A Case of Pemphigus Herpetiformis: An Unusual Variant of Pemphigus

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ABSTRACT:
Pemphigus herpetiformis is a rare subtype of the pemphigus group. Its clinical presentation of vesicles and papules arranged in an annular pattern may mimic other vesiculobullous diseases, particularly dermatitis herpetiformis. However, histopathology and direct immunofluorescence findings are consistent with pemphigus. Most patients exhibit a benign disease course with a favorable response to therapies such as dapsone and corticosteroids. We report the case of a 24-year-old woman presenting with multiple erythematous plaques and vesicles forming an annular pattern on the face, trunk, and extremities, who was diagnosed with pemphigus herpetiformis.
Key words: Autoimmune vesiculobullous, Pemphigus herpetiformis

Introduction

Pemphigus herpetiformis (PH), a rare variant of the pemphigus group, is characterized by clusters of vesicles and papules often arranged in an annular pattern. Autoantibodies against desmoglein 1 and 3 are commonly reported, although the mechanism of antibody development remains unclear[1]. Herein, we report a case of pemphigus herpetiformis in a young Thai woman.

Case report

A 24-year-old female had multiple progressive red plaques and small vesicles arising on normal skin. Some lesions coalesced into annular shapes on her face, trunk, and extremities over nine months (Figure 1). She complained of nocturnal itching that subsided during the day. There were no oral or genital mucosal lesions and no systemic symptoms. Her medical history was unremarkable.

Differential diagnoses for vesiculobullous diseases with an annular or grouped pattern of arrangement included dermatitis herpetiformis (DH), IgA pemphigus, and linear IgA bullous dermatosis (LABD). Skin biopsy revealed subcorneal and intraepidermal separation with acantholysis. The dermis exhibited perivascular lymphocytic infiltration with sparse eosinophils (Figure 2). Direct immunofluorescence revealed positive IgG (3+) and C3 (2+) deposition at the intercellular space (Figure 3), while indirect immunofluorescence revealed circulating IgG anti-intercellular antibodies with a titer >1:40. Anti-endomysial antibodies were negative. Due to the lesion's resemblance to dermatitis herpetiformis, with an annular-shaped pattern distinct from pemphigus vulgaris or pemphigus foliaceus, along with histopathological and immunofluorescence findings consistent with pemphigus, a diagnosis of PH was established based on the diagnostic criteria of Kasperkiewicz and Costa.

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Received: 16 December 2024 Revised: 21 February 2025 Accepted: 8 July 2025

Figure 1 A 24-year-old female with multiple brownish annular papules and plaques with vesicles on the back

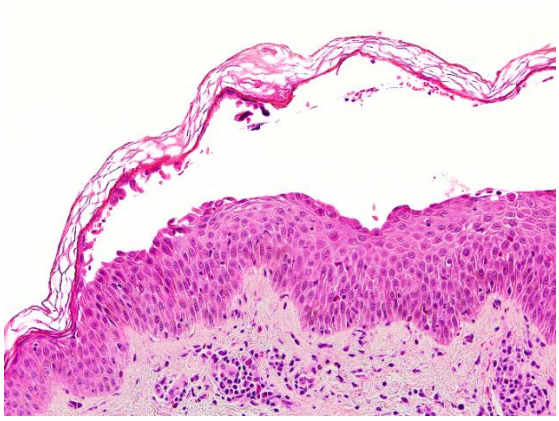

Figure 2 Histopathology showed subcorneal separation with acantholysis and superficial perivascular lymphocytic infiltrates with scattered eosinophils. (H&E, magnification X200)

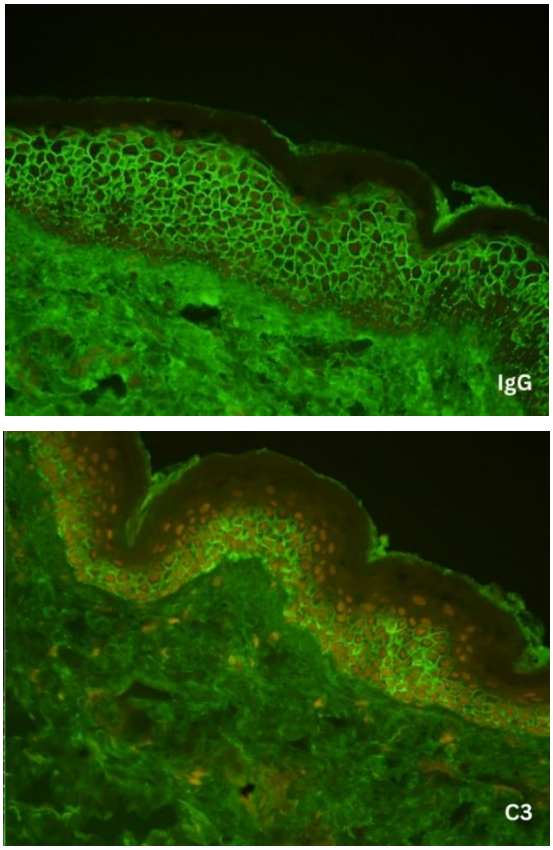

Figure 3 Direct immunofluorescence showed deposits of immunoglobulin G (intensity 3+) and complement 3 (intensity 2+) at intercellular location

The patient was prescribed oral prednisolone (20 mg/day) and dapsone (100 mg/day). After a month of dapsone therapy, she developed hemolytic anemia, prompting a switch to azathioprine (100 mg/day) and colchicine (0.6 mg/day). Prednisolone was tapered over three months, and azathioprine was discontinued after six months without recurrence of vesicles.

