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Case Report

Seborrheic Pemphigus, Antigen Mimicry and the Subsequent-Wrong Diagnostic and Therapeutic Approach?

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Abstract

It is well-established that drugs could be leading cause of occurrence of numerous diseases, including pemphigus, being either inducer or triggering factor of the autoimmunity. Despite medications, it should be kept in mind that chronic or acute infections are also capable of being a trigger in various types of cutaneous eruptions, including pemphigus. The rapidly obtained and uncompleted history for accompanied medication leads to general mistakes in the subsequent treatment approach, as the first step in such cases is discontinuation of the drug-inductor. The absence of this information guaranties the fail of the treatment. On the other hand, the lack of performed screening for chronic or acute hepatitis and tuberculosis is not the only mistake, regarding the high dosage of immunosuppressors that have been planned as regiment and the possible fatal effect on the infection's spread or exacerbation, but also because of the possible triggering ability of chronic or acute infection, which may play also a key role in the generation of antigen- or molecular- mimicry, as a potential source of antibodies reactive with various tissue antigens. It turns out that although the diagnosis of pemphigus in regular cases is usually not a challenge, the treatment occasionally could be, just because of a simple pitfall in anamnesis and screening, as in the presented case. Herein, we present a case of a patient with seborrheic pemphigus, which is strongly demonstrative for these statements, as we want to emphasise the importance of the first and the most powerful clinician's weapons – the patient's history and thorough examination.

Introduction

Pemphigus is a part from the large group of autoimmune bullous diseases with variable clinical manifestation, but common histological and immunofluorescence characteristics, causing blisters and erosions both on the skin and mucous membranes, as a result from autoimmunity to desmosomal cadherins [1]. Pemphigus is divided into two groups, based on the level of acantholysis in the epidermis - pemphigus vulgaris (histologically presented with suprabasal acantholysis) and superficial pemphigus [1][2]. The superficial acantholysis could be seen in pemphigus foliaceus and its milder subtype - pemphigus seborrheicus (PS), which is limited only to seborrheic areas [3]. The other superficial variant is pemphigus erythematosus, also known as Senear - Usher syndrome, which is characterized by immunologic markers both for pemphigus foliaceus and lupus erythematosus, but uncommon mucous membrane involvement [2][3].

Although both genetic and exogenous, stress-related factors have been implicated in the etiopathogenesis of pemphigus in general; antigenic triggering is not yet fully understood [4]. However, it is well-established that drugs could be leading cause of occurrence of the disease, being either inducer or triggering factor [4]. The thorough medical history for accompanying medication is an essential prerequisite for the successful clinical management of pemphigus of any type, as the lack of improvement is often related to simply pit falls in anamnesis, which is unacceptable at the current stage of scientific knowledge. Despite medications, it should be kept in mind that chronic or acute infections are also capable of being a trigger in various types of cutaneous eruptions, including pemphigus [5].

Herein, we present a case, which is strongly demonstrative for these statements, as we want to emphasise the importance of the first and one of the most powerful clinician's weapons - the patient's history, as well as the mandatory screening for infections, prior the introduction of high dosage immunosuppressors.

Case report

A 67 - year - old Caucasian female patient presented with one - year history of spontaneous occurrence of painful erosions on the skin and nasal mucosa. The patient had been diagnosed with seborrheic pemphigus. Seven months prior the current hospitalisation, histologically and immunofluorescently verified and treated in another University dermatological department. The presented medical history reported systemic administration of methylprednisolone x 40 mg i.m/daily, azathioprine 50 mg – 2 x 1 table/daily for one month. The current hospitalisation in a medical institute of MVR - Sofia, Department of Dermatology, Venereology and Dermatologic surgery, was because of the lack of any improvement of the conducted treatment and occurrence of new cutaneous lesions in contrast. The clinical examination revealed multiple blisters and erosions, partially covered with yellow - brownish crusts, disseminated on the seborrheic areas on the sun-exposed zone of the décolletage, presternal, interscapular and paravertebral spaces (Fig.1 a, b). Same lesions were observed on the scalp, while superficial erosions were affected the nasal mucosa and paranasal skin (Fig. 1 c, d). The thorough medical history revealed systemic administration of captopril 25 mg, because of mild arterial hypertension with long-lasting duration. The whole serological screening for HBsAg, Anti Hbs, HIV and quantiferon tests was performed. The revealed titer of antinuclear antibodies (ANA) was 1:100, anti HCV - negative, HIV - negative, quantiferon test - negative, but the anti HBcore total test - positive.

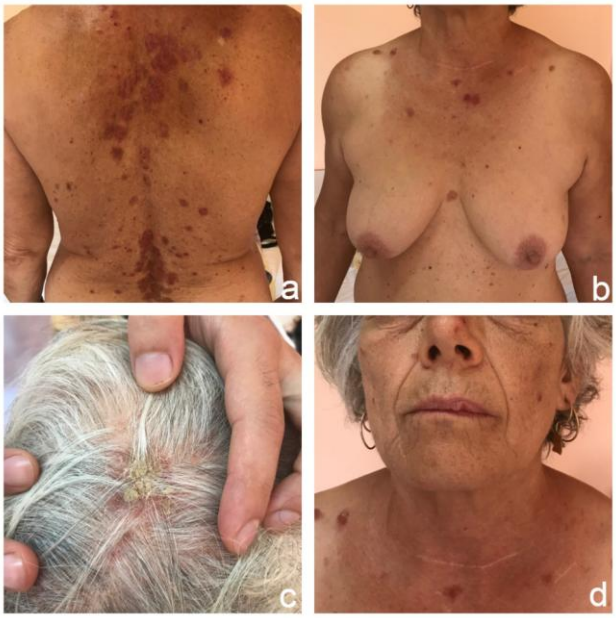

Figure 1: a, b, c, d - Clinical manifestation of a drug-induced pemphigus seborrhoicus, a year after the initial diagnosis

