Recalcitrant case of linear IgA bullous dermatosis in a child

E R N D Gunawardena[1], C Udagedara[2], E M C B Ekanayake[3], G Shopana[4]

Sri Lanka Journal of Dermatology, 2022-2023, **23**: 59-61

Abstract

Linear IgA bullous disease (LABD) is arare autoimmune subepidermal blistering disorder characterized by immunoglobulin class A (IgA) deposits in the basement membrane of the skin. It affects both adults and children. The childhood variant is also known as chronic bullous dermatosis of childhood (CBDC) and unlike in adults it has characteristic clinical findings termed as "string of pearls" or "crown of jewel" appearance of blisters. Most of the patients respond well to dapsone and cortico-steroids. We report a case of a patient with CBDC who had a poor response to the above conventional therapy and had a favorable response to intravenous immunoglobulin (IVIg).

Keywords: Linear IgA disease, chronic bullous disease of childhood, string of pearls, dapsone, IVIg

Introduction

Linear IgA bullous disease is a rare autoimmune blistering disorder with an estimated annual incidence of 0.5 per million in Western Europe. Its prevalence in Sri Lanka or Asia is unknown. LABD has a bimodal age distribution. In children it occurs between the age of 2 to 5 years with a mean age of 4.5 years. IgA autoantibodies target 97KDa and 120KDa antigens which are located on the extracellular domain of BP180[1]. Infections, medications, autoimmune conditions and malignancies can be triggering factors in LABD but such associations in CBDC are rare.

Vesiculobullous lesions are arranged in a herpetiform, annular arrangement which is also known as string of pearl or crown of jewel appearance which is characteristic to CBDC. The lesions have a predilection to flexures mainly the lower trunk, groin, and upper thigh. Mucosal involvement is not a common feature.

The first line treatment for LABD is dapsone but some patients require second line treatment modalities including steroids and other immunomodulators including biologics. No correlation between the severity of blistering and the chronicity of disease exists. The clinical course of the disease is often benign and self-limiting. CBDC remits within 2-4 years. Lesions heal without scarring.

Case report

A previously well, 8 years old girl from Nuwara Eliya presented to the pediatric unit of local hospital with a generalized blistering eruption of four days duration. Initially there were blisters on the right arm which subsequently became generalized involving both upper, lower limbs, trunk and buttocks. Face, palms soles and genitalia were spared. There was no mucosal involvement. They were mildly itchy but not painful. She did not have fever or any associated symptoms. On examination there were annular tense vesiculobullous lesions on normal appearing skin. Characteristic "string of pearls" appearance was noted (Figure 1). Figurate outline could be appreciated in the areas of coalescence (Figure 2). Moreover, central crusting was noted (Figure 3). Systemic examination was normal.

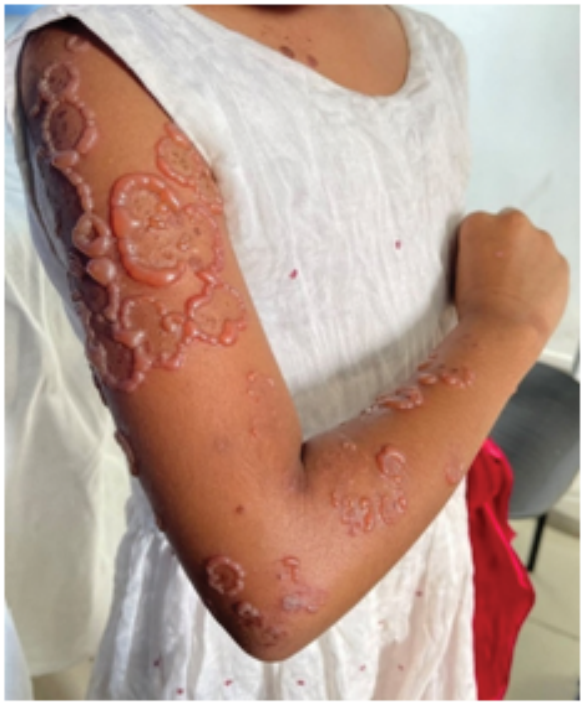

Figure 1. *Characteristic "string of pearl" arrangement of tense blisters.*

[1,3,4]*Registrar in Dermatology,* [2]*Consultant Dermatologist, National Hospital, Kandy, Sri Lanka.*

