Carbamazepine Induced Bullous Pemphigoid in a 49 Year Old Male

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ABSTRACT

Bullous pemphigoid is an autoimmune blistering condition mediated by autoantibodies[1]. It is categorized as an uncommon disorder[2-4], with an estimated incidence of 2.4-21.7 cases per million[2-6] but carries significant morbidity and mortality, warranting clinical awareness and investigation[7,8]. A number of medications have been implicated in the development of bullous pemphigoid including loop diuretics, ace inhibitors, and anti-epileptic drugs.

This is a case report of carbamazepine-induced bullous pemphigoid in a 49-year-old male after taking the medication for almost 30 years. Diagnosis of bullous pemphigoid was based on biopsy histology and immunofluorescence, as well as the presence of BP 180 antibody. Clinical features of extensive rash and bullae were present on dermatological exam. Upon discontinuation of carbamazepine and appropriate treatment of bullous pemphigoid, the patient's condition improved. A thorough analysis of the patient's history and medications did not reveal any other potential triggers of bullous pemphigoid.

The only two previous reports of an association between carbamazepine and bullous pemphigoid are limited by lack of immunologic evidence of diagnosis or the identification of a specific causative agent. To address these limitations, we describe what is to our knowledge, the first reported case of clearly documented association between carbamazepine and bullous pemphigoid.

BACKGROUND

Bullous pemphigoid is an autoimmune blistering condition mediated by autoantibodies[1]. It is categorized as an uncommon disorder[2-4], with an estimated incidence of 2.4-21.7 cases per million[2-6]. Bullous pemphigoid carries significant morbidity and mortality. Mortality rates in the US range from 11-23%[7]. Risks associated with this condition include dehydration, superimposed infection, and scarring[8]. Bullous pemphigoid may develop spontaneously or be triggered by infection or medication. A number of medications have been implicated in the development of bullous pemphigoid including loop diuretics, ace inhibitors, and anti-epileptic drugs[9-11]. There are 2 case reports available which claim an association between BP and carbamazepine[12,13].

CASE

A 49-year-old male, with a past medical history significant for cerebral palsy and seizure disorder well-controlled on carbamazepine, presented with worsening bullous pemphigoid diagnosed at an outside hospital. He was admitted due to worsening of his condition despite topical and oral corticosteroid treatment. The rash presented as blistering on his trunk and all four extremities. There was no mucosal involvement. The patient and his family denied any new medications, foods, illnesses, or environmental exposures. Dermatological exam noted tense bullae filled with clear to straw-colored fluid primarily on the trunk and thighs but also on the more distal extremities. Ruptured bullae with overlying crust were also present, especially on the hands and feet. Nikolsky sign was negative.

The diagnosis of bullous pemphigoid was confirmed with the presence of linear basement membrane deposits on immunofluorescence. Direct immunofluorescence analysis of a skin biopsy demonstrated intralesional IgG deposition and linear immunofluorescence at the dermal-epidermal junction of lesions. Additionally, BP 180 antibody testing was positive with a serum concentration of 126 U/mL.

The patient's home medication list, which included aspirin, lorazepam, trazodone, and carbamazepine, was reviewed to identify potential causes of bullous pemphigoid other than carbamazepine. Other than carbamazepine, none of these medications are associated with serious skin conditions or bullous pemphigoid. Therefore, carbamazepine was discontinued and switched to levetiracetam for seizure prophylaxis. After the removal of carbamazepine and initiation of rituximab for treatment-refractory bullous pemphigoid, no new lesions developed. Six weeks after discharge the patient's condition continued to improve.

