TREATMENT OF LINEAR IgA DISEASE OF CHILDHOOD WITH DAPSONE

JEHAD T. AL-RATROUT*
Department of Dermatology
Qatif Central Hospital
Dammam,Saudi Arabia

Summary :
We describe in this report one of the uncommon acquired blistering disorder of childhood. We relied in our diagnosis on immunofluoresence which eliminates any diagnostic uncertainty because routine histopathology sometimes is of little value in distinguishing between certain bullous disorders. The child currently reported responded dramatically to dapsone with no hematological, renal, hepatic side effects or relapse after follow up for one year.

Case Report :

A one-year-old male child presented with four days history of multiple pruritic, bullous eruptions on the extremities preceded by two days history of flue like symptoms but negative drug history.

Physical examination revealed that the child was well nourished, afebrile with widespread vesicles, tense hemorrhagic bullae on normal and erythematous base, and crusted erosions with few target like lesions (Fig.1). He was admitted with a diagnosis of erythema multiforme but he continued to develop new blisters on the extremities that spread to trunk, perineum, buttocks, abdomen, and face with the scalp less severely affected . Characteristically the new crops of blisters appeared in clusters around resolving lesions (jewel like clustering) (Fig.2) .

The oral and ocular mucosa were not involved as well as the palms and soles.

Routine hematologic , biochemical , serologic investigations, Gram stain for blister fluid, Tzanck smear, throat swab,urinanalysis ,blood culture and glucose -6-phosphatase dehydrogenase were all normal . Staphylococcus -aureus were cultured from the bullous fluid . The patient was homozygous for HLA-B 8 . The antithyroid microsomal autoantibody, antinuclear antibody ,and antismooth muscle antibody were negative.

A perilesional skin biopsy specimen from the trunk revealed a subepidermal bulla. The bullous cavity contained fibrin , neutrophils and few eosinophisls . Few micro abscesses were seen at the tips of dermal papillae. The dermis showed mild perivascular inflammatory infiltrate. The overlying epidermis was intact without necrosis (Fig. 3)

Direct immunofluoresence of perilesional skin showed linear deposits of IgA at the dermo-epidermal junction (Fig.4). Indirect immunofluorescence was not carried out.

Following the previously mentioned histopathology and immunofluorescence results the patient was diagnosed as chronic bullous dermatosis of childhood and treated with IV Flucloxacillin 150 mg Q6hour for two weeks ,repeated culture of the bullous fluid turned to be of normal growth but the lesions continue to erupt daily and since he is G6PD normal we started him on Dapsone, 2 mg / kg /day. The treatment was very well tolerated with no evidence of heamatological side effects. There was rapid improvement within one week with no new lesions and he was discharged home with biweekly follow up for CBC and reticulocyte, and monthly for LFT and RFT. Treatment was tapered after three months to 0.5 m g / kg/ day over six months, and all lesions healed with hyperpigmentaion but no scarring (Fig.5) and he was free of any lesion after one year follow up.

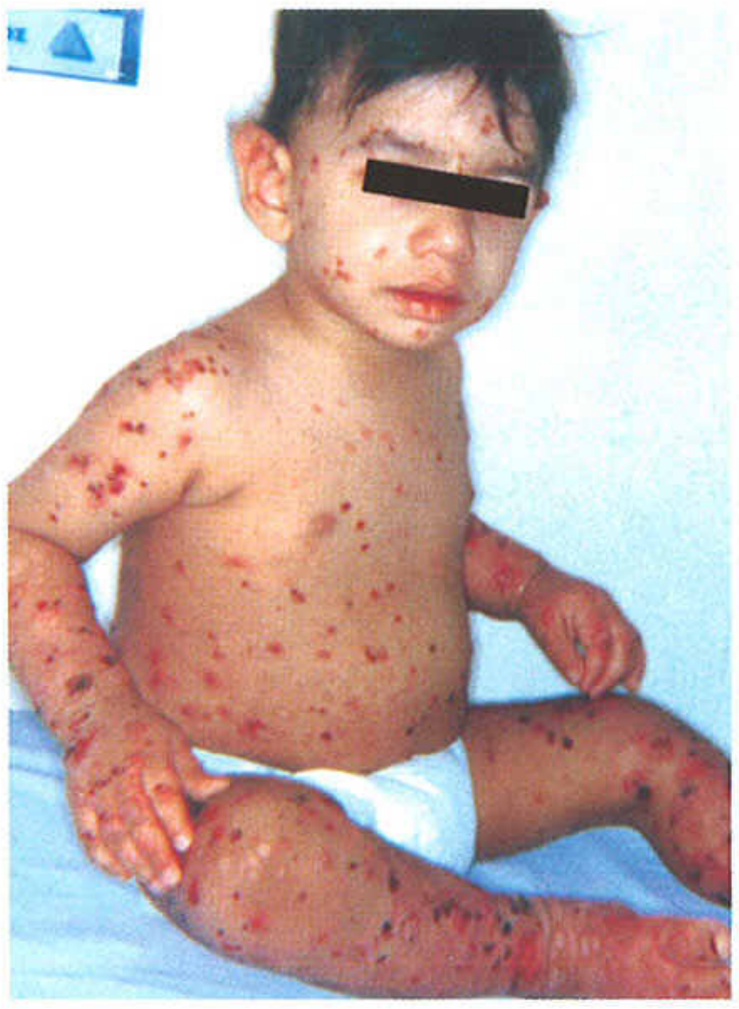

Figure 1: Multiple,tense hemorrhagic bullae on normal and erythematous base and crusted erosions.

