Eosinophilic Pustular Folliculitis: Case Report and Review of the Literature

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Eosinophilic pustular folliculitis (EPF) is a rare dermatosis characterized by recurrent outbreaks of papulopustular skin lesions mainly distributed in seborrheic areas. These eruptions often are associated with peripheral blood eosinophilia and occur mainly on the face, upper back, and upper extremities. There are 3 variants: classic EPF (Ofuji disease), immunosuppression-associated EPF, and infancy-associated EPF. We report a human immunodeficiency virus (HIV)–seronegative patient with classic EPF who responded to treatment with indomethacin.

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Eosinophilic pustular folliculitis (EPF), first described by Ise and Ofuji[1] in 1965 in a Japanese woman, is a rare dermatosis characterized by recurrent outbreaks of papulopustular skin lesions mainly distributed in seborrheic areas. These eruptions occur mainly on the face, upper back, and upper extremities, and often are associated with peripheral blood eosinophilia. There are 3 variants: classic EPF (Ofuji disease), immunosuppression-associated EPF, and infancy-associated EPF. These entities are histologically indistinguishable; however, there are clinical differences. We report a human immunodeficiency virus (HIV)–seronegative patient with classic EPF who responded to treatment with indomethacin.

Case Report

A 36-year-old white man presented with a waxing and waning pruritic rash of 7 months' duration that was first noted on his forearm as small bumps and progressively spread to his trunk and face. On physical examination there were well-demarcated, slightly scaly, erythematous plaques in an annular configuration with follicular papules at the margins and central clearing. The lesions were urticarialike. No pustules were noted. The lesions were present on the back, extensor surface of the arms, chest, abdomen, and forehead, and ranged in size from 2 to 10 cm (Figure 1). His palms and soles were clear of similar lesions.

The patient's medical history was remarkable only for seasonal allergies, asthma, and leukopenia. His medications included fexofenadine hydrochloride and escitalopram oxalate, which he had been taking for several years prior to the cutaneous eruption. This condition had been treated over the last 7 months with various systemic and topical corticosteroids with temporary improvement of the lesions; however, once the medications were stopped, the dermatosis flared.

Laboratory investigations included an antinuclear antibody test, HIV serum assay, and anti-Ro/anti-La antibody test, which were all within reference range. A bone marrow biopsy was performed to work up his leukopenia and the results were negative. The only abnormal laboratory value was an elevated peripheral eosinophil count of 11% (reference range, 0%–6%). To elucidate the cause, a stool sample was obtained for ova and parasites, which also was negative. Skin swabs for microscopy and culture as well as scrapings for mycology were all negative.

Biopsy specimens from the arm and back demonstrated periadnexal inflammatory cell infiltrates composed of lymphocytes, histiocytes, neutrophils, and large numbers of eosinophils. The inflammation surrounded as well as invaded the follicular structures and the follicular epithelium was spongiotic. A similar inflammatory infiltrate also was noted about the adjacent vessels (Figure 2). A periodic acid–Schiff stain was negative for fungi.

