Bullous Pemphigoid Precipitated by Galantamine Hydrobromide

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Bullous pemphigoid (BP) is an acquired autoimmune disease commonly attributed as idiopathic, especially in elderly patients, characterized by subepidermal vesicles and bullae with linear deposits of IgG autoantibodies and complement along the epidermal basement membrane. It also is now commonly accepted that BP can be caused by or associated with drug therapy. We report a case of drug-induced BP (DIBP) likely due to galantamine hydrobromide, a competitive and reversible acetylcholinesterase inhibitor used in the treatment of mild to moderate Alzheimer dementia.

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Autoimmune diseases or autoimmunelike reactions have long been recognized as possible iatrogenic manifestations of drug therapy. Bullous pemphigoid (BP) is an acquired autoimmune disease commonly attributed as idiopathic, especially in elderly patients. It is characterized by subepidermal vesicles and bullae with linear deposits of IgG autoantibodies, especially IgG4, and complement along the epidermal basement membrane. Antibodies can be visualized by direct immunofluorescence, specifically on the BP antigen 2 NC16A domain as well as the BP antigen 1 of hemidesmosomes. It also is now commonly accepted that BP can be caused by or associated with drug therapy. Currently, there are several case reports in the medical literature of drug-induced BP (DIBP) and pemphigoidlike reactions. Some of the more commonly reported drugs include furosemide,[1-3] penicillamine,[4,5] penicillins,[6] amoxicillin,[2] spironolactone,[3] neuroleptic agents,[3] and topical fluorouracil.[7] We report a case of DIBP likely due to galantamine hydrobromide, a medication used in the treatment of mild to moderate Alzheimer dementia.

Case Report

A 79-year-old white woman with a 3-year history of Alzheimer disease presented for evaluation of a pruritic blistering eruption that began on her thighs, later spreading to her trunk and upper extremities (Figure 1). She presented 6 weeks after switching from donepezil to galantamine hydrobromide for her Alzheimer dementia. The eruption developed approximately 10 days prior to her visit to our office. Her medical history included hypertension controlled for several years with metoprolol tartrate, and degenerative arthritis treated with acetaminophen. Her only other medication was a daily multivitamin. Aside from the recent switch to galantamine hydrobromide, there had been no change in her medication for several years. Review of systems was unremarkable except for intense pruritus. Physical examination was remarkable for multiple tense blisters as well as several erosions scattered on the trunk and all 4 extremities. A skin biopsy was submitted for hematoxylin and eosin staining and direct immunofluorescence. The histopathologic findings were consistent with the diagnosis of BP. The patient was instructed to stop taking galantamine hydrobromide and was started on prednisone 40 mg daily. On follow-up 4 weeks later, she had complete resolution of her symptoms, and her skin lesions were mostly healed (Figure 2). Subsequently, prednisone was tapered and completely stopped. She has remained asymptomatic and has had no recurrence of skin lesions 6 months after stopping prednisone.

Comment

There are several characteristics of DIBP that differ from prototypical idiopathic BP. Drug-induced bullous pemphigoid typically occurs in younger patients,

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The authors report no conflict of interest.

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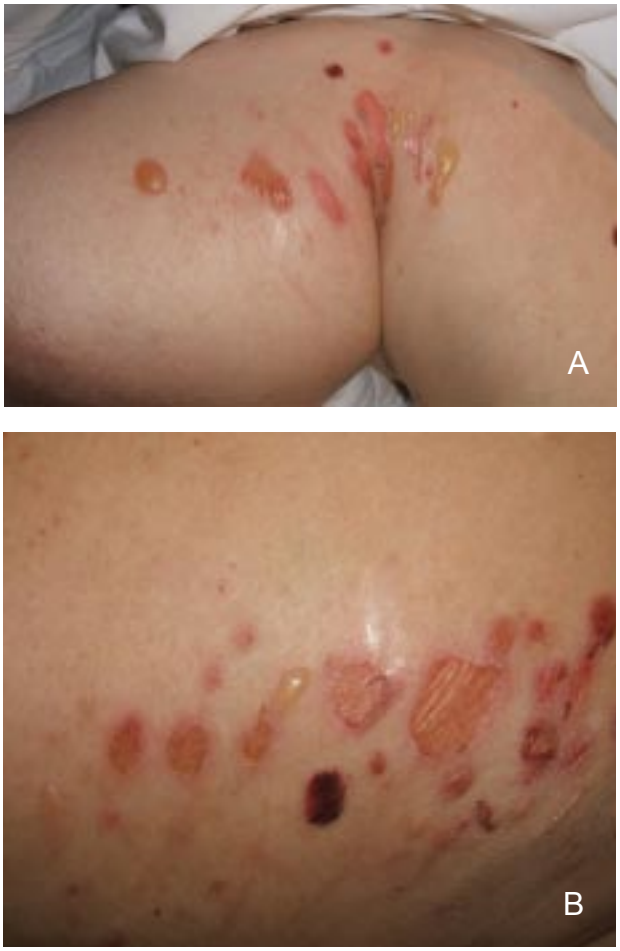

Figure 1. Blistering eruption on the medial thigh (A) and thigh (B).

while BP is most common in patients older than 60 years. Other differences seen in patients with DIBP include bullae on skin that looks healthy, occasional clinical resemblance to erythema multiforme, rapid improvement with use of systemic steroids, positive Nikolsky sign, greater prominence of eosinophilia on histology, and low recurrence rates.[2]

Several pathogenic mechanisms have been proposed for DIBP. One theory is that sulfur-containing drugs may cause a biochemical split between the dermis and epidermis, independent from immunologic mechanisms.[2] An immunologic hypothesis proposes that certain drugs may bind to proteins in the lamina lucida and act as an antigenic hapten, which subsequently activates an immune response.[8] Treatment of DIBP includes removal of the offending agent. Clinical history may dictate the drug to remove.

Galantamine hydrobromide is a competitive and reversible acetylcholinesterase inhibitor. It is believed

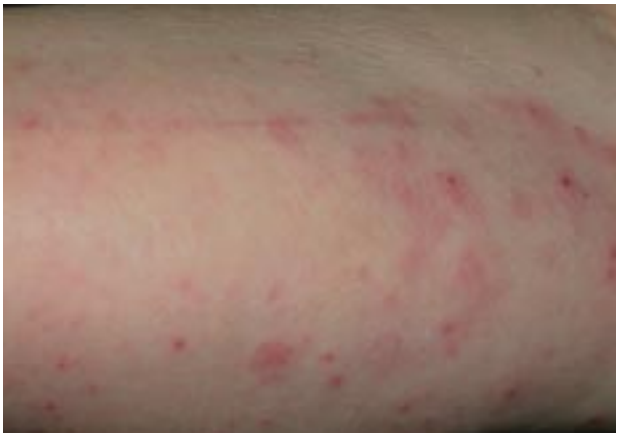

Figure 2. Resolution of lesions 4 weeks after cessation of galantamine hydrobromide.

to work in mild to moderate Alzheimer disease by increasing the concentration of acetylcholine in the brain. There is no evidence that galantamine hydrobromide alters the course of the underlying dementia process.[9] The most common side effects of galantamine hydrobromide are gastrointestinal system disorders. Dermatologic conditions have not been identified as common side effects.[9] Based on a PubMed search of the English-language literature, our case is the first known report of DIBP likely precipitated by galantamine hydrobromide.

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