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Case Report

"Transforming the Beast to A Beauty"- Fifteen Years into the Making - Case Report of Congenital Neurofibromatosis

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Abstract

BACKGROUND: In 1882, the German pathologist Friedrich Daniel von Recklinghausen described a series of patients with a combination of cutaneous lesions and tumours of the peripheral and central nervous system. Succeeding this paper, all of the patients with similar symptoms were given the diagnosis "von Recklinghausen disease". In the 20th century, a distinction was made between Neurofibromatosis type 1 (NF1) and Neurofibromatosis type 2 (NF2) with the help of molecular testing.

CASE REPORT: We are presenting the results from multiple surgical esthetic and reconstructive surgical procedures performed on a female patient with severe congenital neurofibromatosis during 15 years (2000-2015). The external appearance of our patient was not reflected in the general public's beauty standards. Convinced that she was unusual and unaccepted by the society, she gathered all of the strength and became our patient at 15 years of age.

CONCLUSION: Transforming the patient's life in the next fifteen years improved her overall health and her life quality.

Introduction

In 1768, Akenside was the first one to publish a scientifically-based description of a disease that later has been described as Neurofibromatosis type 1 [1]. At that time, he had acknowledged that the monsters of scholars, such as Pare and Aldrovandi, suffered from a disorder of the nerves [2]. The neurofibromas of NF1 were first described in details by Smith in 1849 [2]. In 1882, the German pathologist Friedrich Daniel von Recklinghausen described a series of patients with a combination of cutaneous lesions and tumours of the peripheral and central nervous system [1]. Succeeding this paper, all of the patients with similar symptoms were given the diagnosis "von Recklinghausen disease".

In the 20th century, a distinction was made between Neurofibromatosis type 1 (NF1) and Neurofibromatosis type 2 (NF2) with the help of molecular testing. NF1 evolved from the von Recklinghausen disease, a name which now is only an antiquated synonym for the disease [3]. It has been estimated that in 1 out of every 2500 to 3500 individuals are affected, and only one half are results of the inherited (familial) disorder. The remaining half is considered to be sporadic (de-novo) mutations [4]. The classic manifestation of café-au-lait macules, axillary or inguinal freckling, iris hamartomas (Lisch nodules) and neurofibromas. These findings usually prompt further clinical examination, sometimes requiring genetic testing (in questionable cases) for the mutation of the NF1 gene on chromosome 17q11.2. The consensus for diagnosis of NF1 was developed by the NIH (National Institute of Health) at the National Institutes of Health Consensus Development Conference in 1987, later updated in

1997, which required having two or more of the clinical features shown in Table 1 [5], [6], [7].

Table 1: Clinical features of the patient

NIH diagnostic criteria for neurofibromatosis type 1
6+ café-au-lait macules (prepubertal individuals: bigger than 5 mm and postpubertal individuals: bigger than 15 mm)
Axillary or inguinal freckling
Neurofibromas (2 or more) or one Plexiform neurofibroma
Optic glioma
Iris hamartoma (Lisch nodules, 2 or more)
Bone lesions (sphenoid dysplasia, medullary narrowing or cortical thickening of long bone cortex with or without pseudoarthrosis)
First degree relative with NF1

Ethical Approval: Our patient has been informed of potential publication, has given her consent, and all steps to ensure patient confidentiality have been taken.

Case Presentation

The female patient was only 15 years of age when first presented to our hospital. The first impression was remarkable for her innumerable skin neurofibromas and skeletal abnormalities. Born in 1985 in a small mountain village in the eastern part of Republic of Macedonia, she spends almost her entire life hiding from the public due to her external appearance. Living in an isolated area of a third world country additionally limited her to access appropriate medical care.

The patient had neurofibromas involving almost all anatomical regions of the body, most prominent on the face, head, thorax, hands, feet and the inguinal area. The neurofibromas were ranging in size (from 0.5 to 10 cm in greatest dimension) and in addition to their location were incapacitating her daily living. The patient was not able to walk or use her hands. In addition to the neurofibromas, the patient had multiple café-au-lait macules and cervical ankyloses.