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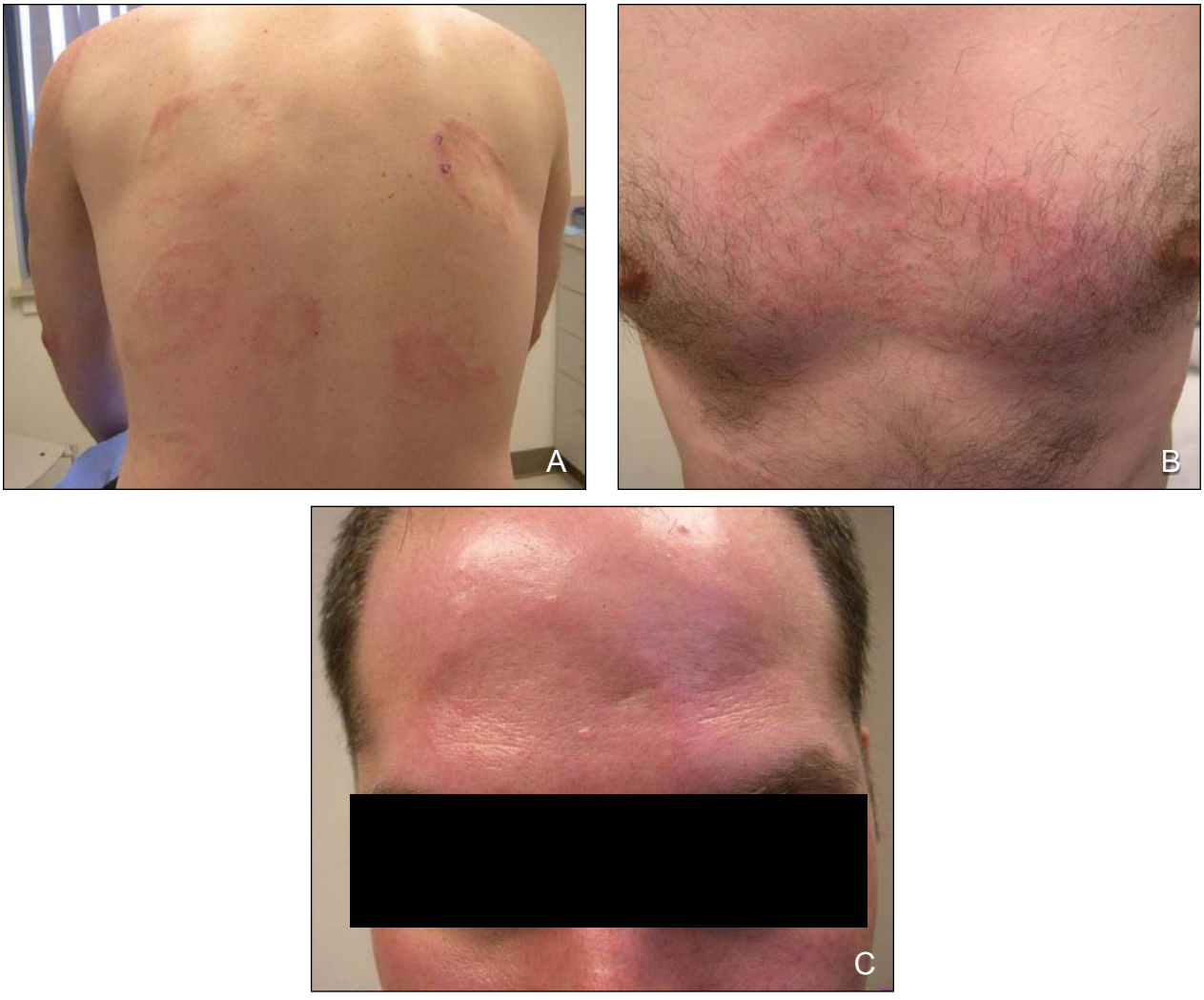

Figure 1. Well-demarcated annular plaques with central clearing were noted on the back (A). An erythematous plaque developed on the chest with follicular papules at the margins (B). A somewhat urticarialike plaque presented on the forehead (C).

A diagnosis of EPF was made and the patient was prescribed indomethacin 50 mg twice daily. After 1 week of treatment, marked improvement was seen in the clinical appearance of the eruptions on his face and trunk. The patient currently is on indomethacin 50 mg once daily with good control.

Comment

Classic EPF, or Ofuji disease, was first described by Ise and Ofuji[1] in 1965 in a Japanese woman with recurrent episodes of follicular pustules accompanied by peripheral blood eosinophilia. By 1970, 3 additional cases were observed and Ofuji et al[2] thus coined the term *eosinophilic pustulous folliculitis*.[3]

Classic EPF is a rare chronic disease characterized by recurrent annular clusters of sterile follicular papules and pustules superimposed on erythematous plaques with central clearing and peripheral extension (Table). Individual clusters last for 7 to 10 days and tend to relapse every 3 to 4 weeks. Resolution of the lesions occasionally leaves residual postinflammatory hyperpigmentation, as seen in our patient.[4]

The face, trunk, and extremities are the sites usually involved, with lesions occurring on the face in 85% of affected individuals and on the back in up to 59% of cases. However, the distribution of lesions also can include the palms and soles, despite the fact that follicles are not found in either palms or soles.[5] Interestingly, palmar and plantar involvement has been reported to affect as many as one-fifth of patients and may be the presenting feature.[6] Mild to moderate leukocytosis with eosinophilia is

