Development of cyclosporine-induced linear IgA bullous dermatosis despite concurrent use of dapsone

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INTRODUCTION

Linear IgA bullous dermatosis (LABD) is a rare subepidermal-blistering disease caused by antibasement membrane IgA antibodies. The exact pathogenesis of LABD remains unknown. In adults, LABD is typically caused by antibiotics, such as vancomycin, penicillins, cephalosporins, and sulfonamides.[1] Antihypertensives, antiepileptics, analgesics, and immunosuppressive medications, such as cyclosporine, have also been implicated.[2] The first step in management is withdrawal of the causative agent. The first-line therapeutic agent is dapsone, and improvement is often seen within days of starting treatment.[1] We present the case of a 27-year-old woman who developed LABD while taking dapsone, the treatment of choice for the disease.

Abbreviation used:

LABD: linear IgA bullous dermatosis

CASE REPORT

A 27-year-old woman with primary aplastic anemia presented to an outpatient dermatology clinic with a 2-day history of a pruritic, blistering rash. She had a remote history of minocycline-induced systemic lupus erythematosus. Her medication list was notable for 225-mg cyclosporine daily (3.1 mg/kg) for aplastic anemia and dapsone 100 mg daily for pneumocystis pneumonia prophylaxis, both of which she began taking 5 months before development of the rash. Of note, she had missed 2 doses of dapsone before presentation but did not have any other recent changes to her medications. Examination revealed tense bullae and erosions with background erythema on the arms, back, and legs (Fig 1, *A*). Several lesions displayed a "crown of jewels" appearance with a central lesion and circumferential vesicles (Fig 1, *B*). Punch biopsy demonstrated subepidermal vesiculation with neutrophils (Fig 2). Direct immunofluorescence test was positive for linear IgA basement membrane deposition. Taken together, this was most consistent with LABD. Trace IgG and C3 were positive, felt to be secondary to epitope spreading. Bullous pemphigoid (BPAG1 and BPAG 2) and epidermolysis bullous acquisita (collagen VII) antibodies were negative.

She was continued on dapsone and cyclosporine at the same doses and was treated with topical high-potency corticosteroids. At 1 month follow up, her lesions completely remitted.

DISCUSSION

Symptoms of LABD typically begin within 1 month of drug administration, but cases have been reported with a latency period of up to 780 days.[1-3] Most frequently observed in children,

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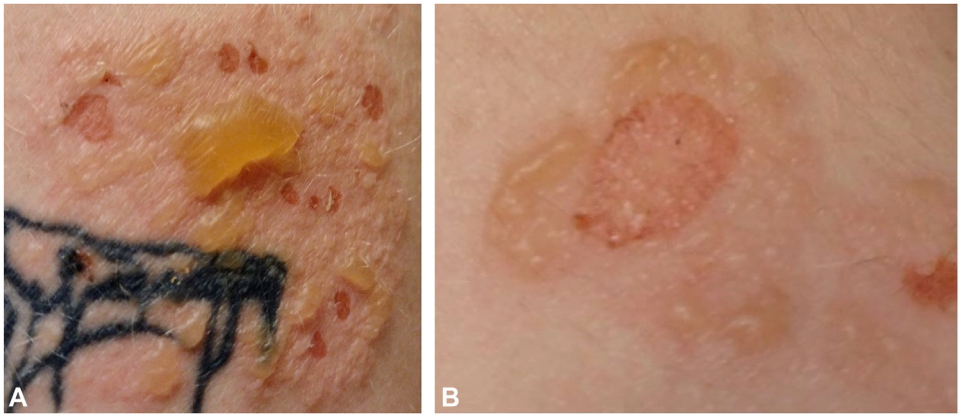

Fig 1. **A**, Tense blisters and erosions on the upper extremity. **B**, Tense vesicles with crown of jewels morphology.

lesions may appear as a "crown of jewels" or "string of pearls" with a central lesion surrounded by vesicles. Biopsy showing subepidermal vesiculation with neutrophils and direct immunofluorescence with linear IgA is diagnostic. These findings paired with negative serologies for anticollagen VII, anti-BPAG1, and anti-BPAG2 antibodies help differentiate the condition from other bullous disorders, such as epidermolysis bullous acquisita and bullous pemphgoid.[1,4]

This patient's characteristic "crown of jewels" rash in combination with linear IgA deposition on direct immunofluorescence strongly suggests LABD, which is unusual because of development of the disease while taking dapsone, the agent of choice to treat LABD. Additionally of interest, cyclosporine could represent an iatrogenic trigger in this patient as she began taking both medications the same month and cyclosporine has been previously implicated in the development of LABD.[2,5]

Due to the established rapid response of LABD to dapsone, it is possible that the patient had developed LABD-associated antibodies during the course of cyclosporine, and her disease was masked by concurrent dapsone use. Dapsone is known to have a half-life of 10 to 50 hours with an average of 30 hours.[6] Our suspicion is that when the patient missed >48 hours of dapsone treatment, her skin disease became clinically evident. This patient's history of autoimmune disease, including drug-induced lupus and primary aplastic anemia, suggests that they may have increased risk of developing LABD.[3] Interestingly, although most patients with drug-induced LABD require withdrawal of the offending agent to achieve lesions resolution, this patient's lesions resolved with resuming dapsone and the addition of topical corticosteroids. Of note,

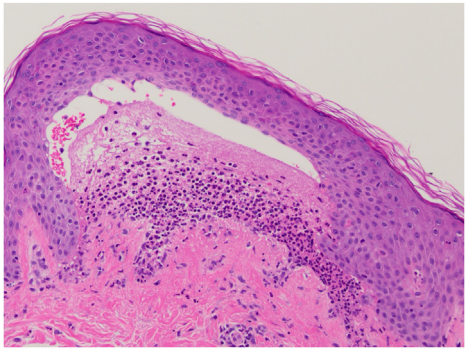

Fig 2. Punch biopsy showing subepidermal vesiculation with abundant neutrophils. (Hematoxylin-eosin stain; original magnification: 20×.)

Petit et al[5] describes a case of LABD suspected to be triggered by cyclosporine, which was continued through treatment. Instead of cyclosporine discontinuation, the medication dosage was decreased, and the patient was started on dapsone and oral steroids with disease improvement.[5]

This patient's case highlights an atypical presentation of LABD with exquisite responsiveness to dapsone and emphasizes the importance of a high index of suspicion for the development of additional autoimmune disorders in patients with known autoimmune disease.

Conflicts of interest

None.

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