The cutaneous form of pemphigus vulgaris of the pemphigus chancre type: clinical and therapeutic implications

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ABSTRACT

Introduction: Pemphigus vulgaris can show non-textbook clinical peculiarities, "pearls".

Case report: A middle-aged male presented with a single desquamating crust with impetiginisation in the parietal area of the scalp present for over 2 years. Clinicians initially suspected microbial causes of the disease, including folliculitis decalvans. The patient was prescribed oral itraconazole, and rifampicin with clindamycin without improvement. Since the H + E examination revealed unequivocal features of pemphigus vulgaris, the patient was referred for proper immunopathological diagnostics. Based on the clinical picture, H + E evaluation, direct immunofluorescence, which showed pemphigus IgG4 deposits, and multiparametric ELISA (increased level of anti-desmoglein 3 IgG antibodies), a cutaneous form of pemphigus vulgaris of the pemphigus chancre type was diagnosed. The patient received intralesional injections of betamethasone dipropionate/betamethasone phosphate and rituximab intravenously (total dose of 2 g) with significant improvement.

Conclusions: This patient illustrates that appropriate treatment, in non-emergency cases, should be implemented only after diagnosing patients at the clinical-laboratory level.

Key words: pemphigus vulgaris, scalp, pemphigus chancre.

INTRODUCTION

Pemphigus vulgaris (PV) belongs to the group of chronic autoimmune bullous diseases. PV is potentially lethal, and autoimmunity involves desmoglein 3 (DSG3) and, less specifically, desmoglein 1 (DSG1). The diagnosis is based on direct immunofluorescence (DIF) of the perilesional tissue, a series of biochemical and molecular tests, and, above all, careful analysis of the clinical presentation of patients, which should enable the selection of appropriate laboratory diagnostics [1]. The spectrum of symptoms and the course of the disease may vary significantly among patients, but the tendency to occupy the area of natural body orifices remains constant [2, 3]. There, as a result of acantholysis, suprabasilar blisters are formed, usually filled with serous fluid. The blisters rupture easily, leaving an erosion, and usually heal without scarring. In a significant number of cases, lesions are observed in the mucous membranes of the oral cavity, especially on the palate. Eruptions may also affect skin appendages, such as hair follicles, eccrine glands, and nail apparatus, where DSG1 and DSG3 are also

expressed [4]. A clinically significant peculiarity of PV is an efflorescence described in only a few classical textbooks as a pemphigus chancre, or a type of the primary symptom, i.e. a long-lasting single lesion [5]. A pemphigus chancre located on the scalp may precede the appearance of PV on the mucous membranes [6]. Such lesions may cause numerous doubts and problems at the stage of diagnosis and treatment due to their often non-stereotypical clinical picture. In the diagnosis of such cases, the use of minimally invasive DIF of scalp-plucked hair (DIFh) has been suggested [6].

OBJECTIVE

Presentation of the case of a patient with PV of the pemphigus chancre type and visualization of diagnostic difficulties at the clinical level related to the differentiation of diseases of the scalp.

CASE REPORT

A middle-aged male presented to the autoimmune bullous dermatoses clinic with a desquamating, scaly crust with impetiginisation located in the parietal region of the scalp. The localized lesion has persisted for more than 2 years. The patient admitted that clinicians initially suspected a microbial cause of the disease, including folliculitis decalvans, prescribing oral itraconazole and rifampicin along with clindamycin. This therapy did not improve the patient's clinical condition.

Only after receiving the result of the examination of the skin section stained with hematoxylin and eosin (H + E), in which unequivocal features of PV were found, such as suprabasilar acantholytic separation in the follicular and extrafollicular epithelium and "tombstoning", the patient was referred for proper immunopathological diagnosis. DIF showed pemphigus IgG4 deposits, while multiparameter ELISA showed an increased level of IgG antibodies to DSG3 (4.08, cut-off 1.0). Based on the clinical picture (fig. 1 A), H + E (figs. 1 B, C), DIF (fig. 1 D) and multiparametric ELISA tests, a cutaneous form of PV of the pemphigus chancre type was diagnosed.

The patient received intralesional injections of a combination of betamethasone dipropionate and betamethasone phosphate. The topical disinfectant and mechanical removal of crusts were also used. The patient was also given rituximab, according to the established scheme, a total of 2 g intravenously, together with oral methylprednisolone at an initial dose of 24 mg daily, then tapered. This combined