Discussion

PH is a rare variant of pemphigus that clinically mimics DH, with vesiculobullous or papular lesions arranged in grouped patterns. Annular-shaped lesions are common, likely due to the centrifugal spread of the inflammatory

process[1]. However, the histological and immunological findings are consistent with the pemphigus group. Direct immunofluorescence typically shows IgG and C3 deposition in the intercellular spaces of the epidermis. Unusual cases with IgA deposition in the intercellular spaces, intra-epidermis, or focal linear basement membrane have also been reported[2,3]. ELISA often detects IgG autoantibodies against desmoglein 1 or 3, though mucosal involvement in PH is rare. This might be explained by the predominant of the autoantibodies against desmoglein 1 as majority of PH serum contained the autoantibodies against desmoglein 1[4]. Recent literature reviews suggest that IgG autoantibodies against desmocollin 1 and 3 may also be present in PH[5]. Diagnostic criteria for PH have been proposed by Kasperkiewicz and Costa (Table 1).

In our case, the patient presented with multiple progressive erythematous plaques with small vesicles that coalesced into annular lesions on the face, trunk, and extremities. These lesions were consistent with previous reports of PH. Additionally, PH can be misdiagnosed as other subepidermal bullous dermatoses, including IgA pemphigus and LABD[6]. However, IgA pemphigus, LABD, and DH can typically be differentiated from PH by the deposition of IgA observed on direct immunofluorescence. Furthermore, the patient reported pruritus, particularly at night, which aligns with previous reports indicating that pruritus is a common symptom in most cases of PH[7].

Histopathological findings in PH are heterogeneous, ranging from eosinophilic or neutrophilic spongiosis to subcorneal or suprabasal separation with varying degrees of acantholysis[7]. Our case exhibited subcorneal separation with minimal intraepidermal involvement, resembling superficial pemphigus rather than subepidermal bullous dermatosis (Figure 2). Direct immunofluorescence revealed intercellular IgG and C3 deposition with a negative result for IgA. This pattern is distinct from the granular IgA deposition observed in DH (Figure 3). Furthermore, indirect immunofluorescence on monkey esophagus substrate excluded DH by confirming the absence of anti-endomysial antibodies, which are typically sensitive in non-gluten-restricted patients[8]. Regarding the detection of autoantibodies, we cannot perform ELISA testing of anti-desmoglein and anti-desmocollin for the definite diagnosis owing to the limitation in our institute.

PH responds well to dapsone and corticosteroids, with some cases requiring additional immunosuppressive agents like azathioprine, methotrexate, or IVIG. Spontaneous resolution is rare[7]. In this case, dapsone induced hemolytic anemia, a known adverse effect, emphasizing the need for close monitoring of complete blood counts. The prognosis of PH is generally benign, but relapses can occur, particularly during steroid tapering. Although some reports associate PH with solid tumors and autoimmune diseases, further studies are needed[1]. Our patient achieved complete remission after the treatment for 8 months and showed no malignancy or autoimmune conditions during one year of follow-up.

Conclusion

We report a rare case of pemphigus herpetiformis, a condition that mimics DH and other vesiculobullous diseases characterized by annular lesion patterns. However, histopathological and immunofluorescence findings confirmed its classification within the pemphigus group. Early recognition is essential, as the treatment approach and prognosis differ markedly from those of other dermatoses.

Table 1 Diagnostic criteria of pemphigus herpetiformis

	Clinical signs	Histology	Immunological
Kasperkiewicz[1] Mandatory: Clinical signs + Direct immunofluorescent microscopy	Grouped (herpetiform) distribution of itching erythematous vesicular/bullous/papular lesions, often in an annular-shaped pattern	Eosinophilic/neutrophilic spongiosis/intraepidermal pustules with or without acantholysis	Direct immunofluorescent study: IgG and/or C3 intercellular pattern on epidermis Indirect immunofluorescent study: IgG intercellular pattern on epidermis Detection of IgG autoantibodies against desmoglein 1 and/or 3 desmocollin 1 and/or 3
Costa[7] Mandatory: 1 clinical + 1 pathological + 1 immunologic	Pruritic herpetiform intact cutaneous blisters with/without erosions	Intraepidermal eosinophils and/or neutrophils	Direct immunofluorescent study: IgG with/without C3 intercellular deposits
	Pruritic annular or urticaria erythematous cutaneous plaque with/without erosions	Intraepidermal split with/without acantholysis	Indirect immunofluorescent study: IgG to epithelial cell surface Detection of circulating autoantibodies against desmoglein (1,3) or desmocollin (1,2,3), or both

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