Verrucous Scalp Plaque and Widespread Eruption

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A 40-year-old Black man presented for evaluation of a thick plaque throughout the scalp (top), scaly plaques on the cheeks (bottom), and a spreading rash on the trunk that had progressed over the last few months. He had no relevant medical history, took no medications, and was in a monogamous relationship with a female partner. He previously saw an outside dermatologist who gave him triamcinolone cream, which was mildly helpful. Physical examination revealed a thick verrucous plaque throughout the scalp extending onto the forehead; thick plaques on the cheeks; and numerous, thinly eroded lesions on the trunk. Biopsies and a laboratory workup were performed.

WHAT’S YOUR DIAGNOSIS?

a. disseminated blastomycosis
b. hypertrophic lupus erythematosus
c. pemphigus foliaceous
d. sebopsoriasis
e. secondary syphilis

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THE DIAGNOSIS:
Pemphigus Foliaceous

Laboratory workup including a complete blood cell count with differential, comprehensive metabolic panel, antinuclear antibodies, Sjögren syndrome A and B antibodies, hepatitis profile, rapid plasma reagin, HIV screen, aldolase, anti–Jo-1, T-Spot TB test (Quest Diagnostics), and tissue cultures was unremarkable. Two 4-mm punch biopsies were obtained from the left cheek and upper back, both of which demonstrated intragranular acantholysis suggestive of pemphigus foliaceous (Figure 1A). A subsequent punch biopsy from the right lower abdomen sent for direct immunofluorescence demonstrated netlike positivity of IgG and C3 in the upper epidermis (Figure 1B), and serum sent for indirect immunofluorescence demonstrated intercellular IgG antibodies to desmoglein (Dsg) 1 on monkey esophagus and positive Dsg-1 antibodies on enzyme-linked immunosorbent assay, confirming the diagnosis.

The patient was started on a 60-mg prednisone taper as well as dapsone 50 mg daily; the dapsone was titrated up to 100 mg daily. After tapering down to 10 mg daily of prednisone over 2 months and continuing dapsone with minimal improvement, he was given 2 infusions of rituximab 1000 mg 2 weeks apart. The scalp plaque was dramatically improved at 3-month follow-up (Figure 2), with partial improvement of the cheek plaques (Figure 3). Dapsone was increased to 150 mg daily, and he was encouraged to use triamcinolone acetonide ointment 0.1% twice daily, which led to further improvement.

Pemphigus foliaceus is an autoimmune blistering disease that most commonly occurs in middle-aged adults. It generally is less common than pemphigus vulgaris, except in Finland, Tunisia, and Brazil, where there is an endemic condition with an identical clinical and histological presentation known as fogo selvagem.1

The pathogenesis of pemphigus foliaceous is characterized by IgG autoantibodies against Dsg-1, a transmembrane glycoprotein involved in the cellular adhesion of keratinocytes, which is preferentially expressed in the superficial epidermis.2,7 Dysfunction of Dsg-1 results in the separation of superficial epidermal cells, resulting in intraepidermal blisters.2,7 In contrast to pemphigus vulgaris, there typically is a lack of oral mucosal involvement due to compensation by Dsg-3 in the mucosa.4 Potential triggers for pemphigus foliaceous include exposure to UV radiation; radiotherapy;
Rituximab with short-course prednisone has been found to be more effective in achieving complete remission at 24 months than prednisone alone. In patients with contraindications to systemic glucocorticoid therapy, rituximab has been shown as an effective first-line therapy.

One-quarter of patients treated with rituximab relapsed within 2 years of treatment (average time to relapse, 6–26 months). High-dose rituximab regimens, along with a higher number of rituximab treatment cycles, have been shown to prolong time to relapse. Further, higher baseline levels of Dsg-1 antibody have been correlated to earlier relapse and can be used following rituximab therapy to monitor disease progression.

The differential diagnosis for pemphigus foliaceous includes disseminated blastomycosis, hypertrophic lupus erythematosus, sebopsoriasis, and secondary syphilis. Disseminated blastomycosis presents with cutaneous manifestations such as nodules, papules, or pustules evolving over weeks to months into ulcers with subsequent scarring. Hypertrophic lupus erythematosus presents with papules and nodules with associated keratotic scaling on the face, palms, and extensor surfaces of the limbs. Sebopsoriasis is characterized by well-defined lesions with an overlying scale distributed on the scalp, face, and chest. Secondary syphilis presents as early hyperpigmented macules transitioning to acral papulosquamous lesions involving the palms and soles.

Diagnosis of pemphigus foliaceous typically is made using a combination of histology as well as both direct and indirect immunofluorescence. Histologically, pemphigus foliaceous presents with subcorneal acantholysis, which is most prominent in the granular layer and occasionally the presence of neutrophils and eosinophils in the blister cavity. Direct immunofluorescence demonstrates netlike intercellular IgG and C3 in the upper portion of the epidermis. Indirect immunofluorescence can help detect circulating IgG antibodies to Dsg-3, with guinea pig esophagus being the ideal substrate.

First-line treatment of pemphigus foliaceous consists of systemic glucocorticoid therapy, often administered with azathioprine, methotrexate, or mycophenolate mofetil. Although first-line treatment is effective in 60% to 80% of patients, relapsing cases can be treated with cyclophosphamide, intravenous immunoglobulin, immunoadsorption, plasmapheresis, or rituximab.

Rituximab is a chimeric monoclonal antibody targeting CD20+ B cells, leading to decreased antibody production, which has been shown to be effective in treating severe and refractory cases of pemphigus foliaceous.

References