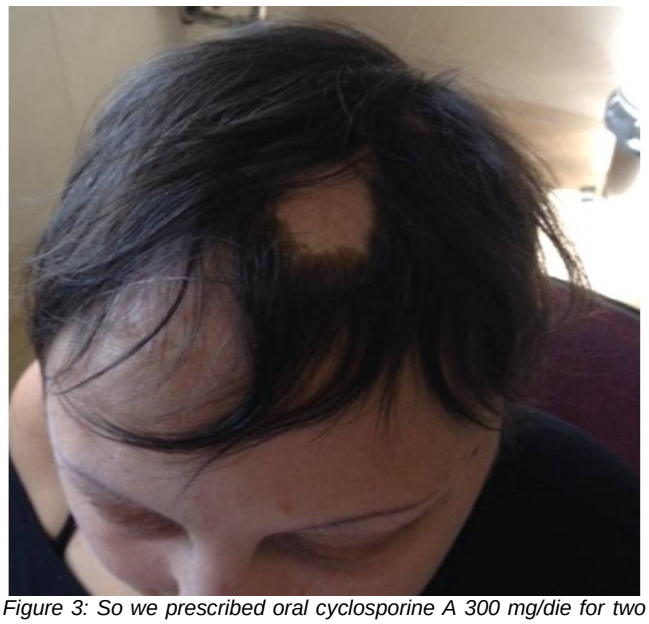

Figure 3: So we prescribed oral cyclosporine A 300 mg/die for two months, and intralesional triamcitolone acetonide once every two weeks. Due to the good clinical response to the therapy and the possible side effects of corticosteroids, after two months, we decided to prescribe the only cyclosporine A 200 mg/die

After one month, we observed the diffuse hair re-growth on the scalp. New eyelashes and eyebrows were also observed (Fig.2).

We decided to reduce progressively the cyclosporine therapy and to stop it. Because of the appearance of new hair loss patches (Fig.3), the patient re-started the treatment with cyclosporine A at a dosage of 200 mg/die. The clinical response was rapid and excellent (Fig.4).

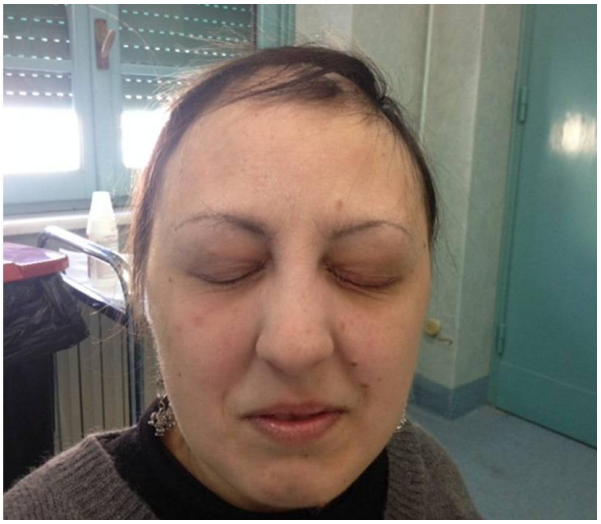

Figure 4: Our patient with complete hair re-growth

During the treatment we constantly evaluated the patient's clinical conditions, monitoring her blood pressure and routine blood test. No side effects or complications had been observed.

Discussion

Turner syndrome (or Ullrich-Turner syndrome) is one of the most frequent chromosomal abnormalities, which results from a sex-chromosomal anomaly characterised by a presence of one normal X chromosome and a missing or structurally abnormal second sex chromosome. It is a rare disease affecting 1:2500 live born girls [4].

Table 1: Characteristic clinical features of Turner syndrome

Skin and adnexa	pterygium; ↑ moles; vitiligo; ↑ growth of body hair (forearm); low-set hair; ↓ hair density; congenital lymphedema of the hands and feet; over the curvature of the nails
Mouth	palate with a pointed arch form ("Gothic" palate); ↓ development of the jaw; mouth as a "carp."
Ears	low implantation; ↓ development of the ear's board; large ears; others malformations; neurosensorial defects
Eyes	alteration in the position and shape of the eyelid (hypertelorism and epicanthal folds); strabismus; dyschromatopsia
Neck	short and squat
Skeletal system	short fingers; widened distal phalanges; ↓ length of the fourth metacarpal bone (XR Archibald sign); cubitus valgus; medial condyle of the tibia agenesia (XR Kosowicz sign); delayed bone maturation (first three years of life, after ten years)
Chest	enlarged; pectus excavatum; hypoplasia and the excessive distance between the mammary areola
Urinary system	horseshoe kidney; renal cysts; unilateral renal agenesis; pelvis and ureters alterations
Cardiovascular system	bicuspid aortic valve; aortic coarctation; aortic valve disease; anomalous venous return of the pulmonary veins; mitral valve prolapse; hypertension; conduction defects
Blood	abnormalities of coagulation factors
Metabolism	abnormal lipid profile (cholesterol, triglycerides) and glucose
Nervose system	defects in visual-spatial and visual-perceptual skills; ↓ motor function (unable to walk before 15 months); ↓ non-verbal memory; ↓ attention
Psychological	disorders in emotional

The Turner syndrome phenotype includes female gender, short stature, primary ovarian failure and some characteristic physical features (tab.1) [5]. Patients with Turner syndrome have an increased incidence of autoimmune disorders (AID), such as Hashimoto's thyroiditis, Grave's disease, celiac disease, inflammatory bowel disease, and diabetes mellitus [6-8].

Even if dermatologic autoimmune diseases (e.g. psoriasis, vitiligo, halo nevi) are well-known in Turner patients (9, 10), only a few cases of associated AA have been reported so far [11-13].

AA is a chronic inflammatory autoimmune disease, characterised by non-scarring hair loss on the scalp or any hair-bearing area of the body. Clinically it may represent in variable patterns, such as patchy, diffuse, reticulate, linear, or opiates-type. Depending on the severity of hair loss, AA may also be classified as localised (few patches of hair loss), subtotal (diffuse alopecia of the scalp), total (complete loss of scalp hair) or universal (complete loss of body hair) [14].

Table 2: Therapeutic options for alopecia areata

Classical treatments	Corticosteroids (topical, intralesional, systemic)
	PUVA-therapy (topical or systemic 8-Methoxypsoralen + UVA)
	Topical immunotherapy (diphenylcycloproperone/DPCP, squaric
	acid dibutyl ester/SADBE)
	Antralin cream or ointment
Aneddotic treatments	Antidepressant
	Hypnotherapy
	Psychological support
	Topical minoxidil
	Topical triiodothyronine
	Garlic gel
	Azelaic acid
	Topical onion juice
	Imiquimod
	Botulinum toxin
	Photodynamic therapy
	Topical phenol
	Excimer lasers
Promising treatments	Azathioprine
	Methotrexate
	Cyclosporine A (topical, systemic)
	Tacrolimus
	Pimecrolimus
	Alitretinoin
	Biological therapies
	Platelet-rich plasma
	UVA1 (340-400 nm)

The course of the disease is highly variable: it may spontaneously regress, be stable or progress to a severe form. Even if numerous treatment options are now available for AA (tab.2), no definitive therapy exists [15, 16].

In our case, the patient showed an excellent clinical response to cyclosporine A treatment, initially combined with intralesional corticosteroids.

In conclusion, the authors have presented this case study to record the possible association of AA with Turner syndrome, and therapeutic validity of cyclosporine in stimulating hair growth where other therapies had previously failed.

References

1. Wolff H, Fischer TW, Blume-Peytavi U. The diagnosis and treatment of hair and scalp diseases. Dtsch Arztebl Int. 2016;113:377–386. PMid:27504707 PMCid:PMC4908932

2. Lazzarini R, Bilac Oliari C, Nasser Erthal AL. Late-onset alopecia areata: descriptive analysis of 30 cases. An Bras Dermatol. 2016;9:844-845. https://doi.org/10.1590/abd1806-4841.20165184 PMid:28099618 PMCid:PMC5193207

3. Alkhalifah A, Alsantali A, Wang E, McElwee KJ, Shapiro J. Alopecia areata update: part I. Clinical picture, histopathology, and pathogenesis. J Am Acad Dermatol. 2010;62:177-188. https://doi.org/10.1016/j.jaad.2009.10.032 PMid:20115945

4. Nielsen J, Wohlert M. Chromosome abnormalities found among 34,910 newborn children: results from a 13-year incidence study in Arhus, Denmark. Hum Genet. 1991;87:81–83. https://doi.org/10.1007/BF01213097 PMid:2037286

5. Bondy CA. Care of girls and women with Turner syndrome: a guideline of the Turner Syndrome Study Group. J Clin Endocrinol Metab. 2007;92:10–25. https://doi.org/10.1210/jc.2006-1374 PMid:17047017

6. Lleo A, Moroni L, Caliari L, Invernizzi P. Autoimmunity and

Turner's syndrome. Autoimmun Rev 2012;11:A538–A543. https://doi.org/10.1016/j.autrev.2011.11.015 PMid:22154619

7. Larizza D, Calcaterra V, Martinetti M. Autoimmune stigmata in Turner Syndrome: when lacks an X chromosome. J Autoimmun 2009;33:25–30. https://doi.org/10.1016/j.jaut.2009.03.002 PMid:19349146

8. Jorgensen KT, Rostgaard K, Bache I, et al. Autoimmune diseases in women with Turner's syndrome. Arthritis Rheum 2010;62:658–666. https://doi.org/10.1002/art.27270 PMid:20187158

9. Watabe H, Kawakami T, Kimura S, et al. Childhood psoriasis associated with Turner Syndrome. J Dermatol 2006;33:896–898. https://doi.org/10.1111/j.1346-8138.2006.00205.x PMid:17169099

10. Brazzelli V, Larizza D, Martinetti M, et al. Halo nevus, rather than vitiligo, is a typical dermatologic finding of Turner's syndrome: clinical, genetic, and immunogenetic study in 72 patients. J Am Acad Dermatol 2004;51:354–358. https://doi.org/10.1016/j.jaad.2003.11.082 PMid:15337976

11. Tebbe B, Gollnick H, Muller R, et al. Alopecia areata and diffuse hypotrichosis associated with Ullrich-Turner Syndrome. Presentation of 4 patients. Hautarzt 1993;44:647–652. PMid:8225974

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Case Report

Pigmented Paraaxillary Located "Complex" Basal Cell Carcinoma Imitating clinically irritated Melanocytic Lesion - Succesfull Surgical Approach in Bulgarian Patient

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Abstract

BACKGROUND: Basal cell carcinoma (BCC) is the most frequently encountered neoplasm worldwide. While nodular BCC is the most frequent clinical subtype, other forms of BCC, such as superficial, cystic, morpheiform, infiltrative, and pigmented may also be encountered.

CASE PRESENTATION: We present the case of a 67-year-old male with a relatively well-defined infiltrative, pigmented plaque with multiple colours and peripheral growth situated in the right axillary region. The histopathologic examination performed after complete surgical excision of the tumour revealed a complex pigmented BCC with macronodular, fibroepithelioma-like, cystic, focally infiltrative and basosquamous features.

CONCLUSION: Uncommon locations of BCCs in sun-protected areas such as the axillary region require a higher degree of suspicion for diagnosis. The complex histology of the presented case, including subtypes with differing biologic attributes, emphasises the importance of histopathological examination in the diagnosis and therapeutic management of BCC.

Introduction

Basal cell carcinoma (BCC) is the most frequently encountered cutaneous neoplasm worldwide, accounting for approximately 90% of all skin cancers [1], with an incidence of 2,000 cases /100,000 population [2]. Most BCCs develop in individuals with Fitzpatrick photo-types I or II and arise in sun-exposed areas, mostly in the head and neck and less frequently in the trunk and limbs [3, 4]. Less than 4% of all BCCs occur in the genital and perianal

region [5]. It is a slow growing tumour with a 0.5% metastatic rate [6], but with a considerable risk of local invasion and destruction if left untreated.

Several risk factors have been described in the pathogenesis of BCC. Long-term exposure to sunlight or artificial ultraviolet light (UV), especially UVB [7], represents the main BCC- inducing factor. Phenotypic and genetic traits (e.g. inherited diseases or syndromes such as basal cell nevus syndrome (Gorlin-Goltz syndrome), xeroderma pigmentosum, epidermodysplasia verruciformis, albinism, and Gardner's syndrome); a familial history of skin cancer; DNA repair deficiencies leading to chromosomal instability; immunosuppression; exposure to other environmental carcinogenic factors (e.g. arsenic, alkylating agents, polycyclic aromatic hydrocarbons) [8]; accidental or therapeutic exposure to ionizing radiation; and repeated cutaneous trauma have also been designated as important factors in the development of BCCs [3, 9, 10, 11].

A constitutive activation of the sonic hedgehog signalling pathway caused by acquired mutations in the PTCH and SMO genes [11], localised in the basal epidermal cell layer represents the early developmental determinant of BCCs, while other molecular alterations of P53 and melanocortin-1 receptor genes also play essential pathogenic roles [13, 14].

Nodular BCC is considered the most frequent clinical subtype, while other forms (superficial, cystic, morpheaform, infiltrative, pigmented tumours, and others) account for less than 10% of all BCCs [15].

Fibroepithelioma of Pinkus is another distinct BCC subtype, mostly found in the trunk; it can resemble an acrochordon, compound melanocytic nevus, melanoma, seborrheic keratosis, or other benign skin lesions [16].

The clinical diversity of BCCs emphasises the importance of histopathological examination in the diagnosis and therapeutic management of BCC. While nodular BCCs have definite clinical and histopathologic features, the other variants (adenoid, cystic, morpheaform, pigmented and others) may show more complex features and less predictable outcomes.

The differential diagnosis can be challenging; the major risk is that of mistaking BCC for benign, harmless lesions [17] or, on the other hand, for more severe, life threatening malignancies such as melanoma.

Standard surgical excision or Mohs micrographic surgery remain the mainstays of localised BCC treatment. In particular situations of inoperable cases, as in patients with locally advanced, metastatic disease or those with severe comorbidities or immunosuppression, BCCs may be approached with more conservative, nonsurgical methods [18].

The following report depicts an unusual case of BCC in a Bulgarian patient with a pigmented skin lesion localised in the axillary region. Histopathologic examination performed after complete surgical excision revealed the diagnosis of a complex pigmented BCC with macronodular, fibroepithelioma-like, cystic, focally infiltrative, and basosquamous features.

Case report

We report the case of a 67-year-old male who presented to the dermatology department with a skin lesion in the right axillary region that had been gradually growing for the past ten years (Fig. 1a). The lesion had bled two days before presentation but was otherwise asymptomatic. The patient did not report any food, or drug allergies or intolerances and his medical history were unremarkable except for benign prostatic hyperplasia. Clinical examination revealed a relatively well defined, infiltrated plaque with an uneven eroded surface, irregular borders, variegated colours, and peripheral growth in the right axillary region, measuring approximately 1x1.5 cm in greatest diameter (Fig. 1b).

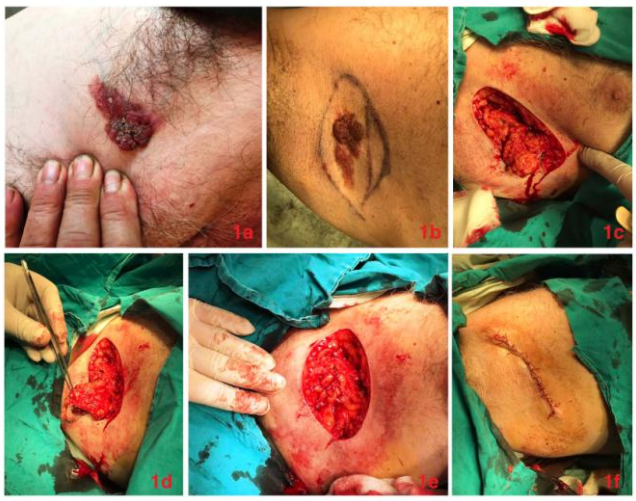

Figure 1: 1a) Clinical appearance of the lesion in the right axillary region; 1b) Preoperative markings showing wide excision margins; 1c) Surgical defect after excision of the lesion; 1d) Further excisional debridement of the subcutaneous fat to ensure complete tumor remova; 1f) Final surgical defect ready for reconstruction; 1f) Primary closure of the defect with interrupted non-absorbable sutures

The differential diagnosis included pigmented BCC, irritated melanocytic nevus, pigmented seborrheic keratosis, benign or malignant adnexal tumours, and melanoma. Paraclinical tests were unremarkable as well, with sinus tachycardia on ECG,

normal abdominal ultrasound, and a chest x-ray showing no visible infiltrations of the lung parenchyma, free costodiaphragmatic recess, and an extended aortic arch. Taking into consideration the history of change and the concern for a possibly aggressive malignant process, the lesion was surgically excised in an elliptical manner with wide margins under local anaesthesia with 2% lidocaine and epinephrine. Primary closure of the defect was achieved (Fig. 1c-f) followed by application of antiseptic ointment dressings. Postsurgical health status was eventless, and the patient was discharged with follow-up instructions. Histological examination revealed a large, complex basal cell carcinoma with several different histopathologic types, including macronodular, fibroepithelioma-like, cystic, focally infiltrative, and basosquamous (Fig. 2 a-h).

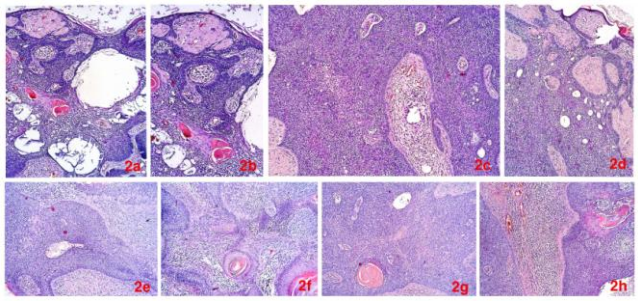

Figure 2: 2a and 2b) These are slightly different views of the same area of the tumour. There are epidermal atrophy and keratin debris above the stratum corneum. The hyalinized papillary dermal material likely represents secondary amyloid formation. The narrow branching cords of basaloid cells extending from the epidermis are reminiscent of fibroepithelioma of Pinkus. Other areas of the tumour show cystic change, and there are islands of keratinization, staining more intensely red, that represent squamoid differentiation within the tumour; 2c) Here, the tumour islands are most consistent with macronodular basal cell carcinoma. They are associated with a cellular, fibrous stroma featuring small vessel proliferation; 2d) The upper ½ of this image displays features of fibroepithelioma of Pinkus; changes in the lower ½ of the image are similar to those in (2c) and are mainly macronodular, with small foci of cystic change. The cellular, fibrotic stroma is evident; 2e) There is a central island of macronodular BCC associated with a cellular fibrotic stroma. The tumor island at the top of the figure (12:00-1:00) shows infiltrative features along its lower edge; 2f) Centrally, there is a distinctly squamoid area, with horn cyst formation (at 6:00) and infiltrative features; this area can be interpreted as a focus of basosquamous carcinoma. Again, there is a cellular, fibrotic stroma with lymphocytic inflammation; 2g) This image shows a macronodular focus of basal cell carcinoma with more subtle squamoid changes and a distinct focus of keratinization (at 7:00); 2h) Islands of macronodular basal cell carcinoma are present at the left and right of the figure. The larger tumour island on the right also shows a squamoid change in its upper portion. Between the two islands is a cellular fibrotic stroma with lymphocytic inflammation.

Many of these types (fibroepithelioma-like, cystic, basosquamous) are indicative of follicular/primary epithelial germ differentiation, while the infiltrative and basosquamous carcinoma areas are associated with more biologically aggressive tumours. The probable amyloid formation seen in Figures 2a and 2b is known to occur in basal cell carcinoma, and derives from degenerated basaloid cells, with modification of keratin filaments into a beta-pleated sheet configuration.

Discussion

Basal cell carcinoma is the most frequent type of skin cancer, and a strong association between its development and long-term sun exposure has been established [19].

However, its development in uncommon locations - such as sun-protected areas - requires a higher degree of suspicion for diagnosis. There exist few reports of axillary BCC cases, with an estimated a prevalence of 0.17%. As of August 2014, there were only 81 cases of axillary BCCs presented in scholarly journals [20]. Cohen observed that these tumours occurred predominantly in Caucasians, without significant BCC-associated risk factors [21]. The histologic sub-types associated with this localisation were mainly superficial or nodular, with an excellent prognosis after complete surgical removal [21]. No case of metastatic spread has been reported. However, the development of axillary tumours in patients with Gorlin-Goltz syndrome emphasises the risk of their inheritance, an important pathogenetic factor that should be thoroughly investigated. Moreover, the report of a linear adamantanoid BCC in the axilla, a sub-type with an increased risk of local invasion and recurrence [22], suggests the need for caution in the diagnosis and management of tumours localised in sun-protected areas.

Because of the wide-ranging clinical differential diagnosis in the presented case, including an array of benign and malignant tumours, histologic evaluation was carried out to determine the correct diagnosis. The peculiarity of our case consisted of its mixed histopathological patterns of macronodular, fibroepithelioma-like, cystic, focally infiltrative, and basosquamous features that have rarely been described in axillary BCCs. Infiltrative and basosquamous carcinomas are considered aggressive tumours, with an increased risk of recurrence and metastases. The treatment approach should focus on surgical excision with free margins to prevent tumour recurrence.

Although the tumour had slowly progressed over the previous ten years, the reason the patient presented for a dermatologic appointment was the acute symptom of bleeding. This reinforces the importance of educational campaigns and dermoscopic screenings for early diagnosis and treatment of skin cancers.

While international reports suggest a worldwide increase in the incidence of non-melanoma skin cancers [23], generally attributed to ultraviolet exposure, it would be useful to study the epidemiology of BCCs that develop in sun-protected areas, to gain more insight into the pathogenesis of this subset of tumours.

In conclusion, uncommon locations of BCCs

in sun-protected areas such as the axillary region require a higher degree of suspicion for diagnosis. The complexity of histopathologic subtypes in the presented case, each with potentially different biologic attributes, emphasises the importance of histopathological examination in the diagnosis and therapeutic management of BCC.

References

1. Urbach F. Incidence of non melanoma skin cancer. Dermatol Clin. 1991;9:751–5. PMid:1934649

2. Dourmishev A, Popova L, Dourmishev L. Basal-cell carcinoma and squamous-cell carcinomas: Epidemiology, location and radiotherapy. Skin Cancer. 1996;11:195–200.

3. Chung S. Basal Cell Carcinoma. Arch Plast Surg. 2012; 39(2): 166–170. https://doi.org/10.5999/aps.2012.39.2.166 PMid:22783519 PMCid:PMC3385325

4. Dourmishev LA, Rusinova D, and Botev I. Clinical variants, stages, and management of basal cell carcinoma. Indian Dermatol Online J. 2013; 4(1): 12–17. https://doi.org/10.4103/2229-5178.105456 PMid:23439912 PMCid:PMC3573444

5. Mulvany NJ, Allen DG. Differentiated intraepithelial neoplasia of the vulva. Int J Gynecol Pathol. 2008;27:125–35. https://doi.org/10.1097/pgp.0b0318134ea34 PMid:18156987

6. Lo JS, Snow SN, Reizner GT, Mohs FE, Larson PO, Hruza GJ. Metastatic basal cell carcinoma: Report of twelve cases with a review of the literature. J Am Acad Dermatol. 1991;24:715–9. https://doi.org/10.1016/0190-9622(91)70108-E

7. Dessinioti C, Antoniou C, Katsambas A, Stratigos AJ. Basal cell carcinoma: What's new under the sun. Photochem Photobiol. 2010;86:481–91. https://doi.org/10.1111/j.1751-1097.2010.00735.x PMid:20550646

8. Cabrera HN, Gómez ML. Skin cancer induced by arsenic in the water. J Cutan Med Surg. 2003;7:106–11. https://doi.org/10.1177/120347540300700202 PMid:12447618

9. Chan PC, Haseman JK, Boorman GA, Huff J, Manus AG, Cardy RH. Forestomach lesions in rats and mice administered 3-chloro-2-methylpropene by gavage for two years. Cancer Res. 1986;46:6349–52. PMid:3779651

10. Kubasiewicz M, Starzy-ski Z. Case-referent study on skin cancer and its relation to occupational exposure to polycyclic aromatic hydrocarbons. I. Study design. Pol J Occup Med. 1989;2:221–8. PMid:2489425

11.Emmert S, Schön MP, Haenssle HA. Molecular biology of basal and squamous cell carcinomas. Adv Exp Med Biol. 2014;810:234-52. https://doi.org/10.1007/978-1-4939-0437-2_13

13. de Zwaan SE, Haass NK. Genetics of basal cell carcinoma. Australas J Dermatol. 2010;51:81–92. https://doi.org/10.1111/j.1440-0960.2009.00579.x PMid:20546211

14. Von Hoff DD, LoRusso PM, Rudin CM, et al. Inhibition of the hedgehog pathway in advanced basal-cell carcinoma. N Engl J Med. 2009;361:1164–1172. https://doi.org/10.1056/NEJMoa0905360 PMid:19726763

15. Saxena K, Manohar V, Bhakhar V, Bahl S. Adenoid basal cell carcinoma: a rare facet of basal cell carcinoma. BMJ Case Rep. 2016;2016:10.

16. Viera M, Amini S, Huo R, Oliviero M, Bassalo S. A New Look at Fibroepithelioma of Pinkus. Features on Confocal Microscopy. J Clin Aesthet Dermatol. 2008; 1(2): 42–44. PMid:21103323 PMCid:PMC2989825

17. Aydin D, Rosenkrantz Hölmich L, Jakobsen LP. Metastatic basal cell carcinoma caused by carcinoma misdiagnosed as acne – case report and literature review. Clin Case Rep. 2016; 4(6): 601–604. https://doi.org/10.1002/ccr3.575 PMid:27398205 PMCid:PMC4891487

18. Lanoue J, Goldenberg G. Basal Cell Carcinoma. A Comprehensive Review of Existing and Emerging Nonsurgical Therapies. J Clin Aesthet Dermatol. 2016; 9(5): 26–36. PMid:27386043 PMCid:PMC4928477

19. Enachescu CI, Mihai MM. Clinical and histological features of basal cell carcinomas. A five-year experience in a dermatology clinic. Rev Chim. 2016;67(9):1701- 1706.

20. Cohen PR. Axillary basal cell carcinoma in patients with Goltz-Gorlin syndrome: report of basal cell carcinoma in both axilla of a woman with basal cell nevus syndrome and literature review. Dermatol Online J. 2014;20(8).

21. Cohen PR. Basal cell carcinoma of the axilla: review of the world literature. Am J Clin Dermatol. 2014;15(2):95-100. https://doi.org/10.1007/s40257-014-0066-8 PMid:24567258

22. Bajaj S, Sharma PK, Kar HK. Linear adamantinoid basal cell carcinoma in the axilla. Dermatol Online J. 2015;21(5). pii: 13030/qt8k0713nb.

23. Mohan SV, ChangAL. Advanced Basal Cell Carcinoma: Epidemiology and Therapeutic Innovations. Curr Dermatol Rep. 2014;3:40-45. eCollection 2014.

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Case Report

Incontinentia Pigmenti: A Case Report of a Complex Systemic Disease

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Keywords: Incontinentia Pigmenti; genodermatosis; NEMO; cutaneous manifestations; systemic disease.

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Abstract

Incontinentia Pigmenti is an uncommon X-linked genodermatosis, caused by mutations in the NEMO gene. It is a systemic disease that involves tissue of ectodermic and mesodermic origin, including cutaneous tissue, teeth, eyes and the central nervous system, amongst other organs. The Authors report a rare case of Incontinentia Pigmenti in a female newborn.

Introduction

First described by Bloch in 1926, and Sulzberger in 1928, incontinentia pigmenti (IP) is a rare X-linked genodermatosis [1, 2], which name is related to the histological characteristics of the lesions in the third stage (or pigmentary stage) of the disease (Tab.1), consisting in the melanin incontinence by melanocytes of the basal epidermal layer and by its presence in the superficial dermis.

IP is a systemic disease which involves tissues of both ectodermic and mesodermic origin, including cutaneous tissue, teeth, eyes and the central nervous system, amongst other organs [3]. It is a hereditary, X-linked dominant disorder, with high penetrance and variable expressivity. It derives by mutations in the NEMO/IKKγ/IKBKG gene, located on Xq28. NEMO is the essential modulator of NF-kB, a transcriptor factor involved in immune and inflammatory responses, and in protecting cells from tumour necrosis factor-induced apoptosis. Disruption of the NEMO gene leads to diminish the NF-kB activity and to increase the cells susceptibility to apoptosis [4, 5]. Also, inflammatory reactions and epidermal eosinophil recruitment, observed in the first stages of IP, seems to be important in the pathogenesis of the disease. It seems possible that the epidermal eosinophil accumulation is related to an eosinophil-selective chemokine (eotaxin), produced by specific leucocytes (e.g. eosinophils, macrophages, T-cells) and some structural cells (e.g. endothelial cells, fibroblasts and epithelial cells) [6].

In male patients, NEMO mutation is linked to their embryonic lethality. Female survival is due to the lyonization phenomenon (or X chromosome inactivation), which occur during early embryogenesis.

Although its epidemiological data are unknown, IP seems to occur in approximately 1 in 40.000 newborns [7]. About 50% of the IP cases have a positive family history of the same disease. The disease is predominant in women (F: M = 37:1). Less than 3% of cases are described in males. Many of them have Klinefelter's syndrome (47, XXY

karyotype), where the second X chromosome seems to play an important role in their survival from the natural intrauterine death. In the other male cases, different genetic mutations have also been described, such as hypomorphic alleles or somatic mosaicism for the common IKBKG deletion [8, 9].

Case report

A newborn female, 20 days old, affected by a diffuse vesciculo-bullous rash showed up to our Clinic (Fig. 1).

The baby was born at term by a spontaneous vaginal delivery, which was carried out after 3 hours by the membranes rupture.

The entire pregnancy had taken place regularly, without any complication.

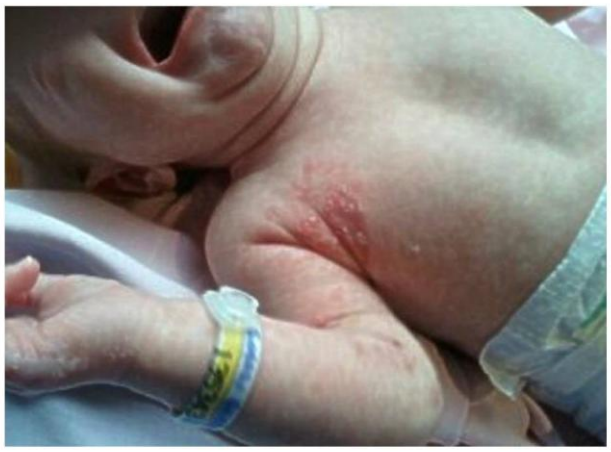

Figure 1: Blisters and bullae, on inflammatory ground, localised on the trunk, in a linear arrangement which follows the lines of Blaschko

The patient's mother was an otherwise healthy single woman of 31 years old. She did not have previous pregnancies or abortions. During her childhood, the woman had suffered from varicella, rubeola, parotitis and rubella.

The woman told us to be affected by epilepsy. Her medical treatment, also during the pregnancy, consisted of carbamazepine. No other diseases or drugs assumptions had been reported. Her familial history was insignificant.

At the mother's clinical evaluation we did not observe any form of cutaneous, nail or hair alterations. Maternal serology was negative for VDRL, HIV, HBV, HCV.

Unfortunately, no news about the newborn's father had been reported to us.

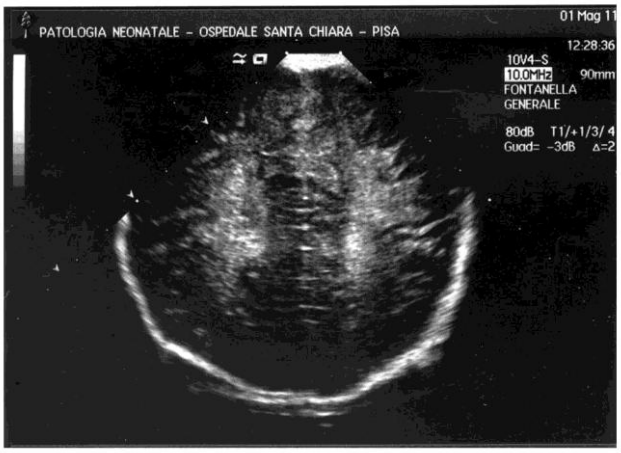

Figure 2: Cranial ultrasound shows an immature central nervous system, as demonstrated by the bilateral periventricular hyperechogenicity of the white substance

During the clinical evaluation, the young patient was 48 cm in height, and 2.6 kg of weight, which is less than normal. She had normal blood pressure, pulse rate and breathing. The musculoskeletal system was normal, except for an hypoplastic mandible. She did not have ocular or abdominal alterations.

From birth, the newborn suffered from seizures. The EEG showed a severely abnormal pattern with frequent multi-focal spikes; the head ultrasound showed a pattern of immature neurological development (Fig. 2). Even if, in a first moment, the neurologist thought how seizures could be the result of the carbamazepine abstinence, seizures never stopped as they were a primary disease.

During the dermatologic examination, we observed clear, tense blister and bullae, on inflammatory base. Lesions were localised on the extremities and the trunk, in a linear arrangement which followed the lines of Blaschko, and seemed to be asymptomatic. The Nikolsky test was negative. No other lesions were observed in the other cutaneous or mucosal areas.

Hairs were less than normal, wiry and coarse. Nails were dystrophic.

Routine blood testing for inflammation, infections and autoimmune diseases were negative, except for a peripheral eosinophilia (> 20%). C-reactive protein and procalcitonin were normal. A punch biopsy performed on a lesion showed, in the epidermis, a mild acanthosis, foci of eosinophilic spongiosis and occasional dyskeratotic keratinocytes. In the same time, the dermis showed an infiltrate of lymphocytes, eosinophils and nuclear dust derived from eosinophilic karyorrhexis (Fig. 3).

