

Eosinophilic pustular folliculitis (EPF): a case report and literature review

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Eosinophilic pustular folliculitis (EPF): a case report and literature review

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Abstract:

Eosinophilic pustular folliculitis (EPF), also known as Ofuji's disease, is a distinctive dermatosis characterized by the appearance of follicular papules or pustules involving the face, trunk and/or extremities. Its variants include a classic type, an HIV-associated type, an infantile type. We here report on a patient with classic EPF, who was successfully treated with oral indomethacin. One year follow up of this case revealed dramatic improvement.

Key words: eosinophilic pustular folliculitis, Ofuji's disease

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บทคัดย่อ:

Eosinophilic pustular folliculitis (EPF) หรือ Ofuji's disease มีลักษณะรอยโรคเป็นตุ่มแดงหรือตุ่มหนองของรูขุมขนที่ใบหน้า ลำตัว และแขนขา พบทั้งในผู้ใหญ่ปกติ ผู้ป่วยโรคเอดส์ หรือในเด็ก คณะผู้รายงานได้นำเสนอผู้ป่วยที่มีลักษณะทางคลินิกและผลชิ้นเนื้อเข้าได้กับโรคนี้ และพบว่ายาารับประทาน indomethacin ให้ผลดีในการรักษา หลังติดตามผู้ป่วยนานหนึ่งปี

คำสำคัญ: eosinophilic pustular folliculitis, Ofuji's disease

Introduction

The first case of eosinophilic pustular folliculitis (EPF) was described by Ise and Ofuji¹ in 1965. This disease may be misdiagnosed due to the clinical findings resembling dermatophytosis, bacterial infection or seborrheic dermatitis. In suspicious cases, laboratory investigations and skin biopsy are necessary for definite diagnosis. Several therapeutic regimens have been reported to control this disease, but no definitively effective therapy has been established. In this report we describe a case of classic EPF (Ofuji's disease) that manifested as erythematous plaques studded with papulo-pustules on the left cheek, with the diagnosis confirmed by histological and laboratory studies. The response to oral isotretinoin, oral indomethacin and the long-term follow-up are discussed.

Case report

A 28-year-old man attended the Trang Hospital skin clinic in January, 2003 having had a history of recurrent erythematous papules, pustules and plaques with peripheral extension and central clearing on both cheeks and the perioral area. There were no indications of his problem being the result of either shaving or sun exposure. A KOH test was used to investigate for fungal disease which proved negative. The patient was diagnosed as possibly having seborrheic dermatitis, pityrosporum folliculitis or perioral dermatitis. Consequently the patient was treated topically with 0.05% betamethasone cream and oral antihistamine. After six weeks, there was no observed clinical improvement. The lesions did not respond to either oral antifungal medication or oral antibiotics. As a result the treatment was subsequently changed to

oral isotretinoin 10 mg once a day. The lesions showed dramatic improvement within two weeks and had completely cleared after eight weeks. But then two months after the drug treatment was stopped the lesions returned.

As Figure 1A shows, by May, 2006 the patient's face had erythematous plaques studded with papules and pustules formed in annular configurations located on the left cheek. Both a KOH preparation for fungal hyphae and an HIV test showed negative. A CBC showed leukocytosis (WBC 11,850/mm³) and eosinophilia (3.5%). Additionally, a skin biopsy from the left cheek was done, whereupon the histopathology revealed folliculitis with infiltration of lymphohistiocytes and eosinophils. (Figure 2) A diagnosis of classic EPF was made based on the typical clinical and histological findings, and indomethacin treatment was prescribed. All eruptions cleared with oral administration of indomethacin 75 mg per day for four weeks (Figure 1B) after which he was treated with indomethacin 25 mg per day. At a one-year follow-up there was no recurrence of the lesions observed.



