A case of linear IgA bullous dermatosis in a glucose-6-phosphate dehydrogenase–deficient child successfully treated with oral erythromycin and topical tacrolimus

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Key words: autoimmune; chronic bullous disease of childhood; erythromycin; g6pd deficiency; linear IgA bullous dermatosis.

INTRODUCTION

Autoimmune blistering diseases (AIBDs) are a group of rare disorders affecting either the skin or mucous membrane or both that rarely affect the pediatric age group. Linear IgA bullous dermatosis (LABD) is the most common among the AIBDs in children which gives rise to the development of subepidermal bullae due to the linear IgA deposition over the basement membrane zone.[1] Clinically, it presents as tense blisters arranged in a polycyclic or annular pattern traditionally referred to as "clusters of jewels" or "string of pearls."[2]

Despite the good prognosis of this condition, treatment is often instituted to shorten the disease duration by controlling and reducing the severity of the blister formation.[2] Conventional first-line treatments for LABD include dapsone or sulfapyridine; however, these may pose potentially serious side effects, and thus, require regular blood-test monitoring.[3]

We report a case of a glucose-6-phosphate dehydrogenase–deficient 11-year-old child diagnosed with LABD wherein dapsone was contraindicated. The patient was treated with oral erythromycin, which provided marked improvement and complete disease remission.

Abbreviations used:

AIBD: autoimmune blistering disease
LABD: linear IgA bullous dermatosis

CASE REPORT

We present a case of an 11-year-old girl from the Philippines who presented with a 3-month history of recurrent, annular, vesiculobullous lesions over the trunk and extremities. No medications were taken or applied before the appearance of the rash. The lesions initially started as few, pruritic, erythematous vesicles over the popliteal area, which were associated with an undocumented fever that only lasted for 3 days. Multiple medical consultations were done, and she was given various systemic antibiotics, such as trimethoprim-sulfamethoxazole, cloxacillin, and cephalexin, as well as topical and systemic steroids, such as clobetasol and prednisone; however, no resolution was noted despite the patient's compliance.

On examination, there were multiple symmetrical, erythematous patches and plaques; some were surrounded annularly by tense vesicles and bullae with moist erosions and hemorrhagic crust over the trunk and extremities (Fig 1). Mucosal surfaces were unremarkable. Nikolsky and Asboe-Hansen signs were both negative.

A 4-mm punch biopsy was done on a vesicle on the upper portion of the arm revealing a subepidermal blister filled with neutrophils and a moderately dense superficial perivascular infiltrate of neutrophils and eosinophils in the dermis (Fig 2).

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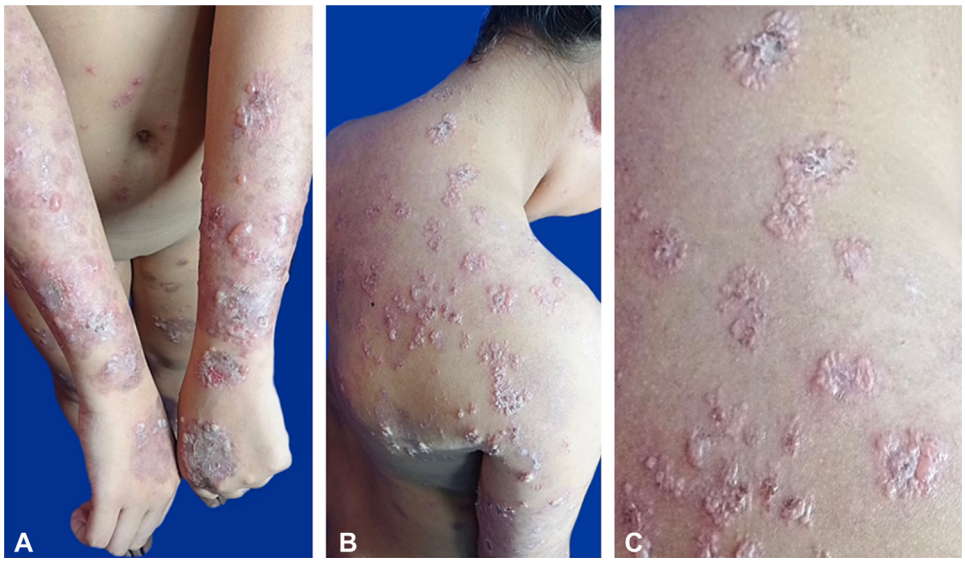

Fig 1. Multiple, symmetrical, erythematous patches and plaques where some were surrounded annularly by tensed vesicles and bullae and some were topped with moist erosions and hemorrhagic crust over the (**A**) extremities and (**B**) back. A closer look of the (**C**) annular vesicles on the back.

