Pemphigus Foliaceus in an Otherwise Healthy 35-Year-Old Male

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Abstract

We report a classic case presentation of the rarely seen disease pemphigus foliaceus in a 35-year-old Salvadorian male with no past medical history. There is no universal gold standard for pemphigus disease treatment, and practitioners and patients should be aware that treatment may need to be adjusted during the clinical course of the disease. Immunofluorescence biopsy and antibody titers can help establish the diagnosis. We discuss the clinical features, pathophysiology, histology, disease course and treatment of pemphigus foliaceus.

Introduction

Pemphigus foliaceus (PF) is a rare autoimmune disorder characterized by subcorneal acantholysis mediated by IgG anti-desmoglein-1 (DSG-1) antibodies. We encountered a case of PF in a Hispanic patient seen initially by the emergency room physician. The clinical presentation of this condition is characterized by often-thick keratotic scale on an erythematous base with neither bullae formation nor mucosal involvement, as was the case with our patient. Immunofluorescence patterns and specific antibody titers help to establish the PF diagnosis; however, the presentation may at times overlap significantly with other forms of pemphigus, so it is important for the practitioner to obtain a biopsy. There is no gold-standard algorithm for pemphigus management,[1] and patients and physicians should be aware that it may be chronic and difficult to treat, requiring multiple follow-ups. Patients should be informed that treatment may need to be adjusted throughout the clinical course of the disease to maintain remission.

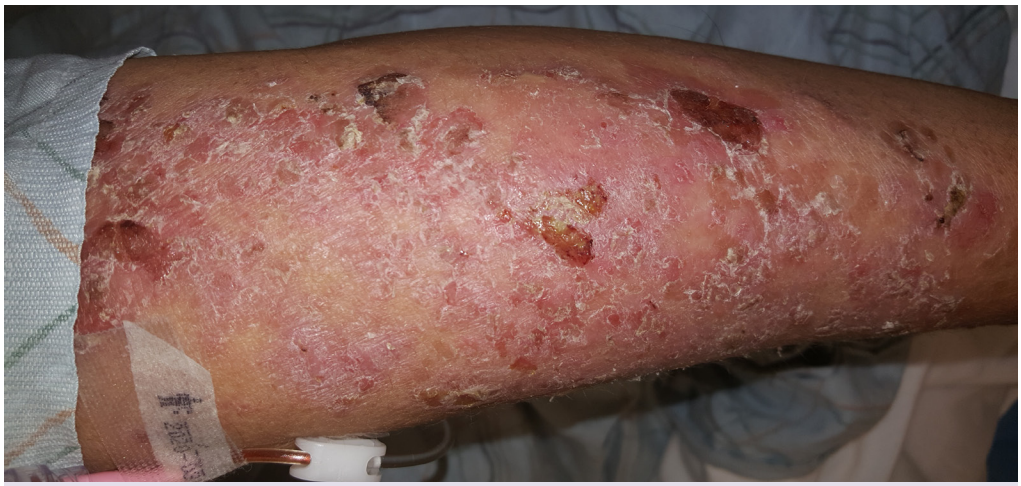

Figure 1. Erythematous, crusted and scaling lesions on the upper extremity.

Case Report

An otherwise healthy, 35-year-old Salvadorian male with no past medical history presented with a three-week history of a cutaneous eruption that began on the face and scalp. It progressed to the chest, back, abdomen, and extremities. He denied pain and had no household contacts with similar symptoms. He denied any medication use. Further, the patient denied both family and personal history of skin diseases. He did report bilateral eye discharge, but denied visual changes, arthralgia, gastrointestinal symptoms, dysphagia, odynophagia, dysphonia, dysuria, and fever.

The patient complained of a warm sensation to the skin and mild pruritus in the involved areas. He denied pain even in denuded or excoriated areas. The mucous membranes were asymptomatic, with no sensations of pain or paresthesia in the oral, genital or ocular mucosae.

Laboratory values were significant only for a leukocytosis of 12,500 and a platelet count of 431,000. Other serum laboratory values, including complete blood count, basic metabolic panel, and lactate level, were unremarkable.

Physical examination revealed diffuse, erythematous, scaly macules, papules, patches, and plaques, with multiple areas where the lesions appeared to be confluent. There were some areas of superficial ulceration and excoriations on the face (especially malar distribution), extremities, and trunk (**Figures 1-4,** p. 41-42). There was thick keratotic debris, most notably on the scalp but also on other involved skin areas, although to a lesser