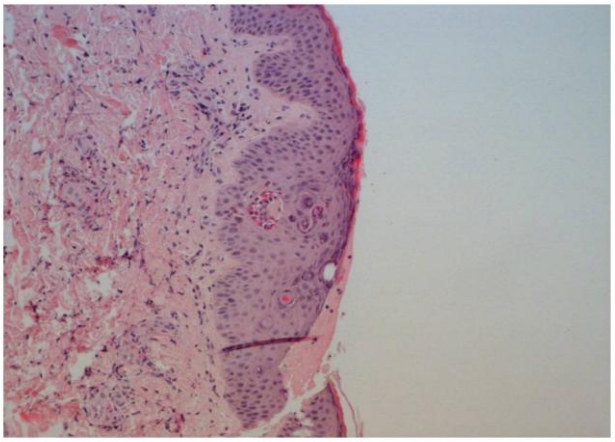

Figure 3: Histology: The epidermis shows mild acanthosis, foci of eosinophilic spongiosis and occasional dyskeratotic keratinocytes. The dermis is characterised by an infiltrate of lymphocytes, many eosinophils and nuclear dust derived from eosinophilic karyorrhexis

On the basis of the patient's clinical pattern and of the histological examination, we made the diagnosis of IP.

Because of the spontaneous improvement and resolution of skin lesions, we prescribed only an antibiotic therapy to avoid secondary infections of the lesions.

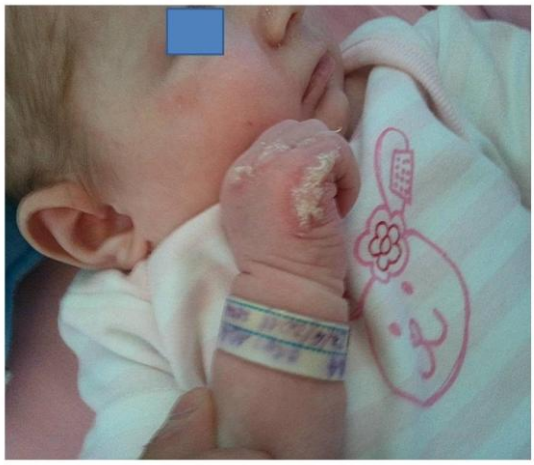

Figure 4: Warty lesions on the right hand

Two weeks later, during a follow-up, the dermatologic manifestations had been changed, as the classic evolution of IP. Linear warty lesions appeared on the side of the previous vesicular-bullous rash.

Discussion

The clinical presentation of IP varies considerably, even among the family members of the same patient [10]. They range from subtle cutaneous and dental involvement to a complex syndrome, sometimes deadly.

Although IP may affect many organs, the cutaneous manifestations are the most commonly described (l). Typically the cutaneous lesions occur along the Blaschko's lines and evolve through four stages (Table 1) [11-13].

The first one (bullous stage) is described in 90% of patients at birth or within the first two weeks of life. Sometimes, it may occur in utero and doesn't progress after birth. Clinically, it is characterised by clear, tense bullae on inflammatory bases. Lesions are mainly described on the extremities (linear pattern) and the trunk (linear or circumferential pattern). Even if the face is usually spared, scalp lesions are quite common. The rash disappears by the age of 18 months. Recurrences can seldom be observed, also several years after the neonatal period, but they are usually shorter and less severe than the original eruption. The second stage (verrucous one) is characterised by a hypertrophic, wart-like rash, with the same localisation of initial lesions. Usually, stage 2 starts between the second and sixth weeks of life and persists for a few months. The third stage (hyperpigmentation stage) is the most characteristic one. It usually begins at the age six-twelve months and persists into the adulthood. Clinically, it is characterised by brownish linear and whorled streaks which follow the Blaschko's lines. The pigmentation ranges in colour from blue-grey or slate to brown. The bizarre splashed or Chinese figure distribution is diagnostic. Linear or macular telangiectasia may also be described. The last stage (fourth stage or atretic one) is described only in 14 % patients. Clinically, it is characterised by hypo pigmentary and atrophic lesions, in the same areas of the previous hyperpigmentation.

Table 1: Stages of incontinentia pigmenti

STAGE	CLINICALCHARACTERISTICS	HISTOLOGIC FEATURES
STAGE 1 – BULLOUS STAGE	Clear, tense bullae and vesicles on inflammatory bases.	Eosinophilic spongiosis, intraepidermal vesicles. Inflammation of the dermis, with a cellular, infiltrate, including numerous eosinophils.
STAGE 2 - VERRUCOUS STAGE	Hypertrophic, wart-like rash.	Dyskeratotic keratinocytes, hyperkeratosis, acanthosis and papillomatosis. Macrophages laden with melanin may be present in the upper dermis. Possible signs of epidermal and dermal inflammation (epidermal spongiosis, cellular infiltrate including numerous eosinophils).
STAGE 3 - HYPERPIGMENTATION STAGE	Brownish linear and whorled streaks.	Melanin incontinence by melanocytes in the basal epidermal layer and its presence in the superficial dermis.
STAGE 4 - ATRETIC STAGE	Hypopigmentary and atrophic lesions.	Epidermal atrophy and decreased, normal or small melanocytes. Skin appendages may be absent.

In realty, the onset and duration of each stage vary among individuals, and not all individuals experience all four stages. Stage 1 and three are more commonly observed than stage 2 and 4. Some patients may show additional cutaneous manifestations such as palmoplantar hyperhidrosis, port wine stain, abnormalities of mammary tissue, hair

(e.g. alopecia, woolly hair) and nails alterations (e.g. onycho- dystrophy, onychogryphosis, pitting, yellow discoloration, subungual and periungual keratotic tumours) [14,15]. Extracutaneous manifestations may also be described.

Among these, the dental abnormalities (e.g. delayed dentition, partial anodontia, hypodontia, abnormally shaped teeth) are the most commonly reported, occurring in more than 80% of all patients [16,17].

Ocular defects occur in about 40% of all the cases. They include strabismus, cataract, conjunctival pigmentosa uveitis, optic nerve atrophy, retinal vascular abnormalities, blue sclera, exudative chorioretinitis, retinal glioma [18].

About 25% of patients have neurological disorders, like seizures, spastic or paralytic quadriplegia, hemiparesis, cerebral atrophy, microcephaly and encephalopathy [19, 20]. The incidence of mental retardation is about 25-35%.

Other extracutaneous manifestations include abnormalities of the musculoskeletal system (e.g. hemivertebra, hemiatrophy, syndactyly, congenital dislocation of the hip, club foot, dwarfism, scoliosis, supernumerary ribs), and of the cardiovascular one (e.g. atrial septal defects, acyanotic tetralogy of Fallot, ventricular endomyocardial fibrosis, tricuspid insufficiency, primary pulmonary hypertension) [21].

Also, immunologic abnormalities are common in IP. They include functional abnormalities of neutrophils and lymphocytes and defects in polymorphonuclear chemotaxis. Eosinophilia up to 50% in the peripheral blood is common in the first inflammatory stage of IP.

Unfortunately, to date, no strict diagnostic criteria for IP exist. The diagnosis is mainly clinical, and it is based on recognition of the typical cutaneous lesions. The presence of dental, hair, nails and ocular alterations support the diagnosis. Peripheral eosinophilia is a suggestive sign in the earlier diagnosis. Eventually, a family history of X-linked inheritance or a history of multiple miscarriages may also support the hypothetic diagnosis.

The diagnosis may be confirmed only with the histological examination of a skin biopsy, and molecular genetic test (NEMO mutation).

In conclusion, because IP is a systemic disorder, a multidisciplinary approach to the patients is crucial. A complete neurologic examination is recommended for all IP infants.

Regular visits to a paediatric ophthalmologist are essential during the first year of life. Laser photocoagulation and vascular endothelial growth factor inhibitor seem to be good treatments for retinal vascular abnormalities [22].

Concerning teeth, a radiologic evaluation and dental intervention by the age of two years is an appropriate therapeutic approach.

The dermatological management in the newborn period is aimed at reducing the risk of infection of blisters using antibiotics and hygienic preventive measures. Spontaneous improvement and resolution of skin lesions is general the rule. Topical and systemic steroids may be prescribed to limit the rash of the first two stages [23]. The use of laser therapies to treat the hyperpigmented lesions of should be discouraged because it has been reported to trigger an extensive vesicular-bullous eruption [24].

References

1. Woon-Kyong Chung, Deok-Woo Lee, Sung-Eun Chang et Al. A Case of incontinentia pigmenti associated with multiorgan abnormalities. Ann Dermatol. 2009; 21: 56–59. https://doi.org/10.5021/ad.2009.21.1.56 PMid:20548858 PMCid:PMC2883371

2. Babu NA, Rajesh E, Krupaa J, Gnananandar G. Genodermatoses. J Pharm Bioallied Sci. 2015;7(Suppl 1): S203–S206. PMid:26015711 PMCid:PMC4439671

3. Hadj-Rabia S, Froidevaux D, Bodak N, Hamel-Teillac D, Smahi A, Touil Y, et al. Clinical study of 40 cases of incontinentia pigmenti. Arch Dermatol. 2003;139:1163–1170. https://doi.org/10.1001/archderm.139.9.1163 PMid:12975158

4. Berlin AL, Paller AS, Chan LS. Incontinentia pigmenti: a review and update on the molecular basis of pathophysiology. J Am Acad Dermatol. 2002;47:169–187. https://doi.org/10.1067/mjd.2002.125949 PMid:12140463

5. Shastry BS. Recent progress in the genetics of incontinentia pigmenti (Bloch-Sulzberger syndrome). J Hum Genet. 2000;45:323-326. https://doi.org/10.1007/s100380070001 PMid:11185738

6. Jean-Baptiste S, O'Toole EA, Chen M et Al. Expression of eotaxin, an eosinophil-selective chemokine, parallels eosinophil accumulation in the vesiculobullous stage of incontinentia pigmenti. Clin Exp Immunol. 2002;127:470-478. https://doi.org/10.1046/j.1365-2249.2002.01755.x PMid:11966763 PMCid:PMC1906303

7. Buinauskiene J, Buinauskaite E, Valiukeviciene S. Incontinentia pigmenti (Bloch- Sulzberger syndrome) in neonates. Medicina (Kaunas). 2005;41:496–499.

8. Buinauskaite E, Buinauskiene J, Kucinskiene V, Strazdiene D, Valiukeviciene S. Incontinentia pigmenti in a male infant with Klinefelter syndrome: a case report and review of the literature. Pediatr Dermatol. 2010;27:492-495. https://doi.org/10.1111/j.1525-1470.2010.01261.x PMid:20807362

9. Song JY, Na CH, Chung BS, Choi KC, Shin BS. A case of a surviving male infant with incontinentia pigmenti. Ann Dermatol. 2008;20:134-137. https://doi.org/10.5021/ad.2008.20.3.134 PMid:27303177 PMCid:PMC4903964

10. Kutkowska-Kaźmierczak A, Obersztyn E, Bonnefont JP, Rosińska-Borkowska D, Mazurczak T, Sobczyńska-Tomaszewska A, Mazurczak T. Variable clinical expression of familial Incontinentia Pigmenti syndrome - presentation of three cases. Med Wieku Rozwoj. 2008;12:748-753. PMid:19305025

11. Ehrenreich M, Tarlow MM, Godlewska-Janusz E, Schwartz RA. Incontinentia pigmenti (Bloch-Sulzberger syndrome): a systemic disorder. Cutis. 2007;79:355-362. PMid:17569396

12. Chung WK, Lee DW, Chang SE, Lee MW, Choi JH, Moon KC. A case of incontinentia pigmenti associated with multiorgan abnormalities. Ann Dermatol. 2009;21: 56–59. https://doi.org/10.5021/ad.2009.21.1.56 PMid:20548858 PMCid:PMC2883371

13. Poziomczyk CS, Recuero JK, Bringhenti L, Maria FD, Campos CW, Travi GM, Freitas AM, Maahs MA, Zen PR, Fiegenbaum M, Almeida ST, Bonamigo RR, Bau AE. Incontinentia pigmenti. An Bras Dermatol. 2014;89:26-36. https://doi.org/10.1590/abd1806-4841.20142584 PMid:24626645 PMCid:PMC3938351

14. Chun SR, Rashid RM. Delayed onychodystrophy of incontinentia pigmenti: an evidence- based review of epidemiology, diagnosis and management. J Drugs Dermatol. 2010;9:350-354. PMid:20514792

15. Chan YC, Happle R, Giam YC. Whorled scarring alopecia: a rare phenomenon in incontinentia pigmenti? J Am Acad Dermatol. 2003;49:929-931. https://doi.org/10.1016/S0190-9622(03)00474-2

16. Santa-Maria FD, Mariath LM, Poziomczyk CS, Maahs MA, Rosa RF, Zen PR, Schüller- Faccini L, Kiszewski AE. Dental anomalies in 14 patients with IP: clinical and radiological analysis and review.Clin Oral Investig. 2016 [Epub ahead]. PMid:27766487

17. Minić S, Trpinac D, Gabriel H, Gencik M, Obradović M. Dental and oral anomalies in incontinentia pigmenti: a systematic review. Clin Oral Investig. 2013;17:1-8. https://doi.org/10.1007/s00784-012-0721-5 PMid:22453515

18. Minić S, Obradović M, Kovacević I, Trpinac D. Ocular anomalies in incontinentia pigmenti: literature review and meta-analysis. Srp Arh Celok Lek. 2010;138:408-413. https://doi.org/10.2298/SARH1008408M PMid:20842883

19. Minić S, Trpinac D, Obradović M. Systematic review of central nervous system anomalies in incontinentia pigmenti. Orphanet J Rare Dis. 2013;8:25. https://doi.org/10.1186/1750-1172-8-25 PMid:23406512 PMCid:PMC3576363

20. Pörksen G, Pfeiffer C, Hahn G, Poppe M, Friebel D, Kreuz F, Gahr M. Neonatal seizures in two sisters with incontinentia pigmenti. Neuropediatrics. 2004;35:139-142. https://doi.org/10.1055/s-2004-815837 PMid:15127315

21. Godambe S, McNamara P, Rajguru M, Hellmann J. Unusual neonatal presentation of incontinentia pigmenti with persistent pulmonary hypertension of the newborn: a case report. J Perinatol. 2005;25:289-292. https://doi.org/10.1038/sj.jp.7211250 PMid:15789024

22. Moreira Neto CA, Moreira AT, Moreira Jr CA. Ophthalmic evaluation, treatment, and follow-up of two cases of incontinentia pigmenti. Arq Bras Oftalmol. 2014;77:47-49. https://doi.org/10.5935/0004-2749.20140012 PMid:25076373

23. Tomotaki S, Shibasaki J, Yunoki Y, Kishigami M, Imagawa T, Aida N, Toyoshima K, Itani Y. Effectiveness of corticosteroid therapy for acute neurological symptoms in incontinentia pigmenti. Pediatr Neurol. 2016;56:55-58. https://doi.org/10.1016/j.pediatrneurol.2015.12.002 PMid:26777982

24. Nagase T, Takanashi M, Takada H, Ohmori K. Extensive vesiculobullous eruption following limited ruby laser treatment for incontinentia pigmenti: a case report. Australas J Dermatol. 1997;38:155-157. https://doi.org/10.1111/j.1440-0960.1997.tb01135.x PMid:9293665

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Case Report

Basal Cell Carcinoma Surgery: Simple Undermining Approach in Two Patients with Different Tumour Locations

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Abstract

Basal cell carcinoma (BCC) is the most common human malignancy, accounting for the majority of all non-melanoma skin cancers (NMSC). In the past several decades the worldwide incidence of BCC has constantly been increasing. Even though it is a slow growing tumour that, left untreated, rarely metastasizes, it has a distinctive invasive growth pattern, posing a considerable risk for local invasion and destruction of underlying tissues, such as muscle, cartilage, bone or vital structures. Advanced BCCs include such locally invasive or metastatic tumours. Complete surgical excision is the standard therapy for most uncomplicated BCC cases with good prognosis and cure rates. Treatment of advanced forms of BCCs poses significant therapeutic challenges, most often requiring complicated surgery, radiotherapy, and/or targeted therapies directed towards the sonic hedgehog signalling pathway (SHH). We present two cases of large BCCs located on the scalp and posterior thorax, which underwent surgical excision with clear margins, followed by reconstruction of the defect after extensive undermining of the skin.

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Introduction

Basal cell carcinoma (BCC) is the most common human malignancy, accounting for the majority of non-melanoma skin cancers, with worldwide incidence rates increasing at least 2-3 fold in the past few decades [1,2]. It is a slow growing tumour with metastatic incidence rates ranging between 0.0028–0.55% [3]. However, in some cases, these tumours display a locally invasive growth pattern that poses a considerable risk of destruction of underlying cartilage, bone, or vital structures. Most BCCs develop in sun exposed areas of fair skinned individuals, mainly on the head and neck, and less frequently on the trunk and limbs [4, 5]. Besides

cutaneous phototype and exposure to UV radiation, other risk factors known to favor the development of BCC include genetic traits (including xeroderma pigmentosum, epidermodysplasia verruciformis, albinism, Gardner's syndrome, a familial history of skin cancer, or DNA repair deficiencies leading to chromosomal instability), immunosuppression, repeated cutaneous trauma, or exposure to ionizing radiation or other environmental carcinogens (e.g. arsenic, alkylating agents, polycyclic aromatic hydrocarbons) [6-8].

We present two cases of BCCs located on the scalp and posterior thorax, managed by complete surgical excision, followed by reconstruction of the resulting defect after extensive undermining of the skin. This technique allowed for subsequent direct closure with simple sutures and an acceptable cosmetic outcome.

Case report #1 - Scalp BCC

An 86 year-old male was presented to the dermatology department for the diagnosis and treatment of a cutaneous tumour located on his scalp, which had been present for more than two years. The patient reported accelerated enlargement of the skin lesion within the last three months, associated with local pruritus and pain, and denied any treatment or medical attention before presentation. His medical history was positive for glaucoma, while the family history was unremarkable for skin cancer or other significant dermatological conditions.

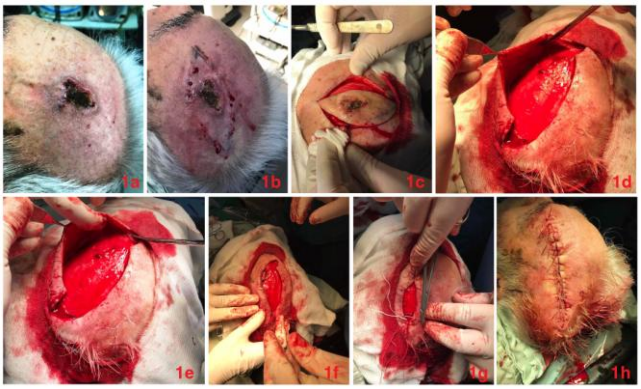

Figure 1: 1a) Cutaneous lesion on the frontoparietal region of the scalp; 1b) Preoperative excision markings with wide margins, bleeding and edema from infiltration of local anesthetic; 1c) Tumour is partially excised showing depth of the excision to the pericranium; 1d-e) Primary surgical defect is extensively undermined in all directions to allow for coaptation of the wound edges; 1f-g) Placement of simple interrupted non-absorbable sutures for scalp defect closure; 1h) Scalp defect is completely reconstructed, ready for antiseptic dressings

Clinical examination revealed a relatively well demarcated, oval shaped cutaneous tumour located on the scalp, featuring a "rolled border" and central ulceration covered by a serosanguinous crust - features consistent with those of basal cell carcinoma (Fig. 1a). Palpation of the submandibular, axillary, preauricular and occipital lymph nodes did not demonstrate enlargement or painful masses. No abnormalities were detected on chest x-ray. Concerning disease progression and invasion, an x-ray of the calvaria did not show any bone involvement. On abdominal ultrasound, prostate hyperplasia, multiple bladder diverticula and a single 1.4 cm cyst of the left kidney were discovered.

After obtaining informed consent from the patient, an elliptical surgical excision of the scalp lesion was performed under local anaesthesia with 2% lidocaine and epinephrine (Fig. 1b–h). The extensive undermining of the post-excisional wound edges was conducted (Fig. 1d-e), followed by primary defect closure by placement of interrupted non-absorbable sutures (Fig. 1f-h) and application of antiseptic dressings. Perioperative antibiotic prophylaxis was performed with administration of 2 grammes of Ceftriaxone q.d. for five days. The patient was discharged with instructions for wound-care and follow-up for suture removal; his postoperative course was devoid of complications. The subsequent histopathological evaluation confirmed the diagnosis of basal cell carcinoma of the scalp. No evidence of metastatic spread was found with imaging procedures or by laboratory blood tests.

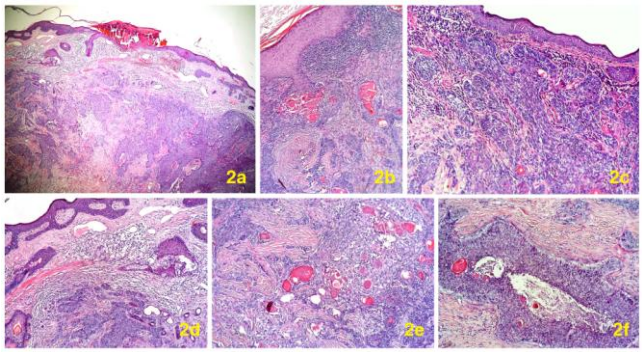

Figure 2: 2a) large dermal tumor; 2b) focal connections between tumor cells and the epidermis; 2c) nodular masses of basaloid neoplastic cells with hyperchromatic nuclei, nuclear pleomorphism, scanty cytoplasm and peripheral palisading of nuclei; 2d) areas of infiltration composed of strands and chords of tumor cells that invade the dermal structures; 2e) foci of abrupt keratinization within some tumor islands; 2f) central necrosis with pseudo-cystic changes

Histopathology: Histopathological examination showed a large dermal tumour (Fig. 2a), focally connected to the epidermis (Fig. 2b), consisting of nodular masses of neoplastic basaloid cells with hyperchromatic nuclei, nuclear pleomorphism, scanty cytoplasm and the peripheral palisading of nuclei typical of basal cell carcinoma (Fig. 2c). There were areas of infiltration composed of strands and chords of tumour cells that invaded the dermal structures (Fig. 2d), as well as numerous foci of abrupt keratinization in the middle of some tumor islands (Fig. 2e). In some areas, there was a cleavage between the tumour cells

and the adjacent fibrous stroma, with mucinous degeneration, and the larger tumour islands showed central necrosis with pseudo-cystic changes (Fig. 2f). These findings were considered typical for a large nodular basal cell carcinoma with infiltrative areas, mucinous stromal degeneration and foci of keratinization.

Case report #2 - Posterior trunk BCC

A 73-year-old male presented to the dermatology department with a large cutaneous tumour located on his posterior trunk that had been slowly growing for more than ten years. The patient denied any treatment or medical attention before the presentation. The patient's medical history revealed previous coronary bypass surgery. At the time of admission, he had been taking a daily dose of acetylsalicylic acid (ASA) as a preventative therapy, which before surgery was replaced with 0.6 ml subcutaneous nadroparin calcium twice daily. On examination, the tumour was located on the left posterior upper trunk. The skin lesion was well marginated, pinkish-grey in colour, with an eroded surface and focal bleeding (Fig. 3a).

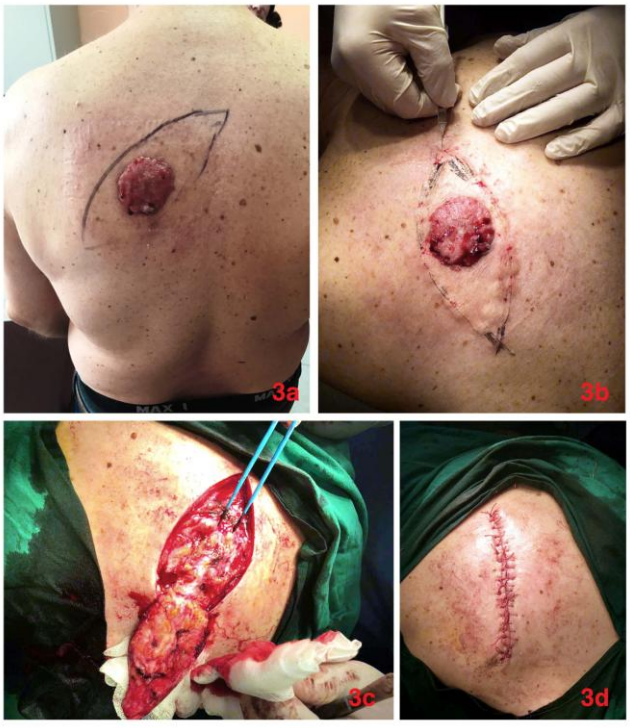

Figure 3: a) Skin lesion on the left posterior upper-trunk region; b) Preoperative excision markings, bleeding and oedema from local anaesthetic infiltration; c) Tumour is partially excised, showing substantial bleeding and performance of electrocautery hemostasis; d) Primary surgical defect is completely reconstructed, ready for antiseptic dressings

No regional lymphadenopathy could be identified by clinical examination. Considering the long duration and morphology, a provisional diagnosis of basal cell carcinoma was made.

Chest x-ray and lymph node ultrasonography of the axillary and inguinal lymph nodes did not show any evidence of disease progression or tumour spread. Abdominal ultrasonography revealed morphologic findings consistent with pyelonephritis and light hydronephrosis and urology and nephrology consults were requested. Informed consent was obtained from the patient before surgery. The upper-trunk skin lesion was then surgically excised in an elliptical manner with wide margins under local anaesthesia with 2% lidocaine and epinephrine (Fig. 3c). Substantial intraoperative bleeding was encountered, and electrocoagulation was employed. Following rigorous hemostasis, the extensive undermining of the wound edges in all directions was performed to allow for direct wound closure. The surgical defect was first approximated using absorbable subdermal sutures followed by placement of simple interrupted non-absorbable sutures (Fig. 3d), and application of antiseptic ointment wound dressings. Postoperative antibiotic prophylaxis consisted of Clarithromycin 500 mg q.d. for ten days. There were no postoperative complications, and the patient was discharged with instructions for daily wound care. Follow-up visits were scheduled, and all sutures were removed at day twenty post-operatively.

Histopathology: The tumour consisted of tightly packed large dermal nodules and interconnecting strands of basaloid cells with monomorphic nuclei, scanty cytoplasm and peripheral nuclear palisading. The majority of tumour nodules showed central cystic degenerative changes and pseudo-glandular spaces with mucinous contents (Fig. 4a-c).

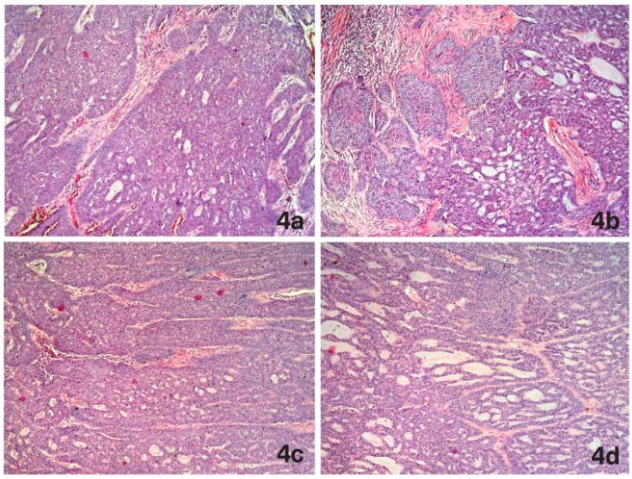

Figure 4: a-c) central cystic degenerative changes and pseudo-glandular spaces with mucinous content; d) cribriform pattern with some resemblances to adenoid cystic carcinoma

Some of these areas resembled the cribriform pattern usually associated with adenoid cystic carcinoma (Fig. 4d). These features were typical for a large nodular basal cell carcinoma with cystic change, sometimes referred to as adenoid basal cell carcinoma.

Discussion

The main molecular alterations responsible for the development of BCCs include the activation of the sonic hedgehog signalling pathway caused by acquired mutations in the PTCH and SMO genes [9] and also mutations in P53 and melanocortin-1 receptor genes [10, 11]. Standard therapy for the majority of BCCs is complete surgical excision, with good prognosis and cure rates. However, advanced BCCs, comprising locally advanced lesions and tumours with metastatic spread, pose significant therapeutic challenges and are, most often, difficult to treat. Advanced BCCs management is complex, requiring complicated surgery, radiotherapy or targeted therapies directed towards sonic hedgehog signalling pathway (SHH), either alone or in combination [12, 13].

Tumour size and location, the patient's general condition, and the physician's experience with particular therapeutic modalities are key considerations. Undermining plastic surgery has proven to be a good alternative to complex grafts or flaps for the treatment of selected cases of locally advanced BCCs, with the advantage of being less traumatic, allowing for good intraoperative control of clinical margins and good esthetic results [14]. Basal cell carcinoma is the most frequent cutaneous neoplasm worldwide. "Advanced" BCC, though a loosely defined term, comprises locally advanced and metastatic tumours. In a systematic review of the literature, Archontaki *et al.* (2009) analysed clinical and paraclinical data of 51 patients diagnosed with giant BCCs [15]. These investigators found a higher incidence of giant BCCs among elderly males aged between 60-70 years old. Tumours developed over a mean period of 14.5 years; they were located mostly on sun-exposed areas, primarily on the back, followed by the face and upper extremities, and with an average diameter of 14.77 cm [15]. Histopathologic examination revealed a predominance of the nodular BCC subtype [15]. There was a very high rate of post-interventional complications, including local recurrences or metastases in 38.3% of cases [15]. Mohs micrographic surgery is currently considered the gold standard therapy for advanced BCCs, followed by wide surgical excision with complete control of tumour margins. Metastatic BCC now has an improved prognosis due to the discovery of targeted therapies directed towards signalling pathways like a sonic hedgehog, including the international availability of new drugs such as vismodegib and sonidegib [16, 17]. Recent research has shown that, even though therapy with hedgehog inhibitors is not always curative for extensive BCCs, when used in conjunction with surgical treatment, it can significantly decrease the morbidity associated with surgical therapy while increasing the chances of obtaining complete resections [20]. Basal cell carcinoma of the trunk accounts for approximately 10 % of all BCCs [18], while those of the scalp region tend to be less common, with incidence rates of 2.6% [19]. Large tumour size and perineural invasion are associated with aggressive subtypes, and incomplete excision rates seem to be higher in such cases [19]. Therefore, Mohs micrographic surgery or standard surgical excision with wide margins is the best treatment options in advanced forms of BCC.

In conclusion, undermining or extendable plastic surgery is a simple surgical approach with proven benefits concerning closing-tension of skin defects, especially in the scalp region. Published data confirm the fact that undermining can decrease tension at the wound margins, allowing good intraoperative control of these margins with diminished trauma when compared to more elaborate plastic surgical procedures and with potentially better results [14, 21].

References

1. Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of the worldwide incidence of nonmelanoma skin cancer. Br J Dermatol. 2012;166:1069–1080. https://doi.org/10.1111/j.1365-2133.2012.10830.x PMid:22251204

2. Karagas MR, Greenberg ER, Spencer SK, Stukel TA, Mott LA. The increase in incidence rates of basal cell and squamous cell skin cancer in New Hampshire, USA New Hampshire Skin Cancer Study Group. Int J Cancer. 1999;81:555–559. https://doi.org/10.1002/(SICI)1097-0215(19990517)81:4<555::AID-IJC9>3.0.CO;2-R

3. McCusker M, Basset-Seguin N, Dummer R, et al. Metastatic basal cell carcinoma: Prognosis dependent on anatomic site and spread of disease. Eur J Cancer. 2014;50:774–783. https://doi.org/10.1016/j.ejca.2013.12.013 PMid:24412051

4. Chung S. Basal Cell Carcinoma. Arch Plast Surg. 2012; 39(2): 166–170. https://doi.org/10.5999/aps.2012.39.2.166 PMid:22783519 PMCid:PMC3385325

5. Dourmishev LA, Rusinova D, and Botev I. Clinical variants, stages, and management of basal cell carcinoma. Indian Dermatol Online J. 2013; 4(1): 12–17. https://doi.org/10.4103/2229-5178.105456 PMid:23439912 PMCid:PMC3573444

6. Cabrera HN, Gómez ML. Skin cancer induced by arsenic in the water. J Cutan Med Surg. 2003;7:106–11. https://doi.org/10.1177/120347540300700202 PMid:12447618

7. Chan PC, Haseman JK, Boorman GA, Huff J, Manus AG, Cardy RH. Forestomach lesions in rats and mice administered 3-chloro-2-methylpropene by gavage for two years. Cancer Res. 1986;46:6349–52. PMid:3779651

8. Kubasiewicz M, Starzy-ski Z. Case-referent study on skin cancer and its relation to occupational exposure to polycyclic aromatic hydrocarbons. I. Study design. Pol J Occup Med. 1989;2:221–8. PMid:2489425

9. Emmert S, Schön MP, Haenssle HA. Molecular biology of basal and squamous cell carcinomas. Adv Exp Med Biol. 2014;810:234-52. https://doi.org/10.1007/978-1-4939-0437-2_13

10. de Zwaan SE, Haass NK. Genetics of basal cell carcinoma. Australas J Dermatol. 2010;51:81–92. https://doi.org/10.1111/j.1440-0960.2009.00579.x PMid:20546211

11. Von Hoff DD, LoRusso PM, Rudin CM, et al. Inhibition of the hedgehog pathway in advanced basal-cell carcinoma. N Engl J Med. 2009;361:1164–1172. https://doi.org/10.1056/NEJMoa0905360 PMid:19726763

12. Berking C, Hauschild A, Oliver Kölbl O, Mast G, Gutzmer R. Basal Cell Carcinoma—Treatments for the Commonest Skin Cancer. Dtsch Arztebl Int. 2014 May; 111(22): 389–395. PMid:24980564 PMCid:PMC4078227

13. Mohan S. V., Chang A.L.S. Advanced Basal Cell Carcinoma: Epidemiology and Therapeutic Innovations. Curr Dermatol Rep. 2014; 3(1): 40–45. https://doi.org/10.1007/s13671-014-0069-y PMid:24587976 PMCid:PMC3931971

14. Tchernev G, Pidakev I, Lozev I, Lotti T, Cardoso JC, Patterson JW. Undermining plastic surgery as a possible option for treating basal cell carcinoma of the forehead. Wien Med Wochenschr. 2017 Feb 13. https://doi.org/10.1007/s10354-017-0542-x

15. Archontaki M, Stavrianos SD, Korkolis DP, Arnogiannaki N, Vassiliadis V, Liapakis IE, Christ H, Rapidis AD, Kokkalis G. Giant Basal cell carcinoma: clinicopathological analysis of 51 cases and review of the literature. Anticancer Res 2009; 29(7):2655-63. PMid:19596942

16. Doan H Q, Silapunt S, Migden M R. Sonidegib, a novel smoothened inhibitor for the treatment of advanced basal cell carcinoma. Onco Targets Ther. 2016; 9: 5671–5678. https://doi.org/10.2147/OTT.S108171 PMid:27695345 PMCid:PMC5028081

17. Wollina U, Tchernev G. Advanced basal cell carcinoma. Wien Med Wochenschr 2013; 163(15-16):347-53. https://doi.org/10.1007/s10354-013-0193-5 PMid:23589318

18. Bogdanić B, Smud S, Bagatin D, Nola M, Mijatović D, Majerović M. Giant basal cell carcinoma of the back: a case report and review of the literature. Coll Antropol. 2009;33(1):315-8. PMid:19408644

19. Cho M, Lee J, James CL, Marshman G, Huilgol SC. Scalp Basal Cell Carcinoma: Review of 2,202 Cases. Dermatol Surg. 2016;42(7):834-41. https://doi.org/10.1097/DSS.0000000000000783 PMid:27243131

20. Ching JA, Curtis HL, Braue JA, Kudchadkar RR, Mendoza TI et all. The impact of neoadjuvant hedgehog inhibitor therapy on the surgical treatment of extensive basal cell carcinoma. Ann Plast Surg. 2015;74 Suppl 4:S193-7. https://doi.org/10.1097/SAP.0000000000000452 PMid:25695449

21. Raposio E, Nordström RE, Santi PL. Undermining of the scalp: quantitative effects. Plast Reconstr Surg. 1998 Apr;101(5):1218-22. https://doi.org/10.1097/00006534-199804010-00007

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Case Report

Asymptomatic Papules and Subcutaneous Nodules as First Sign of Gout

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Keywords: gout; hyperuricemia; tophi; arthropathy; cutaneous manifestations.

