Successful treatment of linear immunoglobulin A bullous dermatosis with dupilumab in a pediatric patient

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INTRODUCTION

Linear immunoglobulin A (IgA) bullous dermatosis (LABD) of childhood is a rare, autoimmune, subepidermal blistering disorder, caused by IgA autoantibodies targeting the basement membrane zone. Affecting mostly children around 4.5 years of age, it has a 1.6:1 female/male ratio and an incidence of 0.69-2.3 cases per-million/year. LABD features pruritic, tense bullae in a "string of pearls" or "crown of jewels" pattern, commonly on the genitalia, face, trunk, and extremities, with a 64% mucosal involvement.[1]

Treating LABD is challenging, as no Food and Drug Administration approved treatments exist, and off-label options such as systemic dapsone are not the ideal choice for those at risk of hemolytic anemia.[1]

Abbreviations used:

IgA: immunoglobulin A
LABD: linear IgA bullous dermatosis

CASE PRESENTATION

A 7-year-old boy was referred as a case of refractory atopic dermatitis not responding to topical treatments. He had no relevant medical history, and no family history of consanguinity, atopy, bullous dermatoses, or genetic syndromes.

Examination revealed scattered, excoriated, erythematous plaques with overlying hemorrhagic crust involving the scalp, trunk, extremities, and perioral areas with a body surface area of >10% (Fig 1, *A*). Tense bullae were also noted on the extremities. There was no mucosal involvement. He had a parent-proxy Peak Pruritus Numerical Rating Scale score of 10.[2]

Biopsy revealed a subepidermal split with focal spongiosis and a superficial dermal perivascular infiltrate, and interstitial mixed infiltrate of eosinophils and neutrophils (Fig 2). Direct immunofluorescence showed a linear IgA and C3 deposition along the basement membrane and was negative for immunoglobulin G, immunoglobulin M, and fibrin. Thus, confirming the diagnosis of LABD.

Laboratory analysis revealed an elevated serum IgA, and a microcytic, hypochromic anemia with a hemoglobin of 6.4 g/dL, and a decreased hematocrit, mean corpuscular volume and mean corpuscular hemoglobin, with an increased red cell distribution width. The patient was referred to hematology and was started on iron supplementation for iron deficiency anemia that was secondary to inadequate dietary intake. Screening for celiac disease and glucose-6-phosphate dehydrogenase deficiency were negative. All proceeding work-up by the hematology team was negative and a diagnosis of dietary-induced iron deficiency anemia was confirmed.

While investigations were pending, the patient was started on oral 0.5 mg/kg/day prednisolone

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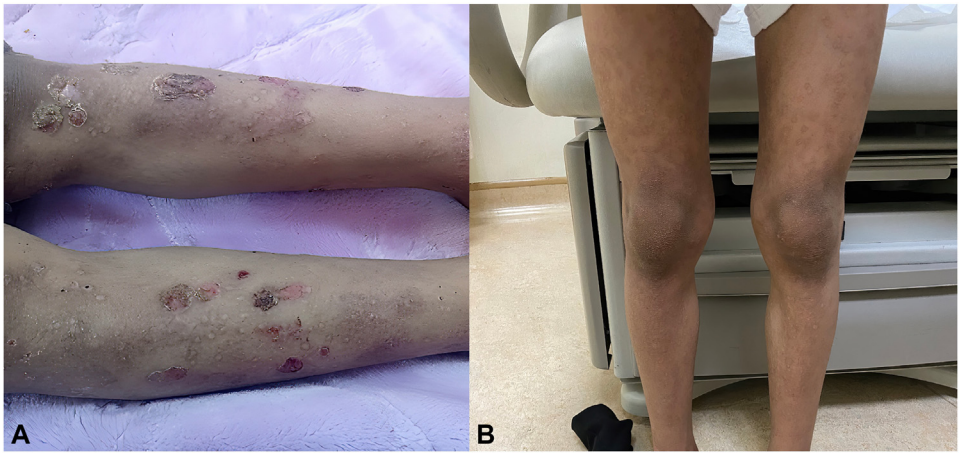

Fig 1. Before dupilumab (**A**): Scattered hemorrhagic crusted and erosive plaques on the bilateral *lower* extremities. After dupilumab (**B**): Scattered hypopigmented and hyperpigmented macules and patches on the bilateral *lower* extremities. No bullae were noted.