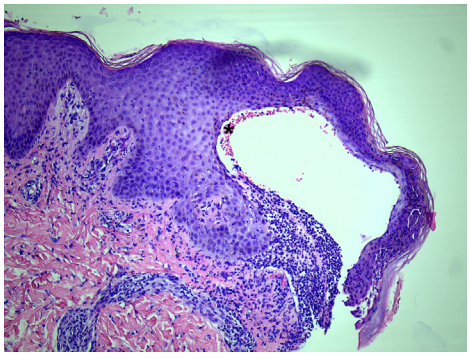

Fig 2. Subepidermal blister filled with neutrophils (asterisk). (Hematoxylin-eosin stain; original magnification: ×10).

Direct immunofluorescence results of a 4-mm perilesional skin sample revealed linear deposition of IgA and fibrinogen at the basement membrane zone (Fig 3).

LABD was confirmed based on the characteristic clinical, histologic, and immunologic findings. Starting dapsone was initially considered; however, the patient was noted to have a glucose-6-phosphate dehydrogenase level of 10.65 U/gHb which is below the normal level for her age (>13.01 U/gHb)

The patient was treated with oral erythromycin stearate 500-mg tablets; 1 tablet taken 3 times a day, and topical tacrolimus 0.03% cream applied twice a day, which resulted in notable improvement of symptoms and clearing of lesions.

After 4 weeks of treatment, the patient achieved complete remission (Fig 4) and had stayed clear for 3 months without any maintenance medications.

DISCUSSION

LABD is a rare AIBD that can occur in both children and adults. Because of the rarity and spontaneous nature of AIBDs in the pediatric population, there are no established or evidence-based treatment guidelines for LABD.[3]

Conventionally, LABD is often treated with dapsone alone or in combination with prednisolone. With dapsone, patients often respond dramatically, as fast as 24 to 48 hours, making it the drug of choice in managing the disease. However, it may cause serious side effects, which can be life-threatening, such as hemolysis and bone marrow suppression, and thus, serial monitoring of blood parameters are necessary.[4,5] Before the treatment initiation, patients should also be screened for glucose-6-phosphate dehydrogenase deficiency to prevent the risk of severe hemolytic anemia.[6]

There were several reports in the literature providing evidences of good clinical response to the macrolide erythromycin. A national survey of the members of the British Society of Dermatology suggests that it can act synergistically and would be beneficial when used with other systemic treatments; however, when used as a sole agent, the sustained improvement is still uncertain.[4] Although several published case reports also provided scientific evidence of good clinical response to erythromycin, a 5-year-old child with frequent relapses was managed and well controlled by continuous daily intake of 250 mg of erythromycin and a 52-year-old man's flare was well controlled by just a 10-day course of the medication.[7] There

