PEMPHIGUS VEGETANS HALLOPEAU - ATYPICAL TRANSITION TO PEMPHIGUS VULGARIS

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Summary

Pemphigus vegetans represents a chronic autoimmune pathology within the bullous skin disorders, being one of the rarest clinical variants of pemphigus vulgaris. Due to its potentially fatal nature, the therapeutic management of patients with pemphigus vegetans always requires a multidisciplinary approach, especially due to the unpredictable nature given by the hyperactive immune status. This case presentation concerns a patient presenting to our clinic with intertriginous vegetative plaques with peripheral pustular clusters, with clinical improvement after administration of low-dose prednisone. The patient subsequently returns for recurrence of the bullous pathology, the lesions being clinically compatible with the classic form of pemphigus vulgaris, on second presentation.

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Introduction

Pemphigus vegetans is considered to be a rare variant of pemphigus vulgaris, constituting approximately 1-2% of all forms of pemphigus. [1] It differs from other forms of pemphigus by the presence of vegetative, warty plaques, especially in the intertriginous areas, as well as involvement of the oral mucosa. Age of onset is usually 40-60 years, and it is more common in women.[2] It can be clinically divided into 2 subtypes: Hallopeau and Neumann. Skin lesions of the Hallopeau form are represented by clusters of pustules that erode and form hypertrophic plaques. It is considered a less severe form with prompt response to treatment and good prognosis. The Neumann variant, has an onset similar to pemphigus vulgaris, with the appearance of friable bullae and erosions, areas on which subsequently form vegetative, exudative plaques in evolution.[1, 3] Prognosis is poorer in the latter form, induction of remission also requires higher doses of corticosteroid treatment, and relapses are more common.[4]

Case presentation

A 57-year-old female patient, smoker, on systemic treatment with itraconazole for onychomycosis, with no other significant personal

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pathological history, presents to our clinic for multiple intertriginous, vegetative erythematous-violaceous plaques. Subjectively, the lesions were accompanied by moderate painful sensation with a burning character. Anamnestically, the patient reports the onset of lesions one month prior to presentation to the hospital, in the form of pustules that subsequently converge and erode. At home she underwent local treatment with antiseptic and hydrating creams, without improvement of the symptoms.

The objective clinical examination showed vegetative, verrucous, exudative plaques with purulent deposits and clusters of millimetric pustules in the periphery of the lesions, variable diameter of the lesions approx. 5-20 cm, located under the abdominal, inguinal, bilateral axillary and submammary fold. Also, in the cephalic, suboccipital, retroauricular and jugal mucosa, the patient had multiple well-demarcated, round-oval erosions of about 1-2 cm in diameter.

At the time of admission, the patient was found with moderate neutrophilia and elevated inflammatory markers, without any other changes in the biological constants. The patient refused to undergo a biopsy, and in these circumstances, the stage diagnosis of Hallopeau's pemphigus vegetans was established on clinical grounds. Systemic treatment with prednisone 0.5 mg/kgc/day and systemic antibiotic therapy with amoxicillin and clavulanic acid is initiated until normalisation of the haemogram. Locally, the lesions were cleansed twice daily with fuchsin-based solution and boric acid 3%. Following a favourable clinical and paraclinical evolution, the patient was discharged with outpatient monitoring of the systemic treatment. Follow-up clinical examination one week after discharge showed remission of the pustules, as well as re-epithelialization of the erosions with areas of incipient post-inflammatory hyperpigmentation, without other subjective complaints.

The patient comes back one month after discharge to our clinic with new bullous lesions with positive Nikolsky sign, along with confluent postbullous erosions. Circumferentially thoracal, as well as palmo-plantar, round-oval flaccid bullae were present on an erythematous background, thin-walled with clear fluid, friable, approximately 1-2 cm in diameter. The postbullous erosions were confluent, variable in size, spontaneously bleeding, with the surface sporadically covered with purulent material. Bilateral jugal mucosal erosions were also present. The scalp (approximately 90% of the surface) showed multiple adherent, hardly removable crusts. Subjectively, the patient described intense pain with a burning character, exacerbated on palpation and when eating. In the intertriginous areas there was residual hyperpigmentation, with smooth, normal-looking tegument, without the presence of new lesions.

In order to support the stage diagnosis of pemphigus vulgaris classic form, the patient agreed to biopsy an intact bulla from the posterior chest. Histopathological examination revealed the presence of suprabasal cleavage, with lymphocytic dermal inflammatory infiltrate, with rare neutrophils and eosinophils, located

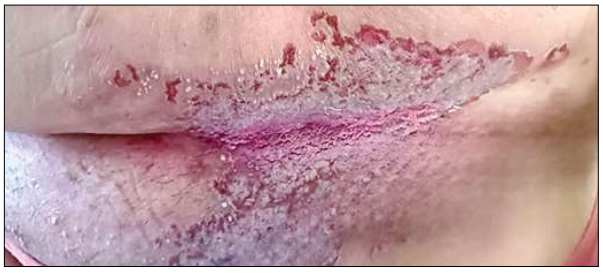


Figure 1. Vegetating plaque localised under the adipous abdominal pannus and peripherally arranged pustular clusters. Lesions are treated with fuchsin-based solution.