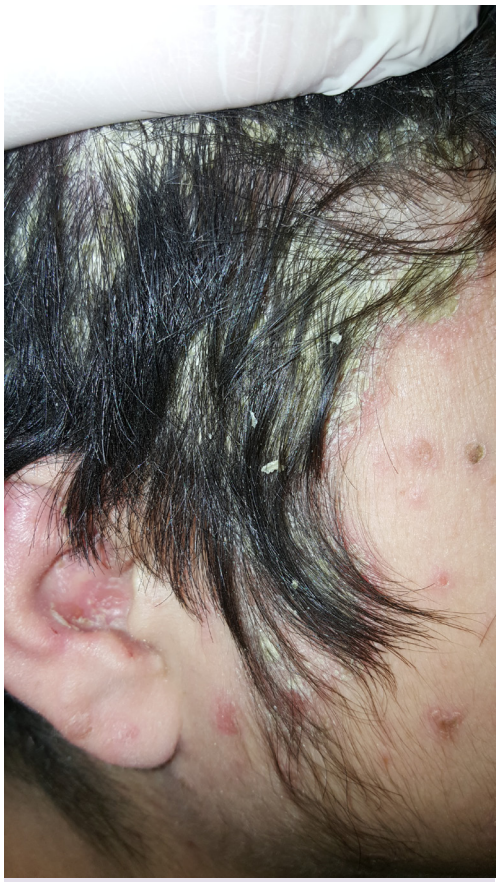

Figure 2. Scaling, erythematous plaques on the scalp.

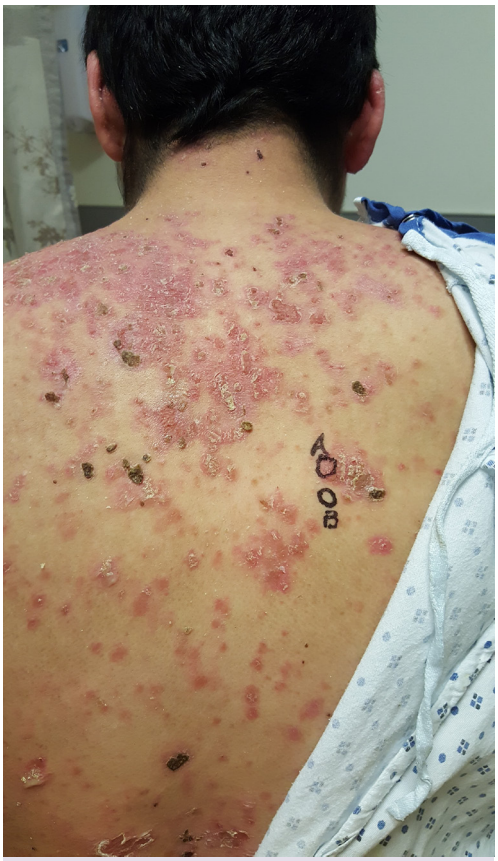

Figure 3. Diffuse, erythematous, scaling and crusting papules and plaques on the posterior trunk.

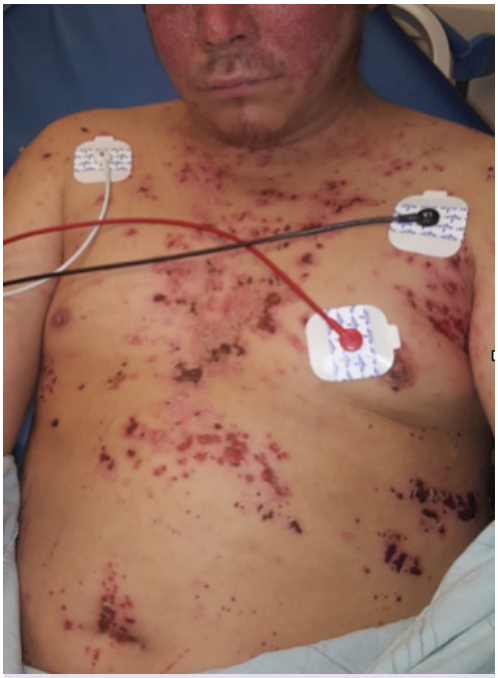

Figure 4. Erythematous, scaling plaques on the face, as well as papules, plaques, erosions and crusting on the anterior trunk.

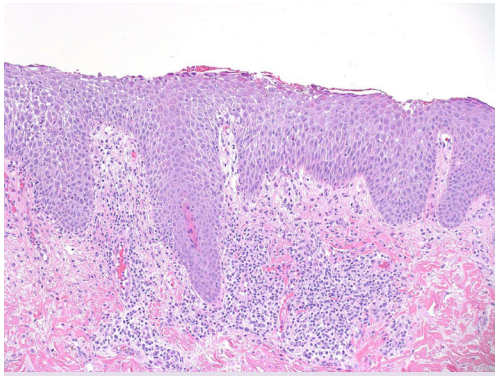

Figure 5. Subtle subcorneal acantholysis (H&E, 20x).

degree. The patient did have injected bilateral conjunctiva with purulent discharge. There was no evidence of oral or urethral mucosal lesions.

A rapid HIV screen was performed in the emergency department with a negative result. He was admitted for treatment of suspected disseminated herpes zoster and started on IV acyclovir. After two days of unsuccessful antiviral treatment, two punch biopsies were performed from both lesional and perilesional skin. They were sent for H&E/PAS staining and direct immunofluorescence, respectively. The acyclovir was stopped and IV fluconazole was started, along with 20 mg IV piggyback methylprednisolone daily. The patient rapidly improved and was discharged after seven days on a five-day oral prednisone taper with instructions to follow up at the community dermatology clinic in one month.