Figure 1A Erythematous papulo-pustule, annular configuration on the left cheek



Figure 1B The lesion had completely cleared after one month of oral indomethacin 75 mg/d

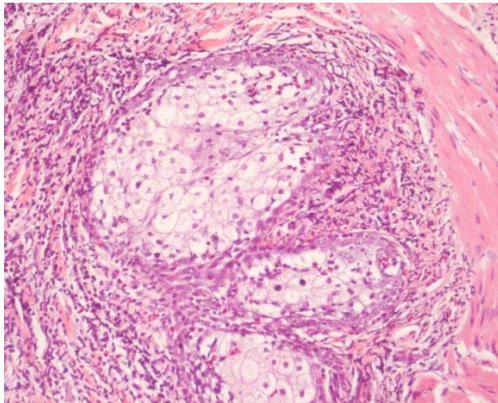


Figure 2 Infiltration of lymphohistiocytes and eosinophils within the follicle

Literature review and discussion

EPF primarily affects adults. It presents as chronic and recurrent annular clusters of sterile erythematous follicular papules and pustules superimposed on plaques with central clearing and peripheral extension. Individual clusters normally last for seven to ten days and tend to relapse every three to four weeks. This has come to be known as classic EPF and is mainly found in Japanese people.² Classic EPF has a peak incidence during the third and fourth decades of life.³⁻⁴ Males are affected more frequently than females. The distribution of classic EPF lesions is concentrated on the face (85% of cases), back and trunk (59%), and other seborrheic areas. Lesions can also occur on the extremities, palms, and soles, despite

the fact that follicles are not found in either palms or soles, and one-fifth of patients display palmoplantar lesions.⁵⁻⁶ Oral mucosal involvement has been described in a German patient with classic EPF.⁷

Two additional types of EPF have also been described, immunosuppression-associated EPF (IS-EPF) (most of which cases are HIV-seropositive) and infancy-associated EPF (I-EPF).⁸⁻¹⁰ Both are indistinguishable histologically from the classic form.

AIDS-associated eosinophilic folliculitis⁸ is different from classic EPF and has three distinguishing features: (1) a different clinical presentation (discrete erythematous urticarial follicular papules are seen in the HIV variant while coalescing papulo-pustular plaques with central clearing and postinflammatory hyperpigmentation are seen in the classic EPF); (2) the universal presence of pruritus; and (3) the usual but not constant occurrence eosinophilia.

I-EPF displays similar sterile papulopustules as classic EPF; however, they are not grouped in annular arrangements.¹¹ Clinical distribution in infants shows predominant folliculitis concentrated on the scalp with occasional spreading to the face and extremities.^{9, 11-12}

Histological examination demonstrates the characteristic features of eosinophils and mononuclear cells infiltrating the pilosebaceous unit and surrounding dermis. "Follicular mucinosis", a reaction pattern associated with lupus erythematosus, photodermatoses, arthropod bites, Hodgkin's disease, and angiolymphoid hyperplasia, may be seen as mucinous degeneration of the sebaceous glands and outer follicular sheath in 40% of EPF cases.^{2, 13-15} Blood eosinophilia is detected in 25-80% of patients and mild to moderate leukocytosis may be present.⁴

The cause of EPF has not been clearly defined but numerous proposed mechanisms include hypersensitivity reactions to various infections, medications, and autoimmune disorders possibly facilitated by skin surface lipid-derived eosinophilic chemotactic and activation factors. Some cases of EPF, particularly IS-EPF, may be caused by immune dysfunction or immune-mediated hypersensitivity to species of the fungus *Malassezia*, two mites (*Demodex folliculorum* and

Demodex brevis), bacteria including *Leptotrichia buccalis*, also medications including carbamazepine, minocycline, allopurinol, timepidium bromide, and indeloxazine.^{2, 16} Other antigen sources, including silicone tissue injections for purposes of nose and chin augmentation, may cause EPF skin reactions.¹⁷ The sebaceous gland, or its skin surface lipid products, may provide a source for antigen-stimulated autoimmune dysfunction or eosinophilic chemotactic factor leading to EPF.¹² An association between immune deficiency and EPF is strongly indicated in IS-EPF. It is thought that eotaxin-1 and T_H2 cytokines play a crucial role in the eosinophil recruitment, inflammation, and tissue damage.¹⁸ Immune dysfunction involving altered chemotaxis, epidermal antibodies, and immunoglobulin levels are associated with EPF.¹⁹ In addition eosinophils have been found to express high levels of neuronal nitric oxide synthase in EPF.²⁰

A differential diagnosis can be challenging, especially in children where infantile acropustulosis, erythema toxicum neonatorum, acne neonatorum, and transient neonatal pustular melanosis should be considered.² In IS-EPF the differential diagnosis is extremely broad, including photodermatitis, opportunistic dermatologic infections, papular urticaria, fungal folliculitis and acne.