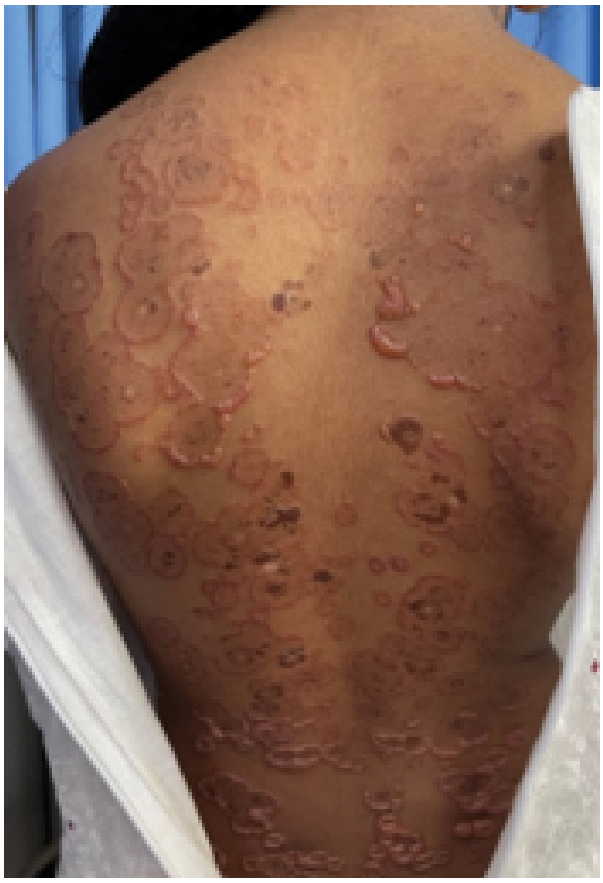

Figure 2. *Figurate outline in areas of coalescence of blisters.*

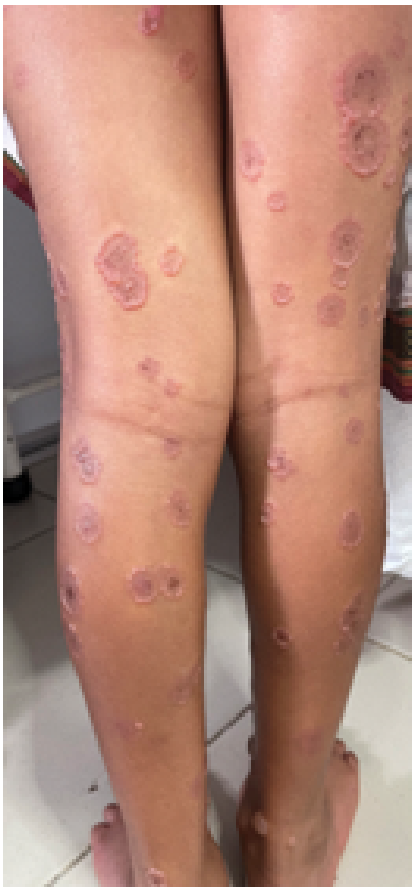

Figure 3. *Vesiculobullous eruption involving legs.*

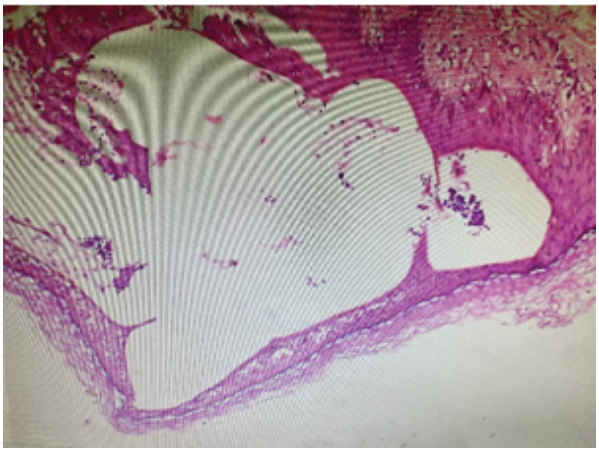

Figure 4. *Subepidermal blister with neutrophil predominance.*

The skin biopsy done at the local hospital was suggestive of linear IgA disease. Complete blood count showed mild leukocytosis of 11×10^9/L. C-Reactive protein, ESR, liver enzymes and renal function tests were normal. Blood picture was normal and G6PD screening test was negative. She was started on dapsone 1 mg/kg/day dose, oral prednisolone 1mg/kg/day and flucloxacillin. As she did not show a favorable response to treatment after one week, she was transferred to the dermatology unit of National Hospital (NH), Kandy for further management.

