Combined dapsone and sulfapyridine for the treatment of therapy-resistant linear IgA bullous dermatosis: Two case reports

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INTRODUCTION

Linear IgA bullous dermatosis (LABD) is a rare autoimmune vesiculobullous disease causing blistering lesions of the skin and mucosa.[1] LABD typically presents in either early childhood or adulthood.[2,3]

The pathogenesis is characterized by a linear deposition of IgA at the dermoepidermal junction.[2] LABD can be idiopathic or drug-induced (typically by vancomycin, β-lactam antibiotics, or nonsteroidal anti-inflammatory drugs).[4] Children frequently present with widespread annular blisters, with predilection of the lower portion of the abdomen, genital areas, and thighs.[5,6] In adults, the clinical presentation varies and annular lesions are less common.[5,7] The reported incidence of LABD varies from <0.5 to 2.3 cases per 1 million population/year.[2]

Dapsone is often reported the most effective drug of choice and is frequently used as first-line therapy. Other treatment options include sulfonamide drugs, such as sulfapyridine/sulfamethoxypyridazine, corticosteroids, colchicine, and other immunosuppressive agents.[2,4,7,8]

Herein, we present 2 case reports of patients with LABD successfully treated with a combination of dapsone and sulfapyridine.

Abbreviation used:

LABD: linear IgA bullous dermatosis

CASE SERIES

Case 1

A 2-year-old, otherwise healthy girl presented with vesiculobullous lesions on the extremities, neck, abdomen (Fig 1, *A*) and, especially, the vulva and buttocks. Complaints of itching and sleep deprivation were reported. The lesions were on an erythematous base and with a rosette-like pattern. Before onset, the patient had diaper dermatitis, treated with oral amoxicillin. Microbiologic test results were negative for herpes and bacteria. Histopathology (including immunofluorescence) confirmed the diagnosis of LABD, revealing a linear IgA deposit at the epidermal basal membrane zone as well as a dermal infiltration of neutrophils.

Treatment with 10 mg/day of oral dapsone was initiated (1 mg/kg/day), and the patient initially responded well. However, after a few weeks of treatment, the disease progressed, with the development of new vesiculobullous lesions in the same regions (Fig 1, *B*). The lesions were painful and pruritic. The treatment was supplemented with 10 mg/day of prednisone as well as a topical steroid treatment and potassium permanganate baths. During the following 6 months, the dapsone dose was slowly increased to 20 mg/day, with varying prednisone dosing, but the disease was never fully controlled by this regimen.

Sulfapyridine (250 mg/day; 23 mg/kg/day) in combination with prednisone was then attempted and later increased to 500 mg/day (44 mg/kg/day). This treatment regimen led to temporary prednisone-related growth suppression and excessive hair growth, and the patient again developed several new bullae. Eventually, a combination of dapsone (10 mg/day) and sulfapyridine (500 mg/day) was initiated.[9] After a few weeks, the patient responded significantly to the treatment

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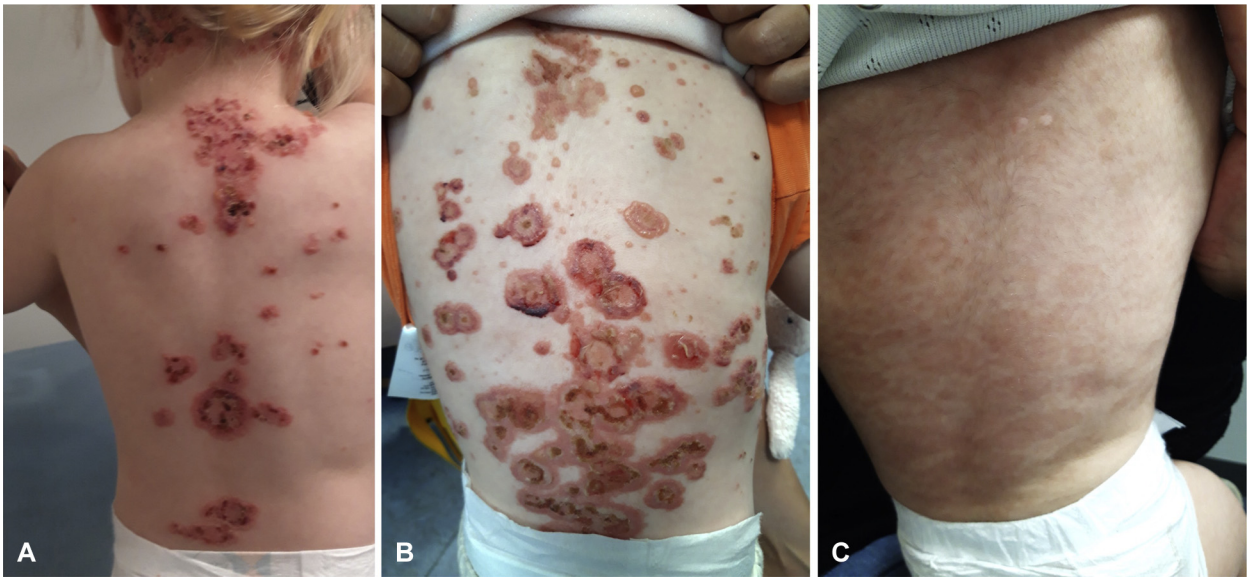