JEHAD T. AL-RATROUT,MD, KFU FELLOWSHIP .
Consultant Dermatologist.
Dammam 31421 P.o.Box 662
Kingdom of Saudi Arabia
Fax: (3) 8917435
E-mail:alratjeh@hotmail.com

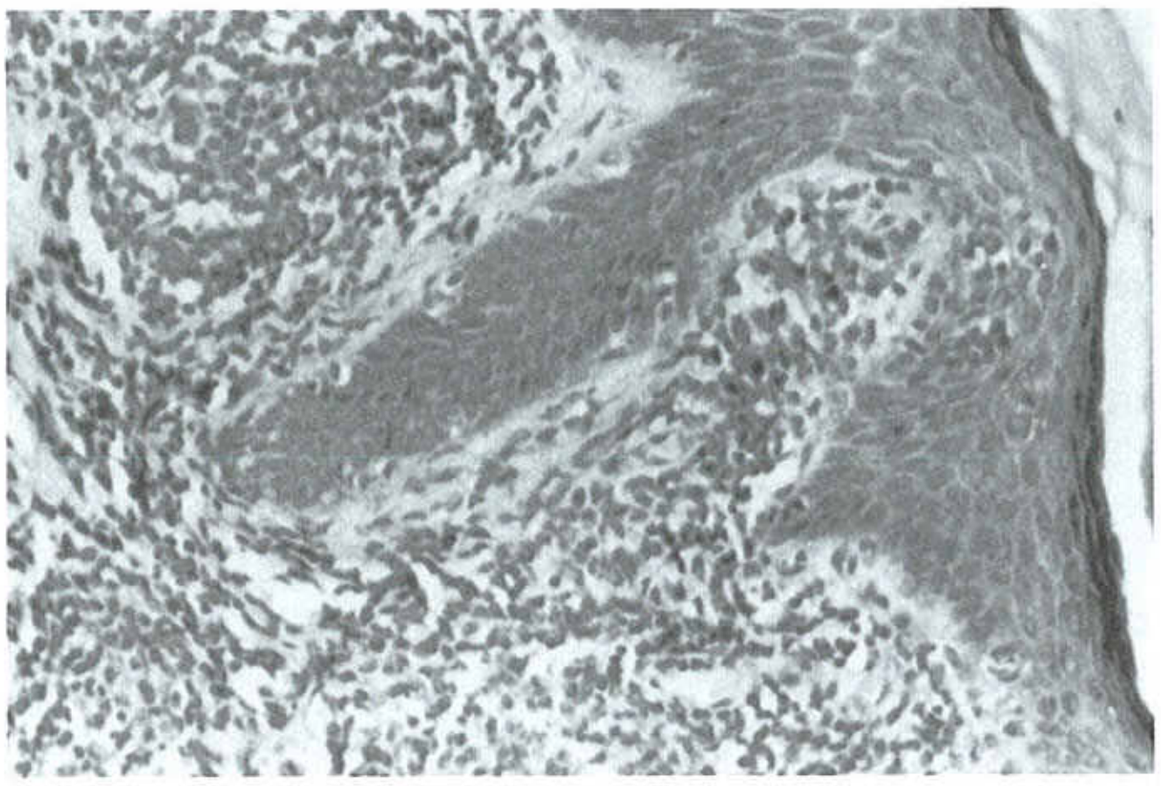

Figure 2: Bullae arranged in a jewel like clustering.