The patient was referred for evaluation of virus load in peripheral blood, to differentiate between chronic and acute infection, as a possible trigger for antigen/ molecular mimicry, which would require adequate therapy, as no such examinations, not therapy had been introduced to that point. The rest of the results from the conducted laboratory blood tests were within the normal range. The histological examination after biopsy demonstrated pseudoepitheliomatous, hyper- and parakeratosis in the epidermis with mononuclear perivascular infiltration in the dermis. The immunofluorescent examination confirmed the diagnosis pemphigus, with intercellular deposition of IgG and C3 in the epidermis. Diagnose of drug-induced seborrheic pemphigus was made, based on the clinical and laboratory findings. The administration of captopril was switched to valsartan 80 mg.

Systemic administration of methylpred-nisolone in a daily dose of 1mg/kg with subsequent reduction and azathioprine 2x50 mg daily was planned as a therapeutic regiment, in case of obtaining negative results from the virus load. Meanwhile, the patient was treated with topical application of clobetasone proprionate 0.05% and oral antihistamines.

Discussion

Since the first reported case of drug-induced pemphigus by penicillamine in 1969 [6], and captopril

in 1980 [7], numerous types of drugs have been implicated in the etiopathogenesis of pemphigus, either as triggers, or exacerbates of the disease, including phenytoin and carbamazepine [4, 8]. Wolf R. et al. suggest back in 1991 that clinical course and behavior of the disease depends mainly on the type of the drug, as the authors first report pemphigus-induced by drugs containing a sulfhydryl radical (as penicillamine) showed spontaneous recovery in up to 52.6%, after the drug discontinuation, in contrast to only 15% spontaneous recovery in pemphigus-induced by other drugs [6]. Since then, it is known that drugs with sulfhydryl radicals induce pemphigus, while drugs without sulfhydryl radicals trigger the occurrence of the disease in predisposed individuals, as the mechanism of drug-induced pemphigus is related mainly to drug's potential to induce acantholysis [8][9].

Despite penicillamine, it is well-established that antihypertensive drugs, namely ACE - inhibitors can trigger pemphigus or induce exacerbation, resembling the mode of action of b - blockers in worsening of psoriasis, gold - provoking lichen ruber planus, estrogens - lupus, etc. [8]. The drug may act either as the main etiological factor for occurrences of otherwise mild and therapeutic responsible with drug discontinuation or as a triggering factor, resulting in idiopathic pemphigus, which is usually more therapeutic - resistant, even after discontinuation of the drug [10]. The investigated autoimmune response is similar in drug-related and non-drug induced disease; both showing have tissue - bound and serum autoantibodies to DSG1 and/or DSG3, suggesting a similar underlying molecular mechanism [11]. While the clinical and histological findings in ordinary pemphigus and the drug-induced one are quite similar and they do not allow such differentiation, the clinician should obtain a very thorough medical history, to avoid deterioration of the disease, in contrast to otherwise correct therapeutic behaviour [8]. However, despite the current state of scientific knowledge, and the lower incidence of drug-induced seborrheic pemphigus recently, inadequate diagnostic and therapeutic behavior could be still seen not only among hypertension specialists, but also among dermatologist, who are obviously not aware that severe pemphigus, which is therapeutically resistant and aggressive in its clinical behavior, may be caused by drugs or triggered by infections also [5][8].

Despite drugs, various bacterial, viral and parasitic agents can activate the T - or B - cellular immunity with subsequent autoimmune response to certain cutaneous tissues, in the framework of so-called Antigen Mimicry [5][12]. And while generation of antibodies in pemphigus subtypes could be as a response to different infectious antigens by antigen mimicry and subsequent epitope spreading, the screening for underlying bacterial or viral trigger and its subsequent elimination are as many essential preconditions for achieving of a clinical remission or satisfactory therapeutic response, as discontinuation of eventual drug - inductor [5, 12]. If both mechanisms could be implicated in the etiopathogenesis, the careful history and adequate screening for underlying infectious trigger should be the first step when dealing with pemphigus. Furthermore, it turns out that although the diagnosis of pemphigus in regular cases is usually not a challenge, the treatment occasionally could be, just because of simple pit falls in anamnesis, as in the presented case. The rapidly obtained and uncompleted history for accompanied medication leads to general mistakes in the subsequent treatment approach, as the first step in such cases is discontinuation of the drug-inductor. The absence of this information guaranties the fail of the treatment. On the other hand, the lack of performed screening for chronic or acute hepatitis and tuberculosis is not the only mistake, regarding the high dosage of immunosuppressors that have been planned as regiment and the possible fatal effect on their spread or exacerbation, but also because of the possible triggering ability of chronic or acute infection, which may play a key role in molecular mimicry, as a potential source of antibodies reactive with various tissue antigens [5]. Our patient achieved significant clinical resolution of the symptoms, soon after the discontinuation of the medication with captopril. A very simple step which can provide rapid and uncomplicated treatment and should be considered in earlier stages of the disease.

With the presented case, we want to emphasize the importance of thorough medical history, in which simply pit falls may vitiate the treatment outcome and prognosis, but also the mandatory need of performance of screening for acute and chronic infection, prior the introduction of high dosage systemic immunosuppressors, including quantiferon test for tuberculosis and hepatitis serology, as a potential source of antigen/molecular mimicry, which is capable to produce antigens, complicating the pathogenesis of otherwise drug-induced pemphigus of various type.

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