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Abstract

The authors describe a case report characterised by asymptomatic papules and non-tender subcutaneous nodules as the isolated manifestations of gout.

Introduction

Gout is a metabolic, well-known disorder, which first descriptions had been reported since the ancient time [1]. Although its prevalence varies among different populations and racial groups, recent epidemiological data underline how gout is becoming progressively common in the Western countries, with an estimated worldwide prevalence of 2.5-3.9%. It is more commonly described in male and adult-senescent patients [2-4].

Gout is caused by disordered purine metabolism, resulting in a hyperuricemic condition, which is defined by an increase in the serum level of uric acid over 7.2 mg/dL. The disease may derive by an overproduction of uric acid (primary gout), by an increased production of a purine or by a decreased excretion of uric acid (secondary gout). Well, known risk factors are obesity, alcohol consumption, purine-rich diet. Additionally, the intake of thiazide diuretics or cyclosporine increases the risk to develop gout [1,5].

A persistent hyperuricemia leads to the accumulation and aggregation of monosodium urate monohydrate (MSUM) crystals, also known as tophi. Tophi gradually deposit and accumulate in the synovial fluid and, less commonly, in other tissue [6]. Cutaneous symptoms may lead to diagnosis [7].

Case report

An overweight, 61-year-old male subject, doctor in general medicine, referred to us with multiple papules and subcutaneous, non-tender, pink-reddish in colour, nodules. Lesions were symmetrically

distributed in the skin upon the elbow of both arms and averaged from 0.2 to 1.3 cm in diameter (Fig.1-2). Both papules and nodules were completely asymptomatic, and they were present by more than three months. No other signs, both local and systemic, of infection or inflammation were detected. The patient denied a history of any form of arthropathy.

There were no hints to local trauma, infections or contact with local irritants.

The patient suffered from a mild form of hypertension, treated with a thiazide diuretic. He showed no familiarity for dermatologic and rheumatologic diseases.

The patient did not refer previous treatments of the lesion, except for 15-days of topical corticosteroid and antibiotics (betamethasone plus gentamicin cream), without any beneficial effects.

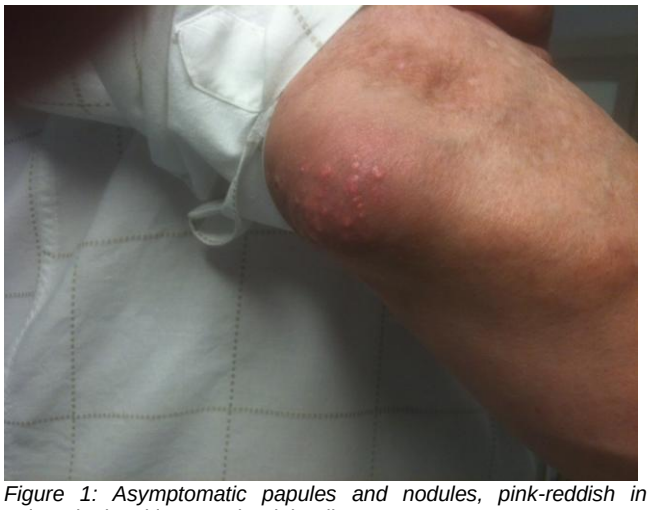

Figure 1: Asymptomatic papules and nodules, pink-reddish in colour, in the skin upon the right elbow

During the clinical evaluation, no other lesions were observed in any other part of the body. A rheumatologic evaluation showed no apparent joint involvement. Routine blood testing for inflammation, infections and autoimmune diseases (ANA, rheumatoid factor, antiphospholipid antibodies) were negative. An excisional biopsy was performed. The histopathological diagnosis of gout tophi was made, which is negatively birefringent under polarised light. Based on the histologic finding, the patient performed an additional laboratory test for uric acid and underwent to an orthopaedic evaluation. While the uric acid resulted to be elevated (15.0 mg/dL), confirming the diagnosis of hyperuricemia, the clinical and X-ray evaluation of the arms, did not show any signs of arthropathy.

Because of the diagnosis of gout, the patient started a diet poor of purines and changed the thiazide diuretic treatment with a beta-blocker drug.

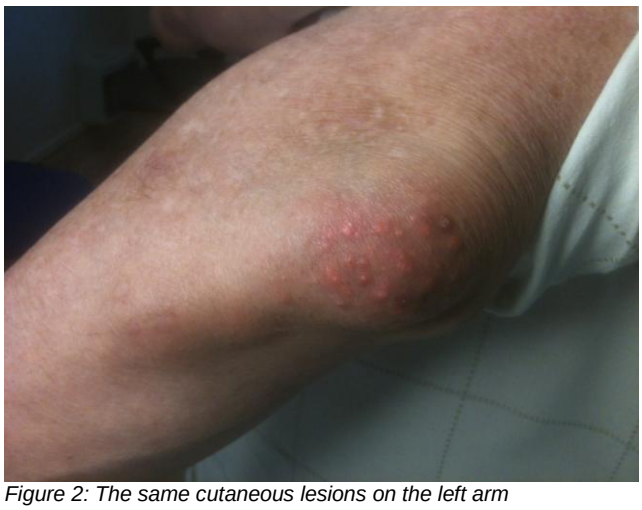

Figure 2: The same cutaneous lesions on the left arm

Finally, he started a proper therapy with allopurinol 300 mg/die.

Discussion

The main clinical characteristic of gout is the arthropathy, due to the deposition of tophi. Even if the great toe is the most commonly affected (podagra), other finger joints, as well as ankle and wrist may also be involved. Initially, there is a typical joint inflammation, characterised by severe pain, erythema and oedema [7]. In some cases, the inflammation of the synovial-based structures (e.g. bursae and tendon) has been described too. If not properly diagnosed and treated, gout arthropathy leads to affect multiple joints, becoming destructive and disabling [8].

Some patients may present the MSUM crystals deposition in the renal system. The phenomenon may vary from a mild and asymptomatic urolithiasis to a severe renal failure [9].

Although rarely, tophi have been reported in other body sites, such as nasal and thyroid cartilages, vocal cords, eyelids, cornea, mitral and tricuspid valves, hyoid bone and spine [10, 11].

Patients with gout may also present a cutaneous involvement, characterised by the development of intradermal or subcutaneous nodules as a sign of the tophi deposition. They are typically described in avascular tissues, such as in the ears (helix and antihelix areas) or in the periarticular acral areas, where they are often associated with an involvement of bursae or tendons [12, 13].

Less commonly, pustules or ulcerations have been described [14]. Rarely, a panniculitis has been reported as a sign of gout. Clinically it is characterised

by nodular lesions, which may ulcerate. It represents an inflammation of the lobular subcutaneous tissue, due to the tophi depositions. Even if lesions may have different localisations, more commonly they are detected on the legs or the trunk [15]

Another rare skin manifestation is the miliarial cutaneous gout (or disseminated one), which is characterised by the diffuse deposition of tophi all over the skin [16,17].

The diagnosis of gout is clinically supported by specific tests. The clinical recognition of tophi is highly suggestive for gout. A synovial aspiration [7] may be useful to detect the presence of MSUM and to exclude the presence of infection. Also, an X-ray may be performed to for the diagnosis of chronic gout [18]. The histologic examination of a lesional biopsy and the laboratory test for the uric acid, lead to the definitive diagnosis.

The principal treatment goals in chronic gout are (a) the symptomatic treatment of the acute joint inflammation and (b) the causal treatment of the underlying metabolic cause, the hyperuricemia. Acute gout should be treated by non-steroidal anti-inflammatory agents (NSAIDs) or cyclooxygenase-2 inhibitors, such as colchicines, and corticosteroids. Even if different medical therapies are available to regulate the uric acid concentration, allopurinol is considered as the first line drug. It acts inhibiting the production of uric acid. A valid alternative to allopurinol is probenecid, which increases the renal excretion of uric acid, by the inhibition of its reabsorption. Recently, febuxostat has been introduced for the treatment of gout. Like allopurinol, it stops the uric acid production by the inhibition of the xanthine oxidase [19]. All these treatments aim to lower the concentration of serum uric acid levels below 360 µmol/L (6 mg/dL).

Surgical removal of tophi is recommended only in patients with severe pain, joint deformities, or cutaneous lesions which tend to enlarge or ulcerate [20]. More recently, a new technique based on Metal-assisted and microwave-accelerated decrystallization (MAMAD), has been proposed for gout's treatment [21].

In conclusion, gout is an important metabolic disease, which derives by a hyperuricemia condition. Even if the arthropathy, due to the deposition of tophi, is most common sign of gout, the disorder may have different clinical manifestations. A proper diagnosis and treatment are fundamental to avoid the chronic course of the disease, which is characterised by disabling arthropathies, and by the risk of renal failure and cutaneous morbidities.

References

1. Nuki G, Simkin P. A concise history of gout and hyperuricemia and their treatment. Arthritis Res Ther. 2006;8:S1. https://doi.org/10.1186/ar1906 PMid:16820040 PMCid:PMC3226106

2. Chen LX, Schumacher HR. Gout: an evidence-based review. J Clin Rheumatology. 2008;14:S55-S62. https://doi.org/10.1097/RHU.0b013e3181896921 PMid:18830092

3. Tausche AK, Jansen TL, Schröder HE, Bornstein SR, Aringer M, Müller-Ladner U. Gout-- current diagnosis and treatment. Dtsch Arztebl Int. 2009;106:549-555. PMid:19795010 PMCid:PMC2754667

4. Gupta S, Yui JC, Xu D, Fitzhugh CD, Clark C, Siddiqui S, Conrey AK, Kato GJ, Minniti CP. Gout and sickle cell disease: not all pain is sickle cell pain. Br J Haematol. 2015; 171(5): 872–875. https://doi.org/10.1111/bjh.13433 PMid:25892648 PMCid:PMC4699866

5. Dalbeth N, House ME, Horne A, Taylor WJ. Reduced creatinine clearance is associated with early development of subcutaneous tophi in people with gout. BMC Musculoskelet Disord. 2013;14:363. https://doi.org/10.1186/1471-2474-14-363 PMid:24359261 PMCid:PMC3878111

6. Chhana A, Dalbeth N. The gouty tophus: a review. Curr Rheumatol Rep. 2015;17:19. https://doi.org/10.1007/s11926-014-0492-x PMid:25761926

7. Köstler E, Porst H, Wollina U. Cutaneous manifestations of metabolic diseases: uncommon presentations. Clin Dermatol. 2005;23:457-464. https://doi.org/10.1016/j.clindermatol.2005.01.008 PMid:16179179

8. Khandpur S, Minz AK, Sharma VK. Chronic tophaceous gout with severe deforming arthritis. Indian J Dermatol Venereol Leprol. 2010;76:69–71. https://doi.org/10.4103/0378-6323.58689 PMid:20061741

9. Roddy E, Zhang W, Doherty M. The changing epidemiology of gout. Nat Clin Pract Rheumatol. 2007;3:443–449. https://doi.org/10.1038/ncprheum0556 PMid:17664951

10. Stark TW, Hirokawa RH. Gout and its manifestations in the head and neck. Otolaryngol Clin North Am 1982;15:659–664. PMid:7133717

11. Verma S., Bhargav P, Toprani T, Shah V. Multiarticular tophaceous gout with severe joint destruction: A pictorial overview with a twist. Indian J Dermatol. 2014;59:609–611. https://doi.org/10.4103/0019-5154.143538 PMid:25484396 PMCid:PMC4248503

12. Chang HJ, Wang PC, Hsu YC, Huang SH. Gout with auricular tophi following anti- tuberculosis treatment: a case report. BMC Res Notes 2013;6:480. https://doi.org/10.1186/1756-0500-6-480 PMid:24256949 PMCid:PMC3843551

13. Liu K, Moffatt EJ, Hudson ER, Layfield LJ. Gouty tophus presenting as a soft-tissue mass diagnosed by fine-needle aspiration: A case report. Diagn Cytopathol 1996;15:246-249. https://doi.org/10.1002/(SICI)1097-0339(199609)15:3<246::AID-DC14>3.0.CO;2-G

14. Filanovsky MG, Sukhdeo K, McNamara MC. Ulcerated tophaceous gout. BMJ Case Rep. 2015;2015.

15. Dahiya A, Leach J, Levy H. Gouty panniculitis in a healthy male. J Am Acad Dermatol. 2007;57(2 Suppl):S52–S54. https://doi.org/10.1016/j.jaad.2006.04.006 PMid:17637378

16. Shukla R, Vender RB, Alhabeeb A, Salama S, Murphy F. Miliarial gout (a new entity). J Cutan Med Surg 2007;11:31–34. https://doi.org/10.2310/7750.2007.00002 PMid:17274936

17. Lo TEN, Racaza GZ, Penserga EG. 'Golden Kernels within the skin': disseminated cutaneous gout. BMJ Case Rep 2013. https://doi.org/10.1136/bcr-2013-009735

18. Neogi T, Jansen TL, Dalbeth N, Fransen J, Schumacher HR, Berendsen D, Brown M, Choi H, Edwards NL, Janssens HJ, Lioté F, Naden RP, Nuki G, Ogdie A, Perez-Ruiz F, Saag K, Singh JA, Sundy JS, Tausche AK, Vaquez-Mellado J, Yarows SA, Taylor WJ. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2015;74:1789-1798.

https://doi.org/10.1136/annrheumdis-2015-208237 PMid:26359487 PMCid:PMC4602275

19. Jansen TL, Richette P, Perez-Ruiz F, Tausche AK, Guerne PA, Punzi L, Leeb B, Barskova V, Uhlig T, Pimentão J, Zimmermann-Górska I, Pascual E, Bardin T, Doherty M. International position paper on febuxostat. Clin Rheumatol. 2010;29:835-840. https://doi.org/10.1007/s10067-010-1457-8 PMid:20401506

20. Chokoeva AA, Tchernev G, Patterson JW, Lotti T, Wollina U. Acute overnight painful swelling of a finger. J Biol Regul Homeost Agents. 2015;29(1 Suppl):1-3. PMid:26016957

21. Toker S, Boone-Kukoyi Z, Thompson N. et Al. Treatment of gout using the metal-assisted and MicrowaveAccelerated Decrystallization technique. ACS Omega. 2016;1:744 −754. https://doi.org/10.1021/acsomega.6b00233 PMid:27917407 PMCid:PMC5131323

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Brief Communication

Mushroom-Like Skin Tumours: Report of Three Cases

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Keywords: Mushroom-like growth; Skin tumours; Melanoma; Merkel cell carcinoma; Basal cell carcinoma; Surgery.

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Abstract

Mushroom like the growth of skin tumour is a rare phenomenon although described already in 1806 by Alibert, who focused on mycosis fungicides. We identified only four case reports in PUBMED database using the terms "mushroom-like growth" and "skin tumour". We analysed our files and identified three elderly female patients (69 to 94 years old). Histological diagnosis was melanoma, Merkel cell carcinoma and basal cell carcinoma. All tumours could be completely removed by wide excision or delayed Mohs surgery. No metastatic spread was noted.

Introduction

Exophytic tumour growth can result in rare cases in a mushroom-like macroscopic appearance. In mycosis fungoides, this peculiar growth pattern is known at least since Alibert (1806) [1], in solid skin tumours, it is extremely rare. We present a collection of tumours from our files to illustrate this phenomenon. In most cases, the only histopathology uncovers the correct diagnosis.

Case series

The cases had been observed at the Department of Dermatology and Allergology. All tumours were subjected to histopathological analysis after complete surgical removal.

Mushroom-like melanoma

A 90-year-old woman presented with a slow-growing exophytic malodorous, oozing tumour on her left calf. She declared that the tumour had been noticed for more than five years. Since it was asymptomatic, she did not care much about. But in the last months, the malodor brought her to the clinic.

On examination, we observed a mushroom-like brownish tumour with a moist surface, about 35 x 30 x 15 mm in size. The tumour was completely excised with a safety margin of 2 cm. The defect was closed by tissue transfer.

Histologic examination revealed an ulcerated, infiltrative, epitheloid cell tumour, sparsely pigmented, with high mitotic activity. Tumour cells were positive for S100 and MART-1. There was a moderate inflammatory infiltrate at the bottom of the lesion. The final diagnosis was nodular melanoma, Clark level IV, tumour thickness 9.0 mm (T4bN0M0, stage IIc). Distal from this lesion another tumour plaque was removed in the same session. Histologic examination confirmed the diagnosis of Bowen's disease.

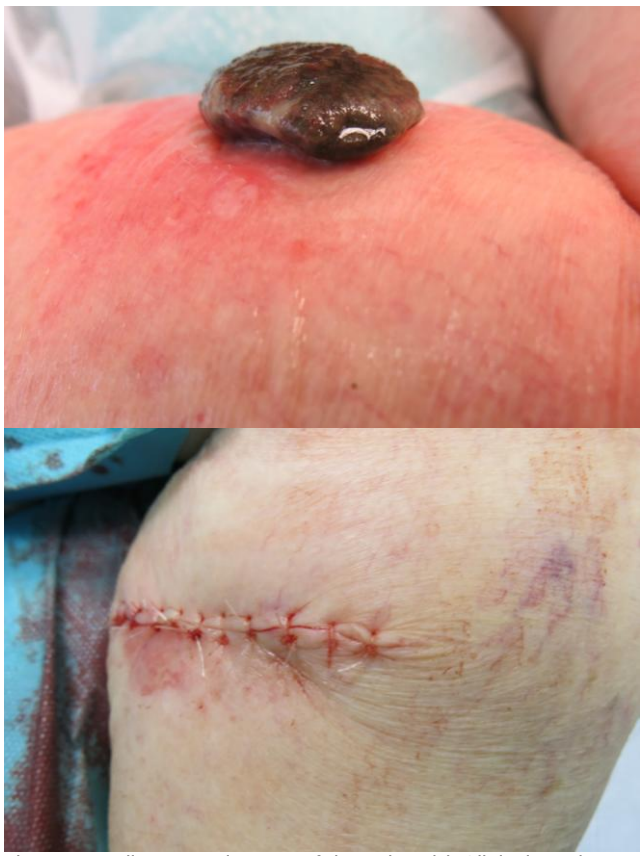

Figure 1: Malignant melanoma of the calve. (a) Clinical mushroom-like appearance; (b) After surgery and defect closure

Staging did not reveal a metastatic spread. Due to the age of the patient neither adjuvant therapy nor sentinel lymph node biopsy has been performed.

Mushroom-like Merkel cell carcinoma

A 69-year-old female patient presented with a soft nodule on the tip of the nose. Tumour history was for about six months. The lesion was symptomless.

On examination, we observed a reddish, exophytic tumour mass of 14 mm in diameter with a mushroom-like appearance (Fig. 2). The tumour was completely excised by delayed Mohs surgery. Histologic investigations demonstrated a nodular dermal tumour composed of basophilic small epitheloid cells with high mitotic activity. There was no connection to the epidermis. Tumour cells were reactive for cytokeratin 20, neuron-specific enolase, synaptophysin, and chromogranin A. On staging, no metastases were noted. The diagnosis of an intermediate type Merkel cell carcinoma was confirmed, T1N0M0 (stage Ia).

After defect closure by Rieger-flap and complete healing, the patient received adjuvant radiotherapy of the tumour basin and regional lymph nodes.

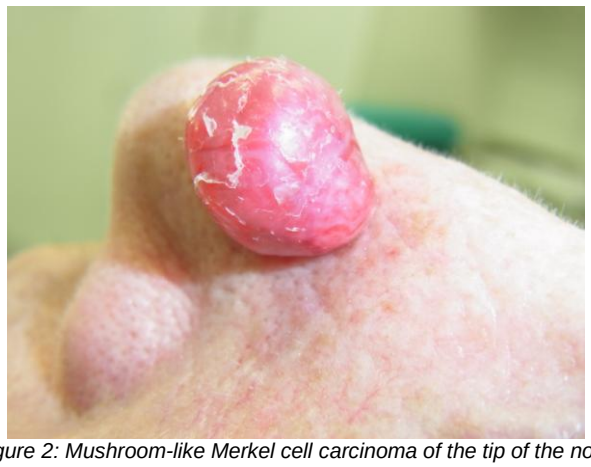

Figure 2: Mushroom-like Merkel cell carcinoma of the tip of the nose

Mushroom-like basal cell carcinoma

A 94-year-old female patient presented with an asymptomatic, exophytic tumour on her right mons pubis was grown for at least five years.

On examination, we observed an exophytic tumour with a flesh-like colour and 1.5 cm in diameter (Fig. 3a). The tumour was painless. We removed the lesion by wide excision with 2 cm safety margin under the suspicion of squamous cells carcinoma or Merkel cell carcinoma. The defect was closed by tissue transfer. Staging with diagnostic ultrasound for regional lymph nodes was unremarkable. Healing was uneventful.

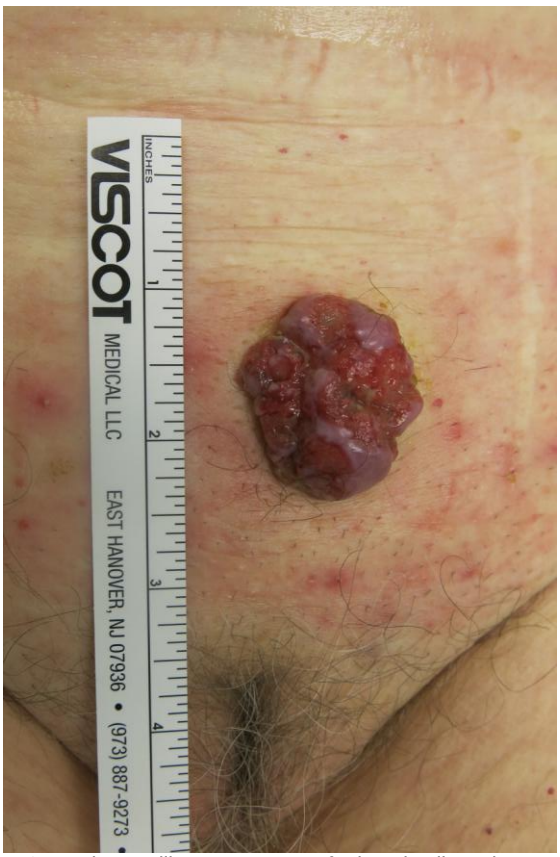

Figure 3: Mushroom-like appearance of a basal cell carcinoma

The histologic investigation described a polypoid, basaloid epitheloid cell tumor with partial regression clefts. It was a mixed solid and adenoid tumour type. The tumour infiltrated deep corium. A mild inflammatory mixed cell infiltrates observed around the lesion. The final diagnosis was basal cell carcinoma.

Discussion

Mushroom-like exophytic tumour growth is a rare phenomenon although it had been described at least since 1806 by Alibert in mycosis fungoides [1]. We described three elderly patients with mushroom-like tumours, melanoma, a Merkel cell carcinoma, and a basal cell carcinoma. It seems surprising that none of these patients had signs of metastatic spread. At least in the case of melanoma and Merkel cell carcinoma, metastasis is not uncommon. Maybe the advanced age of the patients is contributing to this observation.

A mushroom-like basal cell carcinoma of the nose tip had been reported in recent years by Wang et al. (2014) [2]. A mushroom-like cutaneous squamous cell carcinoma of the clear cell/signet-ring cell variant had been observed in a 78-year-old Chinese woman in the right thigh [3]. Mushroom-like soft fibromas of the leg had been identified on chronic lymphedema [4].

In conclusion, the mushroom-like appearance of skin tumours is an exceptionally rare observation. In most cases, the final diagnosis could not be expected by clinical examination. Mushroom-like tumours need a complete surgical removal and careful, histologic examination since often they represent malignancies.

References

1. Makdisi J, Friedman A. Mycosis fungoides--an update on a non-mycotic disease. J Drugs Dermatol. 2013;12:825-831. PMid:23884501

2. Wang JY, Cao HL, Liu LF, Yan JL. Mushroom-like giant basal cell carcinoma on the nasal tip. Dermatol Surg. 2014;40:343-345. https://doi.org/10.1111/dsu.12401 PMid:24372940

3. Wang NR, Wang MM, Zhou L, Liu ZL, Chen NP, Hu JP, Deng YJ, Qi XQ, Huang XF, Su Y, Zhang SY, Tong F, Zhang Y, Lu Q, Zhu ZY, Deng H. Cutaneous clear cell/signet-ring cell squamous cell carcinoma arising in the right thigh of a patient with type 2 diabetes: combined morphologic, immunohistochemical, and etiologic analysis. Diagn Pathol. 2016;11:36. https://doi.org/10.1186/s13000-016-0487-1 PMid:27066782 PMCid:PMC4827219

4. Nakamura S, Hashimoto Y, Nishi K, Takeda K, Takahashi H, Mizumoto T, Iizuka H. Mushroom-like soft fibromas on chronic leg lymphedema. Eur J Dermatol. 2010;20:228-229. PMid:19919910

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Dermatologic Surgery and Dermatologic Oncology as an Essential Part of the Modern Dermatology in Bulgaria

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Keywords: dermatology; dermatologic surgery; dermatologic oncology; melanoma; island flap.

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Abstract

Dermatosurgery and dermatooncology are an integral part of dermatology as a speciality, and this postulate is strictly respected in a high percentage of European dermatological units. Due to the fact that a number of other specialties interweave with the subject of therapy - the surgical treatment of the patient with skin tumors, the positioning of dermatosurgery as part of dermatology is generally controversial (according to some), and at the same time is often the subject of a number of debates and conflicts. These include maxillofacial surgeons, plastic surgeons, regenerative and reconstructive surgeons, surgical and medical oncologist, etc. The advantages of these specialities are mainly based on good medical practice and good surgical techniques that are applied. In contrast, their disadvantages are based on the lack of good awareness of the initial surgical approach as well as the need for time-adjusted and accurately performed additional surgical interventions which should befurthermore careful scheduled with the relevant oncology units. Losing this thread, in practice, it turns out that we are losing the patients themselves or, looking laconically, we are working with reduced efficiency and effectiveness. Although for the last 15 years the positions of these sub-sectors in Bulgaria had been underdeveloped, a certain ascent has been observed nowadays or from a couple of years ago. This advance is undoubtedly due to the influence of the German Dermatological School, presented by Prof. Dr. Uwe Wollina, Head of Department of Dermatology, Venereology and Allergology in Dresden, Germany, as well as due to other respected representative of the Italian Dermatological School - in the face of Prof. Dr. Torello Lotti, Head of the Dermatology Unit at G Marconi University of Rome, Italy.

Introduction

Attested in English in 1819, the word dermatology derives from the Greek δέρματος (dermatosis) [1], genitive of δέρμα (derma), "skin" [2] (itself from δέρω dero, "to flay") and -λογία -logia. Readily visible alterations of the skin surface have been recognised since the dawn of history, with some being treated, and some not. In 1801 the first great school of dermatology became a reality at the famous Hôpital Saint-Louis in Paris, while the first textbooks (Willan's, 1798–1808) and atlases (Alibert's, 1806–1814) appeared in print during the same period [3].

Dermatosurgery and dermatooncology are an integral part of dermatology as a speciality, and this postulate is strictly respected in a high percentage of European dermatological units. Due to the fact that a number of other specialties interweave with the subject of therapy - the surgical treatment of the patient with skin tumors, the positioning of dermatosurgery as part of dermatology is generally controversial (according to some), and at the same time is often the subject of a number of debates and conflicts. These include maxillofacial surgeons, plastic surgeons, regenerative and reconstructive surgeons,

surgical and medical oncologist, etc. The advantages of these specialities are mainly based on good medical practice and good surgical techniques that are applied. In contrast, their disadvantages are based on the lack of good awareness of the initial surgical approach as well as the need for time-adjusted and accurately performed additional surgical interventions which should be furthermore careful scheduled with the relevant oncology units.

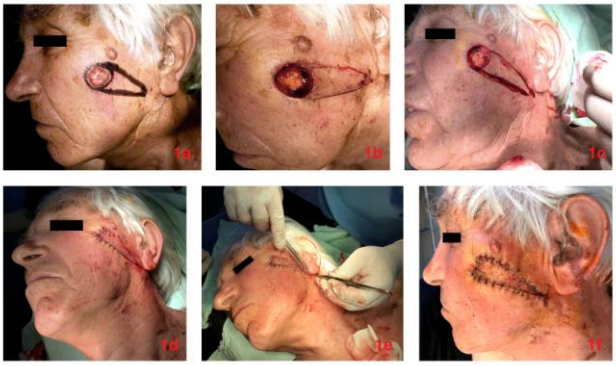

Figure 1: 1a) Island flap. Patient with keratoacanthoma (histopathologically verified after the surgical excision), located in the area of the left cheek, Medical Institute of the Ministry of Interior, Department of Dermatology, Venereology and Dermatological Surgery, 2017, Sofia, Bulgaria; 1b) Oval excision of the primary tumor; 1c) Extension of the wound edges in the shape of triangle peripherally. Preparation of the distal and proximal part of the created skin island; 1d) Transposition of the skin island in the proximal direction followed by careful adaptation of the wound edges; 1e) Adaptation of the distal part of the island; 1f) Post operative clinical finding

Losing this thread, in practice, it turns out that we are losing the patients themselves or, looking laconically, we are working with reduced efficiency and effectiveness.

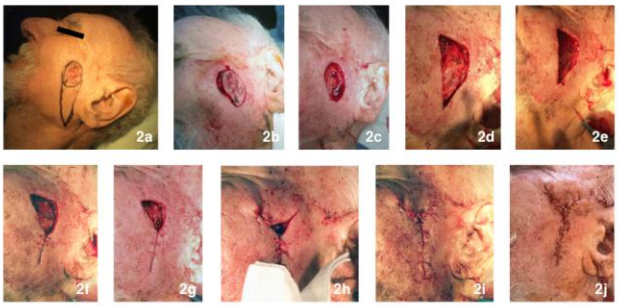

Figure 2: 2a) Patient with basal cell carcinoma of the cheek, preoperative clinical finding. Marking of the resection fields; 2b) Oval excision of the primary tumour with island flap plastic planning. Step by step dissection; 2c) VY flap. Oval excision of the primary tumour and island flap plastic planning. Clinical status immediately after the excision; 2d) Gradual extension of the defect in the shape of a triangle at both of the ends and changing of the primary idea for island flap performance. Medical Institute of the Ministry of Interior, Clinic of Dermatology, Venereology and Dermatological Surgery, 2017, Sofia, Bulgaria; 2e) Gradual extension of the defect in the form of a triangle. Electrocoagulation; 2f) Defect closing from distal to proximal direction. Gradual adaptation of the wound edges by single skin stiches; 2g) Intraoperative finding with minimising the size of the defect by gradually adapting of the wound edges; 2h) Expansion of the defect forward the pre-auricular area, leading to better adaptation of the wound edges; 2i) Post-operative findings; 2j) Post-operative findings. VY flap

Although for the last 15 years the positions of these sub-sectors in Bulgaria had been underdeveloped, a certain ascent has been observed nowadays or from a couple of years ago.

This advance is undoubtedly due to the influence of the German Dermatological School, presented by Prof. Dr. Uwe Wollina, Head of Department of Dermatology, Venereology and Allergology in Dresden, Germany, as well as due to other respected representative of the Italian Dermatological School - in the face of Prof. Dr. Torello Lotti, Head of the Dermatology Unit at G Marconi University of Rome, Italy.

