SHORT COMMUNICATION

A Case of Eosinophilic Pustular Folliculitis with Vegetating Lesions on the Lower Legs and Feet Resembling Pemphigus Vegetans

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Eosinophilic pustular folliculitis (EPF) is an inflammatory dermatosis characterized by erythematous plaques with follicular papules and pustules involving seborrhoeic areas (1). Some reports have described cases of EPF with extrafollicular lesions involving the palmoplantar regions and the nails (1–3). We present here a case of vegetating plaques on the lower legs and feet in a patient with EPF.

CASE REPORT

An 81-year-old Japanese woman presented with vegetating lesions on her lower legs and feet. She had a 14-year history of recurrent erythema with pustules on the face and a 9-year history of recurrent erythema with pustules in the palmoplantar regions. The recurrent facial lesions had been treated with topical metronidazole as rosacea, and the palmoplantar lesions had been diagnosed as palmoplantar pustulosis (PPP), which had been treated with topical betamethasone butyrate propionate at a dermatology clinic. Three months prior to presentation, pruritic vegetating lesions and pustules appeared on her lower legs extending to the feet. Despite treatment with cyclosporine at a dose of 150 mg/day (2.5 mg/kg/day) for a month, vegetating lesions were exacerbated and the patient was referred to our hospital. Physical examination showed pruritic vegetating plaques with scales and pustules on her lower legs and feet (**Fig. 1**a–c). Pruritic erythema with scales was observed in the hypothenar regions and the fingertips, with nail dystrophy sparing the right ring finger (Fig. 1d, e). Pustules and erythema were limited to the lower legs, feet, and hands. Facial and mucosal involvement were not observed on initial physical examination. A biopsy specimen from a vegetating plaque with pustules on the right lower leg showed elongation of epidermal rete ridges with spongiosis, intraepidermal pustules containing eosinophils, and marked eosinophil infiltration around the hair follicles (Fig. 1f). An additional skin biopsy from a pustule on the right sole revealed intraepidermal pustules containing eosinophils, elongation of epidermal rete ridges with spongiosis, and eosinophil

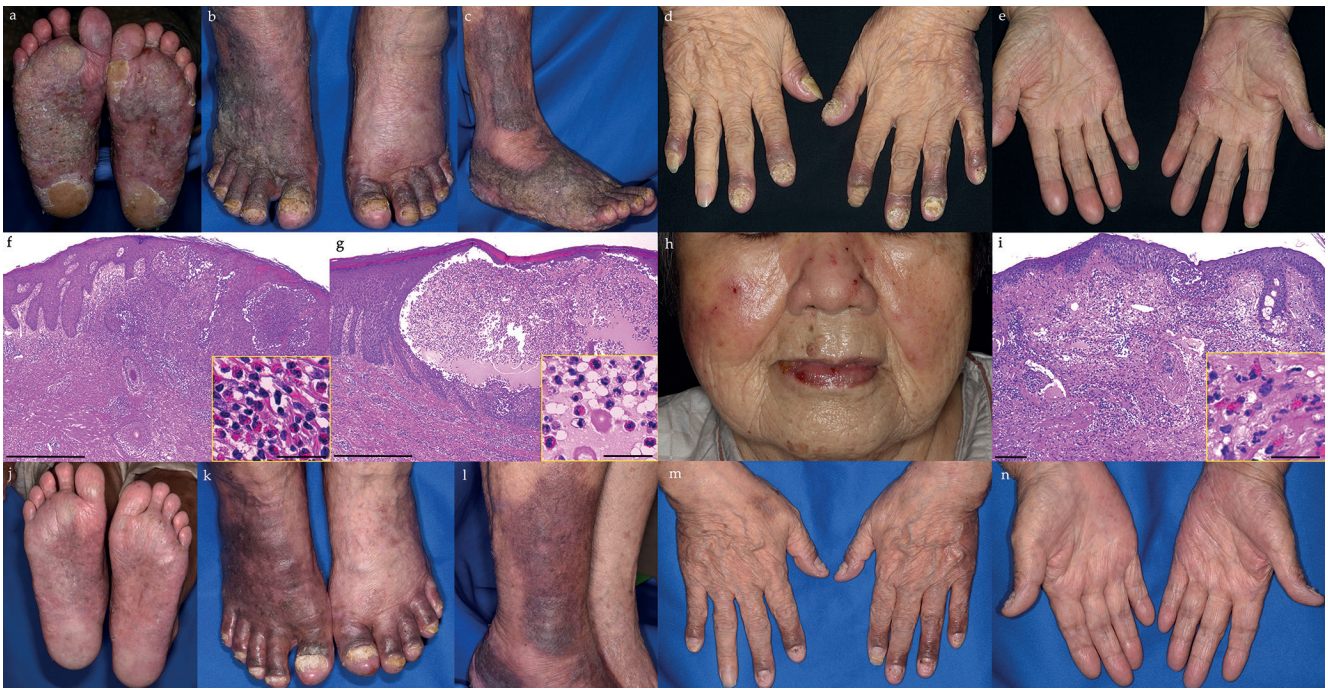

Fig. 1. Clinical and histological findings. (a–c) Pruritic vegetating plaques with scales and pustules on the lower legs and feet. (d, e) Pruritic erythema with scales in the hypothenar regions and the fingertips with nail dystrophy sparing the right ring finger. (f) Skin biopsy from vegetating lesions with pustules on the right lower leg showed elongation of epidermal rete ridges with spongiosis, intraepidermal pustules containing eosinophils, and marked eosinophil infiltration around the hair follicles (haematoxylin and eosin stain: HE, *bar* = 500 μm; *inset*, *bar* = 25 μm). (g) Skin biopsy from a pustule on the right sole revealed intraepidermal multilocular pustules containing eosinophils, elongation of epidermal rete ridges with spongiosis, and eosinophil infiltration in the dermis. (HE, *bar* = 500 μm; *inset, bar* = 25 μm). (h) Pruritic erythema with pustules on the nose and cheeks. (i) Skin biopsy from the pustule on the left cheek revealed marked eosinophil infiltration around the hair follicles (HE, *bar* = 100 μm; *inset*, *bar* = 25 μm). (j–n) Treatment with indometacin farnesil improved the vegetating plaques of lower legs and feet and erythema on the hands within 20 days, leaving post-inflammatory pigmentation on the lower legs, feet, and hands.