The MRI of the head, kyphosis of the spine and ankyloses of the thoracolumbar part, are combined with the different size of round and fairly well-circumscribed nodules. Also, there is neurofibroma in the subcutaneous soft tissue in the forehead, nasal area, intraoral region, upper and lower extremities, sternum, spine and gluteal regions. Serial blood laboratory tests were performed and were within normal limits. The genetic evaluation was not performed for definitive in addition to the clinical diagnosis since it was compliant with the NIH NF1 diagnostic criteria (see Table1). However, maybe one of the most debilitating aspects of the patient's life was her emotional status. Her mental status and intellect were appropriate for her age, and she was attending school until graduation from high school. The everyday stress due to her presence and the constant unpleasant remarks from her peers were leaving scars in her soul much bigger and unbearable if compared to any surgical scars.

After multiple surgical procedures, the results come slowly. She understood and accepted our plan saying "I am a beast, please help me" with despair but and not very hopeful for the future.

The first surgery was performed with general anaesthesia on June 28th 2000, with concentration to the lesions on her face, especially bulky nose and her head (Figure 1).

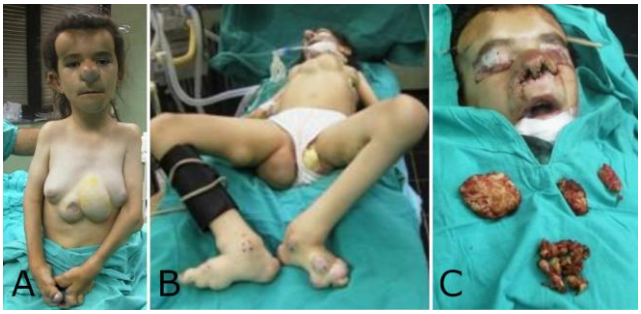


Figure 1: A) Pre-operative presentation (June 28, 2000); B) Pre-operative presentation (June 28, 2000); C) Initial surgery, removal of facial lesion (June 28, 2000)

The second surgery was done the following year in local anaesthesia, since the patient was already experienced and familiar with what to expect. The patient continued to return almost annually for the removal of the lesions.

On March 30th 2011, we came to the point when her psychological and overall health was improving, and we could concentrate more on the smaller lesions on her body which will improve her quality of life even more.

a) b)

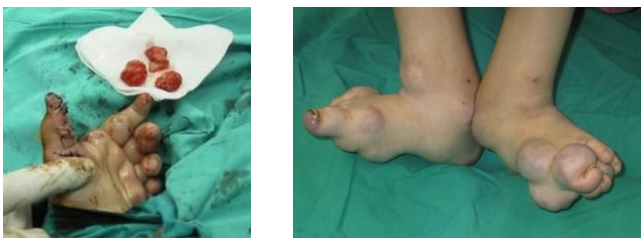


Figure 2: March 30, 2011

Our focus was aimed at restoring her fine motor movement by removing the digital lesions (Figure 2a) and multiple lesions on her bilateral feet, including the lesions affecting the toes (Figure 2b).

After this surgery, the fine motor movements, and use of her hands in general drastically improved. On December 7th 2012, multiple large and diffuse subcutaneous lesions were removed from her anterior thorax region (Figure 3a). The last time we saw the patient was on December 10th 2015. She was functioning on her own and much more independent

than the time we first met her (Figure 3b).

a) b)

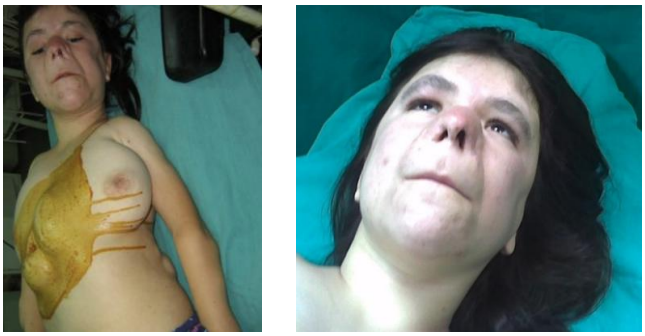


Figure 3: December 7, 2012

The histopathological evaluation of the multiple lesions throughout the years was consistent, showing spindle-cells shaped cells with a scant amount of cytoplasm separated by collagen fibres and myxoid material (Figure 4).