A number of specialists from Bulgaria benefit from the advice and teaching from these already established and internationally respected dermatosurgical and oncological units in Europe (in particular Germany and Italy) within the framework of the international collaboration, currently mediated by the Onkoderma / ADCRSTR cooperation group, the Association for Dermatohistopathological Control, Reevaluation and Subsequent Therapeutic Recommendations.

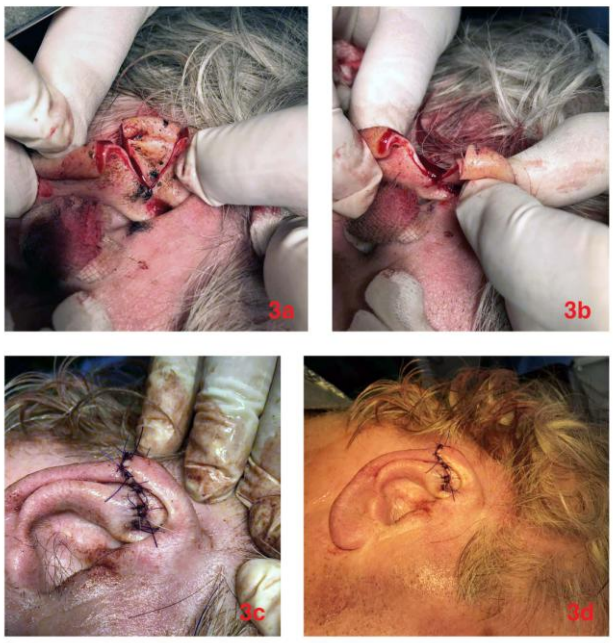

Figure 3: 3a) Intraoperative findings in a patient with a small squamous cell carcinoma of the ear. Triangular excision. Medical Institute of the Ministry of Interior, Clinic of Dermatology, Venereology and Dermatological Surgery, 2017, Sofia, Bulgaria; 3b) Intraoperative defect; 3c) Adaption of the wound edges; 3d) Post-operative findings

The Association for dermatohistopathologic control and subsequent therapeutic recommendations was created, guided by the idea to provide adequate medical care at the European and global level, which is supported basically at national but also at international German and Italian dermatological schools. Among the objectives of the association is to support young physicians in their professional

development as dermatologists and oncologists, integrating international quality of education and training. Despite being a controlling institution for histopathological samples (at the national level) and accurate diagnosis, ADCRTSR.com plays a key and regulatory role in international collaboration and the realisation of numerous innovative projects, namely - projects with the dermatosurgical and dermatooncological division. The influence of the German dermatological school in Dresden, Germany, represented by Prof. Dr. Uwe Wolina and the Italian Dermatological School in Rome, Italy, represented by Prof. Dr. Torello Lotti, is helping in profiling the activity of one of the first non-private clinics with a dermatosurgical and dermatooncological division – the Dermatology unit of the Ministry of Interior Medical Institute, where such a type of skin surgery is performed today in the everyday clinical practice. The international collaboration with renowned international experts is essential for the improvement of both of the primary and specialized national medical care, The Association's members support international collaboration in science, while working hard for the improvement of their knowledge and medical science as a whole, participating in several research projects and publications, as well as in integration of new theories on the etiology and pathogenesis of known diseases and unsolved mysteries in the field of pathogenesis and manifestation of certain diseases. The innovative thinking and dedicated work of our partners cooperate in combating a variety of medical problems.

More than 100 projects have been carried out within the framework of this collaboration over the last 3-4 years, concerning basically the good medical practices and dermatological science, resulting in the maximum of the possible effectiveness regarding the observance of the international standards for dermatologic surgery and oncology. Optimal conditions for the development of the young scientist have also been created meanwhile, in the above-mentioned sub-units as this realisation is still in the stage of everyday improvement. The initial creation of (currently) a small group of specialists, with interest in dermatologic surgery and dermatologic oncology in Bulgaria, leads to increased competitiveness, which inevitably requires also higher qualification - the qualification which is essential as for our survival, as well as the same in patients. Sooner or later the desired effect of the increased effectiveness of the specialised medical assistance, as well as the improved overall survival rate of the patients has been achieved, as a result from the established international relationships and cooperation group.

References

1. δέρμα, Henry George Liddell, Robert Scott, A Greek-English Lexicon, on Perseus.

2. δέρω, Henry George Liddell, Robert Scott, A Greek-English Lexicon, on Perseus Digital Library.

3. Freedberg, et al. Fitzpatrick's Dermatology in General Medicine. (6th ed.). McGraw-Hill Professional, 2003:3.

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Review Article

An Overview on Radiotherapy: From Its History to Its Current Applications in Dermatology

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Keywords: radiotherapy; historical evolution; therapeutic option; cancers; cutaneous malignant diseases.

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Abstract

For more than a century, radiotherapy has been an effective treatment for oncologic patients. The Authors report a brief history of the radiation therapy and its actual indication for the treatments of cutaneous malignant diseases.

Introduction

Radiotherapy (RT), also known as radiation therapy, is a treatment modality based on the use of high energy rays or radioactive substances, to damage tumoral cells and to halt their growth and division.

RT, used alone or in association with different treatments, has been an effective tool for treating cancer for more than 100 years [1].

Also today, it is an important therapeutic tool for the treatment of different kinds of cancer. It is estimated that about two-third of all cancer patients will receive RT as unique treatment or as a part of the more complex therapeutic protocol.

Radiotherapy in the history

Before the advent of ionising particle beams, medicine had few options for treating some diseases, both malignant and benign in nature. The scenario rapidly changed after the discovery of X-rays in 1895 by Wilhelm Conrad Rцntgen [2].

Also before understanding the physical properties of X-rays and their biological effects, one year later their discovery, X-rays were used by Emil Herman Grubbe to treat a patient with breast cancer [3].

In the same year, Antoine Henri Becquerel started to study the phenomenon of radioactivity and to research natural sources of radiation. In 1898, Maria Sklodowska-Curie and her husband Pierre Curie discovered the radium as a source of radiations.

Only three years later, Becquerel and Curie reported on the physiologic effects of radium rays [4].

By the first years of the new century, an increased number of studies reported the use of X-rays and radium in medicine. Skin cancers were the most frequent treated, even because of the low penetration in the tissue of radiations. In the 1910s, Coolidge developed a new device able to emit higher energy X-rays, to treat deeper cancers [5].

In real, due to the lack of knowledge on the properties and mechanism of actions of radiotherapy, the effective, beneficial results in the cancers treatment were poor in comparison to their side effects and physicians started new studies for a better understanding of the treatments [6].

New radioactive isotopes, type of rays and radiation techniques were discovered. Scientists began to understand the nature of radiations, their modalities of actions and the relationship between time and dose of radiations on cell survival. Nevertheless, it was only by 1920s, that physicians understood how the administration of the total radiation dose in fractionated ones was better than a singular treatment session, regarding cancers control and fewer side effects [7].

Another important scientific progress was achieved in 1928 when the International Commission on Radiological Protection (ICRP) was created to address the question of radioprotection [8].

Not less important was the introduction of an ionising chamber in 1932, which made physicians able to measure the radiation dose delivered to the first dose unit (Rцntgen unit) [9].

The successive period, from 1930 to 1950, was characterised by continuos scientifical progress to treat patients affected by deep cancers. This era (also known as Orthovoltage era) was mainly characterised by the use of the radium-based interstitial irradiation (brachytherapy) and by the development of supervoltage X-ray tubes able to deliver energy from 50 kV to 200 kV. The first one modality allowed to the operators to treat the tumour, without an external beam source, limiting the side effects on unaffected tissue. The second one conducted to the introduction of the electron beam therapy, a useful therapeutic option able to deliver higher and variable energies for treating deeper tumours [10].

The studies, which had been conducted in the successive three decades (Megavoltage era), were also focused on the development of more and more innovative radio-therapeutic devices able to treat cancers in the deep tissues. This period saw the introduction of the Cobalt teletherapy, producing high-energy γ-rays [11], and of more potent electron linear accelerators (also known as electron linacs) [12], able to deliver megavoltage X-rays. The new devices were able to deliver a higher dose of energies than the previous ones, making possible the treatment of deeper tumours with a greater skin sparing. Due to the difficulties of managing these sources and the risk to cause an excessive radiation in the tissue surrounding cancer, innovative multi-field plans of irradiations were designed [13].

Radiotherapy was becoming a recognised medical discipline, and the first radiologist associations were being founded. As well as new studies were confirming the efficacy of RT in improving survival of patients with different types of cancers, innovative devices with a computerised control were introduced in the medical practice.

However, a new era in the history of RT was starting. The 1970s and 1980s were characterised by the introduction of innovative devices delivering proton beam. Even if their first clinical use was dated in 1954 [14], was only by the late Seventies that computer-assisted accelerator for protons was successfully applied to treat a different kind of tumours [15].

The major advantage in the use of ion beams is its controllability, which allows providing a superior tool for cancer therapy and difficult-to-treat benign diseases.

Another important progress in radiotherapy was achieved by the end of the 1990s when the introduction of more sophisticated computer allowed the development of a 3D conformal radiotherapeutic device (Stereotactic radiation therapy), able to treat in a more efficacy and safer ways the patients [16].

The new millennium saw the affirmation of the Stereotactic radiation therapy, especially for the treatment of metastatic tumors [17], and the introduction of the adaptive RT (ART), a special form of image-guided radiotherapy (IGRT), that consent of replanning and sometimes optimizing the treatment technique, during the course of radiotherapy when clinically relevant [18].

Types of radiations useful in RT

Radiotherapy is based on the use of two main types of radiation: the electromagnetic and the particulate ones. The first is represented by the X-rays and by the Gamma-rays; the second one by electrons, neutrons and protons.

Radiations may be delivered externally or internally. In the first modality, the beam of radiations is delivered by a source of radiations, which is external to the body; in the second one, a radioactive source is placed inside the lesions that must be

treated.

In general, the choice of the treatment, which has to be used, depends on the localisation, size and type of cancer.

Mechanisms of action of radiotherapy

Even if the interaction radiations-tissue produces numerous effects (Table 1), radiotherapy mainly acts by killing the tumoral cells and halting their ability to reproduce [19]. Those events can be the result of the direct damage of DNA or other important cellular molecules (most commonly described in the case of particulate radiations, such as alpha particles, protons or electrons), or of an indirect cellular damage which occurs after the productions of free radicals (e.g. X-rays or Gamma-rays).

Unfortunately, during radiation therapy, normal cells, especially for those which divide frequently, may also be damaged and killed. This fact may be limited by the focusing the radiation beam on the tumour and by fractioning the total dose of irradiation so that normal tissue can recover and repair itself [20].

Table 1: Effects of radiations on the irradiated tissues

EFFECT	RESULTS
Physics	issue, transfer and absorption of energy
Biophysics	ionisation and excitation phenomenon
Physical-chemical	direct alterations of atoms and molecules or indirect damage through the productions of free radical
Chemical	the breaking of bonds, polymerization or depolymerization phenomenon
Biochemical	molecular alterations
Biochemical-biological	damage to DNA, RNA, cytoplasm, enzymes
Biological	aberrations of various cellular components, morpho-functional and metabolic lesions, damage to the genetic material

Radiotherapy in dermatology

Even if RT is often estimated to be an obsolete treatment available for a dermatologist, it has been used for nearly a century, and today it still represents a valid therapeutic tool even because innovative and more sophisticated techniques have been developed (Table 2) [20].

Radiation therapy may be used in dermatology as a curative treatment or as a palliative one (Table 3). In the first case, it is used to destroy the primary tumour or to reduce the risk of malignant recurrences after the surgical or chemotherapeutic treatment of cancer. In the second case, RT is mainly used to alleviate patient's pain by reducing the tumour's size.

Table 2: Different modalities of radiotherapy available for the treatment of dermatological diseases

TREATMENT	TYPE OF RADIATION	CLINICAL INDICATIONS
Low energy superficial kilovoltage	X-ray	Localised superficial skin cancers
Orthovoltage X-ray	X-rays	Localised superficial skin cancers
High energy megavoltage (MV) photons	X-rays	Rarely used. Skin cancer with deep penetration
Electron Beam Therapy (Linac)	Electrons	Large or thick lesions
Cobalt therapy	Gamma-rays	Like Linac, by which they are often replaced
Brachytherapy	Radioactive sources (e.g. Au, CO, Celsium, Iridium…) localised into tumour tissues (variable energy)	Tumours localised in critical sites

Although the clinical indications for RT are numerous (Table 4) [1], the treatment is more often performed in patients with known melanoma skin cancers (NMSC), such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and Merkel cell carcinoma.

Table 3: Different indications of RT

NATURE OF RADIOTHERAPY	CLINICAL INDICATIONS
THERAPY OF FIRST LINE	Lesions on the face;
	Superficial wide lesions;
	Old patients;
	Patients who cannot be treated surgically;
	Cases in which surgery may lead to important functional damage (e.g. ectropion, paralysis of the facial).
ADJUVANT THERAPY	Positive/close margins after surgical excision of tumour;
	Patients with positive nodes;
	Patients with perineural invasion.
PALLIATIVE TREATMENT	The Late stage of tumours, which could not be treated.

BCC is the most common type of skin cancer, and maybe one of the more common cancer in general. Even if malignant, BCC rarely metastasizes. Usually, it is treated with a simple excision or with Mohs micrographic surgery. Different therapeutic approaches include curettage, electrodesiccation, laser ablation, cryotherapy or medical therapies (e.g. imiquimod, 5-FU).

Table 4: Main dermatological indications for RT

BCC
SCC
Bowen's disease
Erythroplasia
Angiosarcoma
Keratoacanthoma
Melanoma
Merkel cell carcinoma
Cutaneous lymphoma
Kaposi's sarcoma
Fibrosarcoma

RT may be considered as a valid therapeutic options, especially in patients who cannot be surgically operated, in the case of large tumours or not well-defined ones, and finally in the case of cancers involving critical site (e.g. nose, ear). On the other hand, it has been estimated that the use of RT after the surgical excision of the primary tumours, is another valid therapeutic approach for patients with BCC, leading a reduction in the risk of recurrences [21-24] (Table 5, Table 6).

Table 5: Dose recommendation for BCC and SCC, accordingly to the National Comprehensive Cancer Network (NCCN) Guidelines version 2.2014

Tumour diameter (cm)	Dose (Gy)	Margins (cm)	Schedule of sessions
< 2	64	1.0-1.5	32 (6-6.4 weeks)
	55		20 (4 weeks)
	50		15 (3 weeks)
	35		5 (5 days)
≥ 2	66	1.5-2.0	33 (6-6.6 weeks)
	55		20 (4 weeks)
Postoperative adjuvant	50		20 (4 weeks)
	60		30 (6 weeks)

SCC is the second most common cutaneous cancer, and unlike BCC it is characterised by a significant metastatic potential.

Table 6: X-ray therapies most commonly used in dermatology

Modality of irradiation	Energy	Treatment depth
Grenz Rays	10-20 kv	< 1 mm
Contact therapy	40-50 kv	1-2 mm
Short source surface distance	40-50 kv	1-2 mm
Superfical therapy	50-150 kv	> 5 mm
Orthovoltage therapy	150-300 kv	> 5 mm and < 2 cm

Also, in this case, the surgical excision or the MOHS micrographic surgery represent the gold standard treatments. Different approaches include curettage, electrodesiccation and cryosurgery. RT may be considered as a valid therapeutic option, both as primary treatment and as adjuvant therapy for high-risk tumours [25]. In patients with positive nodes, the irradiation may be considered a valid option to their surgical dissection.

Another tumour which benefits of RT is the Merkel cell carcinoma (MCC), a neuroendocrine carcinoma of the skin, highly deadly. In this case, the surgical excision of the primary tumour is recommended such as the successive irradiation of the same site. In the case of positive nodes, they must be irradiated too [26, 27]

Among the other skin tumours, which may be treated with RT, there is the mycosis fungoids, a form of cutaneous T-cell lymphoma. In these cases, RT may be used as a curative treatment of localised form of lymphoma, or as a palliative treatment [28].

Also, the primary cutaneous follicle centre cell lymphoma (FCCL) and the primary cutaneous marginal zone lymphoma (MZL), two types of B cell lymphoma, if not surgically treated, may benefit from the radiation therapy [1].

Finally, there is the Kaposi's sarcoma. Also, in this case, RT may be used as the main treatment, in the case of solitary lesions, or as palliative therapy in the disseminated forms [20, 29].

Particular is the case of melanoma, the most malignant skin disease, characterised to have low radiosensitivity. In this case, the gold standard treatment is represented by surgical excision of the lesion. RT may be considered as therapeutic options only in few selective cases, such as unresectable primary tumours or lentigo malignant. In the other cases, RT is often used with the palliative purpose or as adjuvant therapy for the nodal and brain metastases [30, 31].

The latest introduction of carbon ions in RT seems to open new prospective in the melanoma treatment, even if new studies and researches need to be conducted [32].

References

1. Jonathan D. Tward JD, Christopher J. Anker CJ et Al. Radiation Therapy and Skin Cancer. In Natanasabapathi G. Modern Practices in Radiation Therapy. InTech ed. 2012: 207-246.

2. Rontgen WC. Uber eine neue Art von Strahlen. Vorl¨ aufige Mitteilung. In: Sitzungsberichte¨ der physikalisch-medicinischen Gesellschaft zu W¨urzburg, Sitzung 1985. 30:132–141.

3. Grubbe EH. Priority in the therapeutic use of X-rays. Radiology´ 1933. 21: 156–162. https://doi.org/10.1148/21.2.156

4. Becquerel AH, Curie P. Action physiologique des rayons de radium. Compt. Rend. Acad. Sci. 1901. 132, 1289–1291.

5. Lawrence EO, Livingston MS. The production of high speed light ions without the use of high voltages. Phys. Rev. 1932. 40:19–35. https://doi.org/10.1103/PhysRev.40.19

6. Lederman M. The early history of radiotherapy: 1895–1939. Int. J. Radiat. Oncol. Biol. Phys. 1981. 7: 639–648. https://doi.org/10.1016/0360-3016(81)90379-5

7. Coutard H. Principles of X-ray therapy of malignant disease. Lancet 1934. 2:1–12. https://doi.org/10.1016/S0140-6736(00)90085-0

8. Taylor, L. S. History of the International Commission on Radiological Protection (ICRP). Health Phys. 1958;1:97–104. https://doi.org/10.1097/00004032-195804000-00001 PMid:13598297

9. Thoraeus, R. A. A study of ionization method for measuring the intensity and absorption of roentgen rays and of the efficiency of different filters used in therapy. Acta Radiol. 1932; 15: 1–86.

10. Courant ED. Early Milestones in the Evolution of Accelerators. In Chao AW. Reviews of Accelerator. Science and Technology vol. 1. Ed. World Scientific, Singapore, 2008: 1–5. https://doi.org/10.1142/s1793626808000022

11. Boone MLM, Lawrence JH, Connor WG et al., Introduction to the use of protons and heavy ions in radiation therapy: historical perspective. Int. J. Radiat. Oncol. Biol. Phys. 1977;3:65–69. https://doi.org/10.1016/0360-3016(77)90229-2

12. Fry D W, Harvie RB, Mullett L et Al. A travelling-wave linear accelerator for 4-MeV electrons. Nature 1948;162:859–861. https://doi.org/10.1038/162859a0 PMid:18103121

13. Suit H, Goitein M, Munzenrider J et al., Evaluation of the clinical applicability of proton beams in definitive fractionated radiation therapy. Int. J. Radiat. Oncol. Biol. Phys. 1982;8:2199–2205. https://doi.org/10.1016/0360-3016(82)90570-3

14. Hall EJ. The Physics and Chemistry of Radiation Absorption. In: Radiobiology for the radiologists. 4th edition. Philadelphia: JB Lippincott, 1994:8-10.

15. Ying CH. Update of Radiotherapy for Skin Cancer. Hong Kong Dermatology & Venereology Bulletin.2001; 9(2): 52-59.

16. Mohan, R. Field shaping for three-dimensional conformal radiation therapy and multileaf collimation. Semin. Radiat. Oncol. 1995;5: 86–99. https://doi.org/10.1016/S1053-4296(95)80003-4

17. Milano MT, Katz AW, Zhang H et Al. Oligometastases treated with stereotactic body radiotherapy: long-term follow-up of prospective study. Int. J. Radiat. Oncol. Biol. Phys. 2012; 83: 878–886. https://doi.org/10.1016/j.ijrobp.2011.08.036 PMid:22172903

18. Schwartz DL et al. Adaptive radiotherapy for head-and-neck cancer: initial clinical outcomes from a prospective trial. Int. J. Radiat. Oncol. Biol. Phys. 2012; 83: 986–993. https://doi.org/10.1016/j.ijrobp.2011.08.017 PMid:22138459 PMCid:PMC4271827

19. Veness M, Richards S. Radiotherapy. In: Bolognia J, Jorizzo J, and Schaffer J, eds. Dermatology, vol. 2. Philadelphia: WB Sauders; 2012: 2291–2301.

20. Ying CH. Update of Radiotherapy for Skin Cancer. Hong Kong Dermatology & Venereology Bulletin. 2001; 9(2): 52-58.

21. Cognetta A, Howard B, Heaton H, et. Al. Superficial X-ray in the treatment of basal and squamous cell carcinoma: a viable option in select patients. J Am Acad Dermatol. 2012;67:1237–1241. https://doi.org/10.1016/j.jaad.2012.06.001 PMid:22818756

22. Petit JY, Avril MF, Margulis A, et. al. Evaluation of cosmetic results of a randomized trial comparing surgery and radiotherapy in the treatment of basal cell carcinoma of the face. Plast Reconstr Surg. 2000;105:2544–2551. https://doi.org/10.1097/00006534-200006000-00039 PMid:10845311

23. Zagrodnik B, Kempf W, Seifert E, et. al. Superficial radiotherapy for patients with basal cell carcinoma. Cancer. 2003;98(12):2708–2714. https://doi.org/10.1002/cncr.11798 PMid:14669293

24. Wolstenholme V, Glees JP. The Role of Kilovoltage X-rays in the Treatment of Skin Cancers. European Oncological Disease, 2006;1(1):32-5. https://doi.org/10.17925/eoh.2006.0.1.32

25. Barysch M, Eggman N, Beyeler M, et. al. Long term recurrence rate of large and difficult to treat cutaneous squamous cell carcinomas after superficial radiotherapy. Dermatology. 2012;224:59–65. https://doi.org/10.1159/000337027 PMid:22433440

26. Gillenwater AM, et Al. Merkel cell carcinoma of the head and neck: effect of surgical excision and radiation on recurrence and survival. Arch Otolaryngol Head Neck Surg, 2001; 127(2):149-54. https://doi.org/10.1001/archotol.127.2.149 PMid:11177031

27. Jabbour J. et Al. Merkel cell carcinoma: assessing the effect of wide local excision, lymph node dissection, and radiotherapy on recurrence and survival in early-stage disease--results from a review of 82 consecutive cases diagnosed between 1992 and 2004. Ann Surg Oncol, 2007;14(6): 1943-52. https://doi.org/10.1245/s10434-006-9327-y PMid:17356954

28. Micaily B. et Al. Radiotherapy for unilesional mycosis fungoides. Int J Radiat Oncol Biol Phys.1998;42(2): 361-4. https://doi.org/10.1016/S0360-3016(98)00218-1

29. Cooper JS. The influence of dose on the long-term control of classic (non-AIDS associated) Kaposi's Sarcoma by radiotherapy. Int J Radiat Oncol Biol Phys. 1988;15:1141-6. https://doi.org/10.1016/0360-3016(88)90196-4

30. Farshad, A., et al., A retrospective study of 150 patients with lentigo maligna and lentigo maligna melanoma and the efficacy of radiotherapy using Grenz or soft X-rays. Br J Dermatol. 2002;146(6):1042-6. https://doi.org/10.1046/j.1365-2133.2002.04750.x PMid:12072074

31. Chen, J.C., et al., Stereotactic radiosurgery in the treatment of metastatic disease to the brain. Neurosurgery. 2000; 47(2): 268-79. https://doi.org/10.1097/00006123-200008000-00003 PMid:10942000

32. Kamada, T. Clinical evidence of particle beam therapy (carbon). Int. J. Clin. Oncol. 2012;17: 85–88. https://doi.org/10.1007/s10147-012-0388-6 PMid:22426888

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Review Article

An Overview of Laser in Dermatology: The Past, the Present and … the Future (?)

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Abstract

The authors discuss a brief history of lasers and their use in dermatology. Although the excellent results achieved by the use of laser in dermatology, this special treatment modality is in continuous evolution. At present, new devices have been under development for the therapy of different kind of diseases, while lasers, already in use, has been changing, in order to be more secure, effective and be useful in many others disorders.

History of Laser

Sixty years after its discovery, in a society increasingly invaded by technologies, it is difficult to imagine how, until a few years ago, the laser was only an empirical technique, an academic study, or a futuristic project, as we can read in Tolstoy's novels.

However, if we want to trace the origins of the laser technology; we have to go back to the first years of XX century when Planck and Einstein's discoveries were laying the scientific basis for the development of the laser.

Max Planck dedicated a lot of time in studying the thermodynamic phenomenon of radiation. Finally, in 1900, maybe in his most important study, he discovered the relationship between energy and frequency of radiation and concluded that energy could be emitted or absorbed only in discrete chunks, named “quanta”.

His theory was an innovative one and inspired new physicists, such as Albert Einstein and other. In 1905, Einstein proposed how light delivers its energy in chunks, which were represented by photons, discrete quantum particles.

Later, in 1916, Einstein introduced the concept of stimulated emission: photons, by interacting with excited atoms or molecules, could stimulate the emission of new photons having the same frequency, phase, polarisation and direction of the first one [1].

Table 1: Milestones in the Lasers development

YEAR	PHYSICIANS	DISCOVERY
1960	Ali Javan, William Bennett Jr. and Donald Herriott	Helium-neon (HeNe) laser
1960	Peter P. Sorokin and Mirek J. Stevenson	Uranium laser
1961	Leo F. Johnson and Kurt Nassau	Neodymium-doped solid state laser
1961	J. McClung and Robert W. Hellwarth	Quality switching (Q- switching) technique to shorten the pulse length to nanoseconds
1962	Sumner Mayburg and Jacques Pankove	Semiconductor Diode Lasers
1964	William Bridges	Argon Laser
1964	Joseph E. Geusic and Richard G. Smith	Nd: YAG (neodymium-doped YAG) laser
1964	Kumar Patel	carbon dioxide laser
1967	Bernard Soffer and Bill McFarland	Dye laser
1970	Basov, V.A. Danilychev and Yu. M. Popov	Excimer laser
1972	Charles H. Henry	Quantum well laser
1976	John M.J. Madey	Free-electron laser (FEL).
1994	Jérôme Faist, Federico Capasso, Deborah L. Sivco, Carlo Sirtori, Albert L. Hutchinson and Alfred Y. Cho	Semiconductor laser that can simultaneously emit light at multiple widely separated wavelengths
1996	Wolfgang Ketterle	Pulsed atom laser
1997	Shuji Nakamura, Steven P. DenBaars and James S. Speck	Gallium-nitride (GaN) laser
2009	Chunlei Guo	Femtosecond pulsed laser

Even if the geniality of the Einstein's quantum theory of radiation, the studies, conducted in the successive decades, did not have a great impact in the scientific world. In 1928, the German Ladenburg and Kopfermann reported evidence about the phenomenon of stimulated emission of radiation [2]. Some years later, Fabrikant proposed how stimulated emission, in a gas discharge, may amplify light [3]; while Purcell and Pound described the stimulated emission of radio waves. In 1953, the American Weber proposed a microwave amplifier that was based on stimulated emission in a paramagnetic solid [4].

Nevertheless, it was only in 1954 that Einstein theory became true in practice. In that year the Americans Townes and Weber, and the Russians Basov and Prokhorov, independently reported about their introduction of MASER ("Microwave Amplification by Stimulated Emission of Radiation"), a special device for generating microwave radiation, using excited ammonia molecules into a resonant cavity [5, 6].

While a burst of microwave maser development followed (e.g. in 1956, Bloembergen developed a microwave solid-state maser) [7], some physicists began thinking about extending the maser principle to higher frequencies.

In 1958, Charles Townes and Arthur Schawalow, in a paper published in Physical Review Letters, showed that masers could be theoretically made to operate in the optical and infrared regions [8].

New experimental studies had been conducted by Townes, Schawalow and by the young physicist Gould.

Finally, the 16th may 1960, Theodore H. Maiman, a physicist at Hughes Research Laboratories in Malibu, constructed the first laser, using a cylinder of synthetic ruby, with the ends silver-coated to make them reflective and able to serve as a Fabry-Perot resonator. Maiman used the photographic flash lamp as the laser's pump source [9].

Only two weeks later, Gould and Schawlow built their ruby lasers.

As often happens with great inventions and discoveries, the laser discovery has been questioned for a long time. In 1964, Townes, Basov and Prokhorov received the Nobel Prize for their studies; and in 1977 Gould was recognised as the father of the laser, who also had the merit of first coined the term "Laser" ("Light Amplification by Stimulated Emission of Radiation").

While the scientific group was discussing those diatribes, the Laser was on, and its technology was in continuous progress. On the other hand, it was the time of the Cold War, and the researches about laser, such as for different technologies, were initially addressed to the military area (e.g. laser guide for a precision bomb, used in Vietnam) [10].

Over the years and with the evolution of technology, despite initial impressions, the laser has become a fundamental, irreplaceable and omnipresent device of modern science. Among the years, new and new laser machines, able to develop different radiation beams, have been built and introduced in commerce (Table 1).

Gradually, the laser has found application in various fields of human activity: from telecommunications to industry, from aeronautics to the space conquest, from photography to the creation of three-dimensional images and computer sphere.

Of course, even the medical field could not remain immune to this phenomenon.

As soon as possible, physicians began testing lasers on the medical practice, especially in the branches, such as ophthalmology, where light sources had been widely used for a long time.

In 1961, the Americans Charles Campbell and Charles Koester treated a patient with a retina tumour with a laser. About a week later, Zweng performed successfully a similar operation [10].

By seventies, lasers had been largely used in many medical areas: Kaplan introduced it in plastic surgery; Aronoff and Jako in otolaryngology; Hofestetter in urology; Kiefhaber and Dwyer in gastroenterology and endoscopy; Bellina in gynecology; Abela in cardiology; Ascher in neurosurgery; Lynn-Power in dentistry; Apfelberg for the treatment of vascular lesions; Chekurov, Oshiro and Trelles in rheumatologic and in traumatology diseases.

Even Dermatology was caught by the new technology.

Laser in Dermatology: the past

In 1963, Leon Goldman, also known as the “father of lasers in medicine”, was the first to use the laser in dermatology, thus anticipating an era of unimaginable technological development and innovative therapeutic potential. In his first studies, Goldman reported the effects of Maiman’s laser in the selective destruction of cutaneous pigmented structures, like black hairs [11]. He also described the potential use of ruby laser and the more innovative Q-switched device in tattoo removal and the possible treatment of other pigmented lesions, such as nevi and melanomas. Moreover, Goldman investigated the use of Argon laser in the treatment of vascular malformations, and the use of Carbon dioxide laser for the photo-excision of skin lesions [12].

In 1966, Mester, having discovered the positive effects of low-energy red laser on hair growth in rats, decided to use the same system to stimulate the healing of pressure ulcers.

Only a year later, Dougherty experimented with the use of laser in activating photosensitive substances which were able to bind and destroy cancer cells selectively. This was the origin of photodynamic therapy.

In the same period, Goldman was still studying the effects of different lasers in the treatment of dermatological diseases, underlying the importance of protection measures and suggesting the idea of the laser as a diagnostic tool [13]. In 1973, he also introduced the neo dymium: yttrium- aluminium garnet (Nd: YAG) laser in the treatment of vascular lesions.

In the mid-seventies, the Italian Sesti started on investigating non-surgical lasers in wound healing; in 1976, his team treated successfully a case of a pressure sore.

Also, the Italian scientific group had been contaminated by laser technology and in 1979, the first "Italian Society of Laser Medicine and Surgery” was born.

Nevertheless, was only in 1980 that laser therapy has been deeply revolutionized by the selective photo-thermolysis theory, postulated by Rox Anderson and John Parrish: by the use of specific wavelength, we achieve the destruction of specific molecules (or chromophores), allowing better localization of thermal energy and minimization of damage to the surrounding tissue [14].

Only three years later, Oshiro Atsumi described the use of non-surgical lasers and their mechanisms of action. In the same time, Passerella was studying the laser effects on mitochondria.

In 1984, the Food and Drug Administration (FDA) drew the first guidelines for the use of lasers in various vascular and dermatological lesions. From that era, FDA updates them each year.

The eighties are also characterised by the first use of a photo-acoustic laser in the treatment of penis plastic calcifications, and by the introduction of the lasers-sclerotherapy for the management of telangiectasias of the lower limbs.

Finally, the nineties has been characterised by an increasing of study and case reports of laser resurfacing (Gregory and others), laser hair removal and laser rejuvenation.

Table 2: Surgical lasers

CO_2 laser
Erbium laser
Holmium laser

Laser in Dermatology: the present

By the first researches of Goldman, modern dermatology may have at the disposal of a wide range of laser equipment, often very similar to each other, which can treat, many cutaneous diseases with absolute efficacy and safety [15].

Among the dermatologic lasers, the surgical ones are the more commonly used (Tab.2), especially the carbon dioxide laser (CO_2 laser). Due to its specific wavelength (10600 nm) and to its variable nature and duration of output (continuous, pulsed), CO_2 laser may be useful for the treatment of different skin or mucosal diseases (Table 3) [16-18].

Table 3: Clinical indications for CO_2 laser

Seborrheic keratoses
Actinic cheilitis
Actinic keratoses
Epidermal nevi
Scars
Sebaceous adenomas
Balanite xerotica obliterans
Warts
Basal cell epithelioma
Erythroplasia of Queyrat
Stains (melanin)
Neurofibromas
Oral papillomatosis
Resurfacing and Rejuvenation
Rhinophyma (glandular type)
Syringomas
Trichoepitheliomas
Xanthelasmas
Condrodermatite nodular helix
Skin resurfacing and renjuvenation

Also Erbium: YAG laser (wavelength: 2940 nm) is a useful surgical laser, especially for the treatment of superficial cutaneous lesions and skin refreshing (Table 4) [19].

