

Bullous Pemphigoid: Three Atypical Cases

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Sir,

Bullous pemphigoid (BP) is a relatively common chronic autoimmune subepidermal blistering disease, which frequently occurs in the elderly. Typically, patients with BP present with large tense bullae on an erythematous base, located at the sides of the neck, axillae, groins, upper inner aspects of the thighs and abdomen. Many different clinical variants of BP have been described (1).

The main therapy for BP is based on systemic corticosteroids and immunosuppressants, but alternative treatments (erythromycin, tetracyclines plus niacinamide, and topical high-potency steroids) have been reported to be effective in some cases (1, 2).

We describe three cases of BP that were unusual for clinical presentation, triggering by identified factors and responsiveness to non-conventional treatments.

CASE REPORTS

Case 1

A 59-year-old man presented with bullous eruptions located on his scalp, forehead, and sternal region (seborrheic areas). The tense bullae were 0.5–1 cm in size, on a base that appeared erythematous and covered by greasy scaling. The eruption had been present for a few months (Fig. 1).

Histologically, the blisters were subepidermal with a dense infiltrate of eosinophils. Direct immunofluorescence (IF) studies revealed linear deposition of IgG and C3 at the dermo-epidermal junction. Indirect IF with

NaCl split human skin as substrate showed reactivity of anti-human IgG goat serum on the epidermal side. By immunoblotting on cultured keratinocyte extracts, a 180 kDa BPAG2 antigen was identified in the patient's serum.

A diagnosis of seborrheic BP was made on the basis of the clinical and laboratory findings. The patient had been taking losartan, 25 mg, for hypertension for 6 years. Losartan was withdrawn and deflazacort therapy at 60 mg daily was started. After 10 days, the patient improved clinically, with no development of new lesions. Two weeks later, with no evidence of any lesions, the steroid dosage was gradually tapered and reduced to zero within a month. After 2 months, the patient's blood pressure rose again and, of his own volition, he restarted losartan treatment (25 mg/day). A few days later, eruptions similar to the previous ones appeared on the same sites. Losartan was finally stopped and replaced with a beta-blocker. A topical treatment with clobetasol propionate proved to be sufficient to clear all lesions in a couple of weeks.

Case 2

A 76-year-old man with moderate essential hypertension was being treated with 10 mg enalapril daily for 12 months when he noticed some yellowish pustules and erosions in the perineum and axillae. In time, papillomatous proliferations developed at the sites of the initial pustular lesions and crops of bullae appeared on the vegetating bases and surrounding areas (Fig. 2).



Fig. 1. Patient 1: Seborrheic bullous pemphigoid. Bullae and greasy scaling on the scalp.



Fig. 2. Patient 2: Vegetating bullous pemphigoid. Bullae on and around papillomatous vegetations located on the right axilla.

Cytologic investigation revealed no acantholytic cells. A biopsy of a fresh bulla adjacent to the vegetations showed an inflammatory subepidermal cavity with an eosinophil-rich dermal infiltrate. Direct immunofluorescence of the perilesional skin showed linear staining with IgG and C3 at the dermo-epidermal junction.

These findings were considered to be consistent with the diagnosis of vegetating BP. Enalapril therapy was stopped. Erythromycin 1,000 mg/day was commenced. The patient improved progressively, with no development of new lesions. After 3 weeks, all lesions had cleared.

Case 3

A 76-year-old woman developed a few blisters with an erythematous base on her left leg. The leg had been seriously injured 8 months earlier in a car accident and since then it had become swollen, in comparison with the right leg. A diagnosis of post-traumatic lymphedema had been made by her doctor. A biopsy of a fresh blister with an edematous base showed an intact subepidermal bulla, dermal edema, and a moderate inflammatory infiltrate, with a predominance of eosinophils. Direct immunofluorescence studies showed a linear deposition of IgG and C3 along the basal membrane zone.

A diagnosis of localized BP was made. Treatment with erythromycin, at 1,000 mg daily, was started; no new lesions appeared and a gradual improvement of the skin manifestations was observed. All lesions cleared within a month.

DISCUSSION

The cases reported can be considered as three atypical forms of BP. The first patient, with bullous eruptions localized on seborrheic areas, fits the variant of seborrheic bullous pemphigoid, first described by Schnyder, which may resemble pemphigus erythematous (3). The second patient presenting vegetations and blisters in the axillae and perineum features vegetating bullous pemphigoid. The third patient with blisters confined to a lymphedematous limb is a typical example of localized bullous pemphigoid. This variant of BP may remain localized for years or become generalized (1). In all three cases the histological and immunological findings have substantiated the diagnosis of BP. As for the intervention of triggering factors, circumstantial evidence occurs in each of the cases we have presented.

The first patient had been taking losartan (an anti-hypertensive agent belonging to the angiotensin II

receptor antagonists) for 6 years. When the drug was stopped, the recovery obtained by deflazacort therapy continued even without the steroid treatment, but new lesions appeared soon after losartan was resumed.

The second patient was taking enalapril (an anti-hypertensive agent belonging to the ACE-inhibitors) for one year. This drug has proved to be a triggering factor for pemphigus (4–7) and lichen planus (8) in other patients, so it could well be suspected of having a role in inducing BP.

The third patient had post-traumatic lymphedema, which may have paved the way for the onset of BP lesions (9, 10).

Erythromycin seems to have a significant anti-inflammatory effect and may be of benefit when used alone or in combination with topical steroids in treating BP patients who are not ideal candidates for a systemic steroid (11). High-potency steroids applied to the early lesions may be sufficient to stop or limit the development of blisters in some cases (1).

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