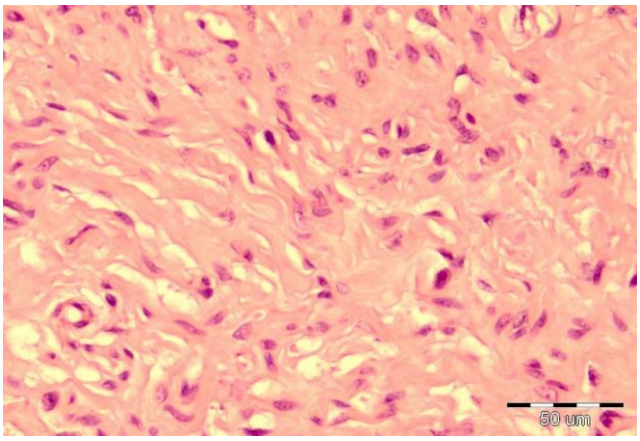


Figure 4: Spindles cells in the fibrous stroma (H&E, 200x)

Immunohistochemical staining with S-100 highlighted the fraction of the cells (Figure 5). Some of the lesions were small (less than 2.0 cm), and others was larger, diffuse and involving nerves (Figure 6). No apparent malignant transformation was identified [8].

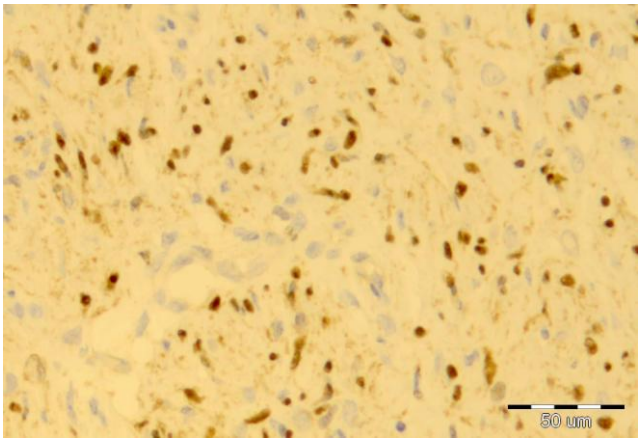
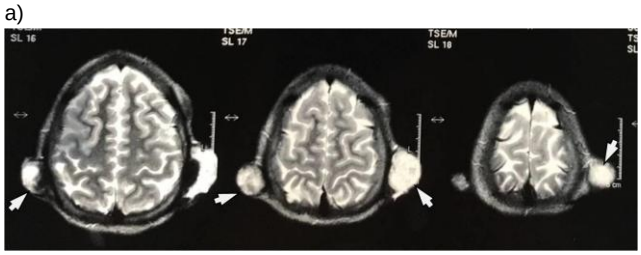


Figure 5: S-100 highlights the Schwann cells (S-100, 200x)

Discussion

Neurofibromatosis type 1 is a genetic disorder that predominantly affected our patient's look [2]. The shame of her physical disabilities attributed to the delay in her family seeking medical help for the multiple deformities [4]. The progression of fibromatoses nodules affected nerves and combined with her spinal ankyloses had limited her mobility, making her dependent on her mother.

a)



b) c)