Table 4: Clinical indications for Er:YAG laser

Sebaceous adenomas
Seborrheic keratosis
Acne scars
Favre-Racouchot disease
Xanthelasmas
Neurofibromas
Epidermal nevi
Spots
Resurfacing and Rejuvenation
Rhinophyma (remodelling phase)
Syringomas
Trichoepitheliomas

Others fundamental dermatologic lasers are the vascular ones, maybe the devices which have most benefited from the continuous technological progress. Even if different types of laser are available for the treatment of different vascular lesions (Table 5) [20-22], the DYE laser (Wavelength: 595 nm) and the Nd:YAG (Wavelength: 1064 nm or 532 nm) is the most commonly used because their safe profiles and their wide areas of clinical use.

Finally, there are the dermatologic lasers useful for aesthetic purposes, such as devices for removal of benign pigmented lesions, hair removal, tattoo removal and patients resurfacing (Table 6) [23-26].

Maybe, this area of laser therapy is the one who most had benefit by the introduction of Q-switched devices.

Table 5: Vascular lasers

Laser	Characteristics	Clinical indications
DYE laser	Liquid solution with a particular pigment (Rhodamine) contained in a cylindrical cell	Pws; facial telangiectasias; spider veins; pyogenic granulomas; Rosacea; pecilodermia of Civatte; cutaneous vascular ectasia
Nd: YAG laser	Crystal of aluminium garnet and yttrium doped with neodymium	Telangiectasias of face and legs, hemangioma, spider veins
Argon laser	Argon	Ruby angiomas, angiokeratomas, Kaposi's sarcoma
Alexandrite laser	Alexandrite	Facial telangiectasias
Diode laser	Semiconductor diode	Telangiectasias
Holmium laser	Solid holmium	Telangiectasias
Krypton laser	Krypton gas	Pws
Ruby laser	Bar of synthetic ruby	Telangiectasia
Copper Vapor laser	Steam copper	Facial telangiectasias

Q-switched lasers produce very short pulses (nanoseconds) with high peak powers (megawatts), allowing better and faster clinical results.

Table 6: Dermatological lasers for aesthetics purpose

CLINICAL INDICATION	LASER
Removal of benign pigmented lesions	Nd: YAG (532 nm), Ruby (694 nm), Alexandrite (760 nm), Nd: YAG (1064 nm)
Hair removal	Ruby (694 nm), Alexandrite (755 nm), Diode (800 nm), Nd: YAG (1064 nm)
Tattoo removal	Nd: YAG 1064 nm (black or dark blue tattoo) or 532 nm (red, violet, pink and brown tattoo), Ruby (black, dark blue, green tattoo), Alexandrite (black, blue and green tattoo)
Not ablative resurfacing	DYE laser, CO_2 Q-switched laser

Laser in Dermatology: … the future (?)

Although the excellent results achieved by the use of laser in dermatology, this special treatment modality is in continuous evolution.

At present, new devices have been under development for the therapy of different kind of diseases, while lasers, already in use, has been changing, in order to be more secure, effective and be useful in many others disorders.

Among the first group of devices there is the Xenon Chloride excimer laser (wavelength: 308 nm), useful for the treatment of autoimmune diseases (e.g. psoriasis, vitiligo, alopecia areata) [27-29], and the low-level laser, which is successfully used for the wounds healing [30, 31].

Among the second group, the Nd: YAG laser is an excellent example of how the technological progress may lead to a wider area of clinical uses, such as the lipolysis and the treatment of onychomycosis [32-34].

References

1. Einstein A. Zur Quantentheorie der Strahlung. Physikalische Gesellschaft Zürich 1916;18:47– 62.

2. Kopfermann H, Ladenburg R. Untersuchungen über die anomale Dispersion angeregter Gase II Teil. Anomale Dispersion in angeregtem Neon - Einfluß von Strom und Druck, Bildung und Vernichtung angeregter Atome. Zschr Physik 1928;48:26– 50. https://doi.org/10.1007/BF01351572

3. Fabrikant VA. Emission mechanism of a gas discharge. PUBLISHER AND TOWN? 1940.

4. Weber J. Amplification of microwave radiation by substances not in thermal equilibrium. Trans Inst Radio Eng PGED 1953;3:1. https://doi.org/10.1109/irepged.1953.6811068

5. Basov NG, Prokhorov AM. Application of molecular beams to the radio spectroscopic study of the rotation spectra of molecules. Zh Eksp Theo Fiz 1954;27:431.

6. Gordon JP, Zeiger HJ, Townes CH. The Maser – new type of microwave amplifier, frequency standard, and spectrometer. Phys Rev 1955;99:1264–1274. https://doi.org/10.1103/PhysRev.99.1264

7. Bloembergen N. Proposal for a new type solid-state maser. Phys Rev 1956;104:324–327. https://doi.org/10.1103/PhysRev.104.324

8. Schawlaow AL, Townes CH. Infrared and optical masers. Phys Rev 1958;112:1940–1949. https://doi.org/10.1103/PhysRev.112.1940

9. Maiman TH. Stimulated optical radiation in ruby. Nature 1960;187:493. https://doi.org/10.1038/187493a0

10. Hecht J. Short history of laser development. Opt. Eng. 2010;49(9): 091002. https://doi.org/10.1117/1.3483597

11. Goldman L, Blaney DJ, Kindel DJ, Franke EK: Effect of the laser beam on the skin. J Invest Dermatol 1963;40:121–122. https://doi.org/10.1038/jid.1963.21 PMid:13948765

12. Goldman L. Historical perspective: personal reflections; in Arndt KA, Noe JM, Rosen S: Cutaneous Laser Therapy: Principles and Methods. New York, Wiley, 1983: p 7. PMid:6872101

13. Goldmann L. Biomedical Aspects of the Laser: The Introduction of Laser Applications into Biology and Medicine. Springer, Berlin, 1967. https://doi.org/10.1007/978-3-642-85797-3

14. Anderson RR, Parrish JA. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. Science. 1983 Apr 29;220(4596):524-7. https://doi.org/10.1126/science.6836297 PMid:6836297

15. Hillegherbersg R. Fundamental of Laser Surgery. Eur J Surg 1997; 163:3-12.

16. Fitzpatrick RE, Goldman MP. CO2 laser surgery. In Goldman M.P., Fizpatrick R.E. Cutaneous laser surgery: the art and science of selective photothermolysis. St. Louis: Mosby-Year Book 1994; 198-259.

17. Fitzpatrick RE, Ruiz-Esparza J. The superpulse CO2 laser. In: Roenigk R.K., Roenigk H. eda. New trends in dermatologic surgery. London, 1993, Martin Dunitz. J Dermatol Surg Oncol, 1994; 20: 449-455. https://doi.org/10.1111/j.1524-4725.1994.tb03215.x PMid:8034839

18. Campolmi P, Bonan P, Cannarozzo G, Mokhtarzadeh S, Gianfaldoni S, Morini C, Bassi A, Lotti T. I laser in dermatologia - Tipologie di apparecchiature e applicazioni cliniche. HiTech Dermo 2010;6:27-35.

19. Zachary CB. Modulating the Er:YAG laser. Laser Surg Med 2000; 26:223-226. https://doi.org/10.1002/(SICI)1096-9101(2000)26:2<223::AID-LSM14>3.0.CO;2-K

20. Dover J S, Arndt KA. New approaches of the treatment of vascular lesions. Laser Surg Med 2000; 26: 158-163. https://doi.org/10.1002/(SICI)1096-9101(2000)26:2<158::AID-LSM6>3.0.CO;2-O

21. Baumler W., Ulrich H., Hartl A, Landthaler M., Shafirsten G. Optimal parameters for the treatment of leg veins using Nd:Yag laser at 1064 nm. Br J Dermatol 2006 Aug; 155(2):364-7. https://doi.org/10.1111/j.1365-2133.2006.07314.x PMid:16882176

22. Goldman M P, Fitzpatrick RE. Laser treatment of cutaneous vascular lesions. In Cutaneous Laser surgery, 2nd edition Mosby St Louis 1999.

23. Tan OT, Morelli JC, Kurban A. K. Pulsed dye laser treatment of benign cutaneous pigmented lesions. Laser Med Surg 1992; 12: 538. https://doi.org/10.1002/lsm.1900120513

24. Haedersal M, Wulf H.C. Evidence – based review of hair removal using laser and light sources. JEADV 2006; 20:9-20. https://doi.org/10.1111/j.1468-3083.2005.01327.x PMid:16405602

25. Grevelink J. M., Duke D., Van Leeuwen R. L. et al. Laser treatment of tattoos in darkly pigmented patients: efficacy and side effects. J Am Acad Dermatol 1996; 34: 653. https://doi.org/10.1016/S0190-9622(96)80068-5

26. Kilmer S. L., Anderson R.R. Clinical use of the Q-Switched Nd:YAG (1064 nm and 532 nm) lasers for treatment of tattoos. J Dermatol Surg Oncol 1993; 19:330. https://doi.org/10.1111/j.1524-4725.1993.tb00354.x

27. Lotti T, Prignano F, Buggiani G. New and experimental treatment of vitiligo and other hypomelanoses. Dermatol Clin 2007; 24 (3): 393-400. https://doi.org/10.1016/j.det.2007.04.009 PMid:17662905

28. Fernández-Guarino M, Jaén P. Laser in psoriasis.G Ital Dermatol Venereol. 2009;144(5):573-81. PMid:19834435

29. Al-Mutairi N. 308-nm excimer laser for the treatment of alopecia areata. Dermatol Surg. 2007 Dec;33(12):1483-7. https://doi.org/10.1097/00042728-200712000-00011 PMid:18076615

30. Medrado AR, Pugliese LS, Reis SR and Andrade ZA. Influence of low level laser therapy on wound healing and its biological action upon myofibroblasts, Lasers Surg Med. 2003;32:239-44. https://doi.org/10.1002/lsm.10126 PMid:12605432

31. Ribeiro MS, Da Silva Dde F, De Araujo CE, De Oliveira SF, Pelegrini CM, Zorn TM and Zezell DM. Effects of low-intensity polarized visible laser radiation on skin burns: a light microscopy study, J Clin Laser Med Surg. 2004;22:59-66. https://doi.org/10.1089/104454704773660994 PMid:15117489

32. Goldman A, Gotkin RH, Sarnoff DS, Prati C, Rossato F. Cellulite: a new treatment approach combining subdermal Nd: YAG laser lipolysis and autologous fat transplantation. Aesthet Surg J. 2008;28(6):656-62. https://doi.org/10.1016/j.asj.2008.09.002 PMid:19083594

33. Bousquet-Rouaud R, Bazan M, Chaintreuil J, Echague AV. High-frequency ultrasound evaluation of cellulite treated with the 1064 nm Nd:YAG laser. J Cosmet Laser Ther. 2009;11(1):34-44. https://doi.org/10.1080/14764170802612968 PMid:19214861

34. Kozarev J, Vižintin Z. Novel Laser Therapy in Treatment of Onychomycosis. J Laser Health Acad 2010;1.

ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2017 Jul 25; 5(4):531-532.
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Otophyma, Rhinophyma and Telangiectatic Rosacea – A Rare Combination in a Female Patient

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Keywords: Rosacea; Otophyma; Treatment; Surgery; Differential diagnoses.

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Abstract

BACKGROUND: Rosacea is an inflammatory facial dermatosis seen more frequently in adults in their second half of life. The phymas are a particular subtype with sebaceous gland hyperplasia and progressive fibrosis.

CASE REPORT: We report on the rare simultaneous occurrence of telangiectatic rosacea, otophyma and rhinophyma in a 50-year-old female with psoriatic arthritis, chronic lymphedema of the legs, and metabolic syndrome.

CONCLUSION: Despite the preference of rhinophyma and otophyma to the male gender, their occurrence in females needs to be considers in the differential diagnosis of dermatoses of head and neck. Early diagnosis and appropriate medical treatment improve outcome and help to avoid surgery.

A 50-year-old woman with a history of psoriatic arthritis, chronic lymphedema of the legs, and metabolic syndrome presented with a combined facial dermatosis and chronic swelling of the outer ears.

On examination, we observed a central facial persistent erythema with some telangiectasias and chronic lymphedema of the cheeks, and irregular nasal surface with redness and some pustules confirming the diagnosis of rosacea, erythematotelangiectatic type, with mild rhinophyma.

The outer ears were characterized by bilateral swelling involving the ear helix, anthelix and conchal fossa with a partial obstruction of the outer ear's canal (Fig. 1a-c). Microbial swabs were taken from there which identified *Pseudomonas aeruginosa*, *Turicella otitidis*, and *Achromobacter*. Mycology remained negative. Imaging by thoracic X-ray, abdominal ultrasound and Duplex sonography were unremarkable.

Figure 1: Clinical presentation. (a) Centrofacial erythema with mild rosacea. (b) and (c) Bilateral otophyma with partial obstruction of the outer ear's canal

The diagnosis of bilateral otophyma with rhinophyma and telangiectatic rosacea was confirmed. We initated systemic drug therapy with minocycline 50 mg twice daily for 6 weeks combined with topical metronidazole ointment for the face and topical fusidinic acid four outer ear's canals.

There was a stepwise improvement of inflammation and swelling. Treatment was well tolerated.

The phymas are part of the rosacea spectrum characterized by sebaceous hyperplasia, fibrosis and localized lymphedema. The most common type is rhinophyma [1]. Otophyma is a rare subtype which can be uni- or bilateral. It affects men more often than women. The disease results in disfigurement of the outer ears. In very rare cases otophyma can be associated with conductive hearing loss because of the obstruction of the external auditory canal. On clinical examination, edematous swelling with or without erythema and peau d'orange appearance are characteristic while papules and pustules are absent [2-9].

Differential diagnosis includes a variety of skin diseases such as relapsing polychondritis, erysipelas, subcutaneous emphysema, contact dermatitis and urticarial, leprosy and auricular petrosis [1, 7].

Treatment is according to recommendations for rosacea in general with metronidazole, azelaic acid, or ivermectin topically, for the inflammatory rosacea and topical alfa-2-adrenergic inhibitor brimonidine tartrate for erythematous rosacea. Tetracycline, azithromycine or isotretinoin are used orally [1, 10].

For treatment of advanced otophyma debulking surgery in analogy to rhinophyma surgery is an option with excision of the lymphedematous skin and defect closure by free skin transplant. Defect closure can be realized with split-skin or full-skin transplants. Decortication is another surgical option using different ablative techniques such as laser, radiosurgery or dermabrasion followed by healing by second intention [8, 9].

In conclusion, the knowledge of the rare rosacea subtype otophyma is important for dermatologists, ENT, and plastic surgeons.

References

1. Wollina U. Rosacea and rhinophyma in the elderly. Clin Dermatol. 2011;29:61-68. https://doi.org/10.1016/j.clindermatol.2010.07.009 PMid:21146734

2. Daniels K, Haddow K. Otophyma: a case report. J Laryngol Otol. 2007;122:524–526. PMid:17517166

3. Carlson JA, Mazza J, Kircher K, Tran TA. Otophyma: a case report and review of the literature (elephantiasis) of the ear. Am J Dermatopathol. 2008;30:61–72. https://doi.org/10.1097/DAD.0b013e31815cd937 PMid:18212550

4. Gupta M, Gupta M, Narang T. Otophyma: a rare and frequently misdiagnosed entitiy. Am J Otolaryngol. 2012;31:199–201. https://doi.org/10.1016/j.amjoto.2008.12.008 PMid:20015739

5. Ekmekci TR, Koslu A, Sakiz D. A case of otophyma. Clin Exp Dermatol. 2005;30:441–442. https://doi.org/10.1111/j.1365-2230.2005.01778.x PMid:15953095

6. Alcántara-Reifs CM, Salido-Vallejo R, Garnacho-Saucedo G, Vélez García-Nieto A. Otophyma: a rare variant of phymatous rosacea. Am J Otolaryngol. 2016;37:251-254. https://doi.org/10.1016/j.amjoto.2016.01.009 PMid:27178518

7. Shuster M, McWilliams A, Giambrone D, Noor O, Cha J. Otophyma: a rare benign clinical entity mimicking leprosy. Dermatol Online J. 2014;21: pii: 13030/qt41p4q5xq.

8. Sharma KS, Pollock J, Hasham S, Brotherston TM. CASE REPORT: Treatment of otophyma: Case report and review of the literature. Eplasty. 2013;13:e18. PMid:23641297 PMCid:PMC3624775

9. Kahn SL, Podjasek JO, Dimitropoulos VA, Brown CW Jr. Excisional debulking and electrosurgery of otophyma and rhinophyma. Dermatol Surg. 2016;42:137-139. https://doi.org/10.1097/DSS.0000000000000560 PMid:26716716

10. Wollina U. Subantimicrobial-dose doxycycline monohydrate in dermatology. Wien Med Wochenschr. 2015;165:499-503. https://doi.org/10.1007/s10354-015-0399-9 PMid:26564206

ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2017 Jul 25; 5(4):533-534.
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Late Onset Achromatic Melanoma Arising in a Giant Congenital Melanocytic Nevus

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Keywords: melanoma; congenital nevus; surgery; progression; outcome; prevention.

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Abstract

A 61-year-old woman, with a lifelong history of a giant congenital melanocytic nevus in the occipital region with secondary development of giant melanoma is presented. Surgical excision was performed, and the histopathological evaluation confirmed the diagnosis of Giant Malignant Melanoma (GMM) with a maximum tumour thickness of 16 mm. Nowadays, there is tremendous uncertainty regarding how giant congenital melanocytic nevi (GCMN) should be treated. The standard approach to patients with late onset giant congenital melanocytic nevi (GCMN is based on two main considerations: (1) obtain an acceptable cosmetic results with the purpose to decrease the psychosocial inconvenience to each patient, and (2) to attempt to minimise the risk of development of malignant transformation. Unfortunately complete surgical removal of the GCMN is usually difficult and very often impossible without subsequent functional or cosmetic mutilations.

A 61-year-old woman, with a lifelong history of a giant congenital melanocytic nevus involving the occipital scalp, posterior neck and shoulders, and upper back, presented with a six-month history of an ulcerated tumour in the occipital region (Fig. 1a, 1b, 1c). Magnetic resonance imaging confirmed the presence of an exophytic cutaneous tumour measuring 11.5 cm in greatest diameter as well as spinal stenosis in the area of C6 and C7. Abnormal laboratory studies included an increased C-reactive protein and an elevated serum S100 level (0.122 mcg/l). Radiographic and ultrasonographic studies failed to show evidence of disease progression to lungs, lymph nodes or abdominal structures. A wide local excision was done, and the histopathology confirmed the diagnosis of malignant melanoma with a maximum thickness of 16 mm (Fig. 1d, 1e, 1f). Additional reexcision with 1,5cm safety margins was planned. Immunohistopathological stainings with HMB-45 (diffusely positive) and S-100 showed a strong positive reaction. The patient denied sentinel lymph node biopsy. Tumour was staged as IIB (T4aN0M0). A prophylactic interferon therapy (3 MU/m^2, 3 x weekly) was planned.

Congenital melanocytic nevus (CMN) is defined, clinically, as a melanocytic lesion present at birth or which develops during infancy from preexistent melanocytes [1, 2]. The risk of developing

melanoma over a CMN is a nowadays very well established subject [1, 3]. It is believed that this risk is directly proportional to nevus size, varying from 2.6% to 4.9% for small and medium nevi and from 6% to 20% for giant nevi [3]. For these reasons, surgical resection of giant congenital nevi is frequently recommended before puberty and when located in areas difficult to monitor [2]. Nowadays, there is tremendous uncertainty regarding how giant congenital melanocytic nevi (GCMN) should be treated. The standard approach to patients with GCMN is based on two main considerations: (1) obtain an acceptable cosmetic result to decrease the psychosocial inconvenience to the patient, and (2) attempt to minimise the risk of malignancy.

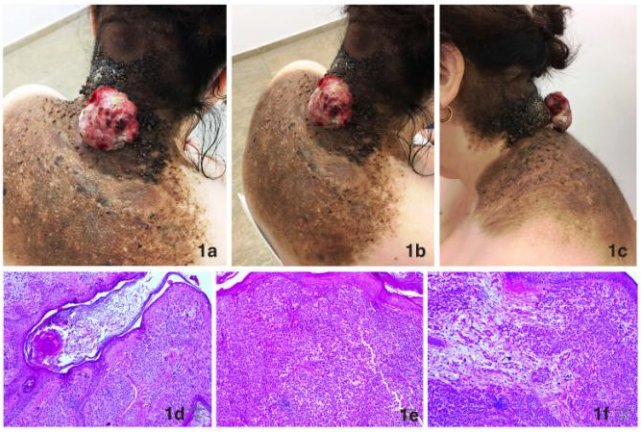

Figure 1: 1a-1c, Clinical pictures of patient with Giant melanoma located on the basis of Giant Congenital Melanocytic Nevus; 1d-1f, Histopathological evaluation showing deep penetrating tumour cells

To date, no absolute guidelines to treat these nevi have been given to our knowledge, and therefore, this subject remains one of the most controversial issues in dermatologic surgery and dermatologic oncology [4-6].

Complete removal of the GCMN is usually difficult and very often impossible without functional or cosmetic mutilation. Moreover, even after complete excision of GCMN down to the muscle fascia, the malignancy risk is not completely eradicated as malignant melanoma can occur at extracutaneous sites [7].

The most promising results of treating GCMN were originally reported by Moss in 1987 [8]. He performed curettage on GCMN during the first weeks of life to remove the superficially distributed nevus cells based on the fact that at that time, there seems to be a cleavage plane between the upper and the lower dermis. This technique offers the best alternative to classic surgery when the nevi are too large to perform complete excision, and it is a technique that is of benefit for these patient groups [9]. Treatment with targeted therapies, after phenotype characterization, should also be considered in selected cases [10, 11].

References

1. Paschoal FM. Nevo melanocítico congênito. An Bras Dermatol. 2002;77:649–656. https://doi.org/10.1590/S0365-05962002000600002

2. Yun SJ, Kwon OS, Han JH, Kweon SS, Lee MW, Lee DY, et al. Clinical characteristics and risk of melanoma development from giant congenital melanocytic naevi in Korea. Br J Dermatol. 2012;166:115–123. https://doi.org/10.1111/j.1365-2133.2011.10636.x PMid:21923752

3. Khashashneh I, Shatnawi M, Tawalbeh A, Alhaji M, Rajjal M. Giant congenital hairy nevus on the scalp. Sudan J Med Sci. 2008;3:343–347.

4. Arons MS, Hurwitz S. Congenital endocellular nevus: a review of treatment controversy. Plast Reconstr Surg. 1983;72:355-365. https://doi.org/10.1097/00006534-198309000-00019

5. Alper JC. Congenital nevi: the controversy rages on [editorial]. Arch Dermatol. 1985;121734-735. https://doi.org/10.1001/archderm.1985.01660060048018

6. De Raeve LE. Management of congenital nevi. Eur J Ped Derm. 1998;8161-164.

7. de David M, Orlow SJ, Provost N et al. Neurocutaneous melanosis: clinical features of large congenital melanocytic nevi in patients with manifest central nervous system melanosis. J Am Acad Dermatol. 1996;35: 529-538. https://doi.org/10.1016/S0190-9622(96)90674-X

8. Moss ALH. Congenital "giant" naevus: a preliminary report of a new surgical approach. Br J Plast Surg. 1987;40410- 419. https://doi.org/10.1016/0007-1226(87)90046-4

9. De Raeve LE, De Coninck AL, Dierickx PR, Roseeuw DI. Neonatal curettage of giant congenital melanocytic nevi. Arch Dermatol. 1996;132(1):20-2. https://doi.org/10.1001/archderm.1996.03890250022005 PMid:8546479

10. Russo A, Ficili B, Candido S, Pezzino FM, Guarneri C, Biondi A, Travali S, McCubrey JA, Spandidos DA, Libra M. Emerging targeted therapies for melanoma treatment (review). Int J Oncol. 2014;45(2):516-24. https://doi.org/10.3892/ijo.2014.2481

11. Bevelacqua V, Bevelacqua Y, Candido S, Skarmoutsou E, Amoroso A, Guarneri C, Strazzanti A, Gangemi P, Mazzarino MC, D'Amico F, McCubrey JA, Libra M, Malaponte G. Nectin like-5 overexpression correlates with the malignant phenotype in cutaneous melanoma. Oncotarget. 2012;3(8):882-92. https://doi.org/10.18632/oncotarget.594 PMid:22929570 PMCid:PMC3478464

ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2017 Jul 25; 5(4):535-536.
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Allergic Maculo-Papular Exanthema Due To Terbinafine

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Keywords: Terbinafine; Exanthema; Antimycotic drugs; Type-IV allergies; Patch test; Prick test.

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Abstract

We report on a 76-year-old male patient who developed a maculopapular generalised exanthema due to terbinafine. Prick test was negative; patch test revealed a positive reaction after 48 h confirming the delayed-type allergic reaction. Non-pustular exanthema has only rarely been reported for terbinafine.

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A 76-year-old male patient presented to our department for Allergology diagnostic. He reported about an itchy dermatosis that developed the year before. He suffered for many years from onychomycosis and recurrent tinea pedum. In May 2016 he was treated for the first time by systemic terbinafine because of tinea pedum. About four weeks later he developed of a generalised maculopapular exanthema. Terbinafine therapy was stopped. The exanthema completely disappeared within two weeks by oral prednisolone in tapering-down doses.

The medical history was negative for atopic diseases and known allergies, but he suffered from a mild depression treated with clomipramine. No other medical drugs were used by our patient.

On examination, we observed a photo skin type II according to Fitzpatrick, tinea pedum, but no urticarial dermographism.

We performed patch test and pricked test with terbinafine. After 20 in, prick test remained negative. Positive control with 0.1% histamine showed an urticarial response of 3 mm to 30 mm with some pseudopodia.

Patch test revealed a positive reaction to the offending drug with multiple papules and erythema (++) after 48 h (Fig. 1).

Terbinafine is a frequently used allylamine antimycotic drug that inhibits squalene epoxidase and thereby ergosterols biosynthesis of fungi [1]. Adverse reactions have been documented with an incidence of 2.7% [2]. The most common findings are acute generalised pustulosis, urticaria, gastrointestinal symptoms, taste loss, and liver toxicity [2-5].

An uncommon adverse effect is the development of drug-induced lupus erythematosus, mostly of the subacute-cutaneous subtype [6], and induction or exacerbation of psoriasis [7].

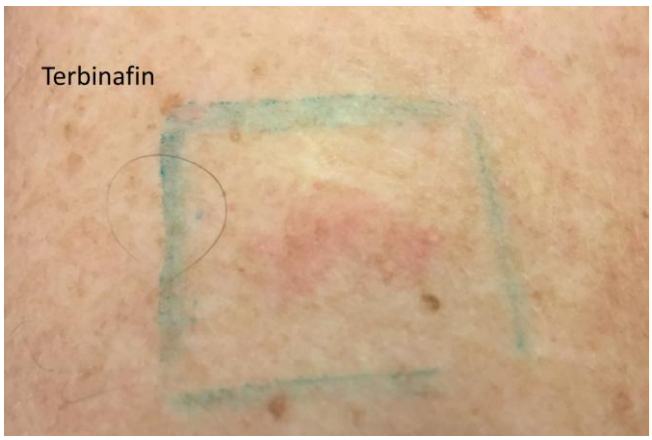

Figure 1: Positive patch test reaction with terbinafine after 48 h

In contrast, to pustular exanthema non-pustular erythema has rarely been described. George et al. (2015) observed a case of pityriasis rosea-like eruption due to terbinafine. Zheng et al. (2017) described a lichenoid drug eruption by terbinafine two weeks after initiation of treatment. Maculo-papular exanthema due to terbinafine has not been described, although it might be underrepresented in the medical literature.

We could confirm the allergic reaction to terbinafine. Although a generalised exanthema had been observed, we identified a type-IV reaction not a type-I reaction to terbinafine. Maculo-papular exanthema and systemic drug-related intertriginous and flexural exanthema (SDRIFE) are the most common symptoms of a delayed drug reaction [8, 9].

References

1. Favre B, Ryder NS. Characterization of squalene epoxidase activity from the dermatophyte Trichophyton rubrum and its inhibition by terbinafine and other antimycotic agents. Antimicrob Agents Chemother. 1996;40:443-447. PMid:8834895 PMCid:PMC163131

2. Ozturk G, Turk BG, Karaca N et al. Generalised pustular eruptions due to terbinafine. Cutan Ocul Toxicol. 2012;31:81-84. https://doi.org/10.3109/15569527.2011.607202 PMid:21888496

3. George A, Bhatia A, Kanish B, Williams A. Terbinafine-induced pityriasis rosea-like eruption. Indian J Pharmacol. 2015;47:680-681. https://doi.org/10.4103/0253-7613.169574 PMid:26729964 PMCid:PMC4689026

4. Sidoroff A. Acute generalised exanthematous pustulosis. Hautarzt. 2014;65: 430-435. https://doi.org/10.1007/s00105-013-2698-7 PMid:24820800

5. Veraldi S, Pontini P, Serini SL. Terbinafine and taste loss. G Ital Dermatol Venereol. 2016;151:308-309. PMid:27176083

6. Lowe GC, Henderson CL, Grau RH, Hansen CB, Sontheimer RD. A systematic review of Drug-induced subacute cutaneous lupus erythematosus. Br J Dermatol. 2011;164(3):465-472. https://doi.org/10.1111/j.1365-2133.2010.10110.x

7. Verros CD, Rallis E. The role of terbinafine in the induction and exacerbation of psoriasis. Int J Dermatol. 2013;52:1155–1156. https://doi.org/10.1111/j.1365-4632.2011.05117.x PMid:22998455

8. Ziemer M. Delayed-type cutaneous drug reactions. Pathogenesis, clinical features and histology. Hautarzt. 2014;65:397-408. https://doi.org/10.1007/s00105-013-2696-9 PMid:24820797

9. Tan SC, Tan JW. Symmetrical drug-related intertriginous and flexural exanthema. Curr Opin Allergy Clin Immunol. 2011;11:313-318. https://doi.org/10.1097/ACI.0b013e3283489d5f PMid:21659857

10. Zheng Y, Zhang J, Chen H, Lai W, Maibach HI. Terbinafine-induced lichenoid drug eruption. Cutan Ocul Toxicol. 2017;36:101-103. https://doi.org/10.3109/15569527.2016.1160101 PMid:26938740

ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2017 Jul 25; 5(4):537-538.
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Circumscribed Lipoatrophy of the Chin after Tooth Extraction

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Keywords: Facial lipoatrophy; Tooth extraction; Facial esthetics; Soft tissue fillers; Autologous adipose tissue transfer.

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Abstract

We describe the rare occurrence of circumscribed facial lipoatrophy after tooth extraction. Correction by minimal invasive esthetic techniques such as soft tissue fillers or autologous fat transfer is possible but was not warranted.

Circumscribed facial lipoatrophy is a rare clinical finding. It has been described as a consequence of trauma, with autoimmune connective tissue disorders like Parry-Romberg syndrome and scleroderma en coup de sabre [1, 2]. Lipoatrophy is a possible adverse effect of drug therapy [3]. It can also develop as a sign of autoaggressive psychiatric disorders [4]

We observed a 50-year-old female with a depression of soft tissue on the right side of her chin that developed about one year ago. The lesions did not show any sign of inflammation (Fig. 1). Touching the area was painless. On palpation, the depressed skin seemed to be attached to the bony structure of the mandibula. There was no opening or secretion.

Her medical history was unremarkable except for a tooth extraction before the appearance of facial lipoatrophy. Oral examination showed the area of tooth loss but no other pathologies (Fig. 2). The routine laboratory was unremarkable. A skin biopsy was suggested, but the patient refused.

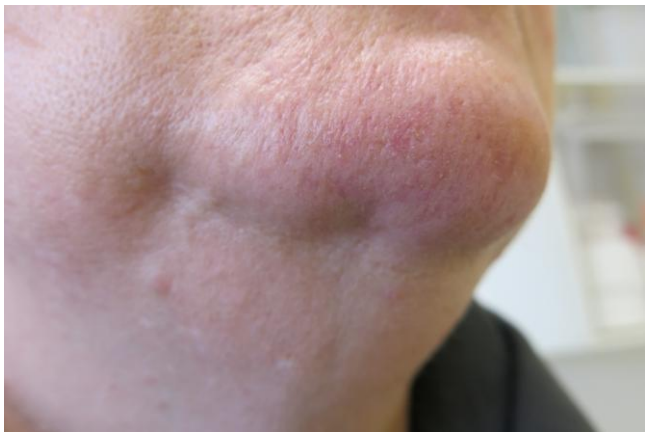

Figure 1: Unilateral depression of soft tissue - circumscribed facial lipoatrophy

Tooth extraction may often lead to alveolar bone resorption. Atrophy of the alveolar ridge can cause aesthetic and surgical problems in prosthetic dentistry [5]. In contrast to this, soft tissue atrophy after tooth extraction is an unusual observation [6].

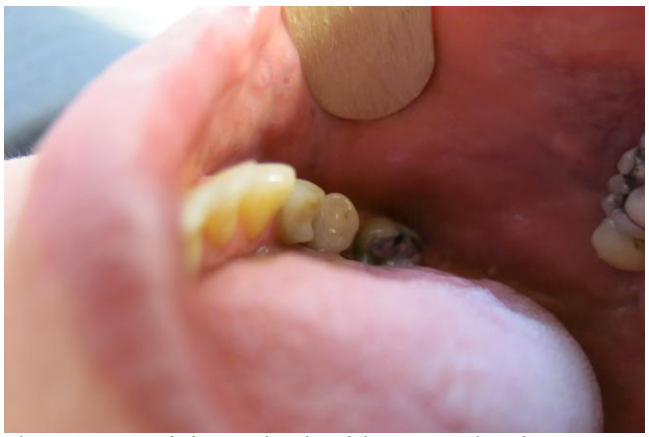

Figure 2: Intraoral view on the site of the extracted tooth

Facial lipoatrophy can be corrected by soft tissue fillers and autologous fat transplants [1, 2, 7], what was not warranted by our patient.