Clinical Characteristics of Eosinophilic Pustular Folliculitis (EPF)

Characteristics	Clinical Features	Age	Race	Sex	Symptoms	Clinical Course
Classic EPF (Ofuji disease)	Annular erythematous plaques studded with papules and pustules with central clearing	Third to fourth decades of life	Asian	Predominantly males	Pruritus	Lesions subside leaving behind postinflammatory hyperpigmentation; recurrences over months
Immunosuppression-associated EPF	Erythematous urticarial papules	Third to fourth decades of life	Any	Homosexual males	Pruritus	Chronic and persistent
Infancy-associated EPF	Multiple sterile papulopustules involving the scalp and brows	Infancy	White	Predominantly males	Pruritus	Self-limiting course with an intermittent recurrence

seen in up to 35% of patients; generally there is no other systemic involvement.[5,7]

Although classic EPF is mainly found in Japanese individuals, the incidence in Europe and the United States has been increasing. Males are affected more frequently than females (5:1 ratio) in all 3 variants of EPF, and the peak age for classic EPF and immunosuppression-associated EPF is the third to fourth decades of life.[4]

It is important to obtain an entire papule or pustule with associated follicle during biopsy to ensure an adequate sample for histologic examination and diagnosis. Because EPF is a folliculocentric finding, serial sections may be needed to examine the inflamed hair follicle. The histopathologic features of all forms of EPF include inner follicular sheath spongiosis and infiltration by eosinophils and lymphocytes in and around hair follicles at the level of the follicular isthmus that may rarely progress to complete destruction of follicles. A reactive follicular mucinosis may be seen as mucinous degeneration of sebaceous glands and the outer follicular sheath in up to 40% of cases.[4]

The pathogenesis of the disease remains unknown. Numerous proposed mechanisms include hypersensitivity reactions to various infections, medications, and autoimmune disorders. Ferrándiz et al[8] proposed that EPF is caused by the overgrowth of *Pityrosporum* species in the follicles. In fact, the seborrheic sites are mainly affected; hence *Pityrosporum* species may play a role in some patients. It also is possible that skin surface lipid-derived eosinophilic chemotactic and activation factors are important in the etiology of the disease. It has been postulated that these lipid-derived eosinophilic chemotactic and activation factors may be arachidonic acid metabolites; this hypothesis is supported by the positive responses that have been achieved with indomethacin therapy, which inhibits cyclooxygenase. Other studies propose the pathogenesis of the disease to involve altered production of cytokines, especially IL-5, which stimulates the activity and proliferation of the eosinophils, and the increased expression of adhesion molecules such as ICAM-1 (intercellular adhesion molecule 1).[4,9,10] In addition, eosinophils have been found to express high levels of nitric oxide synthase, which activates mast cells and eosinophils, thus inflicting epidermal damage.[4,8,11,12]

In some patients EPF has been associated with an immunologic dysfunction, especially those infected with HIV; leukemia; lymphoma; hematologic diseases; and bone marrow transplant.[13]

