

Bullous Pemphigoid with Localized Umbilical Involvement

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Sir,

Bullous pemphigoid (BP) is the most frequent autoimmune bullous disorder. BP is associated with antibodies to two hemidesmosomal proteins, BP180 (type XVII collagen) and BP230 (1). The disorder usually affects elderly people, and severe pruritus is typically present. In the majority of patients, lesions are generalized and are most common on flexural aspects of the limbs and lower abdomen (2). By contrast, localized forms have also been reported at particular sites, including the pretibial area, palmo-plantar region, and genital, perineal, and perianal area, or confined to sites previously affected by, for example, radiotherapy, surgery, trauma, and burns, as well as around stomata and haemodialysis fistulae (2–4). Localized lesions may remain localized or develop into classical BP.

CASE REPORT

An otherwise healthy 61-year-old Caucasian woman presented with a 2–3-year history of itchy erythema and erosions in the umbilical area, which had occasionally lead to a burning sensation and blood-tingled exudation. Treatment with topical antiseptics had not been effective, but the lesions sometimes improved spontaneously. Ultrasound examination had been unremarkable one year previously. Most bacterial swabs had been negative, and candidosis had been excluded repeatedly. No type IV allergy against nickel was reported. The patient was taking fenofibrate, captopril, hydrochlorothiazide, and citalopram for hypercholesterolaemia, arterial hypertension, and depression, respectively, all of which treatments had been initiated without relation to the onset of the skin lesion. On examination, a sharply demarcated erythema, erosions, and a tense vesicle were found in the umbilical area (Fig. 1). The remaining skin and mucous membranes were unaffected.

Histopathology of a lesional skin biopsy showed that the epidermis was completely detached from the dermis and revealed a dense, almost band-like, infiltrate of lymphocytes and eosinophil granulocytes in the underlying papillary dermis. Direct immunofluorescence microscopy of a perilesional skin biopsy showed strong linear staining of C3 and IgG (Fig. 2a) and weaker labelling of IgA at the dermal-epidermal junction. The n-serrated pattern seen in some areas is typically found in diseases with lamina lucida autoantibody reactivity and differentiates them from epidermolysis bullosa acquisita (Fig. 2a, inset) (5). By indirect immunofluo-



Fig. 1. Erythema, erosions, and a tense vesicle in the umbilical area, in an area of approximately 2.5 cm².

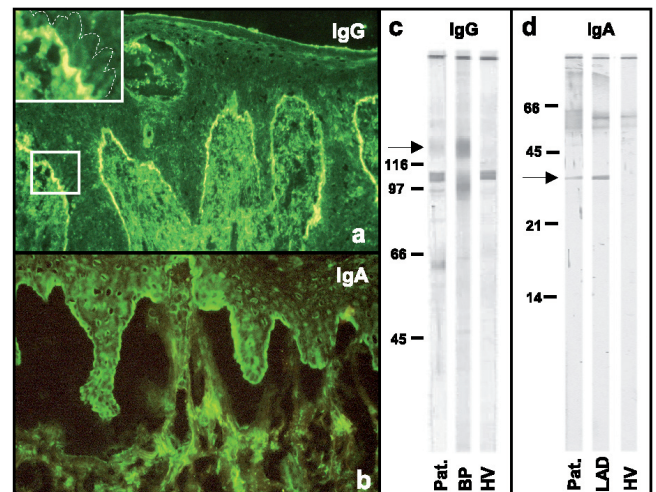


Fig. 2. (a) Linear deposits of C3 at the dermal-epidermal junction by direct immunofluorescence microscopy of perilesional skin. The n-serrated staining pattern seen in some areas (inset, magnified view $\times 3$) excluded the diagnosis of epidermolysis bullosa acquisita (5). The dotted line in the inset highlights the weak n-serrated staining. (b) Weak epidermal binding of IgA autoantibodies by indirect immunofluorescence microscopy on human salt-split skin. (c) The patient's serum (Pat) contained IgG autoantibodies against LAD-1, the soluble ectodomain of BP180, detected by Western blotting using conditioned concentrated medium of cultured human keratinocytes. (d) IgA autoantibodies against the recombinant 16th non-collagenous domain of BP180 (BP180 NC16A) were also found by Western blotting of the patient's serum. The position of the molecular weight markers are indicated on the left side of panels c and d. Arrows mark the position of the relevant target antigens, LAD-1 (c) and BP180 NC16A (d). Sera of patients with classical bullous pemphigoid (BP) and linear IgA dermatosis (LAD) as well as of a healthy volunteer (HV) served as controls (c, d).

rescence (IF) on human 1 M NaCl-split human skin, weak binding of IgA at the epidermal side of the artificial split was shown to be present (Fig. 2b), while no IgG reactivity was found. By immunoblotting of the recombinant 16th non-collagenous domain of BP180 (BP180 NC16A) (6), the immunodominant region in classical BP, serum IgA antibodies were detected (Fig. 2d), whereas IgG reactivity was absent. In addition, the patient's serum contained IgG antibodies to the soluble ectodomain of BP180 (LAD-1) by immunoblotting of concentrated conditioned medium of cultured HaCaT cells (Fig. 2c) (6). The stronger IgG staining by direct IF microscopy and the strong labelling of C3, that can only be weakly induced by IgA autoantibodies, favoured a diagnosis of BP.

The combined use of crystal violet solution 0.1% and betamethasone 0.1% cream resulted in rapid resolution of the lesion. After withdrawal of the topical corticosteroid the lesion recurred, but this was controlled by its re-application once per week. After 20 months, the lesion finally healed completely and the topical corticosteroid was tapered off.

Our patient presented with immunopathological features of BP; however, there were several interesting findings in this case, including the peculiar clinical picture, the combined IgA and IgG response against BP180, and the patient's relatively young age. Interestingly, her lesions were restricted to the umbilicus. While the umbilical area is a predilection site for patients with classical BP (2), BP limited to this region has not been described previously. Periumbilical lesions are also typical for patients with pemphigoid gestationis. Our patient had had two pregnancies without skin lesions or pruritus and gave birth to two healthy children. The specificity of serum autoantibodies has been reported rarely in patients with localized BP. In two patients with lesions limited to the pretibial area and face and scalp, respectively, reactivity against the BP180 NC16A domain was described (7, 8) and in a child with vulval BP, reactivity against LAD-1 was observed (9). In these localized variants including our patient, the autoantibody response is comparable with classical BP and favours the hypothesis that localized forms of BP are not proper entities, but rather represent forms of classical BP with lower disease activity.

The generation of both IgG and IgA autoantibodies against BP180 is also frequently observed in classical BP. Indeed, the majority of BP patients develop, in addition to IgG autoantibodies, IgA reactivity against BP180 (10). It may be speculated that the IgA autoantibodies are due to the relatively young age of our patient. We have previously shown that patients with IgG antibodies to the basal membrane zone are significantly older compared with patients with IgA reactivity (11).

This report describes an unusual case of localized BP and highlights the importance of suspecting BP in chronic pruritic erythema and erosions, even when lesions are restricted to small areas and no obvious blistering is present.

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