In conclusion, circumscribed facial lipoatrophy is a rare sequela after tooth extraction, that can be corrected by minimally invasive procedures established in esthetic medicine [8].

References

1. Rendon MI, Keeling J. Poly-L-lactic acid for the treatment of trauma-induced facial lipoatrophy and asymmetry. Cutis. 2008;81:218-222. PMid:18441843

2. Ortega VG, Sastoque D. New and successful technique for the management of Parry-Romberg syndrome's soft tissue atrophy. J Craniofac Surg. 2015;26:e507-e510. https://doi.org/10.1097/SCS.0000000000002023 PMid:26335318

3. Montessori V, Press N, Harris M, Akagi L, Montaner JS. Adverse effects of antiretroviral therapy for HIV infection. CMAJ. 2004;170:229-238. PMid:14734438 PMCid:PMC315530

4. Bechara FG, Rotterdam S, Stücker M, Hoffmann K, Altmeyer P. A case of localised bilateral lipodystrophy associated with self-injection of xenogenous material. J Dermatol. 2003;30:924-926. https://doi.org/10.1111/j.1346-8138.2003.tb00350.x PMid:14739522

5. Schmidlin PR, Jung RE, Schug J. Alveolar ridge preservation after tooth extraction – a review of the literature. Schweiz Monatsschr Zahnmed. 2004;114:328–336. PMid:15185481

6. Ayhan M, Senen D, Görgü M, Genaağa S, Erdoğan B. Multiple atrophies following tooth extraction. Aesthetic Plast Surg. 2001;25:457-459. https://doi.org/10.1007/s00266-001-0006-x PMid:11731854

7. Lindenblatt N, van Hulle A, Verpaele AM, Tonnard PL. The role of microfat grafting in facial contouring Aesthet Surg J. 2015;35:763-771. https://doi.org/10.1093/asj/sjv083 PMid:26038369

8. Wollina U, Goldman A, Berger U, Abdel-Naser MB. Esthetic and cosmetic dermatology. Dermatol Ther. 2008;21:118-130. https://doi.org/10.1111/j.1529-8019.2008.00179.x PMid:18394086

ID Design 2012/DOOEL Skopje, Republic of Macedonia
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Impetiginized Dyshidrotic Eczema

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Keywords: hand dermatitis; superinfections; St. aureus; clobetasol; skin barrier.

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Abstract

A 16 years old female patient, affected by atopic dermatitis and rhinoconjunctivitis allergica since childhood, requested a dermatologic consultation for lesions which had appeared after 3 months of local treatment with clobethasole propionate. The histological analysis confirmed the diagnosis of dyshidrotic eczema and the microbiological smears demonstrated a significant infection with *Staphylococcus aureus*. The risk of developing corticosteroids' side-effects depends on the potency of the product, extended period of use and the volume of product applied. Clobetasol propionate is a group I- highly potent corticosteroid, which should be used for a maximum period of 2 weeks. Several authors have found that this agent has cumulative depot effect, persisting in the epidermis for 4 days after only one application. Taking together these observations, sustained by the clinical case presented above, we can conclude that the infectious risks associated with topical corticosteroid treatment must not be neglected, particularly since treated patients are fragile, and frequently have multiple well-known risk factors.

A 16 years old female patient, affected by atopic dermatitis and rhinoconjunctivitis allergica since childhood, requested a dermatologic consultation for the lesions presented in Fig. 1a, 1b, which had appeared after 3 months of local treatment with clobethasole propionate for dyshidrotic eczema. The histological analysis confirmed the diagnosis of dyshidrotic eczema and the microbiological smears demonstrated a significant infection with *Staphylococcus aureus*. The pictures show the corpus inflammation and maceration of the skin (Fig. 1a, 1b). After a 10 days treatment regimen with systemic antibiotics (Clarithromycin Retard 500 mg once daily), antihistamine tablets (Bilastine 20 mg) and topical antibacterial agents (silver sulfadiazine), the symptomatology improved significantly.

This complex case reveals a significant immune system dysregulation since the patient had been affected by atopic dermatitis and rhinoconjunctivitis allergica for a long period. As demonstrated by Ambach A et al., these pathologies can be linked to T-cell dysfunction [1].

The risk of cutaneous infections due to topical

corticosteroids is known but has never been thoroughly studied [2]. Z. Boughrara et al. noted cutaneous super-infection in nine of 30 patients receiving topical corticosteroids for bullous pemphigoid, among which there were three cases of fatal necrotizing fasciitis due to Streptococcus A [2].

The risk of developing corticosteroids' side-effects depends on the potency of the product, extended period of use and the volume of product applied [6]. Clobetasol propionate is a group I- highly potent corticosteroid, which should be used for a maximum period of 2 weeks [6]. Research has found that this agent has cumulative depot effect, persisting in the epidermis for 4 days after only one application [3]. Recently, del Rosso highlighted the fact that topical corticosteroids may disrupt the lipid synthesis in stratum corneum, interfering with epidermal barrier recovery [4].

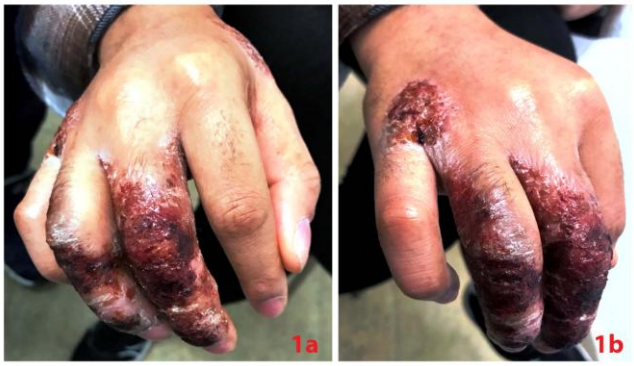

Figure 1: Clinical pictures of a female patient with macerated dyshidrotic eczema and massive superinfection with St. aureus. Yellow-brown colour of the lesions and massive edema

The biomolecular events that facilitate the infection suggest a systemic dysfunction, not limited to the skin district. Indeed, Boudhir H et al. underlined that nodular lesions of Kaposi's disease appeared during treatment of bullous pemphigoid with topical corticosteroids [5].

Taking together these observations, evoked after the analysis of the clinical case, indicate that the infectious risks associated with topical corticosteroid treatment must not be neglected, particularly since treated patients are fragile, and frequently have multiple well-known risk factors.

Taking together these observations, sustained by the clinical case presented above, we can conclude that the infectious risks associated with topical corticosteroid treatment must not be neglected, particularly since treated patients are fragile, and frequently have multiple well-known risk factors.

References

1. Ambach A, Bonnekoh B, Gollnick H. Perforin hyperreleasability and depletion in cytotoxic T cells from patients with exacerbated atopic dermatitis and asymptomatic rhinoconjunctivitis allergica. J Allergy Clin Immunol. 2001;107(5):878-86. https://doi.org/10.1067/mai.2001.114240 PMid:11344356

2. Boughrara Z, Ingen-Housz-Oro S, Legrand P, Duong TA, Roujeau JC. Cutaneous infections in bullous pemphigoid patients treated with topical corticosteroids. Ann Dermatol Venereol. 2010;137(5):345-51. https://doi.org/10.1016/j.annder.2010.03.015 PMid:20470914

3. Abidi A, Ahmad F, Singh SK, Kumar A. Study of reservoir effect of clobetasol propionate cream in an experimental animal study using histamine-induced wheal suppresion test. Indian J. Dermatol. 2010; 55:329-33. https://doi.org/10.4103/0019-5154.74531 PMid:21430883 PMCid:PMC3051290

4. Del Rosso JQ. Topical corticosteroid application and the structural and functional integrity of the epidermal barrier. J Clin Aesthet Dermatol. 2013; 6(11): 20-27.

5. Boudhir H, Mael-Ainin M, Senouci K, Hassam B, Benzekri L. Kaposi's disease: an unusual side-effect of topical corticosteroids. Ann Dermatol Venereol. 2013;140(6-7):459-61. https://doi.org/10.1016/j.annder.2013.04.078 PMid:23773746

6. Tadicherla S, Ross K, Shenefelt PD, Fenshe NA. Topical corticosteroids in dermatology. J Drugs Dermatol. 2009; 8:1093-105. PMid:20027937

ID Design 2012/DOOEL Skopje, Republic of Macedonia
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Frictional Dermatosis in a Courier Driver

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Keywords: Occupational medicine; Frictional hypermelanosis; Differential diagnosis; Histopathology; Driver's seat; Pigmentary disorders.

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Abstract

Frictional hypermelanosis is an uncommon finding in Caucasians. We report the unusual case of 56-year-old male courier driver who developed linear and patchy hypermelanosis of the back caused by the driver's seat. Histology has included other pathologies. Treatment of the asymptomatic hyper pigmentation was not warranted.

Frictional hypermelanosis is an uncommon condition. The clinical finding is characterised by asymptomatic, diffuse, brownish patches located mainly in the skin above bony prominences. Histologically, increased melanin content of the epidermis with or without pigment incontinence, sometimes with amyloid deposits, are characteristic [1].

Friction may have various reasons, such as rubbing skin repeatedly with scrub pads (loofah) or bathroom towels [1], using a washing agent (fifa) during bathing with vigorous friction [2], religious practices [3, 4], clothing [5].

A 56-year-old male patient presented with a linear asymptomatic brownish hyperpigmentation above the breast spine and in the sacral region (Fig. 1 & 2). He used to drive a van as a courier driver for 10 to 12 hours a day. He took no medications and reported no other known complaints or diseases. We took a skin biopsy that confirmed epidermal hypermelanosis and excluded hypermelanocytosis. Amyloid was absent. There was no inflammatory dermal infiltrate as well.

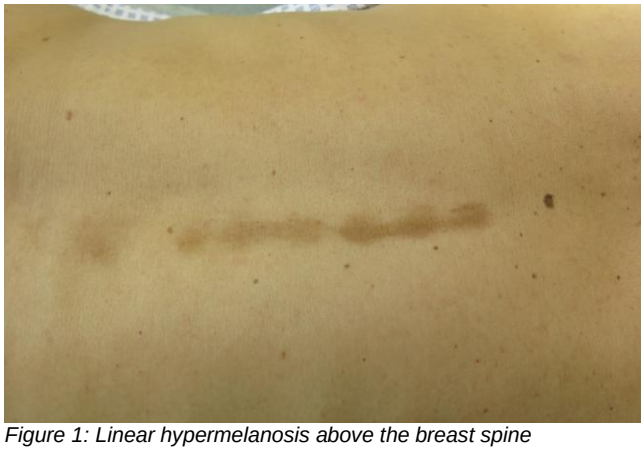

Figure 1: Linear hypermelanosis above the breast spine

Based on history, clinical presentation and histopathology the diagnosis of frictional dermatosis due to the driver's seat was confirmed. No treatment was wanted.

Friction can cause hypermelanosis, lichenoid dermatosis and callus formation. Other causes of circumscribed hypermelanosis include heat, neurocutaneous dysesthesia, post-inflammatory hyperpigmentation, adverse drug reactions, melasma and radiotherapy [6-9].

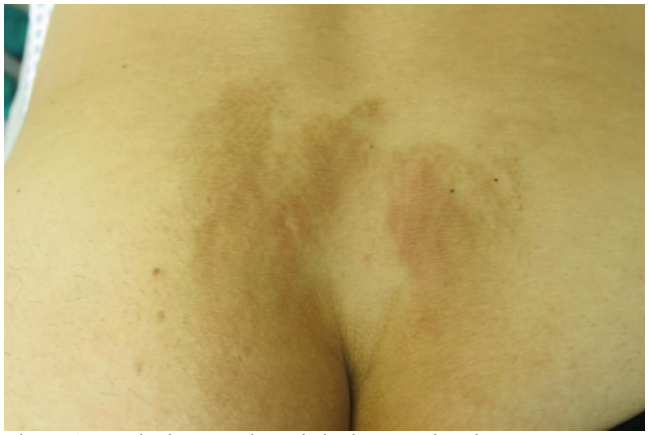

Figure 2: Patchy hypermelanosis in the sacral region

In case of warranted treatment, ablative surgery, cryosurgery, and lasers have been used with mixed results [10].

References

1. Al-Aboosi M, Abalkhail A, Kasim O, Al-Khatib A, Qarqaz F, Todd D, Al-Khidour M, Obeidate F. Friction melanosis: a clinical, histologic, and ultrastructural study in Jordanian patients. Int J Dermatol. 2004;43(4):261-264. https://doi.org/10.1111/j.1365-4632.2004.01606.x PMid:15090007

2. Sharquie KE, Al-Dorky MK. Frictional dermal melanosis (lifa disease) over bony prominences. J Dermatol. 2001;28(1):12-15. https://doi.org/10.1111/j.1346-8138.2001.tb00079.x PMid:11280458

3. Naimer SA, Trattner A, Biton A, Avinoach I, Vardy D. Davener's dermatosis: a variant of friction hypermelanosis. J Am Acad Dermatol. 2000;42(3):442-445. https://doi.org/10.1016/S0190-9622(00)90216-0

4. Papadakis G, Zampelis T, Michalopoulou M, Konstantopoulos K, Rosenberg T, Chatzipanagiotou S. Prayer marks in immigrants from Bangladesh with diabetes who live in Greece. J Immigr Minor Health. 2016;18(1):274-276. https://doi.org/10.1007/s10903-015-0184-2 PMid:25784139

5. Verma SB. Dermatological signs in South Asian women induced by sari and petticoat drawstrings. Clin Exp Dermatol. 2010;35(5):459-461. https://doi.org/10.1111/j.1365-2230.2009.03587.x PMid:19758377

6. Wollina U, Helm C, Hansel G, Köstler E, Schönlebe J. Two cases of erythema ab igne, one with a squamous cell carcinoma. G Ital Dermatol Venereol. 2007;142(4):415-418.

7. Geria AN, Tajirian AL, Kihiczak G, Schwartz RA. Minocycline-induced skin pigmentation: an update. Acta Dermatovenerol Croat. 2009;17(2):123-126. PMid:19595269

8. Wu IB, Lambert C, Lotti TM, Hercogová J, Sintim-Damoa A, Schwartz RA. Melasma. G Ital Dermatol Venereol. 2012;147(4):413-418. PMid:23007216

9. Shumway NK, Cole E, Fernandez KH. Neurocutaneous disease: Neurocutaneous dysesthesias. J Am Acad Dermatol. 2016;74(2):215-228; quiz 229-230. https://doi.org/10.1016/j.jaad.2015.04.059 PMid:26775772

10. Al-Dhalimi MA, Maluki AH, Tauma A. Efficacy and safety of 532-nm and 1,064-nm Q-switched Nd:YAG laser treatment of frictional dermal melanosis over bony prominences (Lifa disease). Dermatol Surg. 2015;41(1):136-141. https://doi.org/10.1097/DSS.0000000000000238 PMid:25533157

ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2017 Jul 25; 5(4):543-544.
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Interstitial Granulomatous Dermatitis (IGD)

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Keywords: IGD; necrobiosis lipoidica; morphea like; prognostic value; plaque; target lesions.

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Abstract

We report the case of a 42 years old male patient suffering from skin changes , which appeared in the last 7-8 years. Two biopsies were performed during the evolution of the lesion. Both showed similar findings that consisted in a busy dermis with interstitial, superficial and deep infiltrates of lymphocytes and histiocytes dispersed among collagen bundles, with variable numbers of neutrophils scattered throughout. Some histiocytes were clustered in poorly formed granuloma that included rare giant cells, with discrete Palisades and piecemeal collagen degeneration, but without mucin deposition or frank necrobiosis of collagen. The clinical and histologic findings were supportive for interstitial granulomatous dermatitis. Interstitial granulomatous dermatitis (IGD) is a poorly understood entity that was regarded by many as belonging to the same spectrum of disease or even synonym with palisaded and neutrophilic granulomatous dermatitis (PNGD). Although IGD and PNGD were usually related to connective tissue disease, mostly rheumatoid arthritis, some patients with typical histologic findings of IGD never develop autoimmune disorders, but they have different underlying conditions, such as metabolic diseases, lymphoproliferative disorders or other malignant tumours. These observations indicate that IGD and PNGD are different disorders with similar manifestations.

We report the case of a 42 years old male patient suffering from skin changes as presented in Fig. 1, which appeared in the last 7-8 years. The physical examination revealed the presence of a large, round, brownish plaque with whitish atrophic dotted areas on its surface, of 8x6 cm, with well-defined margins, located on the posteroinferior region of his left arm. His medical history was positive for insulin dependent diabetes mellitus with an episode of ketoacidosis in the past, chronic pancreatitis, choledocholithiasis, chronic antrum gastritis with negative *Helicobacter Pylori* tests. The patient's blood profile, including routine tests, CRP, C3, C4, *Borrelia Burgdorferi* IgG and IgM, Quantiferon, Ac anti-HBC, Ag Hbs were all within normal levels.

Two biopsies were performed during the evolution of the lesion (in 2012 and 2017 respectively). Both showed similar findings that consisted in a busy dermis with interstitial, superficial and deep infiltrates of lymphocytes and histiocytes dispersed among collagen bundles, with variable numbers of neutrophils scattered throughout (Fig. 2). Some histiocytes were clustered in poorly formed granuloma that included rare giant cells, with discrete

Palisades and piecemeal collagen degeneration, but without mucin deposition or frank necrobiosis of collagen. The clinical and histologic findings were supportive for interstitial granulomatous dermatitis.

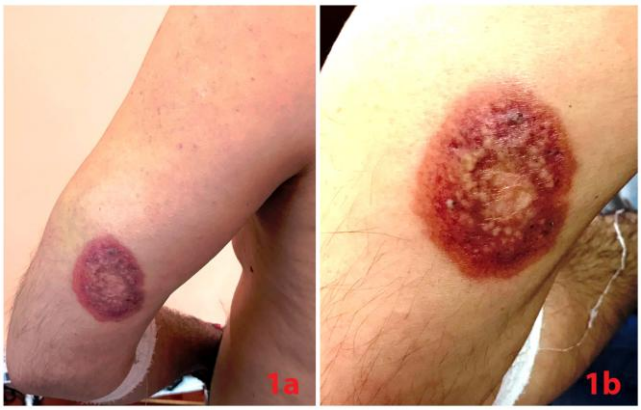

Figure 1: Clinical aspect. a: Large erythematous plaque with dotted whitish areas on the surface; b: Close-up view

Interstitial granulomatous dermatitis (IGD) is a poorly understood entity that was regarded by many as belonging to the same spectrum of disease or even synonym with palisaded and neutrophilic granulomatous dermatitis (PNGD). Although IGD and PNGD were usually related to connective tissue disease, mostly rheumatoid arthritis [1], some patients with typical histologic findings of IGD never develop autoimmune disorders, but they have different underlying conditions, such as metabolic diseases, lymphoproliferative disorders or other malignant tumours. These observations indicate that IGD and PNGD are different disorders with similar manifestations [2].

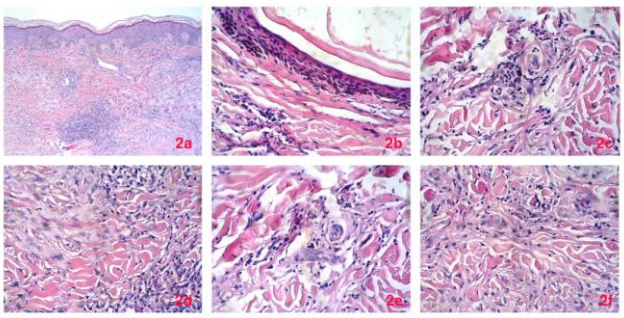

Figure 2: Microscopic features of the cutaneous lesion. 2a) Low power view showing interstitial granulomatous infiltrate, with patchy lymphocytes and vasodilatation; 2b) interstitial inflammation adjacent to a dilated follicle; 2c) interstitial granulomatous infiltrate with a few neutrophils; 2d) higher power view of the interstitial granulomatous infiltrate; 2e) interstitial granulomas with scattered neutrophils – note that mucin deposition is not a prominent feature; 2f) "piecemeal" degeneration of cross-sectional profiles of collagen bundles can be seen along the top of this figure – collagen bundles are surrounded by cleft-like spaces and small macrophages.

From the clinical point of view, the lesions in IGD may be variable: linear rope-like, papular, and even large plaques located on the extensor surface of the extremities [3]. Our main differential diagnosis was necrobiosis lipoidica, usually seen in the context of diabetes mellitus. Although there was a history of diabetes, both biopsies in our case showed no prominent foci of collagen degeneration, and no layering of the histiocytic infiltrate to support this diagnosis.

Other entities that may be brought into discussion when a interstitial granulomatous pattern is encountered microscopically are interstitial granuloma annulare, histiocytoid Sweet syndrome and interstitial drug eruptions, but they could be reliably excluded on clinical basis.

The clinical case presented above shows the complex nature of IGD and its occurrence in non-rheumatologic setting. The presence of an interstitial granulomatous pattern of inflammation in biopsies from patients with systemic disease requires careful attention. The observer should not be sidetracked by the classic association of diabetes with necrobiosis lipoidica and overcall it. Similarly, it is to be kept in mind that IGD may not be necessarily associated with arthritis.

References

1. Sangueza OP, Caudell MD, Mengesha YM, Davis LS, Barnes CJ, Griffin JE, Fleischer AB, Jorizzo JL. Palisaded neutrophilic granulomatous dermatitis in rheumatoid arthritis. J Am Acad Dermatol. 2002;47(2):251-7. https://doi.org/10.1067/mjd.2002.124620 PMid:12140472

2. Peroni A, Colato C, Schena D, Gisondi P, Girolomoni G. Interstitial granulomatous dermatitis: a distinct entity with characteristic histological and clinical pattern. Br J Dermatol. 2012;166(4):775-83. https://doi.org/10.1111/j.1365-2133.2011.10727.x PMid:22059717

3. Tomasini C, Pippione M. Interstitial granulomatous dermatitis with plaques. J Am Acad Dermatol. 2002;46(6):892-9. https://doi.org/10.1067/mjd.2002.120532 PMid:12063487

ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2017 Jul 25; 5(4):545-546.
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Genital Bowen's Disease in a Bulgarian Patient: Complete Remission after Surgical Approach

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Keywords: bowen; genital located; imiquimod; surgical approach; complete remission.

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Abstract

A 60-year-old male patient presented with complaints of persistent red to a brown-colored plaque on his scrotum, with duration of approximately three years. The patient had been treated with oral and topical antifungals for inguinal tinea for several months and after that with topical corticosteroids for eczema for several more months. None of the regimens achieved any therapeutic effect. The histopathological evaluation revealed the presence of atypical keratinocytes in all layers of the epidermis with the altered epidermal pattern, spread parabasal mitotic activity, without secondary satellites, multiple dyskeratotic cells and multinucleated cells. The diagnosis of an intraepithelial non-invasive squamous cell carcinoma, associated with koilocytic dysplasia and hyperplasia was made, meeting the criteria for Bowen disease. An elliptic surgical excision of the lesion was made, while the defect was closed with single stitches, with excellent therapeutic and aesthetic result. First described by John T. Bowen in 1912, Bowen disease (BD) represents a squamous cell carcinoma (SCC) in situ with the potential for significant lateral spread. Treatment options include the application of topical 5-flurorouracil cream – useful in non-hairy areas, imiquimod cream or destructive methods such as radiation, curettage, cryotherapy, laser ablation and photodynamic therapy, especially useful in nail bed involvement. Despite the early lesions, surgical excision is the preferred treatment option, regarding the potential malignant transformation risk.

A 60-year-old male patient presented with complaints of persistent red to a brown-colored plaque on his scrotum, with duration of approximately three years. Meanwhile, the patient had been treated with oral and topical antifungals for inguinal tinea for several months and after that with topical corticosteroids for eczema for several more months. None of the regimens achieved any therapeutic effect. Diabetes type I and pancreatic resection because of alcohol-abused mediated chronic pancreatitis were reported from the medical history. A well-demarcated erythematous macule with a brown periphery and well-defined, unregular borders were observed within the clinical examination, affecting the skin of the left scrotal area, close to the left inguinal fold. Two biopsies were performed for clarifying of the lesion's dignity (Fig. 1a). The histopathological evaluation revealed the presence of atypical keratinocytes in all layers of the epidermis with the altered epidermal pattern, spread parabasal mitotic activity, without secondary satellites, multiple dyskeratotic cells and multinucleated cells. The diagnosis of an intraepithelial non-invasive squamous cell carcinoma, associated with koylocitic dysplasia and hyperplasia

was made, meeting the criteria for Bowen disease (Fig. 1d, 1e, 1f). An elliptic surgical excision of the lesion was made, while the defect was closed with single stitches, with excellent therapeutic and aesthetic result (Fig. 1b, 1c).

First described by John T. Bowen in 1912, Bowen disease (BD) represents a squamous cell carcinoma (SCC) in situ with the potential for significant lateral spread [1]. BD most commonly affects the sun-exposed sites, with approximately equal sexual predisposition ratio [2]. The non-sun-exposed areas of the body are usually predominantly affected in darker-skin patients [2]. While the disease usually affects the head and neck in men, the lower limbs and cheeks are most frequently affected in women [3]. Some lesions contained HPV-18 and 18, which are highly associated with genital bowenoid papulosis, with a tendency for spontaneous regression [3]. Despite that, sunlight could also trigger bowenoid lesions, but they are usually referred to the term “bowenoid actinic keratosis” [4].

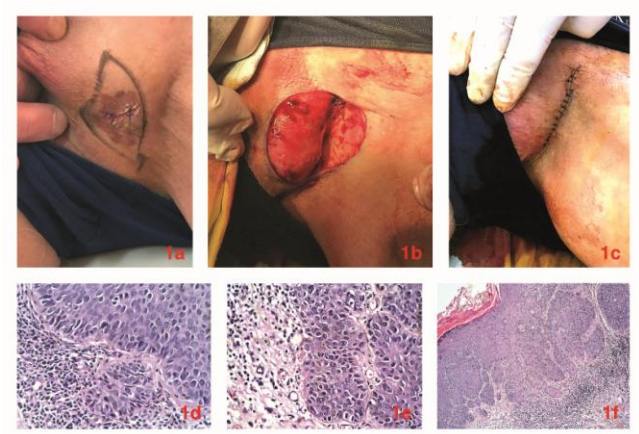

Figure 1: 1a) Clinical manifestation of an erythematous macule with a brown periphery and well-defined, unregular borders, located in the left scrotal area in a 60-year-old male patient. After biopsy; 1b, 1c) Surgical excision. The defect closure with single stitches; 1d, 1e, 1f) Histopathological findings - presence of atypical keratinocytes in all layers of the epidermis with altered epidermal pattern, spread parabasal mitotic activity, without secondary satellites, multiple dyskeratotic cells and multinucleated cells - intraepithelial non-invasive squamous cell carcinoma, associated with koylocitic dysplasia and hyperplasia

The risk of progression to invasive SCC is about 3-5%, as this risk increases up to 10% in genital localisation, as the scrotal SCC is the most common form of it [5]. The presence of ulceration or nodular formation is indicative of malignant transformation, but at later stages [3]. In the past, the association between BD and internal malignancies had been described to vary between 15 and 70% in different studies, as it was mostly reported in a patient with arsenic-induced BD [4]. Nowadays, the disease is not considered as paraneoplastic in general [5].

Treatment options include the application of topical 5-flurorouracil cream – useful in non-hairy areas, imiquimod cream or destructive methods such as radiation, curettage, cryotherapy, laser ablation and photodynamic therapy, especially useful in nail bed involvement [2]. Despite the early lesions, surgical excision is the preferred treatment option, regarding the potential malignant transformation risk [2]. The especially essential diagnostic clue is the presence of koilocytosis in the histological slides, which indicate underlying HPV-infection and further required a surgical excision, instead of the available topical treatment options. The reported case is representative for the importance of biopsy performance in all lesions of unclear dignity, with regret to avoiding diagnostic and therapeutic mistakes which could cost patients’ life. The time needed for misdiagnosis and treatment mistakes is potentially enough for an invasion of the BD into the dermis and malignant transformation into invasive SCC, with an aggressive course and high metastasis rate, which worsens the prognosis and survival rate [4].

References

1. Reizner GT, Chuang TY, Elpern DJ, Stone JL, Farmer ER. Bowen's disease (squamous cell carcinoma in situ) in Kauai, Hawaii. A population-based incidence report. J Am Acad Dermatol. 1994; 4:596-600. https://doi.org/10.1016/S0190-9622(94)70222-5

2. Al-Dawsari NA1, Raslan W, Dawamneh MF.Pigmented Bowen's disease of the penis and scrotum in a patient with AIDS. Dermatol Online J. 2014; 20(4):22337. PMid:24746300

3. Kossard S, Rosen R. Cutaneous Bowen's disease. An analysis of 1001 cases according to age, sex, and site. J Am Acad Dermatol. 1992; 27(3):406-10. https://doi.org/10.1016/0190-9622(92)70208-W

4. Vyas R, Zargar H1, Trolio RD, Di Lorenzo G, Autorino R. Squamous cell carcinoma of the scrotum: A look beyond the chimneystacks. World J Clin Cases. 2014; 2(11):654-60. https://doi.org/10.12998/wjcc.v2.i11.654 PMid:25405188 PMCid:PMC4233419

5. Jaeger AB, Gramkow A, Hjalgrim H, Melbye M, Frisch M. Bowen disease and risk of subsequent malignant neoplasms: a population-based cohort study of 1147 patients. Arch Dermatol. 1999; 135(7):790-3. PMid:10411153

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Verrucous-Keratotic Malignant Melanoma (VKMM)

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Keywords: keratotic melanoma; verrucous melanoma; surgical approach; surgical safety; benign like lesions.

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Abstract

We report a patient with a verrucous keratotic variant of melanoma visiting the policlinic of Medical Institute of Ministry of Interior (MVR-Sofia), Department of Dermatology and Dermatologic surgery, with a keratotic verrucous lesion, located on the right thigh, partially deeply pigmented at upper right quadrant. The lesion had appeared three years ago before her presentation in the policlinic, and it had gradually enlarged and become darker in the last twelve months. The surface of the lesion was covered with thick hyperkeratotic lobules. The histologic evaluation revealed verrucous melanoma with a tumour thickness of 3 mm and Clark Level IV and focal ulceration. The tumour was staged as stage IIB (T3bN0M0). Sentinel lymph node biopsy was planned. Verrucous-keratotic forms of malignant melanoma occur more commonly in women and favour the extremities, but may be found on any anatomic site. Seventy-one percent of this melanoma type are situated on the upper and lower extremities. Although two-thirds of these neoplasms can be can be histologically graded according to the classification of Clark, one-third of these melanomas with marked verrucous hyperplasia and hyperkeratosis of the epidermis do not fit into his classification. Histological classification of patients with a verrucous keratotic type of melanoma may sometimes be extremely difficult. The marked papilliferous architecture of these lesions made an assessment of Breslow depth difficult. The presented case highlights the clinical existence and features of such benign-looking melanomas. It is therefore important for surgical pathologists to recognise this unusual variant of malignant melanoma, as it may be confused both clinically and pathologically with benign lesions.

The verrucous keratotic melanoma seems to be a rare variant of the cutaneous melanoma that can be often misdiagnosed with a benign lesion [1]. We report a patient with a verrucous keratotic variant of melanoma visiting the policlinic of Medical Institute of Ministry of Interior (MVR-Sofia), Department of Dermatology and Dermatologic surgery, with a keratotic verrucous lesion, located on the right thigh, partially deeply pigmented at upper right quadrant (Fig. 1a, 1b). The lesion had appeared three years ago before her presentation in the policlinic, and it had gradually enlarged and become darker in the last twelve months (Fig. 1a, 1b). Physical examination revealed an oval shaped, partially black plaque, slightly elevated, 5.2 x 3.6 cm in size (Fig. 1a, 1b). The surface of the lesion was covered with thick hyperkeratotic lobules. The histologic evaluation (after the surgical removal with 2 cm surgical safety in all directions) revealed Verrucous melanoma with a tumour thickness of 3 mm and Clark Level IV and focal ulceration (Fig. 1c-1f). The tumour was staged as stage IIB (T3bN0M0). Sentinel lymph node biopsy was planned.

Verrucous malignant melanoma (VMM) is a rare variant of melanoma firstly described in 1967 [2]. Both clinically and histologically, it mimics SK [3, 4]. Some intradermal and compound nevi have been described as showing hyperkeratosis, papillomatosis, horn cysts, and lace-like downward growth of epidermal strands [5]. Though specific causative factors linking SK-like epidermal changes are still unknown, it is possible that both nevi and melanomas can release some epidermal cell growth factors, thereby inducing changes in the overlying epidermis [5].

