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Classic form of eosinophilic pustular folliculitis in an immunocompetent girl: rapid and complete resolution after low-dose oral indomethacin treatment

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Abstract

Eosinophilic pustular folliculitis (EPF) is a rare non-infectious pruritic dermatosis, first described by Ise and Ofuji in 1965. We report the case of a 15-year-old immunocompetent girl that presented with a widespread papulopustular eruption four days after her arrival in Japan. The clinical diagnosis of the classic form of EPF was confirmed by histological examination of the lesional skin that revealed an intense, mainly eosinophilic, dermal infiltrate within and around pilosebaceous units. Oral administration of low-dose indomethacin (25 mg/day) led to a complete resolution of the eruption within 6 weeks without causing any side effects. The patient is presently completing a 15-month follow-up and remains free of relapses. To the best of our knowledge, it is the first time that low-dose oral indomethacin is reported to be capable of causing a rapid and complete resolution of the classic form of EPF.

Keywords: eosinophilic folliculitis, indomethacin, eosinophils, prostaglandin D2

Introduction

Eosinophilic pustular folliculitis (EPF) is a chronic, non-infectious pruritic cutaneous disorder of

unknown etiology. It was originally described by Ise and Ofuji in 1965 as a variant of "superficial pustular dermatosis" in a Japanese female patient with recurrent follicular pustules on the trunk and the face accompanied by peripheral eosinophilia [1].

Five years later, Ofuji et al. published three further cases of this dermatosis and coined the term "eosinophilic pustular folliculitis," later also termed Ofuji disease [2]. Clinically, the eruption of EPF, that equally affects both genders, is characterized by sterile papulopustules forming annular plaques with peripheral extension and central resolution. Histologically, a prominent dermal infiltrate dominated by eosinophils is found within and around the pilosebaceous units with occasional formation of eosinophilic microabscesses [2, 3]. Herein, we describe a young immunocompetent female patient with the classic form of EPF who was successfully treated with low-dose oral indomethacin.

Case Synopsis

An HIV-negative and otherwise healthy 15-year-old girl developed a widespread and intensely pruritic eruption four days after her arrival in Japan. Ten days later, she returned to Cyprus and consulted her pediatrician and dermatologist who made the diagnosis of bacterial folliculitis and treated her with various topical (clindamycin, mupirocin) and systemic antibiotics (tetracyclines, erythromycin) over a period of five months. Owing to her poor therapeutic response, she was referred to the Center for Dermatologic Diseases. Her medical history was unremarkable. She had consumed no drugs or herbal remedies prior to the onset of her eruption. Clinical examination revealed a papulopustular eruption (**Figure 1A**) on the trunk, the face, and the extremities, with involvement of hands and feet, focally assuming an annular configuration. Culture of the content of the pustules performed 18 days after the cessation of any treatment with antibiotics and/or

