

following six months, oral glucocorticoids could be reduced to 0.25 mg/kg bodyweight, azathioprine was continued at 1.5 mg/kg bodyweight, and clinical and serological remission was maintained (figures 1C, D).

Due to the variable clinical picture, the diagnosis of PVeg is often challenging. Verrucous plaques involving the finger and nail unit can precede the occurrence of typical PVeg lesions and are prone to be misdiagnosed as acrodermatitis continua suppurativa [3, 4]. Histopathology, DIF, and ELISA are pivotal to confirm the diagnosis and guide treatment [5]. Unlike PVeg which typically affects middle-aged individuals, Pemphigoid vegetans is a rare disease of the elderly which can be differentiated based on histological and immunofluorescence studies [1, 6]. Systemic corticosteroids, combined with immunosuppressive agents, such as azathioprine or mycophenolate mofetil, are considered to be the mainstay for PVeg therapy [1, 7]. For the reported patient, systemic corticosteroids were not applied before acrodermatitis continua suppurativa (which is associated with a glucocorticoid rebound phenomenon [7]) was excluded as a differential diagnosis. Seven-week-long treatment with methotrexate and doxycycline did not prevent progression of the disease and patient morbidity increased. Whereas tetracyclines have been proven effective against PV and PVeg, only methotrexate has been reported as a valuable adjuvant agent for the treatment of PV, with no reports on PVeg [7-9]. IVIG, which are effective for the treatment of steroid-resistant cases of PV [10], stopped lesion progression but did not induce disease remission. Finally, the treatment combination of oral prednisolone and azathioprine was critical for stable improvement of skin lesions. The presented case highlights the diagnostic challenge clinicians face when encountering PVeg patients and the crucial role of systemic corticosteroids for treatment of the disease. ■

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Possible involvement of IgE antibody in epidermolysis bullosa acquisita: detection and correlation

Disease severity of bullous pemphigoid (BP) is reported to be associated with the serum level of IgE anti-BP180 antibody as well as IgG autoantibody [1-3]. However, the involvement of IgE in epidermolysis bullosa acquisita (EBA) remains to be clarified. Here, we describe an EBA patient in whom enzyme-linked immunosorbent assay (ELISA) suggested the existence of IgE anti-collagen VII (col7) antibody. Both IgE anti-collagen VII antibody titre and serum total IgE level changed in parallel with disease activity.

A 69-year-old woman presented with a five-year history of itchy erythema and blisters on the trunk and extremities. Clinical examination revealed multiple thumb nail to palm-sized erosion and thumb nail-sized blisters on the trunk and extremities, as well as nail loss (figures 1A, B). A skin biopsy demonstrated a subepidermal blister with scant infiltration of lymphocytes (figure 1C). Direct immunofluorescent (DIF) staining showed the linear deposition of IgG and complement C3 along the dermal-epidermal junction. Indirect immunofluorescent (IIF) staining with 1 M sodium chloride-split skin revealed linear deposition of IgG on the dermal side (figure 1D). IgE deposition was not detected. Laboratory tests showed elevated serum levels of IgG (1,821 mg/dL) and IgE (898 IU/mL). ELISA for IgG anti-col7 antibody (MBL, Japan) was positive (index: 137.8) while IgG autoantibodies for BP180 NC16a domain and desmoglein 1/3 were negative. We conducted ELISA for IgE anti-col7 antibody using the same ELISA kit with HRP-conjugated anti-IgE antibody (Goat polyclonal, Gene-Tex) on our case and 13 BP patients. The results suggested the existence of IgE anti-col7 antibody in our case (OD of 0.352 in our case vs 0.0858 ± 0.0669 [average $\pm$ 2 SD] in 13 BP patients). The diagnosis of EBA was made based on these findings. The patient's bullous pemphigoid disease area index (BPDAI) score was 65 (erosion/blister). After treatment with 0.5 mg/kg/day prednisone and a total of six courses of double-filtration plasmapheresis (DFPP) and intravenous immunoglobulin infusion therapy, disease activity diminished with reduction of BPDAI score to 17 (Erosion/blister). IgG and IgE anti-col7 antibody titres (16.6 [index] and 0.152 [OD], respectively), total IgE (148 IU/mL), and IgG level (861 mg/dL) also