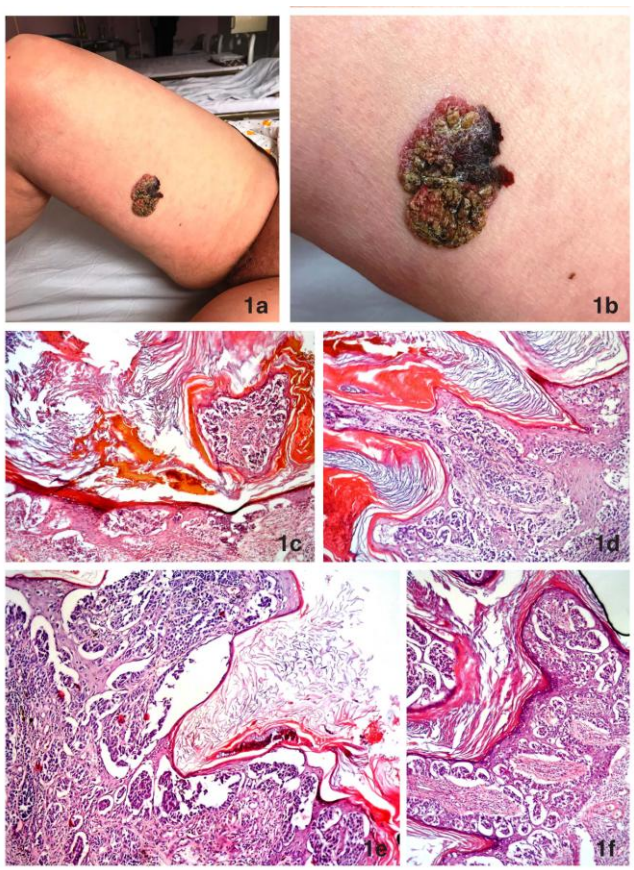

Figure 1: a), b) Large pigmented tumour on the medial aspect of the right thigh. b) Irregularly configurated tumour with verruciform surface and a deeply pigmented macular component in the upper medial part; c), d) e), f) Various aspects of the tumour. Verruciform acanthosis of the epidermis with hyperkeratosis – namely orthohyperkeratosis and columns of parakeratosis. Atypical melanocytes mainly arranged in nests along the dermo-epidermal junction with marked confluence. Consumption of the epidermis in some parts. Some atypical melanocytes also located above the junction. Within the dermis nests and sheets of atypical melanocytes without maturation

Verrucous-keratotic forms of malignant melanoma occur more commonly in women and favour the extremities, but may be found on any anatomic site [3]. Seventy-one percent of this melanoma type are situated on the upper and lower extremities [3]. Although two-thirds of these neoplasms can be can be histologically graded according to the classification of Clark, one-third of these melanomas with marked verrucous hyperplasia and hyperkeratosis of the epidermis do not fit into his classification [3]. Histological classification of patients with a verrucous keratotic type of melanoma may sometimes be extremely difficult [3]. The marked papilliferous architecture of these lesions made an assessment of Breslow depth difficult [6]. The presented case highlights the clinical existence and features of such benign-looking melanomas. It is therefore important for surgical pathologists to recognise this unusual variant of malignant melanoma, as it may be confused both clinically and pathologically with benign lesions [3, 6].

References

1. Matsumoto T, Yokota K, Sawada M, Hasegawa Y, Takeuchi A, Kono M, Akiyama M. Large epidermal cleft formation in verrucous-keratotic malignant melanoma of the heel. J Am Acad Dermatol. 2015;72(1):e37-8. https://doi.org/10.1016/j.jaad.2014.09.044 PMid:25497951

2. Clark WH Jr. A classification of malignant melanoma in man correlated with histogenesis and biologic behaviour. In: Montagna W, ed. Advances in Biology of the Skin, The Pigmentary System, New York: Pergamon Press; 1967: p. 621-47.

3. Kuehnl-Petzoldt C, Berger H, Wiebelt H. Verrucous-keratotic variations of malignant melanoma: a clinicopathological study. Am J Dermatopathol. 1982;4(5):403-10. PMid:7149193

4. Suster S, Ronnen M, Bubis JJ. Verrucous pseudonevoid melanoma. J Surg Oncol. 1987;36:134-7. https://doi.org/10.1002/jso.2930360213 PMid:3657177

5. Requena L, Sánchez M, Requena C. Simultaneous occurrence of junctional nevus and seborrheic keratosis. Cutis. 1989;44:465-6. PMid:2533059

6. Blessing K, Evans AT, al-Nafussi A. Verrucous naevoid and keratotic malignant melanoma: a clinico-pathological study of 20 cases. Histopathology. 1993;23(5):453-8. https://doi.org/10.1111/j.1365-2559.1993.tb00494.x PMid:8314219

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Giant Congenital Melanocytic Nevus (GCMN) - A New Hope for Targeted Therapy?

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Keywords: nevi; congenital nevi; dermabrasion; surgery; NRAS; targeted therapy.

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Abstract

We present a 6-month-old male patient, who was consulted with dermatologist by his parents, because of a pigmented lesion, present since birth, covering almost the all skin of the back and buttocks. A sharply bordered, unequally coloured congenital pigmented nevus, measuring approximately 21 cm in diameter was observed in the whole body skin examination. The lesion was affecting the lower 2/3 of the skin of the back and the top half of the gluteus area, extending to the lateral part of the tors, forward the abdomen and the upper lateral part of the hips, composed by multiple darker-pigmented nests and several lighter areas, with single depigmented zones, hairy surface, irregularly infiltrated on palpation. Congenital melanocytic nevi are presented in approximately 1% of newborns, while giant congenital melanocytic nevi (GCMN) are the most uncommon subtype of them; with occurrence rate 1 in 50,000 births. They affect 2% of a total body surface or presenting in a diameter larger than 20 cm in older children. Although not common, the possible malignant transformation remains one of the most important considerations related to them, as the related lifetime risk of melanoma is 4% to 10%. Treatment recommendations include non-surgical methods as dermabrasion only within the first two weeks of life, for prevention the possible melanocytic deeper migration, while serial surgical excisions or tissue expanders could be useful treatment tool even in later stages. Nevertheless, cosmetic result is not always satisfactory, and the risk of malignant changes remains, in cases of previous melanocytic migration in deeper layer. Recent article suggests the potential role in the treatment of GCMN with NRAS inhibitor trametinib, approved for treatment of advanced melanoma, associated with underlying NRAS mutations. Although promising, the drug could be useful in paediatric patients, only with associated NRAS gene mutation. It is still unclear whether it could be helpful, independent of the NRAS status.

We present a 6-month-old male patient, who was consulted with dermatologist by his parents, because of a pigmented lesion, present since birth, covering almost the all skin of the back and buttocks. A sharply bordered, unequally coloured pigmented nevus, measuring approximately 21 cm in diameter was observed in the whole body skin examination. The lesion was affecting the lower 2/3 of the skin of the back and the top half of the gluteus area, extending to the lateral part of the tors, forward the abdomen and the upper lateral part of the hips, composed by multiple darker-pigmented nests and several lighter areas, with single depigmented zones, hairy surface, irregularly infiltrated on palpation (Fig. 1a, 1b, 1c, 1d). Several satellite pigmented lesions were also observed on the upper and lower extremities, measuring from one to 3-4 cm in diameter, most of them- hairy surfaced. Atopic dermatitis was also seen as an additional abnormality. The performed screening procedures, including MRI and CT, did not reveal any abnormalities, neither data for neurologic involvement.

Congenital melanocytic nevi are presented in approximately 1% of newborns, while giant congenital melanocytic nevi (GCMN) are the most uncommon subtype of them; with occurrence rate 1 in 50,000 births [1]. They affect 2% of a total body surface or presenting in a diameter larger than 20 cm in older children [1]. Although not common, the possible malignant transformation remains one of the most important considerations related to them, as the related lifetime risk of melanoma is 4% to 10% [2]. Treatment recommendations include non-surgical methods as dermabrasion only within the first two weeks of life, for prevention the possible melanocytic deeper migration, while serial surgical excisions or tissue expanders could be useful treatment tool even in later stages [1]. Nevertheless, cosmetic result is not always satisfactory, and the risk of malignant changes remains, in cases of previous melanocytic migration in deeper layer [3].

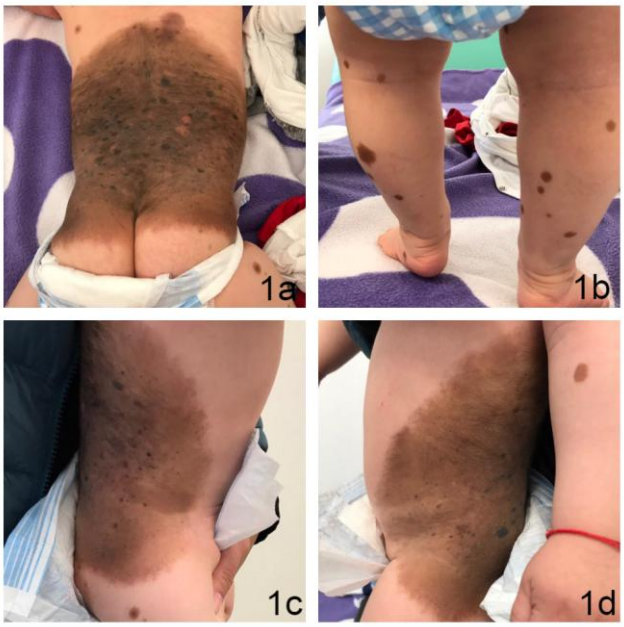

Figure 1: – Clinical manifestation of a giant congenital melanocytic nevus in 6-month-old child, affecting the lower 2/3 of the skin of the back and the top half of the gluteus area (1a), extending to the lateral part of the tors, forward the abdomen and the upper lateral part of the hips (1c, 1d), composed by multiple darker-pigmented nests and several lighter areas, with single depigmented zones, hairy surface, irregularly infiltrated on palpation and several satellite lesions (1b)

Recent article suggests the potential role in the treatment of GCMN with NRAS inhibitor trametinib, approved for treatment of advanced melanoma, associated with underlying NRAS mutations [3]. Although promising, the drug could be useful in paediatric patients, only with associated NRAS gene mutation. It is still unclear whether it could be helpful, independent of the NRAS status. Meanwhile, the future following up of these patients is mandatory [1].

Despite some of the patient could undergo screening by dermatoscopy, this tool is not useful in cases with full-size infiltration and equally dark-brown to black colour, as the remarkable dermoscopic finding could be noted only in the hypopigmented areas, as in the presented cases [4]. The clinical examination could note sigh of infiltration, while PET-scan and reflect confocal microscopy should be added as helpful tools in the following up period. Excision biopsy could be performed in infiltrated areas, but it is not sure and safety enough method for observation of malignant transformation. Therefore, total surgical excisions, by serial operations or tissue expanders remain the most effective treatment option, with minimal risk of malignant transformation and maximal therapeutic effectiveness.

References

1. Ma T, Fan K, Li L, Xie F, Li H, Chou H, Zhang Z. Tissue expansion in the treatment of giant congenital melanocytic nevi of the upper extremity. Medicine (Baltimore). 2017; 96(13):e6358. https://doi.org/10.1097/MD.0000000000006358 PMid:28353563 PMCid:PMC5380247

2. Kopf AW, Bart RS, Hennessey P. Congenital nevocytic nevi and malignant melanomas. J Am Acad Dermatol 1979; 1:123–30. https://doi.org/10.1016/S0190-9622(79)70009-0

3. Recio A1, Sánchez-Moya AI2, Félix V3, Campos Y4. Congenital Melanocytic Nevus Syndrome: A Case Series. Actas Dermosifiliogr. 2017. pii: S0001-7310(16)30371-4. https://doi.org/10.1016/j.ad.2016.07.025

4. Martín-Carrasco P, Bernabeu-Wittel J, Dominguez-Cruz J, Zulueta Dorado T, Conejo-Mir Sanchez J. "Sky Full of Stars" Pattern: Dermoscopic Findings in a Desmoplastic Giant Congenital Melanocytic Nevus.Pediatr Dermatol. 2017. https://doi.org/10.1111/pde.13099

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Syphilis Such As the Other Sexually Transmitted Diseases Are a Cultural Background of Dermatologist

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Keywords: Syphilis; Sexually transmitted diseases; diagnosis; physician; dermatologist.

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Abstract

Syphilis such as the other Sexually transmitted diseases are a cultural background of physician. The authors have presented this case of nodular secondary syphilis for three main reasons. The first one is that, in the last years, syphilis has re-emerged as the problem of public health. The second one is to underline how secondary syphilis, also known as the great imitator, may present itself with numerous manifestations, mimicking different dermatological diseases. Finally, because we want to remember how syphilis and the other sexual transmitted diseases must to be in the cultural background of a dermatologist, and have to be considered in the dermatological differential diagnosis.

An otherwise healthy, 38-years old man showed up to our clinic for nodular lesions in the genital area (Fig.1-2), which was present by eight months. At first, they were localised on his gland and, afterwards, also on the scrotum. History for drug assumption or contact with local irritants was negative. He didn't report any contact with local irritants. The patient did not refer any episodes of high-risk sex and any relevant pathology. He showed no familiarity for lymphoma, lupus and another skin disease.

Because of the chronic disease, the patient had been previously visited by several doctors, not dermatologist ones, without obtaining clinical results. At first, the patient had been visited by his general doctor, who prescribed to him a topical therapy with fusidic acid. Due to the lack of clinical results, the man had a visit with a urologist. The doctor, after examining the lesions, prescribed to the patient a swab test which resulted in being negative. Because of the suspect of an infectious disease, the urologist prescribed to the man a systemic therapy with ciprofloxacin twice a day for a week. For the second time, the patient did not observe any beneficial effects and decided to consult an andrologist. The doctor, after having evaluated the lesions, performed an ultrasound exam, without significant results. Finally, he prescribed to the man a systemic therapy with levofloxacin 500 once a daily for ten days. No clinical effects had been observed. Frustrated by the disease,

the patient decided to consult a dermatologist and referred to us.

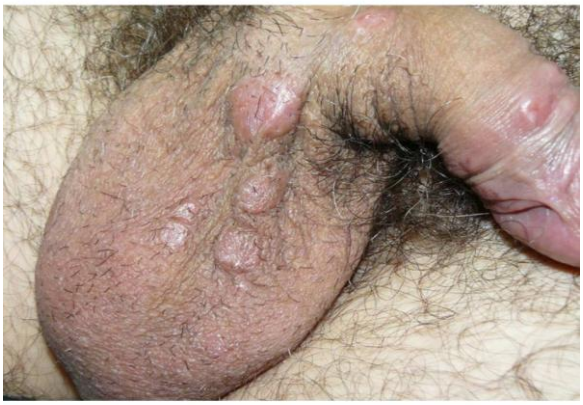

Figure 1: Man, 38 years old, with asymptomatic nodular lesions in the genital area

At genitals examination, we observed numerous subcutaneous hard nodules, with a diameter ranging from a few mm to 2 cm. The skin over the lesions was reddish to brown in colour. No local signs of inflammation or infection were detected. Lesions were asymptomatic. During the clinical evaluations, except for a diffuse lymph-adenopathy, we did not observe significant skin lesions in the other body areas. The patient did not report any disturbance of other kinds. As a result of the clinical and anamnestic evaluation, we advised the patient to perform routine blood tests and specific tests for syphilis.

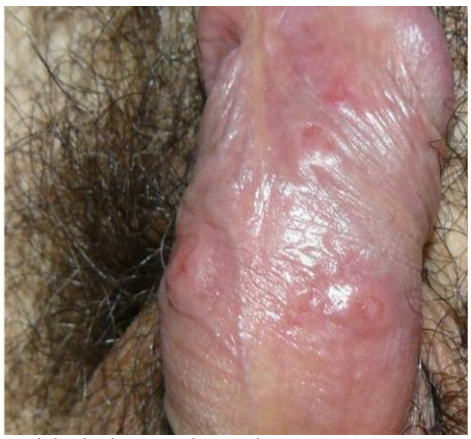

Figure 2: Nodular lesions on the penis

The latter were positive, confirming our suspect of syphilis (RWt +++, RWl ++, VDRL ++, TPHA ++ 1:5120, FTA-ABS-IgG ++, FTA-ABS-IgM +). Only at this moment, the patient admitted having unprotected casual sex. We prescribed to the patient diaminocillina therapy (2400000 U.I./week) for four weeks. Finally, we advised him to abstain from sexual activity and to suggest serological tests to his partners. The patient has been monitored for the duration of treatment. At the end of antibiotic therapy, the patient returned to our observation for a checkup. The lesions were completely healed (FIG.3-4), and serological tests confirmed the improvement of the disease.

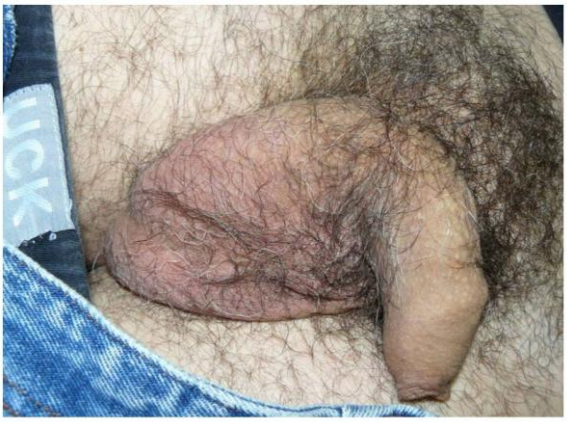

Figure 3: The patient after the treatment

The authors have presented this case of nodular secondary syphilis for three main reasons. The first one is that, in the last years, syphilis has re-emerged as the problem of public health [1-2]. The second one is to underline how secondary syphilis, also known as the great imitator, may present itself with numerous manifestations, mimicking different dermatological diseases [3-6].

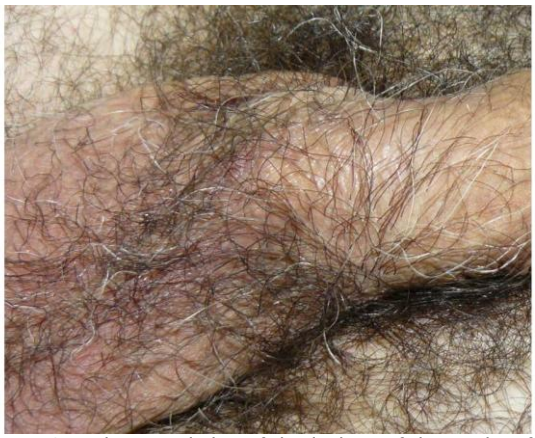

Figure 4: Complete resolution of the lesions of the penis, after the treatment

Finally, because we want to remember how syphilis and the other sexual transmitted diseases must to be in the cultural background of a dermatologist, and have to be considered in the dermatological differential diagnosis.

References

1. Repiso B, Frieyro M, Rivas-Ruiz F, De Troya M. Condom use and number of sexual partners among male syphilis patients who report having sex with men. Actas Dermosifiliogr. 2010;101(10):847-52. https://doi.org/10.1016/j.ad.2010.06.014 PMid:21159260

2. Jebbari H, Simms I, Conti S, Marongiu A, Hughes G, Ward H, Powers C, Thomas DR, Evans B. Variations in the epidemiology of

primary, secondary and early latent syphilis, England and Wales, 1999 to 2008.

3. Schnirring-Judge M, Gustaferro C, Terol C. Vesiculobullous syphilis: a case involving an unusual cutaneous manifestation of secondary syphilis. J Foot Ankle Surg. 2011;50(1):96-101. https://doi.org/10.1053/j.jfas.2010.08.015 PMid:21106408

4. Breznik V, Potočnik M, Miljković J. Papulonodular secondary syphilis in a 52-year-old non-HIV heterosexual patient. Acta Dermatovenerol Alp Panonica Adriat. 2010; 19(4):27-30.

5. Furlan FC, Oliveira AP, Yoshioka MC, Enokihara MM, Michalany NS, Porro AM. Leukocytoclastic vasculitis: another condition that mimics syphilis. An Bras Dermatol. 2010;85(5):676-9. https://doi.org/10.1590/S0365-05962010000500011 PMid:21152792

6. Mullooly C, Higgins SP. Secondary syphilis: the classical triad of skin rash, mucosal ulceration and lymphadenopathy. Int J STD AIDS. 2010;21(8):537-45. https://doi.org/10.1258/ijsa.2010.010243 PMid:20975084

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Dermatosurgery Rounds - The Island SKIN Infraorbital Flap

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Keywords: nonmelanoma skin cancer; surgery; flap; basal cell carcinoma; outcome; cosmetic result.

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Abstract

The main objective in dermatologic surgery is complete excision of the tumour while achieving the best possible functional and cosmetic outcome. Also we must take into account age, sex, and tumour size and site. We should also consider the patient's expectations, the preservation of the different cosmetic units, and the final cosmetic outcome. Various reconstructive methods ranging from secondary healing to free flap applications are usedfor the reconstruction of perinasal or facial defects caused by trauma or tumour surgery. Herein, we describe the nasal infraorbital island skin flap for the reconstruction in a patient with basal cell carcinoma. No complications were observed in operation field. The infraorbital island skin flap which we describe for the perinasal area reconstruction is a safe, easily performed and versatile flap. The multidimensional use of this flap together with a relatively easy reconstruction plan and surgical procedure would be effective in flap choice.

We present an 86-year-old patient with duration of complaints about four years. He was admitted to the clinic, because of the presence of a cutaneous tumor-like formation, painful and exsudative on palpation, located above the left nasolabial fold (Fig. 1a). The clinical examination revealed ulcerated lesion, measuring approximately 2 cm in diameter, covered partially with squamous and crusts, located in regio infraorbitalis sinistra and secreting bloody-purulent discharge (Fig. 1a). Enlarged lymph nodes were not detected, neither data any signs for the dissemination of the process. Arterial hypertension, chronic atrial fibrillation, prostate cancer, liver steatosis, cholelithiasis and cyst of the left kidney were reported as accompanying diseases, as the patient underwent permanent pacemaker implantation, due to extrasystoles. We performed surgical treatment by island plastic in local anaesthesia (Fig. 1b). Initially, the region surrounding the tumour tissue was resected in the form of a deep oval excision forward the underlying muscles, while the bleeding was stopped with cauter (Fig 1c). Two additional deep incisions were also performed, which met each other in the distal part, forming a shape of a triangle, while the contours of the excision were deep to the underlying muscle (Fig. 1d). Bleeding was controlled by cauter. The proximal part of the formed flap was gently dissected in depth to easier

transposition to the regio paranasal (Fig. 1d, 1e). Similarly, the flap was also gently dissected in the distal part of the triangle, regarding the more easily removal of the whole skin island in the proximal direction (Fig. 1e, 1f). The proximal part of the flap was slightly cut, followed by translocation in a proximal direction and adapting it to the edges of the primary shaped skin defect (Fig. 1e, 1f, 1g). Stepwise adjustment of the cutaneous island to the newly created bed, was performed next, as the whole blood supply and innervation of the transported area was preserved (Fig. 1e,1f, 1g, 1h). Postsurgical period underwent without complication, and the condition of the patient was stable. The histopathological evaluation confirmed the diagnosis of ulcerative basal cell carcinoma with clean resection lines, stage 1 (T1 N 0 M0).

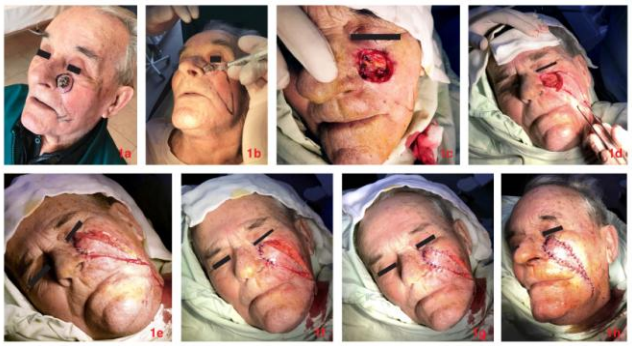

Figure 1: Patients status pre-, intra- and postoperative

The main objective in dermatologic surgery is complete excision of the tumour while achieving the best possible functional and cosmetic outcome [1]. Also, we must take into account age, sex, and tumour size and site [1]. We should also consider the patient's expectations, the preservation of the different cosmetic units, and the final cosmetic outcome [1]. Various reconstructive methods ranging from secondary healing to free flap applications are used for the reconstruction of perinasal or facial defects caused by trauma or tumour surgery [2]. Herein, we describe the nasal infraorbital island skin flap for the reconstruction in a patient with basal cell carcinoma (Fig 1). No complications were observed in operation field. The infraorbital island skin flap which we describe for the perinasal area reconstruction is a safe, easily performed and versatile flap (Fig. 1). The multidimensional use of this flap together with a relatively easy reconstruction plan and surgical procedure would be effective in flap choice.

References

1. Pérez-Paredes MG, Valladares Narganes LM, Cucunubo HA, Rodríguez Prieto MÁ. Shark island flap for reconstruction of nasal ala-perinasal defects.Actas Dermosifiliogr. 2014;105(7):709-11. https://doi.org/10.1016/j.ad.2014.04.002 PMid:24890814

2. Doğan F, Özyazgan İ. New flap for the reconstruction of the perinasal region. Facial Plast Surg. 2014;30(6):676-80. https://doi.org/10.1055/s-0034-1396530 PMid:25536136

ID Design 2012/DOOEL Skopje, Republic of Macedonia
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Lichen Simplex Chronicus as an Essential Part of the Dermatologic Masquerade

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Keywords: lichen simplex; prurigo nodularis; carcinoma; histology; surgery.

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Abstract

A 48 years old female patient had been suffering from the lesions presented for four years. They have started as small, pruritic patches which had been mechanically irritated and grew up in time. The patient had no associated comorbidities or allergies, and she was not under any medication. On physical examination, she presented one erythematous, exudative plaque, with dimensions of 2.5/4 cm, located on the proximal phalanx and interphalangeal articulation of the left thumb. All histopathological features were consistent with the diagnosis of lichen simplex chronicus. Some lesions of lichen simplex chronicus exhibit signs of pseudocarcinomatous, infundibular and sometimes eccrine ductal proliferation of keratinocytes. Although the pseudoinfiltrative aspect of the epithelial proliferation and its pronounced degree might mimic a well-differentiated lesion of squamous cell carcinoma, a lack of cellular atypia and atypical mitotic figures are features that do not support this diagnosis. On the other hand, long lasting lesions of lichen simplex chronicus may lead to alterations in the processes of keratinocyte proliferation and differentiation and eventually give rise to malignant transformation. The best treatment management is a psychodermatological approach, a combination of skin care with psychotherapy, in order to prevent relapses.

A 48 years old female patient had been suffering from the lesions presented in Figure 1a/1b for four years. They have started as small, pruritic patches which had been mechanically irritated and grew up in time. The patient had no associated comorbidities or allergies, and she was not under any medication. On physical examination, she presented one erythematous, exudative plaque, with dimensions of 2.5/4 cm, located on the proximal phalanx and interphalangeal articulation of the left thumb.

A punch biopsy taken from the lesion revealed a markedly hyperplastic epidermis (Fig. 2a), with irregular hyperkeratosis and foci of parakeratosis, a thickened granular zone, acanthosis with irregular rete ridges and a sparse to moderately dense dermal superficial perivascular lymphohistiocytic infiltrate (Fig. 2b). The hyperplastic changes were also present at the level of follicular infundibula, with hypergranulosis and hyperkeratosis in the form of keratotic cysts (Fig. 2c and 2d). The eccrine ducts showed overtly squamous metaplasia. The affected papillary dermis included coarse bundles of collagen arranged in vertically oriented streaks (Fig. 2e). Rare eosinophils dispersed around some widely dilated capillaries,

together with an increased number of fibrocytes, were detected in high power microscopic examination (Fig. 2f). All these features were consistent with the diagnosis of lichen simplex chronicus.

We have taken into consideration the following differential diagnosis: knuckle pads, nodular prurigo, HPV associated lesions or Bowen disease. Lichen simplex chronicus, together with prurigo nodularis, knuckle pads and picker's nodule, represent chronic psoriasiform dermatitides induced by persistent, vigorous rubbing.

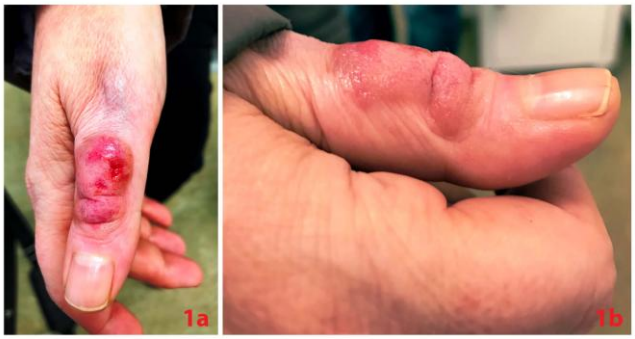

Figure 1: Erythematous, exudative plaque, with dimensions of 2.5/4 cm, located on the proximal phalanx and interphalangeal articulation of the right thumb

They share similar histopathologic features and pathogenic mechanisms. Lichen simplex chronicus is rather a hyperkeratotic plaque, whereas the others are merely papules or nodules produced by the effect of severe and repeated scratching of a cutaneous area located within easy reach of the fingernails [1].

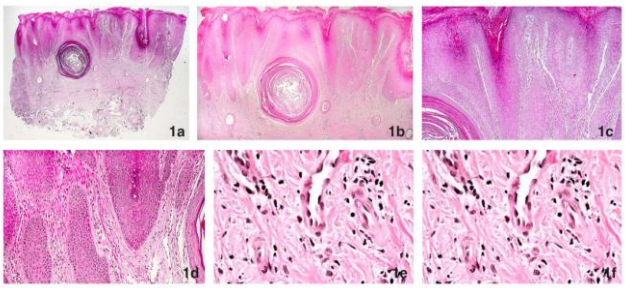

Figure 2: Histopathological features were consistent with the diagnosis of lichen simplex chronicus

Lichen simplex chronicus (LSC) is a chronic skin condition strongly linked with emotional factors which are the source of intense pruritic sensation [1, 2]. As a result of constant scratching or rubbing of the skin, lichenified plaques develop mostly on accessible body areas such as the scalp, head and neck, hands, genitals [3]. Patients with LSC find themselves in a vicious circle, since emotional factors play a key role in the initiation of pruritus and the appearance of the lesions causes more psychological tension [1], sexual dysfunction and sleep disturbances [4]. An JG et al. have shown that the dermatology quality life index (DLQI) was lower in patients with LSC than in those with other dermatological conditions such as psoriasis [5]. LSC patients have also been found to present particular personalities characteristics in comparison with healthy control individuals, such as pain avoidance tendency, more conforming personalities, dependency on other people [6], or even depression and dissociative disturbances [1].

Although not a live threatening condition, the lesions of LSC can become secondary infected or, in rarer instances, they can evolve into squamous cell carcinoma [7]. As was the case here, some lesions of lichen simplex chronicus exhibit signs of pseudocarcinomatous, infundibular and sometimes eccrine ductal proliferation of keratinocytes. Although the pseudoinfiltrative aspect of the epithelial proliferation and its pronounced degree might mimic a well-differentiated lesion of squamous cell carcinoma, a lack of cellular atypia and atypical mitotic figures are features that do not support this diagnosis. On the other hand, long lasting lesions of lichen simplex chronicus may lead to alterations in the processes of keratinocyte proliferation and differentiation and eventually give rise to malignant transformation [8].

The best treatment management is a psychodermatological approach, a combination of skin care with psychotherapy, in order to prevent relapses [1].

References

1.Lotti T, Buggiani G, Prignano F. Prurigo nodularis and lichen simplex chronicus. Dermatol Ther. 2008;21(1):42-6. https://doi.org/10.1111/j.1529-8019.2008.00168.x PMid:18318884

2.Chuh A, Wong W, Zawar V. The skin and the mind. Aust Fam Physician. 2006; 35(9): 723-5. PMid:16969446

3.Rajalakshmi R, Thappa DM, Jaisankar TJ, Nath AK. Lichen simplex chronicus of anogenital region: a clinico-etiological study. Indian J Dermatol Venereol Leprol. 2011;77(1):28-36. https://doi.org/10.4103/0378-6323.74970 PMid:21220876

4.Ermertcan AT, Gencoglan G, Temeltas G, Horasan GD, Deveci A, Ozturk F. Sexual dysfunction in female patients with neurodermatitis. J Androl. 2011; 32 (2):165-9. https://doi.org/10.2164/jandrol.110.010959 PMid:20864649

5.An JG, Liu YT, Xiao SX, Wang JM, Geng SM, Dong YY. Quality of life of patients with neurodermatitis. Int J Med Sci. 2013;10 (5): 593-8. https://doi.org/10.7150/ijms.5624 PMid:23533146 PMCid:PMC3607245

6. Martin-Brufau R, Corbalon-Berna J, Ramirez-Andreo A, Brufau-Redondo C, Liminana-Gras R. Personality differences beween patients with lichen simplex chronicus and normal populations: A study of pruritus. Eur J Dermatol. 2010; 20(3): 359-63. PMid:20388609

7.Wu M, Wang Y, Bu W, Jia G, Fang F, Zhao L. Squamous cell carcinoma arising in lichen simplex chronicus. Eur J Dermatol. 2010; 20(6):858-9. PMid:20959279

8. Tiengo C, Deluca J, Belloni-Fortina A, Salmaso R, Galifi F, Alaibac M. Occurrence of squamous cell carcinoma in an area of lichen simplex chronicus: case report and pathogenetic hypothesis. J Cutan Med Surg. 2012;16(5):350–2. https://doi.org/10.1177/120347541201600513 PMid:22971311

ID Design 2012/DOOEL Skopje, Republic of Macedonia
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Acquired Ulcero-Mutilating Bilateral Acro-Osteopathy (Bureau-Barrière Syndrome)

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Keywords: neuropathy; acquired; eczema; ulcerations; ulcero mutilating lesions; bilateral.

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Abstract

We present a 35-year-old male patient with Bureau-Barrière syndrome. Bureau-Barrière syndrome is an ulcero-mutilating acropathy almost invariably associated with excessive alcohol intake. It presents with a triad of trophic skin changes with recurrent ulcerations, bone lesions and nerve damage. The clinical presentation includes chronic painless plantar ulcerations with periulcerous hyperkeratosis, hyperhidrosis, livedoid skin colour, nail dystrophy, widening and infiltration of the toes and common interdigital mycoses. Other non-specific skin changes related to the alcohol consumption are commonly observed as well. The condition affects mainly middle-aged men suffering from alcoholism. Often a bilateral location at the lower limb of male alcoholics has been described, as in our patient. Successful treatment of the Bureau-Barrière syndrome requires an interdisciplinary approach. Cessation of alcohol intake and smoking is of paramount importance.