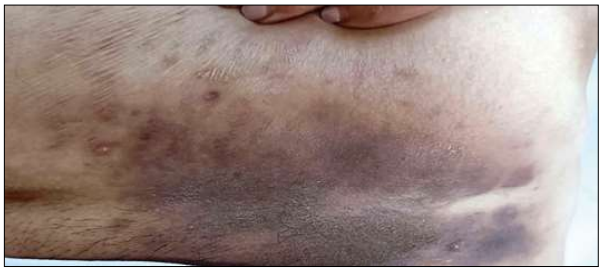
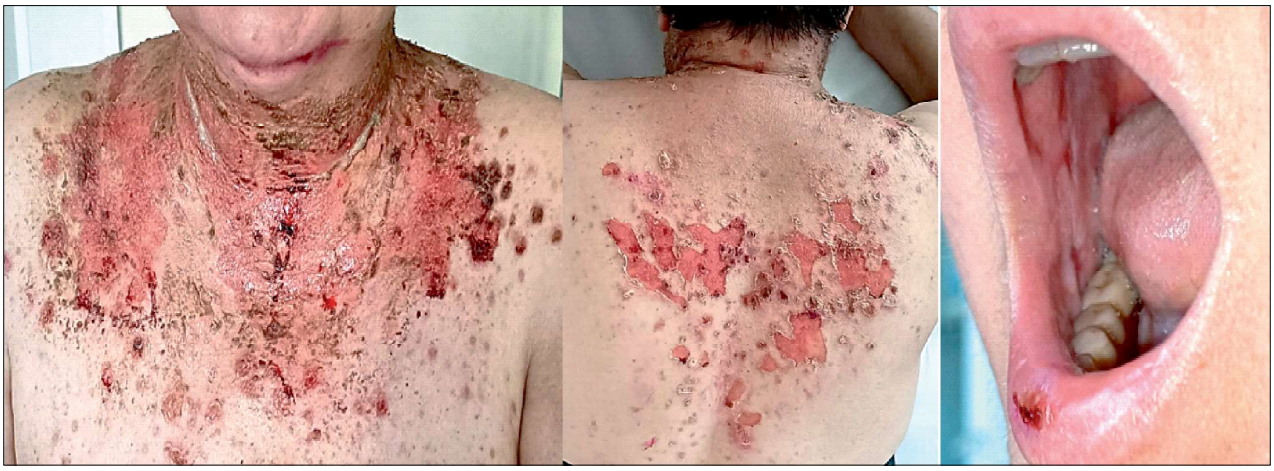


Figure 2. Hypertrophic plaque with postinflammatory hyperpigmentation, left iliac region.



A **B** **C**

Figure 3. ***A)*** *Confluated postbullous erosions - anterior thorax.* ***B)*** *Confluated postbullous erosions – posterior thorax* ***C)*** *Multiple erosions located on the lower lip vermilion and jugal mucosa.*

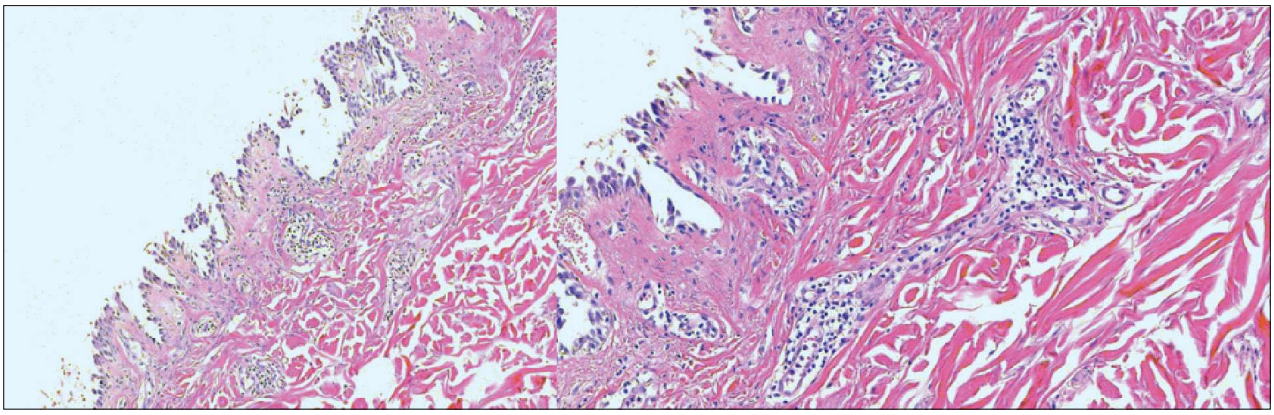


Figure 4. Histopathological features: Intraepidermal suprabasal cleft. Hematoxylin & Eosin.

perivascular and interstitial, thus confirming the nature of bullous pathology.