Fig 1. A, Vesiculobullous lesions at the back at presentation. **B,** Disease progression during monotherapy with dapsone. **C**, Remission of skin lesions achieved with combined therapy of dapsone and sulfapyridine.

combination (Fig 1, *C*). Over the next 6 weeks, the prednisone was tapered off, and no new vesicles or bullae occurred after the introduction of the combination therapy.

Case 2

A 55-year-old man presented to our clinic with a highly itchy rash located on the abdomen, neck, back, and extremities (Fig 2, *A* and *B*). The lesions were annular, with a characteristic rosette-like pattern. The patient reported earlier bullae formations. The patient's comorbidities included hypertension, diabetes, and obesity. Regular medications were thoroughly reviewed, and no new medication had been initiated within the 6 months prior to the disease presentation.

Histopathologic investigations revealed bullae formation and infiltration by neutrophils, and immunofluorescence revealed linear IgA deposits at the dermoepidermal junction compatible with LABD (Fig 2, *E*).

Treatment with dapsone (50 mg/day) was started, in combination with topical steroids and potassium permanganate baths. Initially, the patient experienced a partial response. However, after 1 month, progression occurred, and the dapsone dose was increased to 100 mg/day. After 3 months, the patient developed several new bullae, and the dapsone dose was further increased (150 mg/day), together with a prednisone course (40 mg/day for 2 weeks and then tapered off).

In the following 2.5 years, the disease control was maintained by dapsone treatment and a few courses of prednisone. However, the patient then experienced moderate-to-severe progression, especially involving the hands (Fig 2, *C*) and buttocks, and the treatment regimen was changed from dapsone to sulfapyridine (1000 mg/day, increasing to 1500 mg/day). After a couple of weeks, the patient experienced severe progression, and dapsone (150 mg/day) was reintroduced. On this treatment combination, the patient quickly recovered (Fig 2, *D*), and the skin lesions completely cleared, with only post-inflammatory hyperpigmentation remaining. To date, no relapse has occurred on the treatment combination.

DISCUSSION

LABD is a rare vesiculobullous skin disease characterized by the linear deposition of IgA at the dermoepidermal junction. LABD often has an abrupt onset, with new blister formation, with an annular appearance resembling rosettes.[4] The gold-standard diagnostic method is skin biopsy including direct immunofluorescence, revealing the linear IgA deposits (Fig 2, *E*).[2,10]

The evidence for the current treatment of LABD is limited and based on case reports and case series, and larger controlled trials are lacking.[4,10] Dapsone is generally well tolerated and is often used as a first-line therapy.[2,3] The dose range for the treatment of LABD in adults is 50 to 150 mg/day, while the dose range for children has been reported at 0.5 to