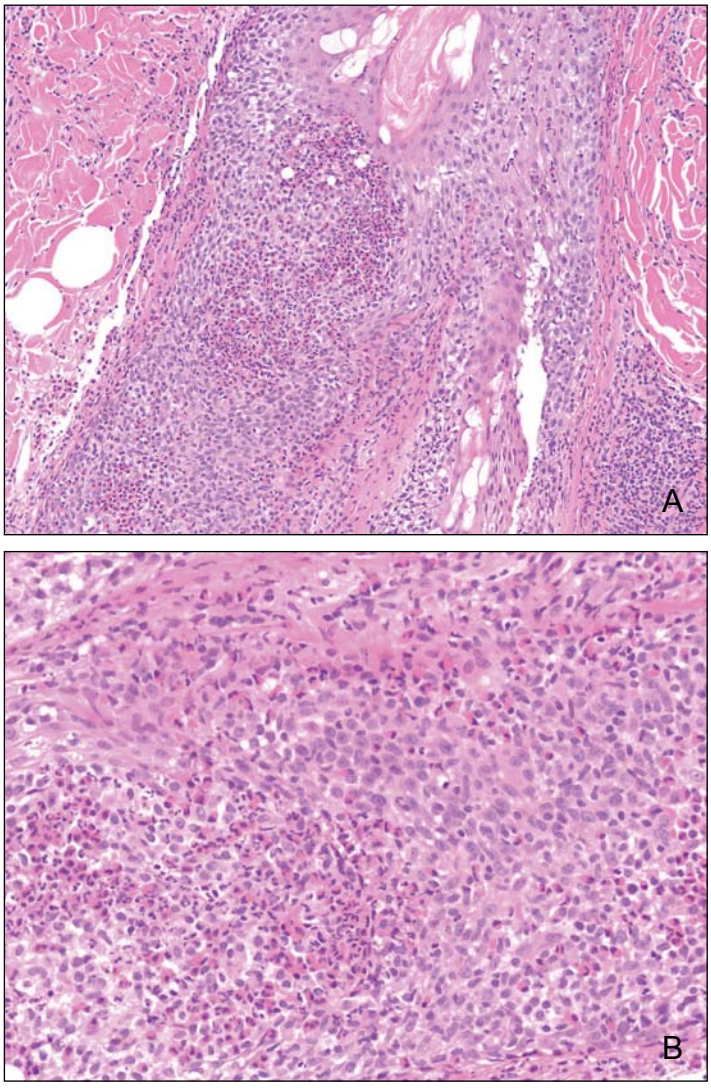

Figure 2. A punch biopsy from the left arm showed hair follicles with a dense mixed inflammatory infiltrate composed of lymphocytes, histiocytes, neutrophils, and eosinophils that surrounded as well as invaded the follicular structures (A) and a punch biopsy from the back demonstrated eosinophils (B)(H&E; original magnifications ×20 and ×40, respectively).

Rosenthal et al[14] suggested that EPF with HIV infection is an HIV-associated eosinophilic folliculitis or immunosuppression-associated EPF, a pruritic, urticarial, and papular eruption first described in 1986 that favors the face, scalp, and trunk.[15] The clinical presentation differs considerably from classic EPF in that neither large pustules nor figurate lesions are observed and the individual lesions are more chronic and persistent. Treatment of the underlying HIV infection with a resultant rise in the $CD4^+$ lymphocyte count may lead to resolution of lesions.[16]

In 1984, Lucky et al[17] reported on EPF in infancy. Infancy-associated EPF is an unusual, self-limiting disorder of unknown etiology that occurs during infancy, usually in boys younger than 1 year. The clinical features include multiple pruritic, sterile, perifollicular papulopustules on an erythematous base. It differs from adult EPF because it primarily involves the scalp and brows and often is accompanied by secondary crusting.[18]

There are numerous proposed treatments of EPF; therefore, no definitively effective therapy has been established. Topical corticosteroids tend to be the first choice for all 3 types of EPF. Other beneficial treatment modalities that have been reported include oral corticosteroids, UV therapy in the form of UVB and psoralen plus UVA, metronidazole, isotretinoin, dapsone, itraconazole, cetirizine hydrochloride, and topical tacrolimus.[16,19] Classic EPF often is treated with indomethacin 50 to 75 mg daily and other nonsteroidal anti-inflammatory drug derivatives; drugs that reduce the production of arachidonic acid metabolites should be the treatment of first choice in patients with classic EPF.[4]

The prognosis for EPF is poor because the clinical course tends to be chronic and relapsing

for years in many patients, and once treatment is discontinued, relapses often are observed.

Conclusion

Eosinophilic pustular folliculitis is a rare complex disease with a pathogenesis that is mostly unknown. This disease affects not only Asian individuals but other races as well and should be considered in the differential diagnosis when folliculitis does not respond to typical treatment modalities. Eosinophilic pustular folliculitis is most likely a multifactorial immune system reaction pattern to a variety of antigenic stimuli. Further investigation into the role of specific chemokines including eotaxin-1 and nitric oxide synthase may provide a clearer understanding of EPF. Future treatment modalities may involve eotaxin antibodies and antagonists and nitric oxide inhibitors aimed at eosinophils infiltrating the follicular epidermis.[4] The choice of the most suitable drug will be possible once its mechanisms are better understood.

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