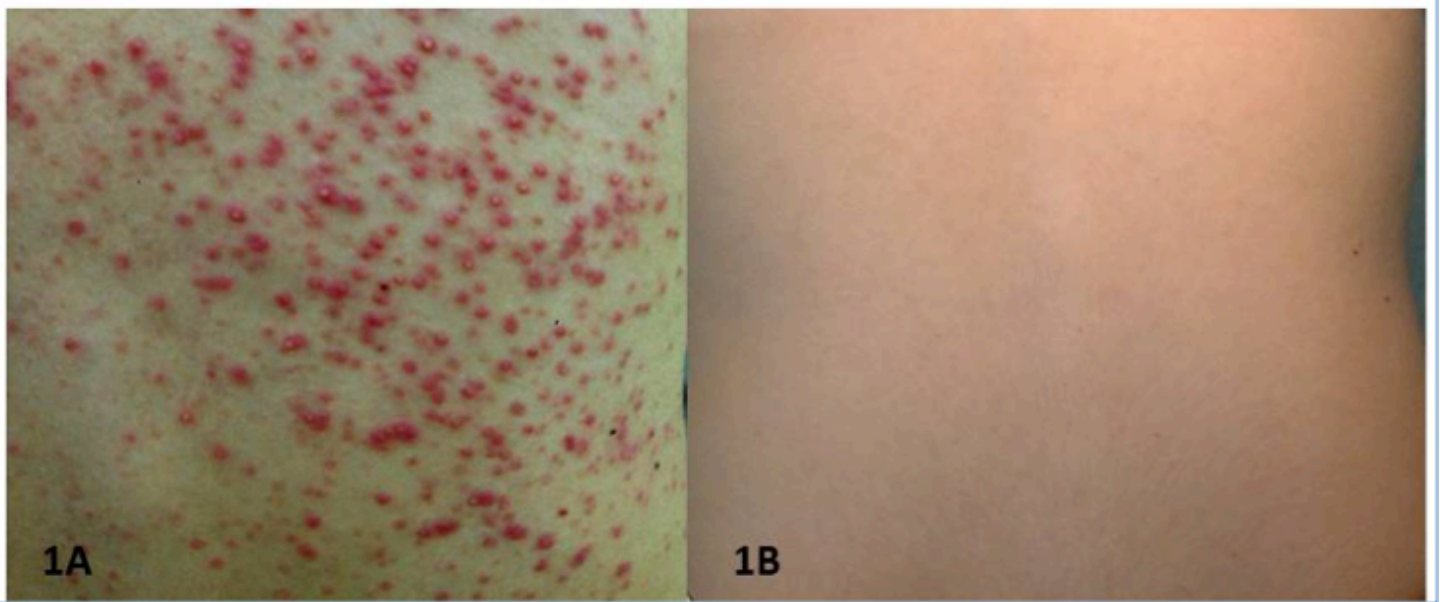


Figure 1. A) Clinical aspect of the papulopustular eruption prior to onset of therapy. B) Complete resolution of lesions after 6 weeks of continuous oral indomethacin treatment.

antiseptic drugs, was negative. Routinely performed hematological, serological, and biochemical tests revealed normal or negative findings, whereas no peripheral eosinophilia could be detected.

The clinical diagnosis of the classic form of EPF was histologically confirmed (Figures 2A, B) and oral treatment with low-dose indomethacin (25 mg/day) was initiated. After one week of treatment, there was an impressive regression of the lesions, which completely resolved after 6 weeks of continuous treatment (**Figure 1B**). The patient exhibited no side effects related to indomethacin. She is presently completing a 15-month follow-up and has showed no relapses.

Case Discussion

Apart from the classic form of EPF described by Ofuji et al. [2], that affects otherwise healthy individuals, three additional variants of this disorder have been recognized: 1) An infantile variant (I-EPF) mainly occurring in non-Japanese infants [4], 2) An immunosuppression-associated variant (IS-EPF), which is further subdivided into three subtypes, related to HIV-infection, malignancy (particularly hematologic), and bone marrow or peripheral blood stem cell transplantation, respectively [5], and 3) A rare drug-induced variant, which is associated with the administration of medications such as, carbamazepine, minocycline, indeloxazine

hydrochloride, and allopurinol [6-8].

EPF clinical variants share the same histological features, but reveal several distinct differences with regard to the morphology and distribution of cutaneous lesions (**Table 1**), [9-11].

The clinical features of the case presented here, were compatible with the classic form of EPF. However, hematological investigations performed upon presentation of the patient to our center (six months after onset of the disease) revealed no peripheral eosinophilia (3% eosinophils), which is known to occur only during the acute phase of the disease.

The etiopathogenesis of EPF still remains unknown. It has been suggested that EPF most likely represents a multifactorial immunological reaction pattern to antigenic stimuli of diverse origin, which may cause an alteration of the immunological balance in the microenvironment of sebocytes leading to production of prostaglandin D2 [10]. The latter and its metabolite 15-deoxy- Δ 12,14-prostaglandin J2 (15d-PGJ2) induce an upregulation of eotaxin-3 (chemoattractant for eosinophils) in sebocytes and cause the eosinophilic infiltration around the pilosebaceous units [12, 13]. Interestingly, a lipid-soluble eosinophilic chemotactic factor could be identified in scale-extracts of skin lesions in patients with the classic form of EPF [14].

Table 1. Clinical forms of eosinophilic pustular folliculitis.

EPF variants	Clinical features
1. Classic	Most patients reveal groups of sterile papulopustules superimposed on annular plaques with central clearing and peripheral extension. Rarely no macroscopic pustules can be observed. In most cases involvement of face, neck, upper back, hands and feet. Scalp is rarely affected.
2. Infantile	Most patients reveal groups of papulopustules (mostly localized on the scalp) that tend to resolve spontaneously. Occurrence of annular plaques is rare. No involvement of hands and feet.
3. Immunosuppression-associated 3.1. HIV-infection 3.2. Malignancy (particularly hematologic) 3.3. Bone marrow or peripheral stem cell transplantation	Highly pruritic urticarial follicular papules (head, neck, trunk). Annular plaques are seen in 50% of the patients. No involvement of hands and feet.
4. Drug-induced	Generalized and disseminated papulopustules Occurrence of annular plaques is rare. No involvement of hands and feet. Usually resolution upon discontinuation of the causative drug +/- topical or systemic corticosteroids.

In the patient reported here no definite etiological factor could be detected. The question as to whether the occurrence of the disease four days after her arrival in Japan is a mere coincidence or could be related to her possible exposure to a yet unknown etiological factor abundantly occurring in this country remains to be elucidated.

