



Eosinophilic Pustular Folliculitis of Infancy

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Abstract

Eosinophilic pustular folliculitis (EPF) is a rare, idiopathic, recurrent, self-limiting disease. It presents as sterile papulopustules located on the scalp and sometimes also on other body parts, without signs of systemic illness. Ten percent of cases occur in infants, mainly before the age of 6 months. The etiology is unknown. Eosinophilic pustular folliculitis of infancy (EPFI) is often underdiagnosed and overtreated, especially in a vulnerable population like preterm infants. We present a female neonate, born prematurely at a gestational age of 25 weeks. She developed recurrent papulopustules on an erythematous base with crustae. After initial treatment with antibiotics and antifungal agents, she was diagnosed with EPFI. We discuss the differential diagnosis and management of EPFI and its possible relationship with the immunological immaturity associated with preterm birth.

Keywords: Eosinophilic pustular folliculitis; Newborn; Infant; Premature; Hyper-IgE syndrome

Introduction

Eosinophilic pustular folliculitis (EPF), also known as Ofuji disease, is a rare, idiopathic, inflammatory skin disease. Eosinophilic pustular folliculitis of infancy (EPFI) accounts for 10% of all EPF cases. It occurs four times more often in (Caucasian) boys than girls [1,2]. The timing of first presentation ranges from birth to 1.5 years; 70% presents before the age of 6 months [2]. It is a recurrent disease in all children with outbreaks every 1-12 weeks, each lasting 1-4 weeks [1,2]. In 80%, the disease spontaneously resolves around the age of 3 years [2].

At presentation, infants have sterile papulopustules on an erythematous base. The lesions are always located on the scalp and in 65% also on other body parts, without signs of systemic illness. Lesions form groups, sometimes with secondary crusting. Unlike adult eosinophilic folliculitis, lesions lack the typical halo [1,3]. After remission, local hyperpigmentation can be seen. Recurrences are often located at hyperpigmented old lesion sites.

Laboratory investigations reveal blood eosinophilia in up to 83% of cases. This might be an underestimation, since blood eosinophilia is only present in the acute phase of the outbreak [2,4]. Microbiology shows negative cultures for bacteria, fungi, and viruses although secondary infection with *Staphylococcus aureus* might occur [1]. At a young age, it may be difficult to differentiate between EPFI and hyper-IgE syndrome (HIES, Job syndrome), since both are accompanied by papulopustular dermatitis, often located on the scalp and face, with crustae associated with *S. aureus* and folliculitis with eosinophilic infiltrates. Both disease entities feature blood eosinophilia. Moreover, elevated IgE levels may be absent in infants with HIES [5].

Histology in EPFI reveals folliculitis in only 62% of cases whereas folliculitis is obligatory in the adult counterpart [1-3]. Punch biopsy of the skin shows dense eosinophilic infiltrates in most patients. These are located in the dermis and can be arranged in a peri- or interfollicular fashion. Lymphocytes and histiocytes can also be present [1]. Further histological findings are subcorneal pustules and spongiosis in the epidermis [6,7].

The cause of EPFI is unknown. Hypersensitivity reactions, immunologic, hormonal, and genetic etiologies have been suggested [3,8,9].

Case Presentation

A female neonate was born prematurely at 25 weeks and 6 days of gestation due to cervical insufficiency. Shortly after birth, intravenous treatment with fluconazole was initiated and continued for 14 days because of a generalized erythematous skin rash with a positive skin swab for *Candida albicans*. Considering the unexplained prematurity, the skin rash, and a C-reactive protein

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Figure 1: Patient's right cheek, showing confluent papulopustules on an erythematous base.



Figure 2: Patient's scalp with crops of papulopustules and crustae.

(CRP) level of 28 mg/l, we also suspected a perinatal infection, for which a 7-day course of antibiotics (amoxicillin and gentamicin) was prescribed. During the first 2 days of her life, she was ventilated and treated with surfactant because of infant respiratory distress syndrome (IRDS). No corticosteroids were administered. Her father was allergic to cats, dogs, dust mite and several fruits and vegetables in his childhood. These allergies resolved within 2 years. There was no family history of similar skin lesions or recurrent infections.

At the age of 5 weeks, she developed progressive erythematous papulopustules with crustae on the scalp, cheeks, and in the supra-auricular region (Figure 1 and 2), without any signs of systemic inflammation. Routine laboratory investigations, including leukocytes and CRP, were normal. She was initially treated with topical fusidic acid and intravenous Flucloxacillin and Fluconazole. These medications were discontinued after a week when blood cultures and regular skin swabs turned out negative for bacteria and fungi.

Two weeks later, new lesions appeared on the same sites as the old, healing lesions. Additional lesions emerged on the abdomen. Initially, no treatment was started. However, because of the progressive nature of the lesions and the vulnerability of this preterm infant, treatment with intravenous Flucloxacillin and oral Fluconazole was started again for a week. This time, a lesion swab showed secondary infection with *S. aureus*.

Specialists in paediatric dermatology and paediatric infectious diseases and immunology were consulted. A differential diagnosis was made, mainly comprising EPFI and HIES. Additional laboratory investigations were carried out. Leukocyte differentiation demonstrated 17% eosinophils (normal <6%), 23% neutrophils (normal 15%-60%), and 46% lymphocytes (normal 12%-68%).

