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Unilateral, localized bullous pemphigoid in a patient with chronic venous stasis

Connie R. Shi, BS,a,b Alexandra Charrow, MD, MBE,b,c Scott R. Granter, MD,a,d Alexander Christakis, MD,d and Erin X. Wei, MD,a,b
Boston, Massachusetts

Key words: anti-BP230 antibody; bullous pemphigoid; localized bullous pemphigoid; venous stasis.

INTRODUCTION
Bullous pemphigoid (BP) is a systemic, autoimmune bullous disease that classically presents as widespread urticarial plaques or tense bullae. Localized variants of BP are rare with approximately 100 cases reported. We present a unique case of unilateral, localized BP in the setting of venous stasis.

CASE REPORT
An 84-year-old woman with a history of chronic left lower extremity edema in the setting of thrombophlebitis and venous thrombosis presented with a 1-year history of bullous lesions isolated to the left lower extremity. Treatment of the bullous lesions with topical antibiotics, intravenous antibiotics, and a brief prednisone taper led to minimal improvement. Current medications included aspirin, cetirizine, losartan, nifedipine, pantoprazole, pravastatin, rivaroxaban, and mesalamine. These were chronic medications that the patient had been taking for at least a year before onset of her symptoms.

Examination found numerous tender, hyperpigmented plaques with tense bullae and erosions limited to the left lower leg, ankle, and dorsal foot (Fig 1). The rest of the findings on skin examination were unremarkable. Punch biopsies were taken from lesional and perilesional skin of an intact bulla. Histologic examination found dermal chronic inflammation with numerous eosinophils (Fig 2, A). Direct immunofluorescence found strong linear staining for IgG, IgA, and C3 at the dermoeidermal junction (Fig 2, B). Enzyme-linked immunosorbent assay for BP230 antibodies was positive at 13.9 U (normal ≤ 6), whereas results were negative for BP180 and collagen VII antibodies. Tissue culture was positive for Pseudomonas aeruginosa and Corynebacterium striatum. Fungal and mycobacterial cultures were negative.

These findings were suggestive of unilateral, localized BP with superimposed wound infection.

Fig 1. Clinical image of bullous lesions on the left lower extremity. Numerous tender, hyperpigmented plaques with tense bullae and erosions.

Abbreviation used:
BP: bullous pemphigoid
Initial treatment with ciprofloxacin, 500 mg twice daily for 10 days, and topical triamcinolone 0.1% ointment twice daily resulted in decreased drainage but minimal improvement of bullae formation. The patient opted for continued trial of topical therapy and deferred systemic treatment because of concerns about associated side effects. Topical triamcinolone ointment with compression therapy and leg elevation led to clinical improvement with healing of previous lesions and no new development of bullous lesions.

DISCUSSION

Localized BP is most frequently reported to arise in sites of prior radiation, representing approximately 30 of the 100 published cases.1 Other reports have noted development of localized BP in sites of lymphedema, surgical scars, fistulas, and stoma.2,3 Dyshidrosiform pemphigoid, a form of BP localized to palmoplantar areas, has also been described. To our knowledge, venous stasis has not been reported as a predisposing factor for BP. Anti-BP230, an antibody to an intracellular antigen in the basal keratinocyte, is believed to be nonpathogenic in most BP patients. Additionally, up to 7.4% of healthy individuals have circulating BP230 antibodies.4 It is unknown if this patient had baseline anti-BP230 antibodies before the onset of her venous disease or if anti-BP230 antibodies were generated from venous dermatitis through recognition of alarm signals from stressed tissue.5 The physical and immunologic changes associated with chronic venous stasis may have predisposed the patient to autoantigen presentation, generation of autoreactive T cells, and subsequent autoantibody producing B cells. Notably, the anti-BP230+, anti-BP180− immunologic profile observed in our patient has also been described in the case of a patient who had localized BP in a bandlike pattern on the bilateral lower extremities.6 Furthermore, 6 in a series of 8 patients with localized BP were found to be anti-BP230+ and anti-BP180− in one study.7

We hypothesize that pre-existing epidermal inflammation in the setting of venous stasis could represent the triggering factor for the generation of localized disease phenotype in this patient. This process may be analogous to Koebnerization, a well-known isomorphic phenomenon seen in other inflammatory diseases,8 in which trauma induces the development of specific inflammatory responses in susceptible individuals. Although the mechanism remains unclear, Koebnerization is thought to involve dysregulation of immunologic and vascular factors in sites of trauma.9 Venous stasis leads to extravasation of blood and plasma constituents, including circulating mediators of innate and adaptive immunity, into the surrounding tissue.

This case raises the possibility that BP preferentially presents in sites of inflammatory injury in patients with certain clinical and molecular profiles. Determining the local inflammatory milieu and distinct molecular profiles of patients who develop limited disease may shed light on BP pathogenesis. Ultimately, treatment of local inflammatory processes—in this patient, venous stasis—may be essential in treating many patients with autoimmune bullous disease.

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