A punch biopsy of the back with H&E stain revealed a subtle subcorneal acantholysis suspicious for pemphigus foliaceus. Direct Immunofluorescence showed weak cell-surface staining with IgG and IgA, as well as patchy staining of fibrinogen connective-tissue fibers. The sample was negative for both IgM and C3 (**Figure 5**).

The patient presented approximately one month later to the community outpatient dermatology clinic as directed, showing only mild to moderate improvement of the condition. He was started on mycophenolate mofetil at a dose of 2 g daily and a five-day prednisone taper. At follow-up, he reported improvement while on the prednisone taper but a rebound after its completion despite the mycophenolate addition. He is currently being maintained on the mycophenolate and 10 mg of oral prednisone daily. The condition has improved slightly, but flares persist.

Discussion

There are six major types of disorders in the pemphigus family, features of which can overlap in the same patient: pemphigus vulgaris, pemphigus herpetiformis, IgA pemphigus, paraneoplastic pemphigus, drug-induced pemphigus, and pemphigus foliaceus. Pemphigus foliaceus has three subtypes: 1) classic or sporadic PF, 2) pemphigus erythematosus, a more limited form of the disease, and 3) endemic PF (fogo selvagem), typically seen in indigenous South American populations. The three entities present with identical histological findings.

While pemphigus foliaceus occurs globally, the epidemiology of the disease can change based on location. For example, in Brazil, endemic PF occurs 20 times more frequently than pemphigus vulgaris.[5] In a Finnish study, pemphigus erythematosus was the most common pemphigus disorder out of 44 patients, and pemphigus vulgaris and pemphigus foliaceus occurred at the same rate.[6] A study of 148 pemphigus patients in Turkey found that 83.1% of patients had pemphigus vulgaris, 8.8% had pemphigus foliaceus, and 4% had pemphigus erythematosus.[4] HLA polymorphisms can be dependent on the geographic location of patients, which may account for the regional variations in pemphigus-foliaceus epidemiology.

Pemphigus foliaceus is a rare immunobullous disease that can have localized or diffuse manifestations. It typically occurs in patients aged 40 to 60 years and affects males and females equally.[2] Classic features of PF include erythematous papules and plaques with crusting, scaling and erosion, without mucosal involvement, on the face, scalp and trunk, often called a "seborrheic" distribution. It commonly presents as erosions demonstrating a positive Nikolsky sign, as pemphigus vulgaris does. Patients are rarely ill-appearing. The most severe form of PF presents with exfoliative erythroderma.[2] In all forms, there are detectable serum IgG antibodies against DSG-1. The primary histologic feature is subcorneal acantholysis. This finding may be indistinguishable from that seen in bullous impetigo, with which it shares a common autoantigen. The key to PF diagnosis is direct immunofluorescence (DIF) demonstrating IgG autoantibodies and C3 on the epidermal cell surface. Pemphigus foliaceus has been associated with several HLA polymorphisms, indicating a genetic predisposition.[3]

Endemic PF, also known as fogo selvagem, presents like other PF subtypes but is most commonly seen in Brazilian patients.[11] It is also found elsewhere in South America as well as in Central America, Algeria, Finland, Morocco and Tunisia.[5] Patients tend to be young adults who spend a good deal of time in outdoor activities.[12] The incidence of new cases increases at the end of the rainy season.[5] The disease tends to occur in patients of lower socioeconomic status, and the condition improves when the living conditions improve.[13] It is associated with IgM and IgE antibodies against DSG-1.[12] Patients with endemic pemphigus foliaceus have an association with HLA class II alleles, indicating a possible underlying genetic susceptibility in these patients.[14] There is evidence that a prior antigenic response to an environmental factor may help trigger the DSG-1 antibodies.[12] More specifically, patients may have IgG1 against DSG-1, but the onset of clinical disease appears to be associated with a significant rise in IgG4.[15] The condition typically affects the face and upper trunk. There is a localized form, which has a good prognosis and may spontaneously remit. The generalized form tends to be more aggressive.[11] Systemic corticosteroids are the therapy of choice for endemic PF.

Pemphigus erythematosus (PE), also known as Senear-Usher syndrome, can present as vesicles, bullae, or scaly plaques over seborrheic areas, the malar area, the trunk or the extremities.[3,16] PE is considered a localized form of pemphigus foliaceus. It shares features with lupus erythematosus, including a positive ANA and histological findings of IgG or IgM granular deposits and C3 at the dermoepidermal junction.[16] However, most patients with PE do not have lupus erythematosus. Cases have shown a possible link between psychiatric disorders and pemphigus, with a recent report of two cases of pemphigus erythematosus associated with bipolar disorder.[17] There are also several cases of thymoma associated with pemphigus erythematosus.[18-20]

Conclusion

We report a case of pemphigus foliaceus in an otherwise healthy 35-year-old male. The clinical presentation of this condition is often characteristic but may overlap significantly with other forms of pemphigus. Immunofluorescence patterns and specific antibody titers may help to establish this rare diagnosis. Patients and clinicians should be aware that there is no universally accepted treatment algorithm, and thus treatment will vary from patient to patient in order to establish optimal remission.

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