Systemic treatment with prednisone 1 mg/kgc/day and antibiotic therapy according to the antibiogram was initiated. Locally, exudative postbullous erosions were treated twice daily with 3% boric acid and fuchsin solution. After moistening the crusts with saline solution methylprednisolone aceponate-based preparations were applied. During hospitalisation, the patient developed cortisone diabetes, and glycaemia was rebalanced by insulin administration according to the scheme established by the diabetologist. The evolution was slowly favourable over 6 weeks, with crusting of the erosions and subsequent re-epithelialization of the tegument.

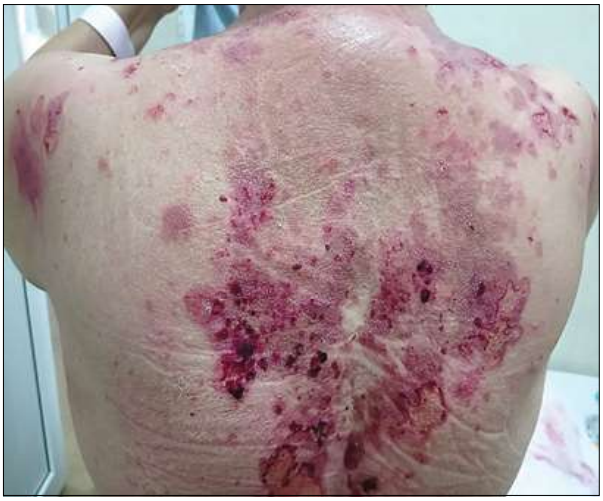


Figure 5. Re-epithelialization of the tegument ½ upper back. Postbullous erosions ½ lower back.

Discussions

Pemphigus is a globally occurring, potentially fatal, bullous autoimmune dermatosis divided into 4 major categories: vulgaris (most common), foliaceous, paraneoplastic and the IgA form.[5] The vegetative form is considered to be a rare subtype of pemphigus vulgaris, with a higher prevalence among women in their 4-6th decade of age.[6] The etiopathogenesis of the disease involves anti-desmoglein 3 and anti-desmoglein 1 IgG antibodies, as well as anti-desmoglein 1 and 2 antibodies.[7] Factors triggering the autoimmune response include viral infec-tions, diet, contact allergens or medication, especially those with sulfhydryl and amide groups such as captopril, other ACE inhibitors or diclofenac.[8] Clinically, pemphigus vegetans is characterised by hypertrophic plaques located mainly intertriginous, with peripherally arranged pustular clusters.[9] Oral lesions often represent the mode of onset of the disease. The mechanism of vegetation formation is poorly understood and is currently linked to epithelial proliferation and eosinophilic chemotaxis following strong anti-genic stimulation.[2] Histopathologically, besides suprabasal acantholysis, characteristic of this form is the presence of epidermal hyperplasia, papillomatosis and eosinophilic abscesses.[4] Diagnosis of the vegetant form is established on the basis of clinical appearance, histopathological examination and the presence of autoantibodies.[7] The current therapeutic standard is broadly based on systemic immunosuppression, either classically with corticosteroids or with azathioprine, dapsone or methotrexate and cyclophosphamide as viable alternatives.[8] It has been shown that the administration of biological therapy, specifically treatment with Rituximab, a monoclonal antibody against CD20, is effective in pemphigus, reducing the need for corticosteroid or other immunosuppressive treatments.[10]

Our case was challenging in terms of diagnostic difficulties, disease progression, and therapeutic management. Initially, the lesions were clinically compatible with the Hallopeau subtype of pemphigus vulgaris, with prompt response to low-dose corticosteroid treatment and rapid remission. The evolution of the disease following gradual tapering of corticosteroid therapy, however, was atypical, the lesions developing the clinical character of classic pemphigus vulgaris with slow response to high-dose systemic corticosteroid therapy. The palmoplantar involvement during the second flare also reveals the unusual character of the clinical transition between forms and subtypes of pemphigus vulgaris.

Conclusions

The atypical transition from the rare form of Hallopeau's pemphigus vegetans to the classic form of pemphigus vulgaris highlights the dynamic nature of autoimmune dermatoses and raises the question of unravelling the immunological mechanism underlying the pathology, the control of which is the key to therapeutic success. This case presentation also reveals the importance of careful long-term monitoring of patients in order to detect erly any changes that could change the clinical classification of a pathology, thus instituting promptly and successfully an appropriate therapeutic protocol through a multidisciplinary dermatologist-infectionist-immunologist collaboration.

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Conflict of interest
NONE DECLARED

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