Linear IgA bullous dermatosis of childhood: Response to thalidomide

Sir,

Linear IgA bullous dermatosis (LABD) of childhood is a self-limiting, autoimmune blistering disorder. It usually presents in children less than five years of age and undergoes spontaneous resolution within two to four years of onset in most patients. We report a case of childhood LABD persisting into adulthood and responding favorably to thalidomide.

In 1997, an eight and a half years old male child weighing 30 kg, diagnosed with LABD, on treatment with 20 mg prednisolone for a year, presented with active disease and Cushingoid features [Figure 1]. His diagnosis was confirmed with histopathology [Figure 2a] and immunofluorescence studies [Figure 2b]. Specific anti-gliadin antibodies were negative, colonoscopy and computed tomography

(CT) scan of abdomen and chest failed to reveal any abnormality. His 8 am serum cortisol levels were undetectable. After ruling out anemia and a G6PD deficiency, we added 25 mg of dapsone per day and gradually increased it to 100 mg. This controlled the disease effectively. Unfortunately, the patient became anemic and his reticulocyte count increased to 5%. Since methemoglobin and sulfhemoglobin levels were within normal limits (WNL), dapsone was continued at a reduced dose of 25 mg daily for a year. The disease remained active. Persistent anemia and a raised reticulocyte count pointed to dapsone intolerance. To reduce the dapsone toxicity, we introduced cimetidine in a dose of 200 mg daily, with prompt improvement in hemoglobin and reduced reticulocyte counts.[1] The lack of local availability and cost of cimetidine necessitated its discontinuation. We tried cefadroxil 500 mg daily which helped to reduce the steroid requirement as erythromycin was ineffective in doing the same.[2] The disease persisted. Addition of methotrexate (2.5 mg/wk for three months) and later azathioprine (50 mg/day for three months) failed to

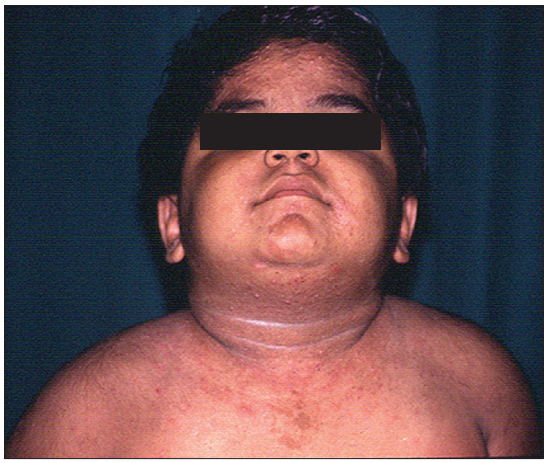

Figure 1: Cushingoid features due to chronic steroid therapy

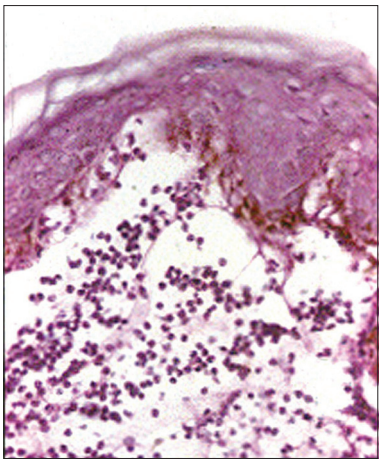

Figure 2a: Photomicrograph showing a subepidermal split with predominant neutrophilic infiltrate (H and E, ×400)

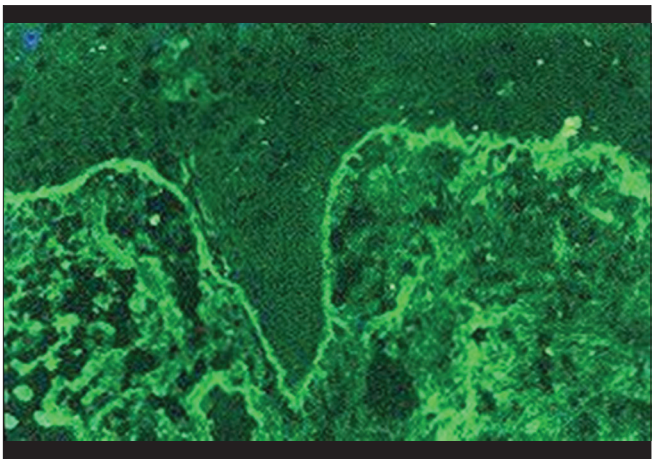

Figure 2b: Direct immunofluorescent study shows linear IgA deposit at the dermal-epidermal junction (×400)

