Localized pemphigus herpetiformis: two case reports

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ABSTRACT

Pemphigus herpetiformis (PHF) is a rare variant of pemphigus that combines the clinical features of dermatitis herpetiformis and immunopathological features of pemphigus. In previous case reports, distribution of lesions is usually generalized, involving trunk and limbs. We report two cases of localized PHF presenting with grouped pustules on bilateral dorsal feet and left preauricular area, respectively. Microscopic examination showed neutrophilic spongiosis, subcorneal pustules, and focal acantholysis. Both direct immunofluorescence of Case 1 and indirect immunofluorescence of Case 2 revealed moderate deposition of IgG in the intercellular space of upper epidermis. Based on the typical histologic features and immunopathological findings, diagnoses of PHF were made. However, the atypical and localized clinical presentation rendered the process of reaching a diagnosis more difficult. PHF should be added in the spectrum of differential diagnosis of localized pustular disorders.

KEYWORDS

Localized Pemphigus herpetiformis Pustules

Introduction

Pemphigus herpetiformis (PHF) is a rare variant of pemphigus that combines the clinical features of dermatitis herpetiformis and immunopathological features of pemphigus. Many synonyms (dermatitis herpetiformis with acantholysis, sulfonamide-responsive pemphigus, mixed bullous disease) were used up till 1975 when the term “pemphigus herpetiformis” was coined by Jablonska et al.¹

Since then, several case reports in the literature have described the clinical variety of PHF.²⁻⁸ We report two atypical cases of localized form of PHF. Common to previous case reports is a clinical presentation of wide-spread distribution of lesions, usually involving both the trunk and limbs.

Case reports

Case 1

An 80-year-old man with a 6-year history of prostate cancer and who was under regular hormonal therapy came to our clinic due to progressively itchy and painful skin lesions (which had lasted for weeks). Physical examination showed erythematous patches with desquamation and multiple pustules on bilateral dorsal feet (Figure 1A). Examination with 10% potassium hydroxide revealed no fungal hyphae or spores.

Histopathological examination showed spongiosis and subcorneal pustules composed of many neutrophils and eosinophils (Figure 1B). Focal acantholytic keratinocytes were also observed under higher magnification (Figure 1C).

Direct immunofluorescence showed moderate deposition of immunoglobulin (Ig) G and complement 3 in the intercellular space of the upper epidermis (Figure 1D). Immunofluorescence for IgA, IgM, and fibrinogen were negative. Diagnosis of PHF was made according to the distinct clinical features...
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diagnoses included dermatophytosis, superficial pemphigus and subcorneal pustular dermatoses. Direct immunofluorescence was not performed because autoimmune bullous disease was not clinically suspected initially. Indirect immunofluorescence from patient’s serum using monkey esophagus as substrate was arranged and revealed moderate deposition of IgG over the intercellular space of the epidermis (Figure 2D). Although indirect immunofluorescence for IgA was not performed, PHF was diagnosed according to strong IgG intercellular deposition and superficial subcorneal acantholysis. She received treatment with oral antihistamine and topical steroid for preauricular lesions. The clinical condition improved 2 weeks after treatment and was without recurrence in the 2-year follow-up period.

Discussion

The clinical distribution of PHF, in the few case reports is almost invariably generalized. The characteristic skin manifestations of PHF are pruritic erythematous vesicular, bullous, and pathological findings. Low dose systemic steroid prednisolone (20 mg/day) was given and clinical response was good. The pustules subsided rapidly after 2 weeks of therapy. We tapered off systemic steroid a month and a half later; no recurrence was noted at subsequent follow-ups. Unfortunately, the patient’s prostate cancer progressed with multiple bone metastases a year after the initial diagnosis of PH. The patient died in 2 years; there was no skin lesion recurrence during this period.

Case 2

A 55-year-old woman without significant past medical history presented with itchy skin lesions for several months. Physical examination showed grouped herpetiform pustules on erythematous patches over left preauricular area (Figure 2A). Tzanck smear and microscopic examination with 10% potassium hydroxide of the lesions on left preauricular area were negative.

Histopathological examination of skin biopsy specimen from preauricular lesions showed subcorneal pustules and focal acantholysis (Figures 2B and 2C). The differential diagnoses included dermatophytosis, superficial pemphigus and subcorneal pustular dermatoses. Direct immunofluorescence shows IgG deposition over the intercellular space of upper epidermis (400×).
or papular lesions in herpetiform pattern involving both the trunk and limbs, similar to those of dermatitis herpetiformis. Rare clinical presentations include measles-like lesions or urticarial plaques. Presence of pustules in PHF has been reported before, but the distribution was much wider (abdomen, back, leg, forearm, wrist). Localized PHF was atypical and rare, which made the clinical diagnosis of pemphigus more difficult.

The differential clinical diagnoses in our cases might have included herpes infection, dermatophytosis, contact dermatitis with secondary bacterial infection or other rare bullous disorders, such as subcorneal pustular dermatosis and IgA pemphigus. The strong deposition of IgG and absence of IgA immunofluorescence excluded the possibility of IgA pemphigus. Pemphigus was not suspected in Case 2; as a result, immunofluorescence examination was not ordered at first. Later on, positive results from indirect immunofluorescence performed allowed us to reach the final diagnosis. A previous study reported that less than half of patients with PHF had a positive indirect immunofluorescence. For physicians, this highlights the importance of recognizing the clinical features of localized immunobullous disease for making appropriate investigations including skin biopsy and direct immunofluorescence examination.

The histopathological findings in PHF are characterized by intraepidermal blisters or subcorneal pustules, but not prominent acantholysis. These features make the histological diagnosis more difficult because similar findings are also present in pustular psoriasis, subcorneal pustular dermatosis, bullous impetigo, acute generalized exanthematous pustulosis, subcorneal pustular dermatosis-type IgA pemphigus and dermatophytosis. All these clinical entities have neutrophil exocytosis in the spongiotic epidermis with variable eosinophils in the infiltrate. A careful comparison of the clinical presentation and immunofluorescence staining of each case are necessary for correct diagnosis. Moreover, the intraepidermal neutrophilic infiltrate and intercellular IgG deposition can be present in cases of pemphigus foliaceus; this should not result in diagnostic problems however, due to the completely different clinical presentation of pemphigus foliaceus.

Localized pemphigus vulgaris (PV) has been reported previously, and its presentation can be very similar to...
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the current cases. Differentiating between these two entities however, may rely on (1) more pustules in patients with PHF while erosions and crusts in those with PV; (2) histologically subcorneal and intraepidermal acantholysis in patients with PHF while suprabasal acantholysis in those with PV; (3) serologically, mainly anti-desmoglein-1 autoantibodies in patients with PHF while mainly anti-desmoglein-3 autoantibodies in those with PV. Neither Immunoblot nor ELISA was performed in our cases due to patients’ inactive status shortly after treatment.

PHF was rarely associated with malignancies, although links with some cancers such as prostate cancer have been noted. The skin lesions in Case 1 were clinically irrelevant to his prostate cancer status however, and should therefore not be considered a paraneoplastic process.

In conclusion, PHF does not always assume a generalized presentation. When it is localized, the clinical and histopathological diagnosis can be very difficult; making the correct diagnosis therefore relies on a positive immunofluorescence result. Thus, when approaching presentations of localized clusters of vesicles or pustules, one should always bear in mind the possibility of such a differential diagnosis.

References