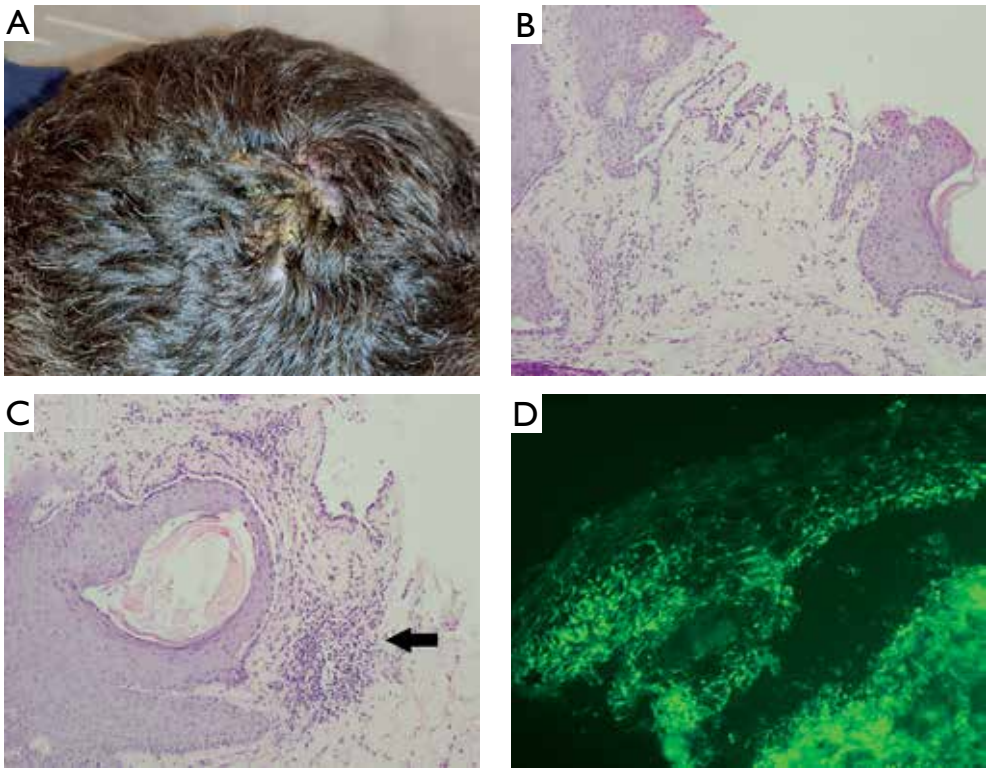

Figure 1. A middle-aged man with the cutaneous form of PV of the pemphigus chancre type. A single desquamating, scaly scab in the parietal area of the scalp (**A**). Suprabasilar acantholysis with tombstoning in the extrafollicular epithelium (**B**) and suprabasilar acantholytic dissection in the follicular epithelium with ectopic lymphoid structure (ELS) indicated by the arrow (**C**) (original lens magnification 20×). Pemphigus IgG4 deposits in the follicular and extrafollicular epithelium presenting dewdrops on a spiderweb appearance in DIF visualized with a blue light-emitting diode microscopy (**D**) (original lens magnification 40×)

treatment allowed for a significant improvement in the patient's clinical condition.

DISCUSSION

Lesions in the scalp always require a thorough and detailed differential diagnosis from the clinician, which should include not only infectious diseases, cancer, psoriasis, allergic or seborrheic dermatitis to name just a few, but also autoimmune diseases. Due to the abundant expression of DSG1 and DSG3, the scalp is a predilection site for PV [3]. The frequency of involvement of this area in patients is estimated between 16% and 60%, while lesions in this area appear first in the course of the disease in as many as 9–15% of patients. In the literature, they have been described as hard, scaly lesions or erosions, which rarely can lead to the development of scarring alopecia in the course of the disease. However, the abundant expression of pemphigus antigens in hair follicles allows for a highly effective diagnosis of PV by DIFh using confocal microscopy [7]. Several patients were described in the literature indexed in the PubMed database, in whom tufted hair folliculitis developed on the scalp in PV lesions that persisted for a long time, even for about 20 years [8]. More broadly, PV should be considered in the differential diagnosis of the causes of folliculitis decalvans.

One should remember the multiplicity of clinical pictures that can be presented by patients with bullous diseases. PV in our patient took the clinically misleading form of pemphigus chancre. Persistent pemphigus inflammatory lesions may be a result of a focal autoimmune response sustained by ectopic lymphoid-like structures (ELSs) (fig. 1 C), which are responsible for the local production of autoantibodies to DSG1 and DSG3. The local nature of this process may contribute to resistance to systemic treatment [9], suggesting the potential benefits of intensive local treatment, conceptually even surgical. Paradoxically, ELSs can localize the pemphigus process, reducing the risk of its generalization, which may be beneficial for patients. This type of aggressive treatment was used in the presented patient, who received intralesional injections of a combined glucocorticosteroid (GCS) preparation together with the systemic treatment, which led to control of the disease process.

Rituximab, a chimeric human-mouse monoclonal antibody that binds to the CD20 antigen present on the surface of B lymphocytes, which leads to the destruction of B lymphocytes through various mechanisms, is also successfully used in the treatment of PV. The effectiveness of PV treatment with rituximab has been confirmed by numerous clinical trials, which enabled the introduction of this drug in this indication both in the United States and in the European Union. Rituximab can be considered a highly effective and well-tolerated drug in PV therapy, allowing for a reduction in the dosage of GCS in moderate and severe cases [10]. The described case confirms the above reports, showing the positive effect of combination therapy after the use of a total dose of 2 g of intravenous rituximab. Rituximab therapy followed the intralesional injections of GCS in order to prevent the expected spreading of PV lesions as the titre of IgG antibodies to DSG3 was high.

On the side note of the described case, it should be emphasized that mastering the stereotypical clinical and laboratory features of diseases is the basis of good practice. Non-stereotypical casuistry is simply a supplement to this good practice, not a replacement for it.

CONCLUSIONS

Diseases from the group of autoimmune bullous dermatoses should be an important element in the differential diagnosis of lesions on the scalp. It is important to perform a thorough examination of a patient with scalp lesions, also by inspecting the mucous membranes, as pemphigus lesions in this area may co-occur or be preceded by the appearance of a pemphigus chancre on the scalp. A careful clinical examination should speed up the necessary laboratory diagnostic process. Due to diagnostic and therapeutic difficulties at the clinical level, immunopathological tests should be considered, which should minimize treatment failures.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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