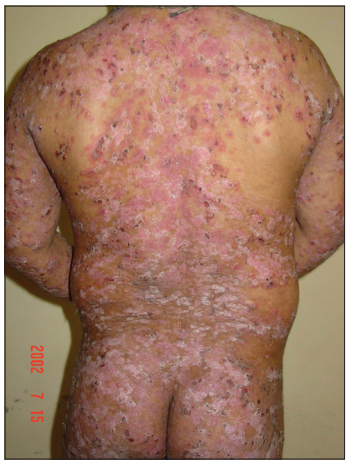

Figure 3a: Active disease pre-thalidomide therapy

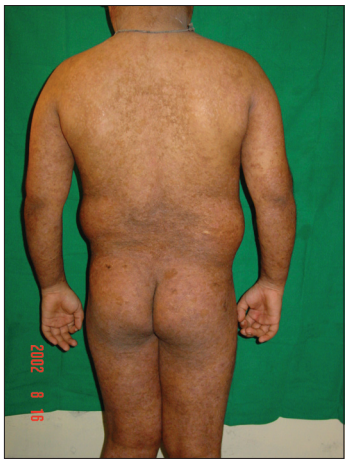

Figure 3b: Dramatic clearance of lesions within one month with thalidomide

improve the disease. Two years on, with the disease still showing no signs of remission, we introduced cyclosporine at 4 mg/kg/day.[3] He showed a remarkable improvement, enough to reduce his steroid dose to 2.5 mg/day, but the prohibitive cost of the medication resulted in its discontinuation. The ensuing flare-up was severe. With few options remaining, thalidomide was introduced at approximately 3 mg/kg/day [Figure 3a] with a cessation of pruritis within a week, and a clearing up of all lesions within a month [Figure 3b]. This dose was continued for a year and it allowed the steroid dose to be tapered to 2.5 mg/day. After a one-year complete disease-free period, he developed intractable leg pain which was unresponsive to non-steroidal anti-inflammatory agents. On discontinuing, his pains disappeared and reappeared on starting thalidomide again. Within two days of stopping the drug, the disease relapsed in a milder form. He was then maintained on a cocktail of 25 mg dapsone, 2.5 mg prednisolone, cefadroxil 500 mg and hydroxyzine 10 mg which he is on till date. Any change in this results in a flare-up of the disease. In 2009, our patient was 20 years old with active disease.

Dapsone is considered to be the drug of choice for LABD. Combination with cimetidine increases its tolerance and reduces hemato-toxicity by inhibiting the formation of hydroxylamine metabolites of dapsone.[1] In our patient, cyclosporine, as a second-line drug, was successful in controlling the disease compared to other usually listed drugs. This is consistent with the observation of Young HS and Coulson IH.[3] Although thalidomide has been tried in pemphigus vulgaris, cicatricial pemphigoid and Hailey-Hailey disease, there are no reports of its use in the treatment of LABD. We had a dramatic response with thalidomide with total clearance in one month, and while on treatment, he was disease-free for one year. We postulate that it could be working by inhibition of Interleukin-12 which is a potent pro-inflammatory cytokine.[4] Thalidomide can be considered as a therapeutic option in resistant cases. A point of caution is to watch out for signs of neuropathy which could become irreversible.[5] The persistence of disease in our patient represents the possibility of a childhood LABD continuing into adult form of the disease and presenting a therapeutic dilemma.

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REFERENCES

1. Rhodes LE, Tingle MD, Park BK, Chu P, Verbov JL, Friedmann PS. Cimetidine improves the therapeutic/toxic ratio of dapsone in patients on chronic dapsone therapy. Br J Dermatol 1995;132:257-62.
2. Kenani N, Mebazaa A, Denguezli M, Ghariani N, Sriha B, Belajouza C, *et al*. Childhood linear IgA bullous dermatosis in Tunisia. Pediatr Dermatol 2009;26:28-33.
3. Young HS, Coulson IH. Linear IgA disease: successful treatment with cyclosporine. Br J Dermatol 2000;143:204-5.
4. Moller DR, Wysocka M, Greenlee BM, Ma X, Wahl L, Flockhart DA, *et al*. Inhibition of LI-12 production by thalidomide. J Immunol 1997;159:5157-61.
5. Crawford CL. Thalidomide-induced neuropathy. Mayo Clin Proc 2002;77:1395.