Various regimens including topical and systemic steroids, topical tacrolimus, systemic dapsone, sulphonamides, macrolides, tetracyclines, cyclosporine, retinoids, and systemic and topical antifungals have been used in the treatment of the classic form of EPF with variable results [15]. In 1984 Hosokawa and Asada were the first to report the favorable therapeutic response of EPF to oral indomethacin, which is administered at daily doses ranging between 75 and 150 mg [16]. Indomethacin is thought to exert its therapeutic effects through inhibition of cyclooxygenase leading to decrease in prostaglandin D2 and eotaxin-3 production by the sebocytes and through interaction with the prostaglandin D2 receptor [17].

In view of the serious side effects mostly occurring after prolonged treatment with high doses of indomethacin (cardiovascular, gastrointestinal, hepatic, hematological, renal), it is generally recommended that the lowest effective dose of this drug is used for the shortest duration possible

in order to minimize the potential risk particularly for a cardiovascular and gastrointestinal adverse event. Our patient's eruption had been resistant to a variety of topical and systemic agents and treatment was started with a daily oral dose of 25 mg indomethacin. Within one week, this led to an impressive therapeutic response and to a complete resolution of the lesions within 6 weeks without causing any side effects. To the best of our knowledge, it is the first time that low-dose oral indomethacin is reported to be capable of causing a rapid and complete resolution of the classic form of EPF.

Conclusion

The purpose of the present case report is twofold: 1) to familiarize the physicians with the clinical features of the classic form of EPF, and 2) to draw their attention to the impressive therapeutic response of the latter to low-dose oral indomethacin. Obviously, no reliable conclusions can be drawn from our experience in a single case. We feel, however, that in view of the rapid and impressive therapeutic response observed in our patient to a daily oral dose of 25 mg indomethacin, it might be worthwhile, particularly in children with EPF, to start oral indomethacin administration with low doses, in order to avoid the occurrence of adverse reactions possibly associated with the higher doses of this compound.

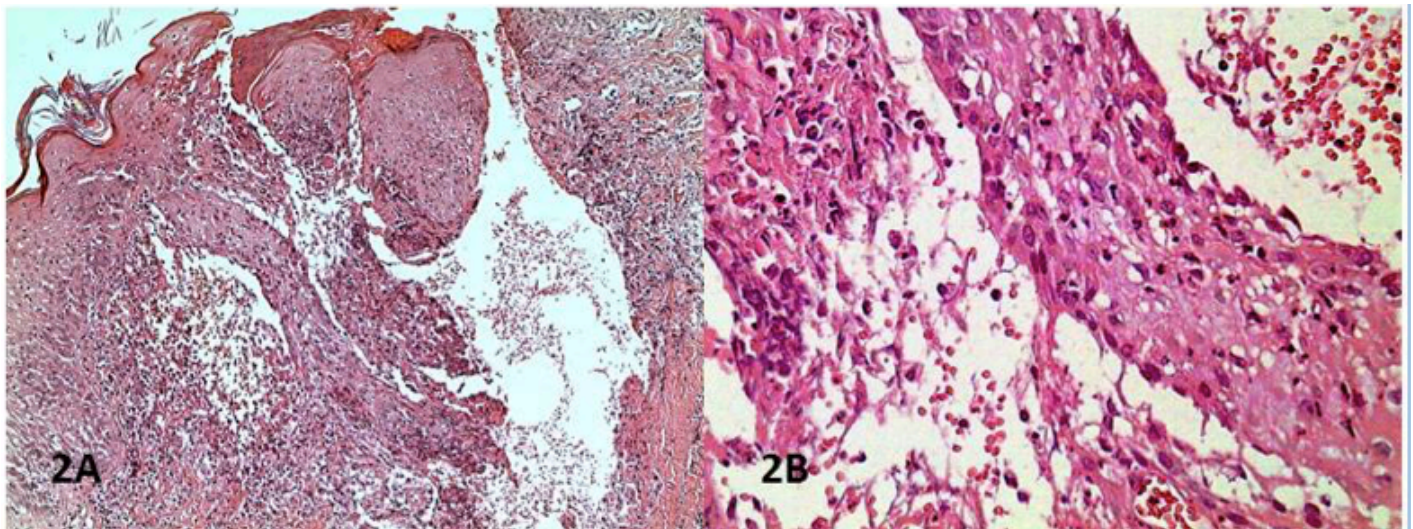


Figure 2. Histological section of a lesional skin biopsy from the patient with eosinophilic pustular folliculitis. A) Heavy infiltration and destruction of the follicle. (H&E, 20%); B) Higher magnification reveals mostly eosinophils among the inflammatory cells (H&E, 40%).

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