We present a 35-year-old male patient, admitted urgently for the first time to the clinic of dermatology and dermatologic surgery with chronic deep ulceration on the toes of both feet, severe generalised itching, malaise, pain in the sacrum area and fever (Fig. 1a, 1b). The patient was hospitalised previously with the diagnosis of osteoarthritis purulenta digitorum pedis dextra, requiring surgical excision with synovectomy and sequesters removal. Also, his past medical history included childhood atopic dermatitis with allergic rhinoconjuctivitis. Examination revealed severe swelling of the toes of both feet with a deep ulceration to the depth of the underlying tendon on the plantar surface of the left thumb (Fig. 1c). Superficial ulcerations were also observed on the plantar surface of the right thumb (Fig. 1d). The skin of both lower legs was markedly erythematous with an eczematous eruption, fine desquamation and yellowish secretion (Fig. 1b). The toenails showed bilateral onychodystrophic changes secondary to underlying onychomycosis without previous therapy (Fig. 1a, 1b). On the skin of the extensor surfaces of both hands, there were multiple excoriations, lichenification and solitary nummular plaques with a diameter of 1 to 3 cm. Alcohol-induced hepatic steatosis, chronic focal calculous cholecystitis

and splenomegaly were established by the laboratory screening. Significantly increased values of CRP (80.1 mg/l) and GGT (1969.0 IU/l) were observed. A considerably increased Anti-streptolysin titer from 1600 IU/ml (normal range up to 200 IU/ml) with fever suggested secondary erysipelas (cellulitis). Neurological clinical examination revealed polyneuropathy with distal hypoesthesia, impaired sense of space, decreased superficial and deep distal sensation and vegetative trophic changes. Electrophysiological studies showed evidence of axonal degeneration of motor fibres of n. peroneus, n. tibialis in the distal segments and sensory fibres of n. suralis, indicating severe distal sensorimotor polyneuropathy - axonal type. Radiculopathy of the sensory root S1 was established as an additional finding. Hemangiomas in L3 and L4, unrelated to the radicular symptoms were also observed.

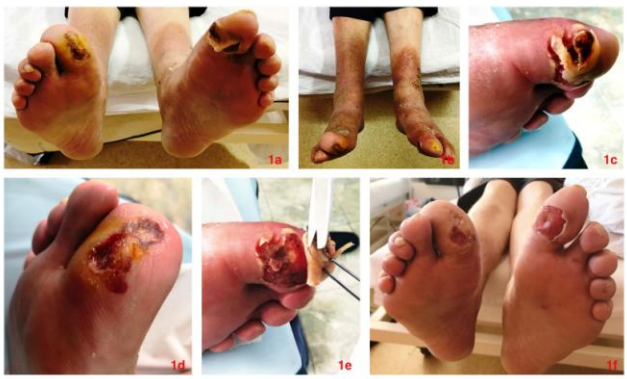

Figure 1: Typical clinical findings in a patient with Bureau-Barrière syndrome

Despite the ulcerative changes in the thumb of the lower limbs, radiographic evidence of osteomyelitis was missing. Based on the medical history of osteoarthritis purulenta digitorum pedis, chronic bilateral ulceration of the toes with the initiation of unilateral elephantiasis of the thumb; vegetative disturbances (pronounced facial erythrosis and hyperhidrosis), history of regular alcohol consumption and bilateral symptomatic polyneuropathy with the acquired, non-familial form of ulcerative ulcero-mutilating bilateral acro-osteopathy type Bureau-Barrière. The therapy included Clindamycin 600 mg/3 x daily iv for seven days, followed by Ciprofloxacin 500 mg/2 x daily 5 days per os in combination with dual antihistamine therapy: levocetirizine, dihydrochloride 5 mg 1x/day, of the lower limbs (with metabolic - toxic genesis), the patient was diagnosed chloropyramine hydrochloride 20 mg 1x day intramuscularly; prednisolone 30 mg per day in a reduction regimen for 4 days; with topical application of iodine povidone 10% ointment for the ulcerations on both great toes; Cliochinolum/Flumethasonum cream for nummular eczematoid lesions 2x per day (Fig. 1d, 1f). A mechanical removal of the hyperkeratosis of both thumbs was also performed, after an initial good therapeutic response (Fig. 1d, 1e, 1f). The polyneuropathy was treated with piracetam 1200 mg (1/1/0) for an initial period of 30 days in combination with pentoxifylline 400 mg (1/0/1) with subsequent dose reduction of the piracetam; Vitamin B12-1000 UI intramuscular application – 1x per day for 10 days, followed by 500 UI every 2 weeks for a total period of 3 months. A significant improvement of neurological symptoms was observed.

Bureau-Barrière syndrome is an ulcero-mutilating acropathy almost invariably associated with excessive alcohol intake. It presents with a triad of trophic skin changes with recurrent ulcerations, bone lesions and nerve damage. The clinical presentation includes chronic painless plantar ulcerations with periulcerous hyperkeratosis, hyperhidrosis, livedoid skin colour, nail dystrophy, widening and infiltration of the toes and common interdigital mycoses [1, 2]. Other non-specific skin changes related to the alcohol consumption are commonly observed as well. The condition affects mainly middle-aged men suffering from alcoholism [1, 3]. Often a bilateral location at the lower limb of male alcoholics has been described, as in our patient [2, 3].

Although the etiologic role of alcohol is well established, the exact pathogenesis is still unclear. The mechanical theory underlines microtraumatism as the main mechanism, whilst the sympathetic theory focuses on the vasomotility dysfunction. An integrative theory combines the former and the latter.

The differential diagnosis of Bureau-Barrière syndrome includes the inherited Thévenard's disease with a positive family history, Charcot's neuropathy in patients with diabetes mellitus, and syringomylelia. In the latter case, pain is lesser than joint of bone destruction suggest, that also means it is not completely painless [4]. Tethered cord syndrome is a rare condition with associated hyperhidrosis [5], and last not least infectious diseases such as borelliosis and leprosy have to be considered [6, 7].

Successful treatment of the Bureau-Barrière syndrome requires an interdisciplinary approach [1, 2]. Cessation of alcohol intake and smoking is of paramount importance.

References

1. Thoma E, Ruzicka T, Donhauser G, Albrecht T, Braun-Falco O. [Clinical aspects and therapy of Bureau-Barrière syndrome. Observations of 17 cases with review of the literature]. Hautarzt. 1993;44(1):5-13. PMid:8436512

2. Dissemond J, Knab J, Goos M. [Bureau-Barrière syndrome of the hand. A case report on an unusual localization]. Hautarzt. 2004;55(4):371-5. https://doi.org/10.1007/s00105-003-0648-5 PMid:15146886

3. Shibuya N, La Fontaine J, Frania SJ. Alcohol-induced neuroarthropathy in the foot: a case series and review of literature. J Foot Ankle Surg. 2008;47(2):118-24. https://doi.org/10.1053/j.jfas.2007.12.009 PMid:18312919

4. Alnot JY, Rossarie R, Welby F. [Syringomyelia and associated bone and joint diseases]. Rev Chir Orthop Reparatrice Appar Mot. 2007;93(3):269-76. https://doi.org/10.1016/S0035-1040(07)90249-4

5. Wollina U, Mohr F, Schier F. Unilateral hyperhidrosis, callosities, and nail dystrophy in a boy with tethered spinal cord syndrome. Pediatr Dermatol. 1998;15(6):486-7. https://doi.org/10.1046/j.1525-1470.1998.1998015486.x PMid:9875980

6. Wollina U, Krönert C, Heinig B. Bilateral callosities, plantar ulcers and peripheral neuropathy in a 15-year-old nondiabetic boy--think of neuroborreliosis. J Eur Acad Dermatol Venereol. 2005;19(2):259-60. https://doi.org/10.1111/j.1468-3083.2005.01012.x PMid:15752310

7. Riyaz N, Sehgal VN. Leprosy: trophic skin ulcers. Skinmed. 2017;15(1):45-51. PMid:28270310

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Severe Acne Inversa - Dermatosurgical Approach in a Bulgarian Patient

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Keywords: dermatosurgical approach; invasive approach; hidradenitis suppurativa; acne inversa; treatment outcome; secondary healing.

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Abstract

We present a 55-year-old male patient - a smoker, admitted to a Medical Institute of MVR (Ministry of the interior, Sofia, Bulgaria), on occasion of pain and swellings, located in the area of both axillae, accompanied by purulent discharge, with bloody admixtures. Bilateral localised cystic rose above the skin surface, hyperpigmented nodules interconnected with multiple fistulas, was observed within the dermatological examination, resulting in a limitation of the possibility of movement of the hands in all directions. A subjective complaint of pain was obtained on palpation. Solid bilateral axillar cicatrices - formation was also established, which additional impeded the movements of the upper limbs. The disease was generalised affecting additional inguinal, femoral and perineal areas, while at this stage the patient refused categorically eventual photo documentation of them. The diagnosis of acne inversa was made based on the available clinical and para-clinical data, as dual antibiotic therapy with Clindamycin 300 mg, two times per day was initiated for two months, in combination with rifampicin 300 mg, two times per day also for two months. This led to a significant improvement in the clinic symptoms and the patient was hospitalised for radical surgery. A surgical management of the clinical findings was planned by an interdisciplinary team including surgeons and dermatologists. The procedure was performed under general anaesthesia. After a thorough cleaning of the operative field, a radical excision of the lesion in the left axillary and para axillar region was performed, comprising the skin and subcutaneous tissue forward the fascia pectoralis. Tissue was dissected in depth in the form of number 4, thereby creating the conditions for adaptation of the initially encountered communicating with each other skin defects. Two tubular drains were placed, followed by gradual suturing of skin and subcutaneous tissue with final applying of a sterile dressing. Effective medical treatment of patients (as in our case) with severe AI is limited. Adalimumab is the first biological approved for moderate to severe AI but does not result in stable CR (cure rate). Therefore its use in a neoadjuvant setting is under investigation. Wide local excision significantly reduces pain and improves the quality of life of AI patients. While local recurrences rate is low, the satisfaction with the cosmetic results is high. The recurrence rate is dependent on the region affected and the type of surgery. While in the axillary region primary closure may be used to reduce the time to healing, anogenital AI has the lowest recurrence rate of healing by secondary intention.

We present a 55-year-old male patient- a smoker, admitted to a Medical Institute of MVR (Ministry of the interior), on occasion of pain and swellings, located in the area of both axillae, accompanied by purulent discharge, with bloody admixtures. Bilateral localised cystic rose above the skin surface, hyperpigmented nodules interconnected with multiple fistulas, was observed within the dermatological examination, resulting in a limitation of the possibility of movement of the hands in all directions. A subjective complaint of pain was obtained on palpation. Solid bilateral axillar cicatrices - formation was also established, which additional impeded the movements of the upper limbs (Fig. 1b, 1f).

The disease was generalised affecting additional inguinal, femoral and perineal areas, while at this stage the patient refused categorically eventual photo documentation of them. The diagnosis of acne inversa was made based on the available clinical and para-clinical data, as dual antibiotic therapy with Clindamycin 300 mg, two times per day was initiated for two months, in combination with rifampicin 300 mg,

two times per day also for two months. This led to a significant improvement in the clinic symptoms (see preoperative images) (Fig. 1f) and the patient was hospitalised for radical surgery.

Laboratory investigations demonstrated severe ongoing inflammation and superimposed infection with *St. aureus* (leukocytosis of 21.3 Gpt/l, in normal range between 3.5-10.5, agranulocytosis 91.8%, with a normal range up to 70%, highly increased CRP, haemoglobin 89 g/l (normal range 120-180 g/l). Erythrocyte transfusion in combination with systemic cefazolin 2g/3 times per day for a total period of seven days was initiated, leading to an improvement of the clinical situation and laboratory aberrations. A surgical management of the clinical findings was planned by an interdisciplinary team including surgeons and dermatologists. The procedure was performed under general anaesthesia. After a thorough cleaning of the operative field, a radical excision of the lesion in the left axillary and para axillar region was performed, comprising the skin and subcutaneous tissue forward the fascia pectoralis (Fig. 1a, 1c, 1d, 1e). Tissue was dissected in depth in the form of number 4, thereby creating the conditions for adaptation of the initially encountered communicating with each other skin defects (Fig. 1c, 1d, 1e). Two tubular drains were placed, followed by gradual suturing of skin and subcutaneous tissue with final applying of a sterile dressing.

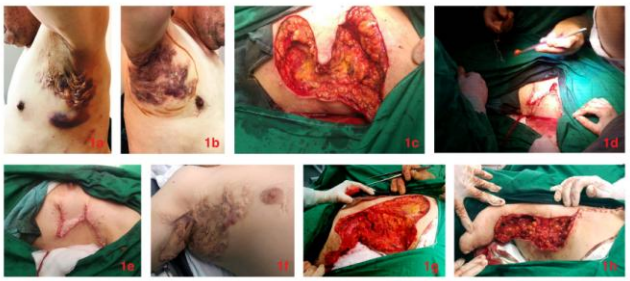

Figure 1: Radical excision of the lesion in the left axillary and para axillar region was performed, comprising the skin and subcutaneous tissue forward the fascia pectoralis. Tissue was dissected in depth in the form of number 4, thereby creating the conditions for adaptation of the initially encountered communicating with each other skin defects. Two tubular drains were placed, followed by gradual suturing of skin and subcutaneous tissue with final applying of a sterile dressing.

A radical excision of the right axillar fossa was also performed, including also the skin and subcutaneous tissue of the para axillar and axillary region (Fig. 1g). A thorough hemostasis was made with a partially adjusting of the wound in its two poles, while a relatively large portion of the defect was let to heal secondary, because of lack of tissue (Fig. 1h). The postoperative period underwent without complications.

Hidradenitis suppurativa (HS) or acne inversa (AI) is a debilitating suppurative disease of the apocrine/follicular glands. Medical treatment has some efficacy at early-stages but is costly and requires frequent physician visits. The advanced disease usually requires surgical intervention [1].

AI is not easily treated as a rule. Although not uncommum – it affects about 1% of adult population in Europe - AI is often misdiagnosed outside specialised clinics and inappropriately treated as a simple boil or abscess [2]. In recent years, guidelines have been developed, based both of expert opinion and the available literature. A multifaceted approach is necessary as AI lesions include as inflammation (amenable to medical treatment) as well as fibrosis (amenable to surgery only). The recommended antiinflammatory therapies encompass both antimicrobials and regular anti-inflammatory drugs [2].

Treatments with the following agents seem to be possible: clindamycin, tetracycline, rifampicin, ertapenem, dapsone, triamcinolone, infliximab, adalimumab, and anakinra, but only adalimumab has been approved in Europe. All other treatments are off-label [2]. The current approach to the management of fibrotic lesions is surgery since it is not susceptible to medical treatment. A comprehensive three-pronged approach with adjuvant therapy, medical therapy, and surgery is recommended [3].

The list of comorbidities and complications associated with AI is extensive [4]. Among the complications of AI, squamous cell carcinoma is considered the most severe. More than 90 cases of patients AI developing squamous cell carcinoma have been identified. Most of the squamous cell carcinomas appear on the perineal or buttock areas with a 2-year survival rate of less than 50%. Those authors believe that the development of squamous cell carcinoma in patients with acne inversa is a typical condition of an immunocompromised district [5]. The "immunocompromised cutaneous district" is a novel concept that applies to an area of diseased or injured skin where local immune control has been altered, thereby permitting the development of a dysimmune reaction, infection or tumour confined to the diseased or injured site [5].

Effective medical treatment of patients (as in our case) with severe AI is limited. Adalimumab is the first biological approved for moderate to severe AI but does not result in stable CR (cure rate). Therefore its use in a neoadjuvant setting is under investigation [6].

Wide local excision significantly reduces pain and improves the quality of life of AI patients. While local recurrences rate is low, the satisfaction with the cosmetic results is high [7, 8]. The recurrence rate is dependent on the region affected and the type of surgery. While in the axillary region primary closure may be used to reduce the time to healing, anogenital AI has the lowest recurrence rate of healing by secondary intention [4, 8].

References

1. Wollina U, Koch A, Heinig B, Kittner T, Nowak A. Acne inversa (Hidradenitis suppurativa): A review with a focus on pathogenesis and treatment. Indian Dermatol Online J. 2013;4(1):2-11. https://doi.org/10.4103/2229-5178.105454 PMid:23439959 PMCid:PMC3573446

2. Andersen RK, Jemec GB. Treatments for hidradenitis suppurativa. Clin Dermatol. 2017;35(2):218-224. https://doi.org/10.1016/j.clindermatol.2016.10.018 PMid:28274363

3. Zouboulis CC, Desai N, Emtestam L, Hunger RE, Ioannides D, Juhász I, Lapins J, Matusiak L, Prens EP, Revuz J, Schneider-Burrus S, Szepietowski JC, van der Zee HH, Jemec GB. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. J Eur Acad Dermatol Venereol. 2015;29(4):619-44. https://doi.org/10.1111/jdv.12966 PMid:25640693

4. Wollina U, Langner D, Heinig B, Nowak A. Comorbidities, treatment, and outcome in severe anogenital inverse acne (hidradenitis suppurativa): a 15-year single center report. Int J Dermatol. 2017;56(1):109-115. https://doi.org/10.1111/ijd.13393 PMid:27495143

5. Fabbrocini G, Ruocco E, De Vita V, Monfrecola G. Squamous cell carcinoma arising in long-standing hidradenitis suppurativa: An overlooked facet of the immunocompromised district. Clin Dermatol. 2017;35(2):225-227. https://doi.org/10.1016/j.clindermatol.2016.10.019 PMid:28274364

6. Ingram JR. Interventions for hidradenitis suppurativa: updated summary of an original Cochrane Review. JAMA Dermatol. 2017; https://doi.org/10.1001/jamadermatol.2017.0432

7. Wollina U, Tilp M, Meseg A, Schönlebe J, Heinig B, Nowak A. Management of severe anogenital acne inversa (hidradenitis suppurativa). Dermatol Surg. 2012;38(1):110-7. https://doi.org/10.1111/j.1524-4725.2011.02157.x PMid:22092781

8. Posch C, Monshi B, Quint T, Vujic I, Lilgenau N, Rappersberger K. The role of wide local excision for the treatment of severe hidradenitis suppurativa (Hurley grade III): Retrospective analysis of 74 patients. J Am Acad Dermatol. 2017; pii: S0190-9622(17)30149-4.

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Multiple Primary Recurrent Basaliomas (mPR-BCCs) of the Scalp with Cranial Bone Invasion

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Keywords: basal cell carcinoma; cranial bone invasion; adequate therapy; surgery; selctrosurgery.

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Abstract

We present a 68-year-old patient with multiple primary infiltrative BCCs in the scalp area, initially treated 14 years ago with superficial contact X-ray therapy, end dose 60 greys, followed by electrocautery (x2) several years later. He presented in the dermatologic policlinic for diagnosis and therapy of two additional, newly-formed pigmented lesions, and because of an uncomfortable, itchy, burning sensation in the area where lesions had been treated years before. Screening cranial computer-tomography (CT) examination revealed two deformities in the form of tumor-mediated osteolysis, affecting the diploe of the tabula externa on the left parietal and parasagittal areas. Complete excision with removal of periosteum and partial removal of the tabula externa was planned with neurosurgeons at a later stage. BCC is one of the most common malignant skin tumours of the head and neck region (about 90% of cases) and is characterised by a significant potential for local infiltration and destructive growth. Recurrent, invasive BCC of the scalp and calvarium is a difficult problem for which universally accepted treatment protocols had not been established. The primary treatment of aggressive BCCs is surgical, with a thorough examination of excision margins to ensure complete resection. Procedural-based options include standard excision, curettage, curettage with electrodessication, and Mohs micrographic surgery (MMS), with MMS being the gold standard for the definitive treatment of BCC. Improper removal or electrocautery (as in our case) of the several aggressive forms of BCC seems to be a particular problem, and not only for dermatologic surgeons. The risk of subsequent invasion and destruction of the cranium, underlying dura, and cranial nerves by basal cell carcinoma (BCC) is extremely low, with an estimated incidence of 0.03%, but is a potential complication over time. Computed tomography is the modality of choice for detecting tumour invasion into bone, which commonly appears as irregular demineralization or osteolysis.

We present a 68-year-old patient with multiple primary infiltrative BCCs in the scalp area, initially treated 14 years ago with superficial contact X-ray therapy, end dose 60 greys, followed by electrocautery (x2) several years later (Fig. 1a). He presented in the dermatologic policlinic for diagnosis and therapy of two additional, newly-formed pigmented lesions, and because of an uncomfortable, itchy, burning sensation in the area where lesions had been treated years before (Fig. 1a-d).

Screening cranial computer-tomography (CT) examination revealed two deformities in the form of tumor-mediated osteolysis, affecting the diploe of the tabula externa on the left parietal and parasagittal areas. Complete excision with removal of periosteum and partial removal of the tabula externa was planned with neurosurgeons at a later stage. BCC is one of the most common malignant skin tumours of the head and neck region (about 90% of cases) and is characterised by a significant potential for local infiltration and destructive growth [1]. Recurrent, invasive BCC of the scalp and calvarium is a difficult problem for which universally accepted treatment protocols had not been established [2]. The primary

treatment of aggressive BCCs is surgical, with a thorough examination of excision margins to ensure complete resection [3]. Procedural-based options include standard excision, curettage, curettage with electrodessication, and Mohs micrographic surgery (MMS), with MMS being the gold standard for the definitive treatment of BCC [4].

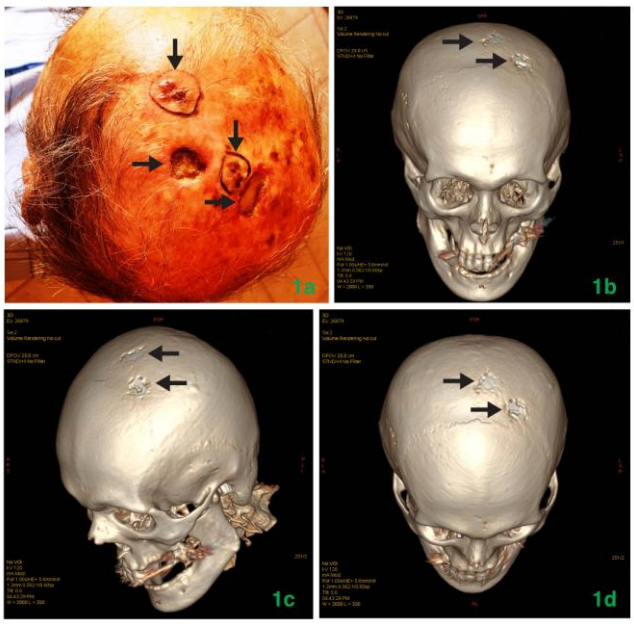

Figure 1: Lesions of the scalp in our patient. 1a) Ulcerated lesions - see horizontally oriented arrows. Horizontally oriented arrows also show histopathologically verified infiltrative BCCs that had been treated in the past. Vertically oriented arrows show newly pigmented BCCs; 1b-d) Horizontally oriented arrows show the older BCCs, treated in the past via radiation and elctrodesiccation

Improper removal or electrocautery (as in our case) of the several aggressive forms of BCC seems to be a particular problem, and not only for dermatologic surgeons. The risk of subsequent invasion and destruction of the cranium, underlying dura, and cranial nerves by basal cell carcinoma (BCC) is extremely low, with an estimated incidence of 0.03%, but is a potential complication over time [5]. Computed tomography is the modality of choice for detecting tumour invasion into bone, which commonly appears as irregular demineralization or osteolysis [5].

References

1. Rasulić LG, Jovanović MD. Surgical treatment and dilemmas in the treatment of basal cell carcinomas with intracranial propagation. Vojnosanit Pregl. 2014;71(11):1045-8. https://doi.org/10.2298/VSP1411045R PMid:25536808

2. Cho GJ, Wang F, Garcia SM, Viner J, Hoffman WY, McDermott MW, Pomerantz JH. Recalcitrant Invasive Skin Cancer of the Scalp: Combined Extirpation and Microsurgical Reconstruction Without Cranioplasty. J Craniofac Surg. 2017;28(2):325-330. https://doi.org/10.1097/SCS.0000000000003384 PMid:28045814

3. Naumann IC, Cordes SR. Giant basal cell carcinoma of the forehead with extensive intracranial involvement. Ann Otol Rhinol Laryngol. 2007;116(9):663-6. https://doi.org/10.1177/000348940711600907 PMid:17926588

4. Blackmon J, Machan M, Rajpara A, Beatty R. Recurrent basal cell carcinoma with intracranial invasion: a case report and literature review. Dermatol Online J. 2014;20(7). pii: 13030/qt11t0g5h8.

5. Kleydman Y, Manolidis S, Ratner D. Basal cell carcinoma with intracranial invasion. J Am Acad Dermatol. 2009;60(6):1045-9. https://doi.org/10.1016/j.jaad.2008.10.005 PMid:19467376

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Medical History

History of the Baths and Thermal Medicine

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Abstract

Hot Springs and Thermal Medicine are an important cultural background all around the world. The authors briefly describe the history of the spa from its origins to today.

Introduction

Thermal Medicine is a discipline which studies and teaches the characteristics of thermal treatments, their biological and pharmacological actions, and therapeutic effects.

The beneficial effects of thermal cures are well-known since the ancient time, when men discovered the importance of water as an essential element for human life, and built the first civilities near to seas and rivers [1]. Indians and Greeks thought that the water was on the basis of the world (Archè) and of the human being. Also in the Genesis of Bible, water has been described as the origin of cosmos.

It was not long before men were discovering the beneficial properties of water, like its healing and disease-protecting effects. Due to its importance, water was seen as magic and considered a gift of the divinity. Egyptians and Israelites used to plunge themselves in the sacral water of Niles and Jordan, Hindus in the Ganges river for healing their soul and body.

In Egyptian times the water has also been used for hygienic and cosmetology purposes. It seems that Egyptian women used to practice water vapours to be more beautiful, and the legendary Cleopatra used to make wraps with mud from the Dead Sea, to maintain her legendary beauty. Nevertheless, it was by the Greeks that thermalism was born [2].

Due to the supernatural power attributed to the warm waters and their vapours, it's not surprising how the first Thermal arose near the temples and

natural hot springs. Ancient Greeks well-knew the beneficial properties of sulphurous springs, especially for healing skin diseases and for relieving muscular and joint pain. In the Homeric poems and Hesiod, many references are made to the use of restorative baths. Also, some of Greece's famous philosophers, such as Hippocrates and Plato, wrote of the benefits of hydrotherapy. Hippocrates dedicated a large section to thermal water in his work "De is, a quiz at loci", in which he described the chemical and organoleptic water features, and the effects of hot and cold baths on the human body. The philosopher proposed the hypothesis that all the human diseases started in an imbalance of the bodily fluids. To restore the balance, changes of habits and environment were advised, included bathing, perspiration, walking, and massages. For this reason, baths were often associated to a gymnasium. A body massage with oil and unguents was introduced after the bath, to restore the skin properties and to relax the patient.

Over time, new baths, both public and private ones, were built inside of various cities.

Even the Etruscans have given great importance to the use of water, not only for its cleanliness and cosmetic properties but also for the healing one. That is why they built spring terms near their town.

If thermalism was born in the ancient Greek, was only by the Roman time that it experienced its gold age [3]. Taking the lead from the Greeks, Romans considered bathing as a regular regimen for health.

With Romans thermal baths became a social experience for everyone. In a first time, numerous baths (Balnea), both private and public, had been constructed in Rome and conquered lands all over Europe. Balnea were also built in private houses, often with special areas dedicated to the sauna or the massage. The advent of the aqueducts, led to the building of magnificent edifices (Thermae) with a capacity for hundreds or thousands of people. From being a good regimen for human health, thermalism became an important experience for socialising, relaxation and working. The new thermal centres (or SPA, "Sanus per Aquam"), in addition to balnea, consisted of gardens, shops and libraries. The Roman Thermae also had a medicinal emphasis, and they were largely used as recuperation centres for the wounded military soldiers. Roman legionaries, fatigued by wars, used to relax and to treat their sore wounds and tired muscles through natural spring water. Many physicians, such as Galen and Celso, studied the water compositions, its effects and clinical indications. Some of the Thermae were addressed for their therapeutical properties. Hydrology became a real science: thermal treatments were prescribed with specific indications to follow and underwent to a medical surveillance [4].

Unfortunately, in the middle age, the progressive decline of the Roman Empire, the barbarian invasions and the spread of Christianity, lead to the thermal crisis. Thermae became progressively desert. Baths were accepted only as a cleaning or a therapeutic tool [4]. On the other hand, at the same time, physicians continued to study the different types of water, underlining their specific clinical indications (e.g. sulphurous water was recommended for skin diseases, while the salsobromoiodic one was recommended for female sterility).

In the Renaissance era, spas and hydrology were revalued [5]. New scientific studies have been conducted and, due to the introduction of printing, they began to spread on a large scale. Spa treatments became more targeted and specific for the treatment of various medical conditions.

Laicality of medical thermalism reinforced more and more during the illuminism and consolidated in the XVIII and XIX centuries. At this age, the scientific progress made the medical hydrology an experimental science and not more an empirical one. The biochemical studies on mineral waters underlined their properties and clinical indications. Doctors were convinced that for each disease there was an appropriate medicinal spring. By this point of view, Vincent Priessnitz [6] and Sebastian Kneipp may be considered as the two fathers of the modern balneotherapy (medicinal use of thermal water) and hydrotherapy (immersion of the body in thermal water for therapeutic purposes).

Combined treatments, such as herbal baths, mud packs, active physical exercises, massages, and diets, were developed too. Often large and beautiful gardens were built near the new spas, underling the importance of the combination ecology-hydrology [7]

Finally, in this period, important scientific institutions and famous academy schools were founded to study thermalism in many European countries.

Table 1: Main dermatological diseases which may be treated with thermal medicine

Psoriasis
Acne
Atopic dermatitis
Contact dermatitis
Seborrheic dermatitis
Collagen vascular disorders

The next Belle Epoque saw the emergence of "Elitist Thermalism". Throughout Europe and the Americas, the Spas were on the rise. Grand hotels, casinos, bar and restaurants arose, near the spa resorts. The new thermal centres were integral parts of gentility life, a meeting centre for the elite and a place of creativity for painters and composers.

After two World Wars, the popularity of the thermal baths decreased again. The destruction of the baths reduced to ruins, the socio-economic crisis, the

progress of chemistry and pharmacology radically changed the way of taking baths.

Thermalism became a social form of hydrotherapy, open to a larger public, and thermal cures were included in the therapeutic program of the national health system (Table 1).

With the beginning of the twenty-first century, water has regained its importance due to the therapeutic experience of the physicians, and to the new studies of hydrology, pharmacology and biochemistry [8, 9]. In particular, due to the contribution of Chinese, American and Spanish studies [10], thermal cure have now assumed a preventive, therapeutic and rehabilitative value in many diseases including collagen vascular disease [11].

Maybe the most important innovation in thermalism is that the classical concept of cure is now joined to the concept of wellness, with an extraordinary flourish of parallel and complementary activities. New spas tourism is developing [12, 13].

Nowadays, health and wellness tourism is a rapidly growing sector of the tourism industry, and it has increased its activity worldwide. The tourism is directed not only to a physical and psychological improvement but also because it is a cultural and relaxing experience.

References

1. Cancellieri M. L'acqua come segno di vita: modi e tecniche di utilizzo nel mondo romano alla luce della documentaz'one archeologica. Med Secoli. 1995;7:451-460. PMid:11623481

2. Melillo L. Thermalism in ancient world. Med Secoli. 1995;7:461-483. PMid:11623482

3. Cilliers L, Retief FP. Medical practice in Graeco-roman antiquity. Curationis. 2006;29:34-40. https://doi.org/10.4102/curationis.v29i2.1071 PMid:16910132

4. Masetti A. "Salus per Aquam": terme e termalismo nella storia. G Med Mil. 2011;161:11-16.

5. Palmer R. "In this our lightye and learned tyme": Italian baths in the era of the Renaissance. Med Hist Suppl. 1990;10:14-22. https://doi.org/10.1017/S0025727300070964

6. Skopec M. Vincent Priessnitz and the Vienna Medical School. Wien Klin Wochenschr. 1991;103:506-508. PMid:1949807

7. Grossi F. Parks and hydro-mineral springs in the classical world and in the contemporary era. Place in therapeutics. Clin Ter. 1997;148:549-565. PMid:9494258

8. Suárez M, González P, Domínguez R et Al. Identification of organic compounds in San Diego de los Ba-os Peloid (Pinar del Río, Cuba). J Altern Complement Med. 2011;17:155-165. https://doi.org/10.1089/acm.2009.0587 PMid:21309710

9. Borroni G, Brazzelli V, Fornara L et al. Clinical, pathological and immunohistochemical effects of arsenical-ferruginous spa waters on mild-to-moderate psoriatic lesions: a randomized placebo-controlled study. Int J Immunopathol Pharmacol. 2013;26:495-501. https://doi.org/10.1177/039463201302600223 PMid:23755765

10. International Society of Hydrothermal Techniques Newsletter March 2016.

11. Wollina U, Uhlemann C. Die klassischen Kollagenosen"-Pathogenese und Therapieansätze. Physikalische Medizin, Rehabilitationsmedizin, Kurortmedizin. 1994;4(01):22-6. https://doi.org/10.1055/s-2008-1061998

12. Wollina U, Uhlemann C. The classic "collagen diseases" - pathogenetic and therapeutic methods of approach. Phys Med Rehab Kuror. 1994;4:22-26. https://doi.org/10.1055/s-2008-1061998

13. Costa C, Quintela J, Mendes J. Health and Wellness Tourism: A Strategic Plan for Tourism and Thermalism Valorization of São Pedro do Sul. In: M. Peris-Ortiz, J. Álvarez-García Eds). Health and Wellness Tourism. Springer International Publishing Switzerland, 2015:21-30. https://doi.org/10.1007/978-3-319-11490-3_2

14. Li Castri A. Thermal Baths and Wellness in Italy. Press Therm Climat. 2009;146:265-272.