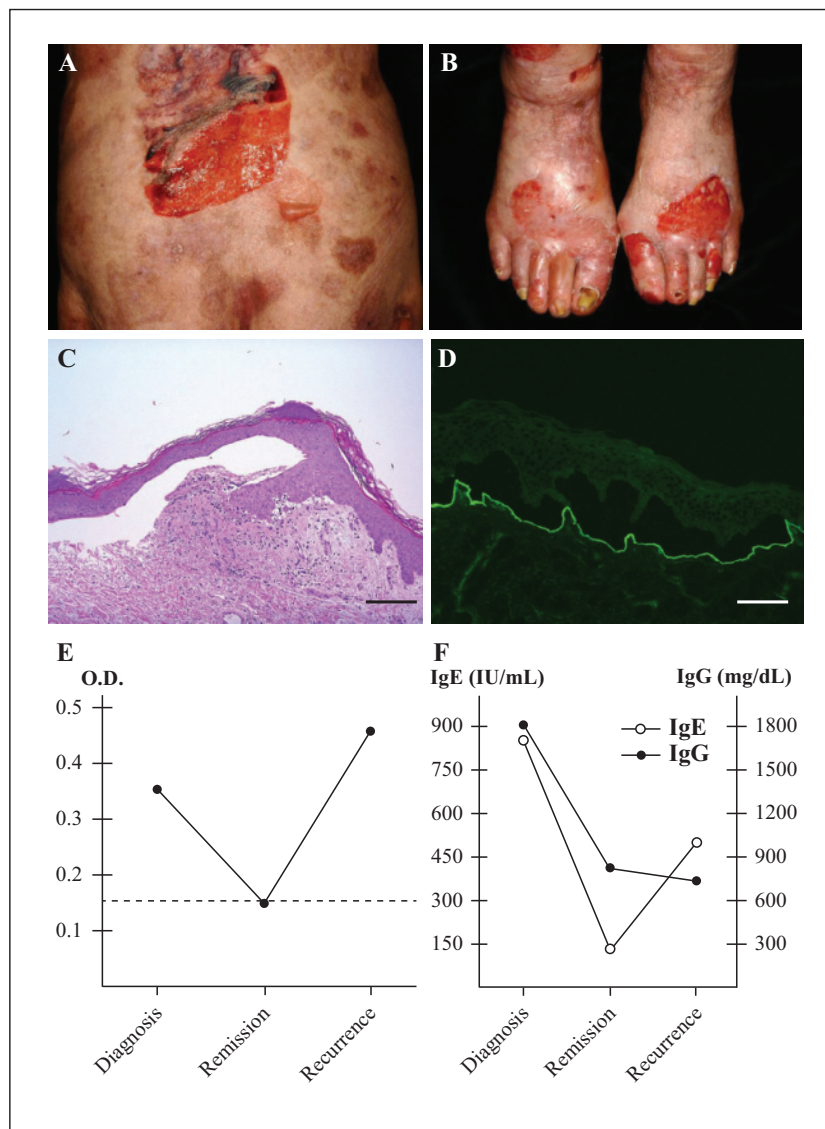


Figure 1. Clinical manifestation of the palm-sized erosive lesion with thumbnail-sized blisters on the back (**A**) and feet (**B**); toenail loss is also observed. **C**) The lesional skin shows a subepidermal blister with scant infiltration of lymphocytes (haematoxylin-eosin staining; $\times 100$; bar = 100 μm). **D**) Split-skin indirect immunofluorescent analysis shows linear deposition of IgG on the dermal side. ($\times 100$; bar = 100 μm). **E**) IgE reactivity against col7 in sera at disease diagnosis and during remission and recurrence, measured using HRP-conjugated anti-human IgE antibody and a commercially available ELISA kit (MBL, Japan); dots show the OD values of IgE anti-col7 antibodies and the dotted line indicates the threshold which is based on average OD value + 2 SD of the sera from 13 BP patients. OD values for IgE anti-col7 antibody are higher than the threshold at diagnosis and recurrence, and correlate with disease activity. **F**) Serum total IgE and IgG levels at the time of diagnosis, remission and recurrence; the white circles indicate serum total IgE levels and the black circles indicate total serum IgG. Total IgE concentration also correlates with disease activity.

decreased. Prednisone at 0.4 mg/kg/day and cyclosporine at 1.5 mg/kg/day sustained the patient's condition for a month. Thumb nail-sized erosive lesions then developed on the trunk and the BPDAl score slightly elevated to 23 (erosion/blister). IgG and IgE anti-col7 antibody titres (27.6 [index] and 0.469 [OD], respectively) and total IgE (554 IU/mL) also increased while serum total IgG level slightly decreased (742 mg/dL). A further two courses of DFPP were performed and there has been no recurrence for three months.