infiltration to the dermis (Fig. 1g). Direct immunofluorescence from the right lower leg lesion was negative. Laboratory results showed an increase in white blood cells (10,600/μL; normal, ≤9,000/μL) and eosinophils (17.6%; normal, ≤5%); neither human immunodeficiency virus antibody titre, anti-desmoglein 1, 3 antibodies, nor anti-BP180 NC16a antibody was detected. A bacterial culture from the pustules on the right lower leg revealed the growth of *Staphylococcus aureus*. Etretinate at 20 mg/day and diaphenylsulfone (DDS) at 75 mg/day were started. The lesions responded poorly to these treatments, and subsequently pruritic erythema with pustules developed on her nose and cheeks after 2 weeks of these treatments (Fig. 1h). A bacterial culture from the pustules on the face was negative. A skin biopsy from the pustule on the left cheek revealed marked eosinophil infiltration around the hair follicles and intraepidermal pustules containing eosinophils (Fig. 1i). Etretinate was stopped, while continuing the DDS at 75 mg/day and starting indometacin farnesil at 400 mg/day. All lesions except for the nail lesions completely improved within 20 days after starting treatment with indometacin farnesil (Fig. 1j–n). These findings corroborated the diagnosis of EPF. DDS and indometacin farnesil were tapered off at 8 and 10 weeks, respectively. After 2 weeks of cessation of indometacin farnesil, multiple pustules erupted on the face and feet. Indometacin farnesil at 400 mg/day was restarted, resulting in the rapid improvement of erythema and pustules within 1 week. There has been no recurrence with indometacin farnesil for 6 months.

DISCUSSION

The typical clinical manifestation of EPF is characterized by sterile follicular pustules or papules involving seborrhoeic areas, but lesions may also involve extrafollicular regions including the palmoplantar regions and the nails (1–3). We report here a case of EPF with vegetating plaques and pustules on the lower legs and feet accompanied by nail dystrophy. To the best of our knowledge, there is no previous report of EPF with vegetating plaques.

In a previous study of EPF in Japanese patients, palmoplantar pustular eruption was observed in 38 out of 207 patients (18%) (2). Umegaki et al. (3) also reported the 2 cases of EPF showing palmoplantar lesions with nail deformity. Biopsy from the nail bed revealed parakeratosis, spongiosis and interface dermatitis with eosinophils, as well as lymphocytes. Similarly, PPP is characterized by pustules, erythema and scaling localized to the palmoplantar regions, which can resemble EPF (4). In a previous report of PPP, eosinophils infiltration in the dermis was observed in 11 out of 40 patients (28%), and eosinophils in the pustules or vesicles in 6 out of 13 patients (46%) (4). Eosinophilic infiltration was also seen in the palmoplantar lesions of EPF (2, 3), as shown in PPP. Therefore, it is challenging to distinguish EPF from PPP when the skin lesions are localized to the palmoplantar regions. Indeed, the current case was initially diagnosed with PPP based on the palmoplantar erythema and pustules. Clues for the diagnosis of EPF include folliculitis with eosinophils infiltration involving seborrheic areas and a positive response to oral indometacin (5). In the current case, the presence of eosinophils infiltration around the hair follicles from the lower leg and facial lesion as well as the successful treatment with oral indometacin led to the diagnosis of EPF.

Because the current case presented with vegetating lesions accompanied by nail dystrophy, the clinical differential diagnosis included pemphigus vegetans. Pemphigus vegetans is characterized by vegetating plaques typically localized to the intertriginous areas (6). Moreover, pemphigus vegetans with distal and nail involvement has been reported, as seen in the current case (7). Although the pathogenesis of the development of vegetating lesions remains unknown, *Staphylococcus spp.* may contribute to the development of vegetating lesions because *Staphylococcus spp.* has been detected in the vegetative lesions of pemphigus vegetans and pemphigoid vegetans patients (7–9). Several studies revealed that *S. aureus* can modify the immunological milieu in the colonization region (10, 11). Extracellular vesicles, which are released from *S. aureus*, enhanced the production of eotaxin and macrophage inflammatory protein-1α (10), which play a critical role in the recruitment of eosinophils (12). Moreover, the production of interleukin (IL)-4 and IL-17, which are known to induce keratinocyte proliferation (13, 14), is also induced by the application of *S. aureus* extracellular vesicles (10). In addition, staphylococcal enterotoxins enhance the expression of IL-22 in keratinocytes and increase the number of T lymphocytes expressing IL-22 (11), which play a role in epidermal hyperplasia (15). Indeed, *S. aureus* application causes immune cell infiltration and epidermal thickening in atopic dermatitis models (10, 11). In the current case, a bacterial culture from the vegetating lesions revealed the growth of *S. aureus*, while the lesions on the face were shown to be sterile pustules. These facts indicated that colonization of *S. aureus* might be responsible for developing vegetating lesions through the disturbance of the immune balance.

The current case highlights vegetating plaques as one of the clinical manifestations of EPF. Because of the clinical similarities between EPF and other entities, it is important to confirm the perifollicular infiltration of eosinophils and the rapid and positive response to oral indometacin for diagnosing EPF.

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