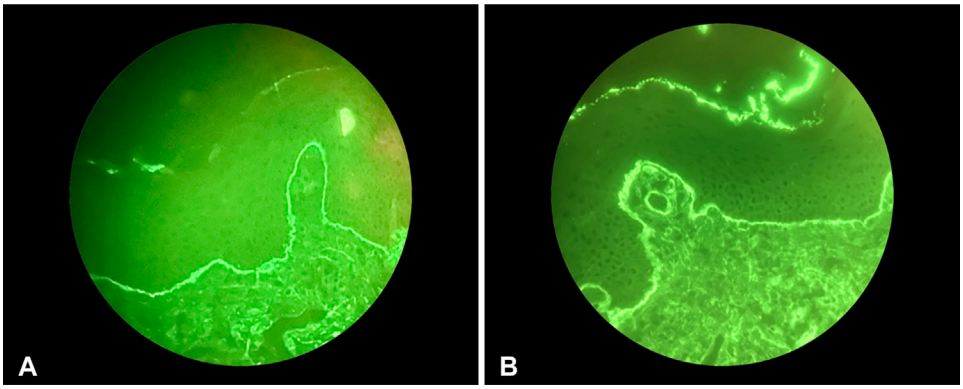

Fig 3. Direct immunofluorescence of perilesional skin showing linear deposition of (**A**) IgA +1 and (**B**) fibrinogen +2 in the basement membrane zone.

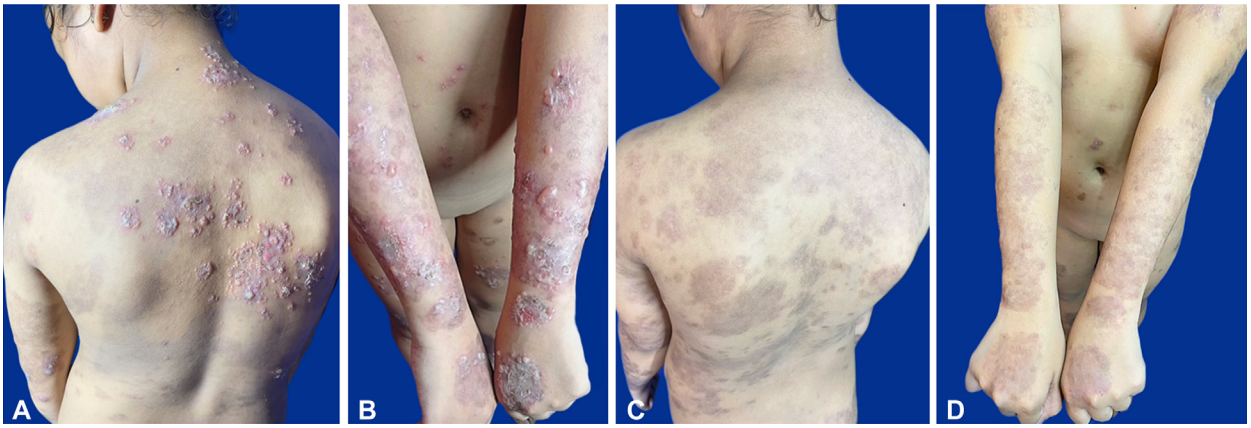

Fig 4. Comparison photos (**A** and **B**) on the day of consultation and (**C** and **D**) after taking erythromycin for 4 weeks. It is notable that the resolution of the lesions leaves only postinflammatory hyperpigmentation with no scarring and milia formation.

is also an anecdotal report of an adult male with chronic renal failure diagnosed with LABD who's disease activity was controlled and responded well to erythromycin even before undergoing intravenous immunoglobulin therapy.[8] The mechanism of this favorable effect in LABD is thought to be more through erythromycin's antiinflammatory rather than its antimicrobial effect. The macrolide erythromycin inhibits neutrophil chemotaxis in vivo and releases lysozyme and b-glucuronidase, which negates the inflammation.[9]

Most untoward reactions to oral administration of erythromycin are not life-threatening and usually limited to gastrointestinal upset. The most common side effects among the pediatric age group include "…dose-related abdominal cramps, nausea, vomiting, diarrhea, and gas."[10] In our patient's case, the abdominal cramps were simply managed by taking the medication an hour after meals, which afforded relief. The 4-week course of oral erythromycin was well-tolerated by the patient without any problem.

In conclusion, the existence and emerging number of cases of LABD reported to have a good clinical response to antibiotics cultivate the foundation and instigation for a treatment with good tolerability and efficacy that is comparable with traditional therapies. Erythromycin, in particular, has shown promising results in the management of LABD in this case. With a low index of side effects and no requirement for regular blood-test monitoring, this treatment is a particular advantage in the pediatric age group. This successful treatment with erythromycin suggests that it can be considered in patients with contraindications to the first-line treatment of LABD.

Conflicts of interest

None disclosed.

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