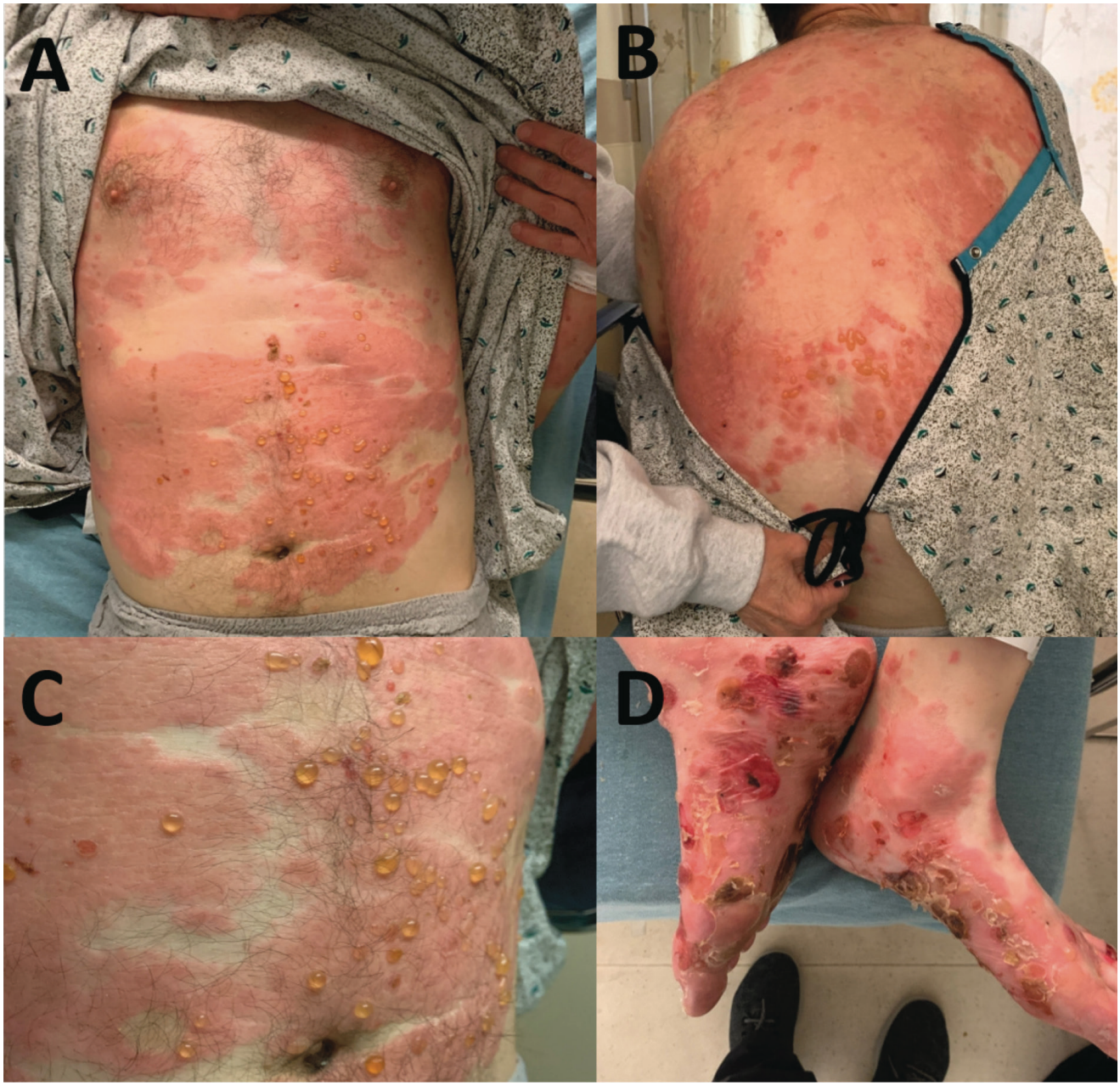

Figure 1: Physical exam findings of widespread bullous skin eruption. Multiple tense bullae present on trunk and ruptured bullae present on distal extremities.

DISCUSSION

Carbamazepine is an anticonvulsant that is associated with serious, even fatal dermatologic reactions, including Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis[14]. Autoimmune blistering conditions such as bullous pemphigoid are not among the known skin reactions caused by carbamazepine. There are only two reports of an association between carbamazepine and bullous pemphigoid[12,13]. The first describes the development of bullous pemphigoid after carbamazepine overdose. However, direct immunofluorescence was not conducted and serum studies were reported to be negative. The second report describes the development of bullous pemphigoid in a patient taking carbamazepine, zonisamide and minocycline. Lesional biopsy plus direct and indirect immunofluorescence indicated bullous pemphigoid as the diagnosis. However, clinical

improvement was noted after the removal of all three medications and reintroduction was not attempted with any of the implicated medications. Moreover, results of drug-induced lymphocyte stimulation tests for carbamazepine, zonisamide and minocycline hydrochloride were negative.

This study has overcome the limitations of previous reports. Bullous pemphigoid was confirmed clinically with improvement after the removal of carbamazepine, immunohistologically with biopsy and direct immunofluorescence, and serologically with the identification of BP 180 antibodies. The probable relationship between the adverse effect of bullous pemphigoid and carbamazepine was also indicated with use of the Naranjo Adverse Drug Reaction Probability Scale, which is consistent with our conclusion that carbamazepine was the likely cause of bullous pemphigoid[15]. The primary limitation of this study is that reintroduction of carbamazepine was not attempted.

Thus, we present this as the first report of proven bullous pemphigoid in association with carbamazepine use. The goal of this report is to create awareness of this association in order to encourage clinical vigilance and the reporting of similar findings in the future.

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