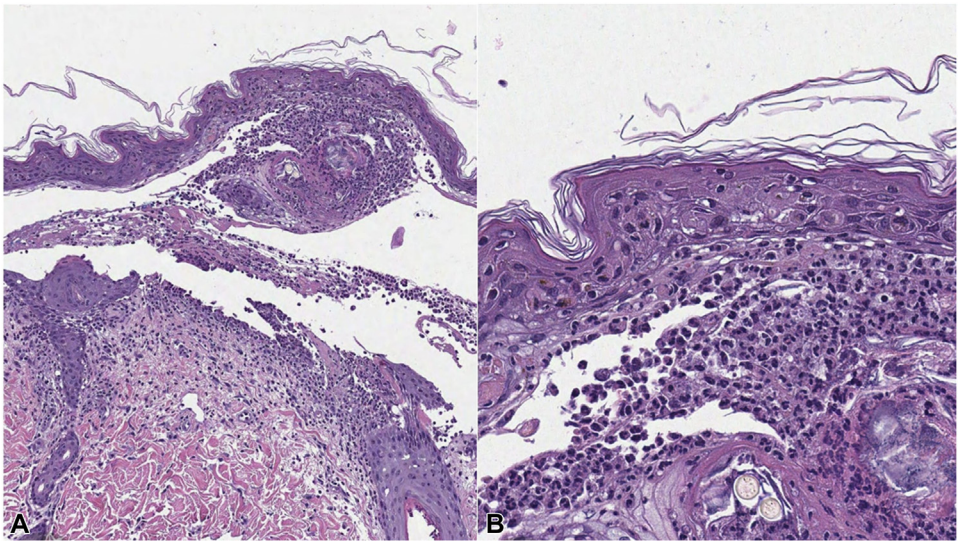

Fig 2. Histopathological result of the biopsy from the lesion of the child with LABD. A subepidermal split with focal spongiosis, and a superficial dermal perivascular infiltrate and interstitial mixed infiltrate of eosinophils and neutrophils (hematoxylin and eosin, magnification ×10 **A** and magnification ×20 **B**). *LABD*, Linear IgA bullous dermatosis.

taper for 3 weeks, topical corticosteroids and tacrolimus, topical mupirocin, and emollients.

As work-up by the hematology team at the time, was still pending, and the patient continued to flare, given the risk of hemolysis, dapsone was avoided, and off-label dupilumab (600 mg loading dose followed by 300 mg monthly subcutaneous injections) was initiated.

At 1-month follow-up, he had a significant improvement in his pruritus and denied any new lesions. By 4-month follow-up, the patient had a complete resolution of his bullae and pruritus with a parent-proxy Peak Pruritus Numerical Rating Scale score score of 0 (Fig 1, *B*).

DISCUSSION

Due to its rarity and lack of Food and Drug Administration approved treatment, LABD in children is difficult to treat. Systemic dapsone is the most common first-line treatment.[1] However, it's typically avoided in patients that are at risk for hemolytic anemia such as those with glucose-6-phosphate dehydrogenase deficiency. In such cases, other measures are typically warranted.

Second-line treatments include colchicine, corticosteroids, rituximab, intravenous immunoglobulin, mycophenolate mofetil, and nicotinamide. Furthermore, omalizumab may also help treat adults with LABD.[1,3,4]

Dupilumab, a human, monoclonal immunoglobulin G4 antibody, inhibits interleukin-4 and interleukin-13 signaling by binding to interleukin-4 receptor-alpha leading to downregulation of immunoglobulin E, cytokines, and chemokines. This cascade of events may reduce inflammation and pruritus.[5] The exact mechanism of action in patients with LABD is unknown. Dupilumab is Food and Drug Administration approved for the treatment of atopic dermatitis and has been reported to help treat other bullous dermatoses, namely, bullous pemphigoid and pemphigus vulgaris.[5,6] To our knowledge, this is the first reported case of successful treatment of LABD with dupilumab in the pediatric population.

Our findings suggest that dupilumab may help treat pediatric patients with LABD. More research is warranted to further study the clinical effects of dupilumab for the treatment of LABD in the pediatric population.

Conflicts of interest

None disclosed

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