Painful Oral, Groin, and Scalp Lesions in a Young Man

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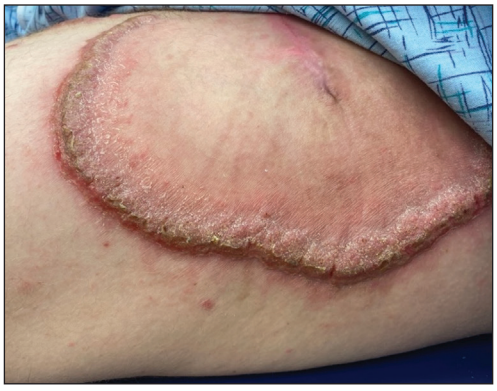

A 27-year-old man presented to the dermatology department with painful oral and groin lesions of 2 years' duration as well as lip ulceration that had been present for 1 month. The patient also reported moderately tender scalp and face lesions that had been present for several weeks. The lip ulceration was previously treated by his primary care provider with valacyclovir (1 g daily for 2 weeks) without improvement. Six months prior to the current presentation, we treated the groin lesions as condyloma involving the perineum and genital region at our clinic with no response to cryotherapy, topical imiquimod, or extensive surgical excision with skin grafting. Pathology at the time showed condyloma but was negative for human papillomavirus. Physical examination at the current presentation revealed superficial erosions along the vermilion border. The oral mucosa exhibited cobblestoning, and fissures were present on the tongue. Eroded pink plaques studded with vesicles were present on the vertex scalp and left chin. The bilateral inguinal regions extending to anterior-lateral upper thighs and posterior buttocks revealed erythematous, arcuate, and annular erosive plaques with verrucous hyperkeratotic borders and fissuring on the leading edge. Pink erosive and verrucous erythematous plaques were noted on the penile shaft, scrotum, and perineum. Punch biopsies of the scalp and left anterior thigh as well as direct immunofluorescence were performed.

WHAT'S YOUR **DIAGNOSIS?**

a. bullous pemphigoid
b. bullous systemic lupus erythematosus
c. dermatitis herpetiformis
d. pemphigus vegetans
e. pemphigus vulgaris

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THE **DIAGNOSIS:** Pemphigus Vegetans

Histopathologic examination of the biopsies from the scalp and left anterior thigh revealed suprabasal clefting with acantholytic cells extending into the follicular infundibulum with eosinophilic pustules within the epidermis. The dermis contained perivascular lymphohistiocytic and eosinophilic inflammatory infiltrates without viral cytopathic effects (Figure 1). Direct immunofluorescence revealed strong IgG and moderate IgA pericellular deposition around keratinocyte cytoplasms (Figure 2). Serologic evaluation demonstrated anti–desmoglein 3 antibodies. Based on the clinical presentation and histopathologic correlation, a diagnosis of pemphigus vegetans was made.

Pemphigus vegetans is a vesiculobullous autoimmune disease that is similar to pemphigus vulgaris but is characterized by the formation of vegetative plaques along the intertriginous areas and on the oral mucosa.[1] It is the rarest variant of all pemphigus subtypes and was first described by Neumann in 1876.[2] There are 2 subtypes of this variant: Hallopeau and Neumann, each with unique characteristics and physical manifestations. The Hallopeau type initially manifests with pustular lesions that rupture and evolve into erosions that commonly become infected. Gradually they merge and multiply to become more painful and vegetative.[3] It has a more indolent course and typically responds well to treatment, and prolonged remission can be reached.[4] The Neumann type is more severe and manifests with large vesiculobullous and erosive lesions that rupture and ulcerate, forming verrucous crusted vegetative plaques over the erosions.[5] The erosions along the edge of the lesions induce new vegetation, becoming dry, hyperkeratotic, and fissured.[3] The Neumann type often requires higher-dose steroids and typically is resistant to treatment.[4] Patients can present with oral stomatitis and occasionally can develop a fissured or cerebriform appearance of the tongue, as seen in our patient (Figure 3).[1,2] Nail changes include onychorrhexis, onychomadesis, subungual pustules, and ultimately nail atrophy.[5]

Pemphigus diseases are characterized by IgG autoantibodies against desmoglein 3 and/or desmoglein 1. These are components of desmosomes that are responsible for keratinocyte adhesion, disruption of which results in the blister formation seen in pemphigus subtypes. The unique physical manifestation of pemphigus vegetans is thought to be due not only to autoantibodies against desmogleins 1 and 3 but also to autoantibodies against desmocollin 1 and 2.[1]

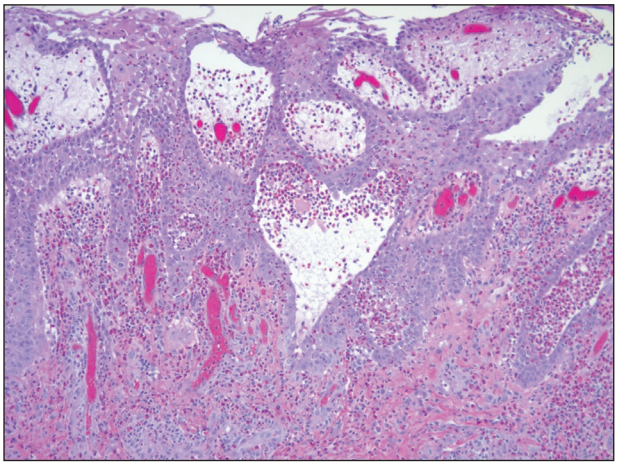

FIGURE 2. Pemphigus vegetans. Punch biopsy showed diffuse eosinophilic infiltrate with suprabasal clefting and acantholytic cells extending into the follicular infundibulum (H&E, original magnification ×40).