Involvement of IgE autoantibody has been reported in BP and MMP [4, 5]. Although the relationship between clinical

manifestation of MMP and IgE anti-laminin332 antibody is still obscure [6], IgE-anti BP180 antibody titre is correlated with disease activity in BP [1-3]. IgE antibody can bind BP180 and may potentially cause eosinophil degranulation, resulting in blister formation in BP [5]. As for EBA, one article described the association between EBA disease activity and IgE for several antigens including dust and house mites, as well as *Candida albicans* [7]. In our case, besides the negative results of fluorescent enzyme immunoassay testing for these allergic antigens at the time of recurrence, the ELISA suggested the existence of IgE anti-col7 antibody, the titre of which changed along with disease severity

(figure 1E) (0.352 at diagnosis, 0.152 during remission, and 0.469 during recurrence over a threshold of 0.153 which was determined as an average + 2 SD based on the results from 13 BP patients). Total IgE itself also correlated with disease activity while total IgG did not (figure 1F).

Although specific IgE antibodies for col7 were detected with ELISA, IgE deposition was not detected on DIF or IIF. Circulating IgE anti-laminin 332 antibodies have been reported to be detected by immunoblot analysis, but were not detected in immunofluorescence studies [6]. The same discrepancy is also reported for BP [8, 9] and this was claimed to derive from overwhelming levels of IgG directed to the same antigen [9].

In our case, IgE anti-col7 antibodies and total IgE level correlated with disease activity. Further studies are needed to clarify the involvement of IgE class antibodies in disease activity. ■

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Corticosteroid-resistant prurigo nodularis: a rare syringotropic variant associated with hypohidrosis

There are no strong theoretical grounds that topical corticosteroids may improve the outcome of prurigo nodularis (PN). Rather, topical corticosteroids may paradoxically induce a new onset of recalcitrant PN or worsen pre-existing quiescent PN. Here, we present four recalcitrant PN cases treated with potent topical corticosteroids, who showed complete or significant regression of lesions after discontinuation of topical corticosteroid therapy combined with a moisturizer as the treatment modality. Our cases indicate that use of topical corticosteroids is not always beneficial, but rather, is paradoxically associated with later development of corticosteroid-resistant PN.

Case 1 was an 11-year-old girl who presented with pruritic papules/nodules on her buttocks. The area affected had slowly increased in size and number and involved the right buttock in a well-defined area despite treatment with clobetasol propionate (CP) 0.05% ointment (a Class 1 topical corticosteroid). The pruritic lesions consisted of excoriated brownish-red papules/nodules, crusts, and patchy hyperpigmentation. Many papules/nodules had markedly increased in size and number, especially at the areas aggressively treated with CP (figure 1A). A skin biopsy of the papule showed acanthosis and hyperkeratosis with a mixed syringotropic infiltrate containing lymphocytes and eosinophils in the dermis (figure 1B). Skin dryness was noted on normal-appearing skin surrounding the PN papules. Indeed, skin surface hydration (SSH) status, measured using a SKICON-200 (IBS Ltd, Hamamatsu, Japan), in the normal-appearing skin surrounding PN papules on the left buttock was reduced to 15.4 μ S, as compared with 95.6 μ S on the unaffected site of the forearm, suggesting a disturbance of sweating due to aggressive use of topical corticosteroid.

Four PN patients including Case 1, who had been refractory to potent topical corticosteroids, were recruited and their clinical and histological features were analysed. These PN lesions were clinically characterized by red to reddish-brown flat or dome-shaped nodules/papules appearing on the dry skin, however, the clinical presentation was heterogeneous among the patients. In some patients, particularly in children, the eruption was subacute and composed of intensely pruritic multiple papules/nodules characterized by less firm and less infiltrated eruptions, which resembled that of prurigo simplex subacuta [1, 2]. The corticosteroid-resistant PN lesions were usually asymmetrically distributed and were predominantly located in the extensor surfaces of extremities, although some lesions were also seen on the abdomen, buttocks, and breasts. Typical histopathological patterns of change were noted in the majority of biopsy specimens; essentially, all specimens were microscopically identical and most specimens showed syringotropic infiltration of lymphocytes (figure 1B).

Sweating responses under quiescent conditions (basal sweating) and after thermal stimulus (inducible sweating) were evaluated using a recently established quantitative method, referred to as “impression mold technique” (IMT), to evaluate individual sweat gland/duct activity to produce