At NH-Kandy the skin biopsy was repeated along with a punch biopsy from perilesional skin for direct immunofluorescence (DIF). Skin biopsy of this patient revealed subepidermal bullae with neutrophilic predominance (Figure 4) and DIF indicated linear IgA deposition along the basement membrane suggestive of linear IgA disease.

Cyclosporin was added to the treatment regime since the patient had a very slow response to treatment and had a generalized severe eruption. Betamethasone with aqueous cream was used as topical therapy.

The patient was discharged 2 weeks after admission following complete remission and was followed up at the clinic setting. Prednisolone and cyclosporin

were tapered gradually over the course of two months. Dapsone was continued at the same dose. One week after prednisolone was completely tailed off from the treatment regime, she relapsed. She developed tense blisters arranged in an annular array involving arms, thighs, and trunk. This episode was less severe compared to the previous episode. She was recommenced on steroids 1mg/kg/day. As she was getting new lesions in spite of dapsone and immunosuppression therapy, IVIG was commenced, 2g/kg over 3 days and she had a marked response. Lesions healed without scarring. Steroids and dapsone were gradually tailed off. She didn't have new lesions over the follow-up period of 6 months.

Discussion

Currently there are no guidelines regarding the management of LABD or CBDC, although numerous treatment options have been utilized and reported in the literature, mainly in the form of case reports and retrospective studies[2].

LABD responds well to dapsone and steroids. The response to dapsone is usually seen within 48-72 hours of starting treatment. Sulfonamides such as sulphapyridine can be used as an alternative treatment but is considered inferior to dapsone. Anti-inflammatory antibiotics such as flucloxacillin, doxycycline, erythromycin have a place in management of CBDC which is mainly precipitated by infections.

In resistant and severe cases or patients with G6PD deficiency or sulfur allergy immunomodulators such as ciclosporin, azathioprine, mycophenolate mofetil, IVIg and even rituximab have been used with promising results[3].

There are case studies where ciclosporin, a calcineurin inhibitor which suppresses T cell activation was used as an adjunct to dapsone and steroids for CBDC[3]. Ciclosporin should be continued for at least 3 months to prevent recurrence according to literature.

IVIg modulates the activation and effector functions of B and T lymphocytes, neutralizes pathogenic autoantibodies, interferes with antigen presentation and has a strong anti-inflammatory effect which depends on its interaction with the complement system, cytokines and endothelial cells. The immunomodulatory potential of IVIg in patients is thus a result of a variety of complex mechanisms that act in synergy. There are trials which have used IVIg in LABD in adults but reported cases in CBDC are scarce. In our case scenario IVIg was used as a successful treatment modality for CBDC.

Here we highlight the use of IVIG in a refractory case of CBDC as an effective treatment option with less side effects in a child.

References

1. Christopher M. Hull, John J. Zone. Dermatitis Herpetiformis and Linear IgA Bullous Dermatosis. In:Jean L. Bolognia, Julie V. Schaffer, Lorenzo Cerroni, eds. Dermatology. 4th Edition. *Elsevir* 533-7.
2. Khan M, Park L, Skopit S. Management Options for Linear Immunoglobulin A (IgA) Bullous Dermatosis: A Literature Review. *Cureus* **15**(3): e36481.
3. Mitra D, Bhatnagar A, Singh GK, Sandhu S. Successful Treatment of Refractory Chronic Bullous Disease of Childhood with Rituximab. *Indian Dermatol Online J.* 2022; **13**(2): 248-51. doi: 10.4103/idoj.idoj_223_21. PMID: 35287397; PMCID: PMC8917490.