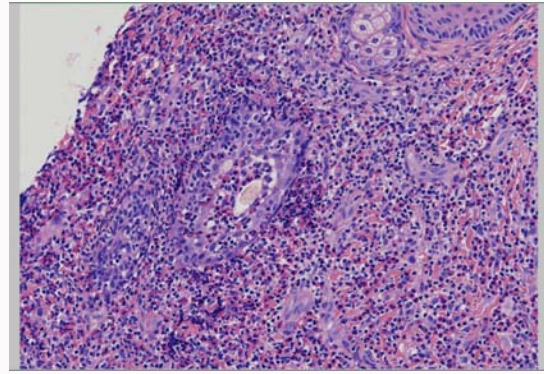


Figure 3: Haematoxylin-eosin stain, close up. Dermis and hair follicle infiltrated by many eosinophilic granulocytes.

The absolute blood eosinophil count was $2.78 \times 10^9/l$ (normal $<0.6 \times 10^9/l$). The serum IgE level was $<2 U/ml$ (normal $<2 U/l$) and a dihydrorhodamine (DHR) flow cytometric assay (i.e. granulocyte function test) to assess oxidative burst in our patient's neutrophils was normal.

To confirm our clinical suspicion of EPFI, a punch biopsy from a scalp lesion was performed. This revealed a superficial dermal infiltrate with a preponderance of eosinophils located in and around a follicle with follicular destruction (Figure 3). The epidermal epithelium showed spongiosis with eosinophilic and neutrophilic infiltration. Periodic-Acid Schiff (PAS) staining was negative for fungal infection.

We diagnosed our patient with EPFI. Her further clinical course was uneventful. At this moment, she is 4 months old and thriving at home. Recurrences are becoming less elaborate and less frequent. The absolute blood eosinophil count decreased to $1.04 \times 10^9/l$. Outpatient follow-up with determination of the serum IgE level at the age of 1 year is planned to rule out HIES.

Discussion

We describe an extremely preterm female infant having recurrent eruptions of erythematous papulopustules with crustae, predominantly located on the face and scalp, starting at the age of 5 weeks. Although clinical and biochemical signs of systemic inflammation were absent, she was treated twice with antibiotic and antifungal medication, without a clear response. Eventually, the age of onset, appearance, typical localization, and the recurrent and self-limiting nature of the eruption, in combination with blood eosinophilia and lack of systemic inflammation, led to a diagnosis of EPFI, which was confirmed with a skin biopsy.

Primary infectious causes of papulopustular lesions in newborns, such as bacterial (impetigo, listeriosis, pustular folliculitis), viral (herpes simplex, varicella), fungal (*Candida albicans*, *malessezia*), and parasitic (in older patients scabies) infections should always be considered and, if likely, ruled out by appropriate microbiological investigations [1-3,6,8-10].

The differential diagnosis of noninfectious papulopustular lesions in newborns consists of EPFI, HIES, erythema toxicum neonatorum, transient neonatal pustular melanosis, infantile acropustulosis, Langerhans cell histiocytosis, miliaria pustulosa, acne neonatorum, incontinentia pigmenti, pustular psoriasis, and transient myeloproliferative disorder [1-3,6-10]. It is especially challenging to differentiate between EPFI, erythema toxicum neonatorum,

infantile acropustulosis, and HIES [1,3,6,10]. These eruptions can have a rather similar appearance, with lesions situated on the scalp, and eosinophilic infiltrates seen in histological specimens. Both EPFI and infantile acropustulosis (IA) are recurrent. However, lesions are mainly located on the hands and feet in IA. Also, neutrophils, not eosinophils, are the prevailing leukocytes found in the pustules of IA. Erythema toxicum neonatorum has an onset before the age of 2 weeks. HIES can hardly be differentiated from EPFI at a young age, neither clinically nor histologically. Many patients with HIES were initially diagnosed with EPFI in their early years. Inasmuch as HIES entails a risk of skeletal abnormalities and severe infections, among others, children diagnosed with EPFI should be invited for follow-up [2]. Also because of the positive cultures for *Candida albicans* and *Staphylococcus aureus*, we still acknowledge the possibility of HIES in our patient.

Despite the unclear etiology of EPFI, there are several speculative causes, as mentioned above. We believe that an immunological cause is plausible, since EPFI is frequently found in (extremely) preterm infants, who lack a properly developed immune system. Often, these preterm infants have a history of systemic candida infection, [11] as was the case in our patient. This also implies an increased vulnerability of immunocompromised patients for EPFI. Furthermore, EPFI is seen in immunocompromised adults with human immunodeficiency virus (HIV) and malignancies, such as T-cell lymphoma [12].

Treatment of EPFI with topical corticosteroids should only be given to patients with complaints of pruritus. Antibiotics should be reserved for patients with secondary infection of the lesions. Other treatment modalities have not been proven effective and since the disease is self-limiting, they carry a large risk of side effects and overtreatment.

In conclusion, EPFI should be considered when newborns or infants have a papulopustular eruption, especially when it is recurrent, located on the scalp, and accompanied by blood eosinophilia. Early recognition may preclude unnecessary treatment, although this remains difficult considering the vulnerable nature of this population and the serious differential diagnoses.

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