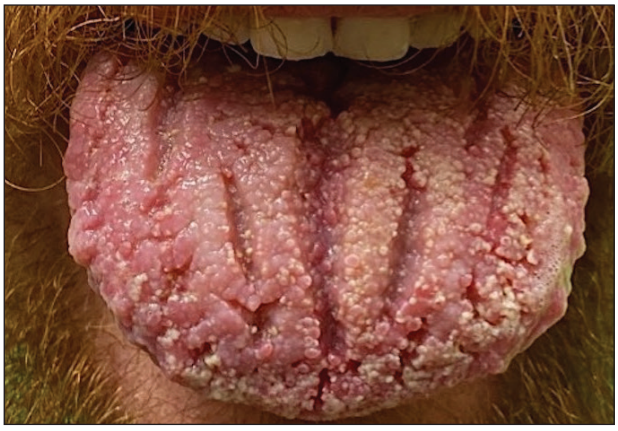

FIGURE 1. Fissures and cerebriform appearance of the tongue in pemphigus vegetans.

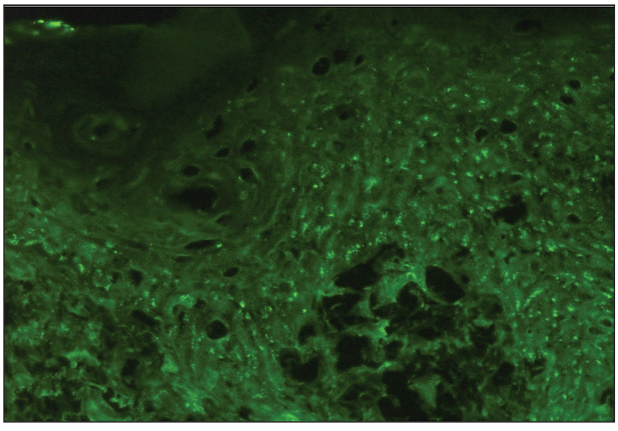

FIGURE 3. Direct immunofluorescence showed pericellular IgG and IgA deposition.

Histopathologic examination reveals hyperkeratosis and pseudoepitheliomatous hyperplasia with acantholysis that creates a suprabasal cleft. Basal cells remain intact to the basement membrane by hemidesmosomes, resulting in a tombstone appearance. The Hallopeau type typically manifests with a large eosinophilic inflammatory response, leading to eosinophilic spongiosis and intraepidermal microabscesses. The Neumann type manifests with more of a neutrophilic and lymphocytic infiltrate, accompanied by the eosinophilic response.[1] For evaluation, obtain histopathology as well as direct immunofluorescence or enzyme-linked immunosorbent assay to look for intracellular deposition of desmoglein autoantibodies.

First-line treatment for pemphigus vulgaris and its variants is rituximab, an anti-CD20 monoclonal antibody. It has also been shown to have therapeutic benefit with combination of corticosteroids and rituximab. Corticosteroids should be given at a dose of 1 mg/kg daily for 2 to 4 weeks. Other immunosuppressive agents (steroid sparing) include azathioprine, dapsone, mycophenolate mofetil, methotrexate, cyclophosphamide, cyclosporine, and intravenous immunoglobulin. Pulse therapy with intermittent intravenous corticosteroids and immunosuppressants is another second-line therapeutic option. Topical therapeutic options include steroids, tacrolimus, and nicotinamide with oral tetracycline at onset and relapse. The goal of therapy is to maintain remission for 1 year then slowly taper treatment over another year.[1]

Our patient initially was treated with prednisone, and subsequent courses of azathioprine and mycophenolate mofetil failed. He then was treated with 2 infusions of rituximab that were given 2 weeks apart. He was able to taper off the prednisone 1 month after the last infusion with complete remission of disease. He has been disease free for more than 9 months postinfusion.

Differential diagnoses for pemphigus vegetans can include bullous pemphigoid, bullous systemic lupus erythematosus, dermatitis herpetiformis, and pemphigus vulgaris. Lesion characteristics are key to differentiating pemphigus vegetans from other autoimmune blistering disorders. Bullous pemphigoid will manifest with tense blisters where pemphigus vulgaris will be flaccid; this is due to the difference in autoantibody targets between the conditions. Diagnosis depends on clinical presentation and histopathologic findings.

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