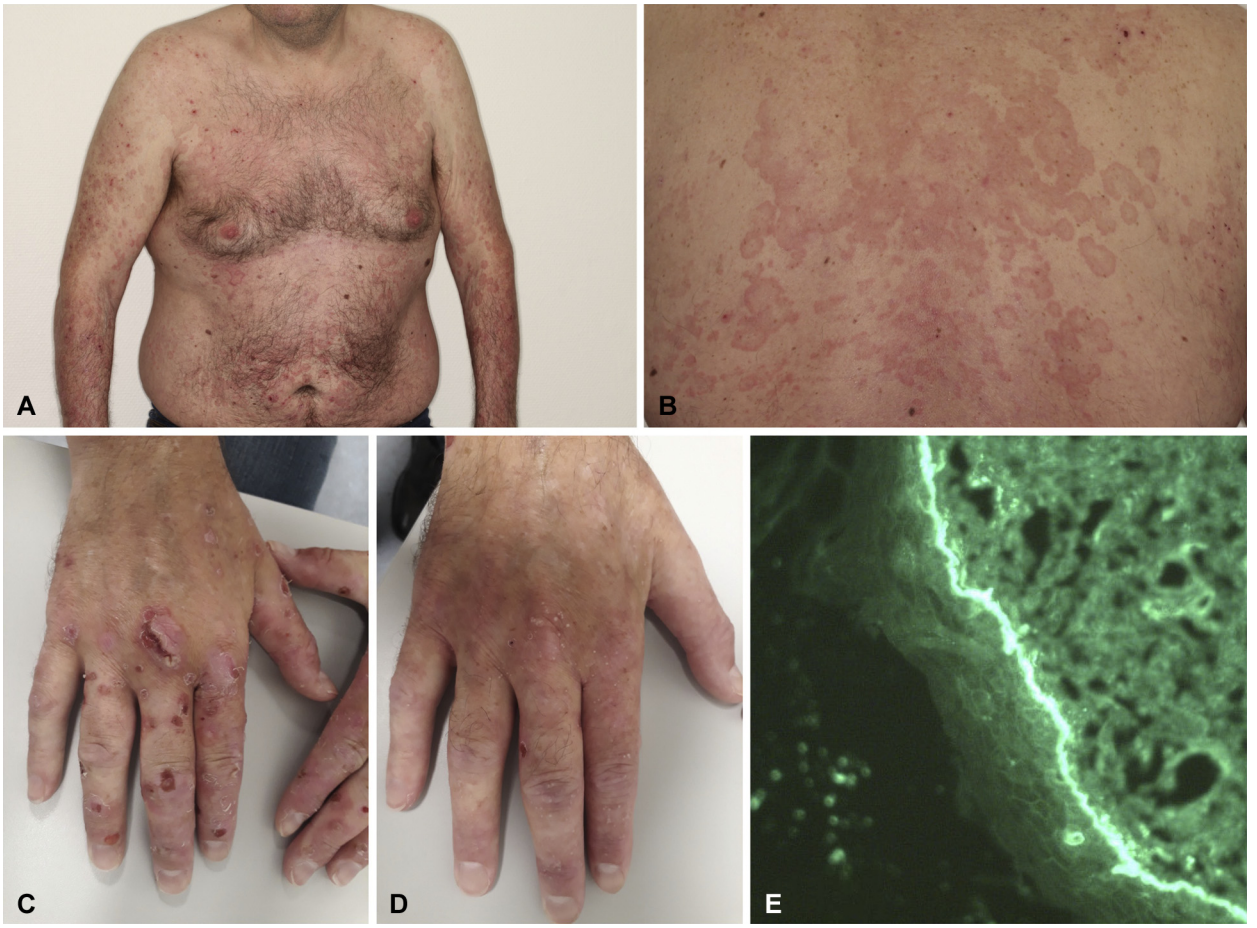

Fig 2. A, Annular exanthema at the trunk and extremities at presentation. **B,** Annular exanthema at the back at presentation. **C,** Disease progression involving the hands during dapsone monotherapy. **D,** Remission of skin lesions achieved with combined therapy of dapsone and sulfapyridine. **E,** Histopathology of skin lesion (right thigh) with immunofluorescence confirming the linear deposition of IgA at the dermoepidermal junction (fluorescein isothiocyanate anti-IgA stain; original magnification: ×200).

2 mg/kg/day.[4] Hematologic parameters should be monitored, since hemolysis (especially in patients with glucose-6-phosphate dehydrogenase deficiency), methemoglobinemia, and agranulocytosis are potential adverse effects.[4] Sulfonamides have been reported as an effective treatment for LABD.[4] However, the availability of these agents is limited in some countries. The sulfapyridine dose for the treatment of LABD in adults is 1000 to 1500 mg/day, while the dose range for children has been reported at 15 to 60 mg/kg/day.[4] Adverse effects, including agranulocytosis, hemolysis, and elevated liver enzymes, may occur but are generally well tolerated.[2,3] Recommendations for the treatment of therapy-resistant LABD are lacking, although various options, including intravenous immunoglobulin, rituximab, tumor necrosis factor-α inhibitors, omalizumab, and a combination therapy of dapsone and sulfapyridine, have been suggested.[4,9]

We present 2 cases with histologically verified LABD. In both cases, initial monotherapy with dapsone or sulfapyridine was not sufficient to treat the skin lesions. However, the combination of dapsone and sulfapyridine effectively resulted in full, lasting remission in both patients.

In conclusion, in LABD cases where both dapsone and sulfapyridine monotherapy have been attempted, combination therapy with dapsone and sulfapyridine should be considered.

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Conflicts of interest

None disclosed.

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