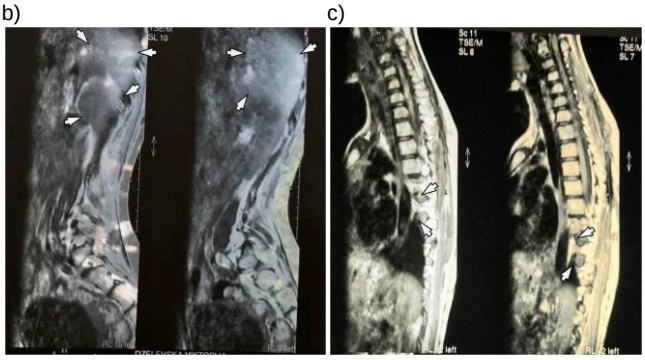


Figure 6: a) MRI of the head; b) MRI of the body; c) MRI of the spine

The solution for the inability to walk the family had overcome by carrying the patient rather than seeking a permanent medical solution. None of the siblings or close relatives is known to have NF-1, which is not an uncommon finding. Her surgical treatments have abruptly stopped in 2015, after the death of her mother who was her principal caregiver and support throughout her life.

The initial operation involved removing the huge neurofibromas from the head and face region. Within the subsequent fifteen years (2000 – 2015) an additional ten surgical procedure was performed in various regions of her body, all of them in local anaesthesia. Her wounds were healing fairly quickly. In each of the wounds, only one drain was left for only one day. We performed to used stitches Vicryl 4-0. No complications were observed, including infections and keloid formations. After the removal of numerous neurofibromas, we release some peripheral nerves structures, and she has achieved complete restoration of movement in her upper extremities to the point that she can perform delicate tasks with her hands. Our last communication was 16.09.2018 when she gave us the consent form to publish her pictures.

In conclusion, the goal of any esthetic intervention in congenital disorder illness is to re-establish near “normal” contour. Immediate results are evident on the patient’s psychological wellbeing. The elimination of unusual appearance contributed and brought out our patient’s pleasant appeal to those that surround her.

The known risk of malignant transformation of the plexiform and intraneural neurofibromas currently has been estimated to be up to 5-10%. Aside from the risk of malignant transformation and deceptive physical deformity, psychological trauma, such as depression and anxiety, almost inevitably accompany physical deformities. Often the suffering does not end with only the patient but continues with the family thus burdening a wider circle of people.

References

1. Gerber PA, Antal AS, Neumann NJ, Homey B, Matuschek C, Peiper M, Budach W, Bölke E. Neurofibromatosis. European journal of medical research. 2009; 14(3):102. PMid:19380279 PMCid:PMC3352057

2. Brosius S. A history of von Recklinghausen's NF1. J Hist Neurosci. 2010; 19(4):333-48. https://doi.org/10.1080/09647041003642885 PMid:20938857

3. Anderson JL, Gutmann DH. Neurofibromatosis type 1. Handb Clin Neurol. 2015; 132:75-86. https://doi.org/10.1016/B978-0-444-62702-5.00004-4 PMid:26564071

4. Evans DG, Howard E, Giblin C, Clancy T, Spencer H, Huson SM, Lalloo F. Birth incidence and prevalence of tumor-prone syndromes: estimates from a UK family genetic register service. American journal of medical genetics Part A. 2010; 152(2):327-32. https://doi.org/10.1002/ajmg.a.33139 PMid:20082463

5. DeBella K, Szudek J, Friedman JM. Use of the national institutes of health criteria for diagnosis of neurofibromatosis 1 in children. Pediatrics. 2000; 105(3):608-14. https://doi.org/10.1542/peds.105.3.608 PMid:10699117

6. Gutmann DH, Aylsworth A, Carey JC, et al. The diagnostic evaluation and multidisciplinary management of neurofibromatosis 1 and neurofibromatosis 2. JAMA. 1997; 278(1):51-7. https://doi.org/10.1001/jama.1997.03550010065042 PMid:9207339

7. Neurofibromatosis. Conference statement. National Institutes of Health Consensus Development Conference. Arch Neurol. 1988; 45(5):575-8. PMid:3128965

8. Fletcher CD. WHO Classification of Tumours of Soft Tissue and Bone. World Health Organization, 2013.