There are multiple treatment options for EPF.⁴ Topical corticosteroids tend to be the first choice for all three types of EPF⁴ and they have shown a good response rate in both children¹⁰ and adults. The utilisation and efficacy of other therapies seems to depend on the variant of EPF. UVB phototherapy was the treatment of choice for patients with difficult-to-treat EPF associated with HIV.²¹ Oral indomethacin is an effective medication for treatment of classic EPF and has a mild adverse effects profile. It is the first line of oral medical treatment for classic EPF in adults not infected with HIV.²² In 1989 Nishimura reported a case of EPF effectively controlled with topical indomethacin.²³ In 1993 Lee et al. reported successful treatment of EPF with oral indomethacin in Singapore.^{3, 24} In 1998 seven cases of EPF were reported in Thailand in which oral indomethacin showed good results.²⁵ In 2002, in a study of EPF treatment by Ishiguro et al., of 20 patients with EPF, eleven were treated with oral indomethacin, of whom eight responded completely and three had a partial

response.²⁶ The effective dosage of indomethacin in these studies ranged from 50–75 mg/day. Tang et al. made a retrospective study of 23 patients with classic EPF, and found that the majority of patients (90%) treated with oral indomethacin had had a good response. The basis for the efficacy of indomethacin is complex. The drug, a potent cyclooxygenase arachinodic acid metabolite, is a chemotactic factor for eosinophils, neutrophils, lipids and prostaglandins. It decreases the local production of these arachinodic acid-derived chemotactic factors, which are thought to play a role in the pathogenesis of EPF.²⁴ The remission of EPF is associated with increased serum concentrations of interferon (IFN- γ) with no essential change of serum levels of IL-4. Indomethacin may encourage remission of EPF by altering cytokine production.²⁷

In 1989, isotretinoin (1 mg/kg/day) was reported as having been successful in treating (although not curing) EPF in a 30-year-old man.²⁸ The patient saw dramatic improvements in a two-week period but withdrawal of the drug was followed by a recurrence of symptoms, after which the reintroduction of isotretinoin was successfully used to reduce the symptoms. Isotretinoin exerts anti-inflammatory effects by its direct action on PMNs, reduction of chemotactic activity, and a diminution in the local synthesis of arachinonic acid-derived eosinophilic cationic factor.²⁹

In 2000, 0.1% tacrolimus ointment applied twice daily was used to treat one patient with EPF in whom other treatments had been unsuccessful.³⁰⁻³¹

The prognosis for EPF is relatively poor with the traditional course tending towards chronicity and relapses for years in many patients. Complete remission can be achieved in some patients with indomethacin and more recently with tacrolimus.

In our patient, following the clinical manifestations which had lesions appearing bilaterally on the cheeks and perioral area, the clinical diagnosis included perioral dermatitis and the treatment of choice was 10 mg per day of oral isotretinoin. The lesions showed a dramatic improvement within two weeks and were completely healed after eight weeks. Withdrawal of oral isotretinoin after two months was followed by a recurrence of the lesions. Definitive diagnosis of this case was classic EPF according to histopathological

examination and laboratory tests, thus the patient was treated with indomethacin 25 mg/tab, three tablets per day for one month. He showed better results so we reduced the drug dosage to one tablet per day for three months and one tablet every other day for the last month. At a one-year follow-up there were no visible signs of any new lesions and the patient continued to take indomethacin 25 mg/tab every other day for maintenance. In this case the clinical improvement resembled other case reports.

Conclusion

Increased awareness of EPF is important as it can mimic other common skin disease. In cases of follicular pathologies which do not respond to conventional therapies, it necessary to take into consideration the possibility of EPF. Oral isotretinoin could show success in treating, but not curing. An oral indomethacin was efficacious as had been previously reported. Therefore it was necessary to evaluate the features as a whole, so that the patients may get benefit of reduced cost and time for treatment.

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