

Bullous pemphigoid localized in a primarily hemiplegic distribution



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INTRODUCTION

Bullous pemphigoid (BP) is an autoimmune disease that results in the formation of tense bullae, usually affecting the elderly population.¹ The pathogenesis involves deposition of IgG autoantibodies in basement membrane hemidesmosomes followed by complement activation and subsequent recruitment of inflammatory cells.^{1,2} Clinically, this activity results in the formation of tense subepidermal blisters and urticarial papules and plaques, most commonly affecting flexural areas, the abdomen, and thighs.² During the last decade, several observational studies have reported associations between BP and several neurologic disorders, including dementia, Parkinson disease, bipolar disorder, epilepsy, multiple sclerosis, and stroke.¹ We present a case of BP in a patient with a recent cerebrovascular accident (CVA), primarily involving the same side of the body affected by the stroke.

CASE REPORT

A 76-year-old man with left-sided hemiparesis secondary to a CVA 1 year prior, presented with a 3-month history of blisters most prominent on his left upper extremity and left trunk and, to a lesser extent, along the right knee and right elbow. The lesions reportedly began as small papules that grew in size and eventually became bullous. The patient denied fevers or chills, exposure to new medications, or history of similar lesions.

On examination, there was evidence of erythematous edematous plaques, some with overlying tense bullae and central erosions, scattered predominantly on the left shoulder, left axilla, and left abdomen (Fig 1). There was marked edema of the left hand with several coalescing erythematous

Abbreviations used:

BP: bullous pemphigoid
BPAG: bullous pemphigoid antigen
CVA: cerebrovascular accident

papules distributed on its dorsal aspect (Fig 2). A few erythematous papules were scattered on the bilateral elbows and knees (Fig 3). The remainder of the patient's physical examination was notable for left-sided hemiparesis.

Workup included viral and bacterial culture to exclude an infectious etiology of bullous lesions. A punch biopsy found subepidermal bulla formation and numerous eosinophils lining up along the dermoepidermal junction (Figs 4 and 5). Direct immunofluorescence found linear deposition of IgG and C3 consistent with the clinical impression of BP. A trial of clobetasol 0.05% cream resulted in only minimal improvement, so tetracycline, 500 mg 4 times a day, nicotinamide, 500 mg twice a day, and oral prednisone, 20 mg daily, were added with significant improvement in bullous lesions.

DISCUSSION

This case highlights a case of BP likely associated with a recent CVA, given the temporal relationship and coinciding distribution. A meta-analysis of 14 studies provided support for associations among BP and several neurodegenerative diseases, including CVA, Parkinson disease, dementia, epilepsy, and multiple sclerosis.^{1,3-5}

The mechanism likely involves epitope spreading, a process by which normally immune-tolerated epitopes and antigens provoke an immune

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Fig 1. Erythematous edematous plaques around the left axilla and arm with overlying tense bullae and central erosions.

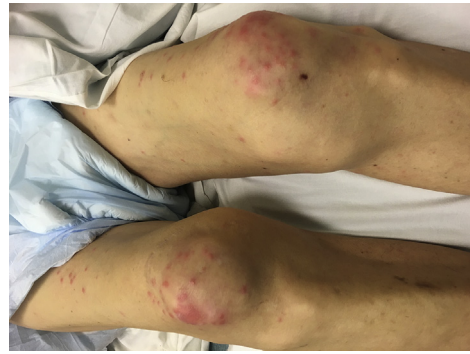


Fig 3. Erythematous edematous papules scattered on the bilateral knees.



Fig 2. Marked edema of the left hand with coalescing erythematous papules distributed along dorsal aspect.

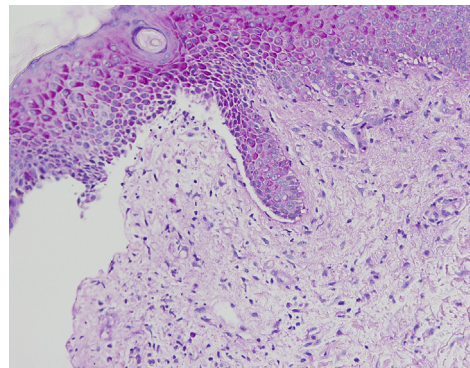


Fig 4. Histologic sections show subepidermal bulla formation with scattered eosinophils in the dermis. (Hematoxylin-eosin stain.)

response via molecular mimicry.⁶ Normally, the brain is an immune-privileged site. However, the aforementioned neurologic diseases cause successive microtrauma and local inflammation in the brain, which likely damage the blood-brain barrier and result in exposure of bullous pemphigoid antigen (BPAG).⁴ BPAG proteins exist as both epidermal and neural tissue isoforms and function as cytoskeletal proteins in hemidesmosomes.^{1,5} Exposure of neural BPAG epitopes and subsequent generation of autoantibodies that also target epithelial BPAG proteins likely cause the characteristic inflammatory cascade in the dermoepidermal junction seen in BP.^{1,7}

Several cases of BP in hemiplegic patients have been documented in case reports, often presenting

on the same side as the hemiplegia.⁸ The bilateral presence of IgG autoantibodies has been documented in these patients, despite their unilateral presentations of BP. Given that the autoantibodies formed from epitope spreading are present systemically, it is reasonable to infer that the hemiplegic side is likely associated with an intrinsic abnormality that makes it particularly susceptible to BP development. It has been conjectured that immune dysfunction in the hemiplegic side may be causative, possibly owing to local alteration in neurotransmitter concentrations and neuropeptide balances.⁹ However, a recent report of unilateral BP and hemiplegia on opposite sides of the body suggests that perhaps multiple mechanisms may be involved in laterality.¹⁰ In this case, the patient's hemiplegia likely conferred increased susceptibility to more severe disease on the affected side, given the more prominent involvement of the patient's left side despite bilateral involvement of the elbows and knees.

The exact mechanisms linking BP to neurodegenerative diseases and hemiplegia are not entirely elucidated and require further investigation. The

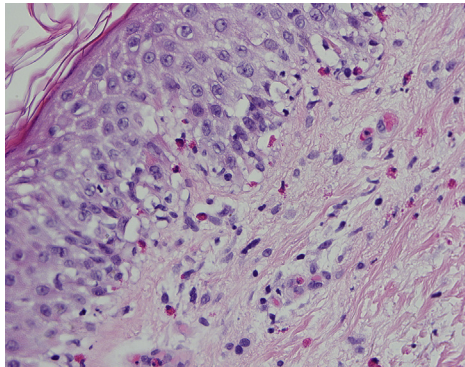


Fig 5. Histologic sections show numerous eosinophils lining up along the dermoepidermal junction. (Hematoxylin-eosin stain.)

proposed mechanism involving epitope spreading and local susceptibility is plausible for the development of BP in this patient and further supports the relationship between BP and stroke.

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