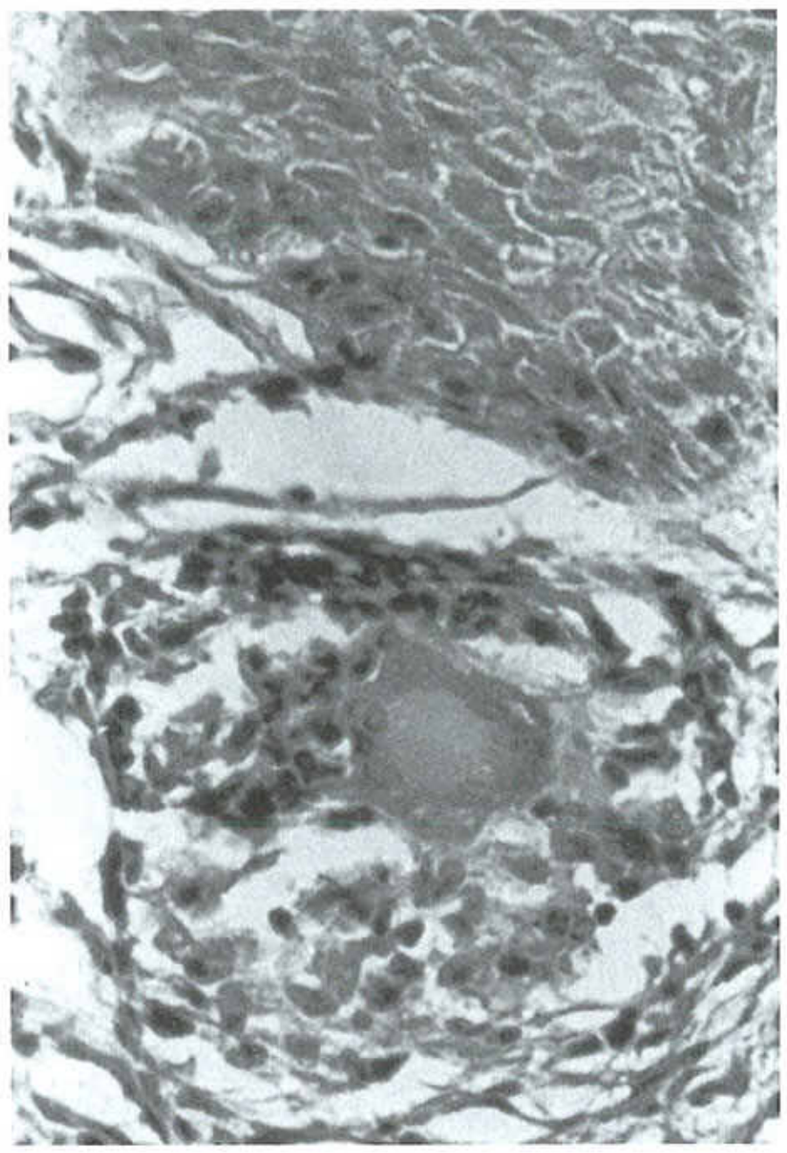

Figure 3: Subepidermal blister with neutrophils in the dermal papillae with perivascular infiltrate in the dermis. H/E 10x10

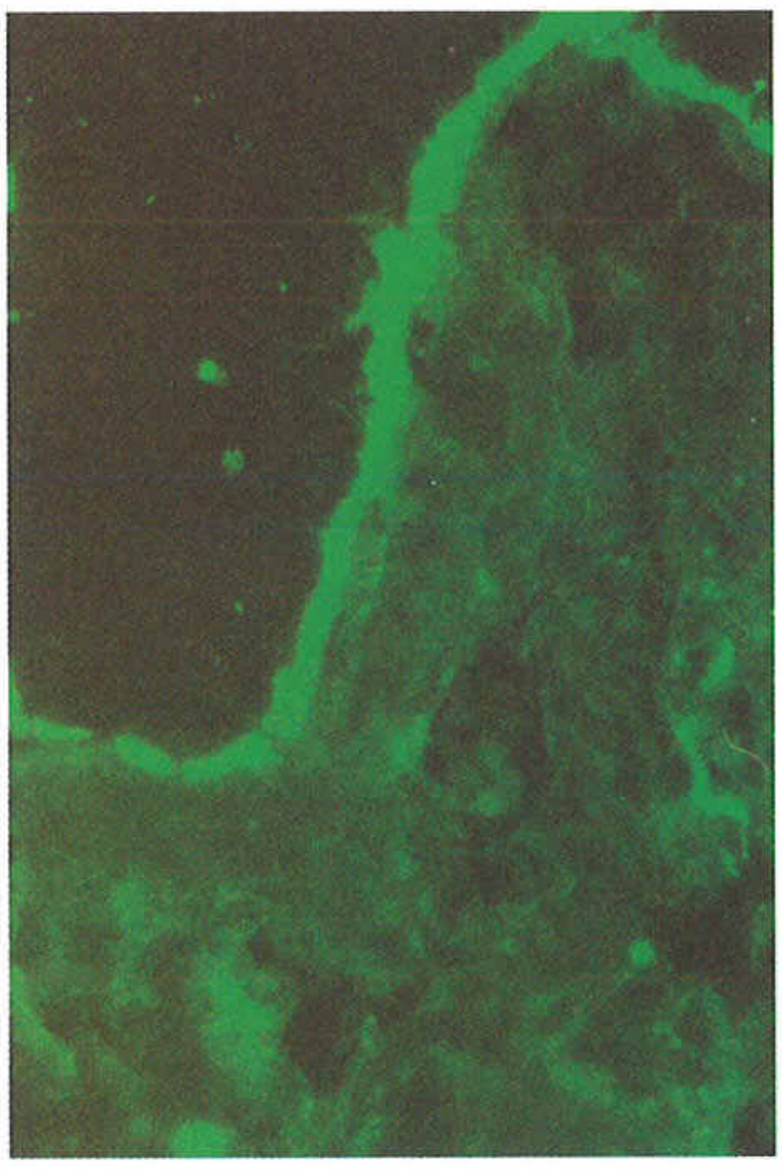

Figure 4: Direct immunofluorescence showing a linear deposition of IgA at the dermoepidermal junction (magnification 40x10).

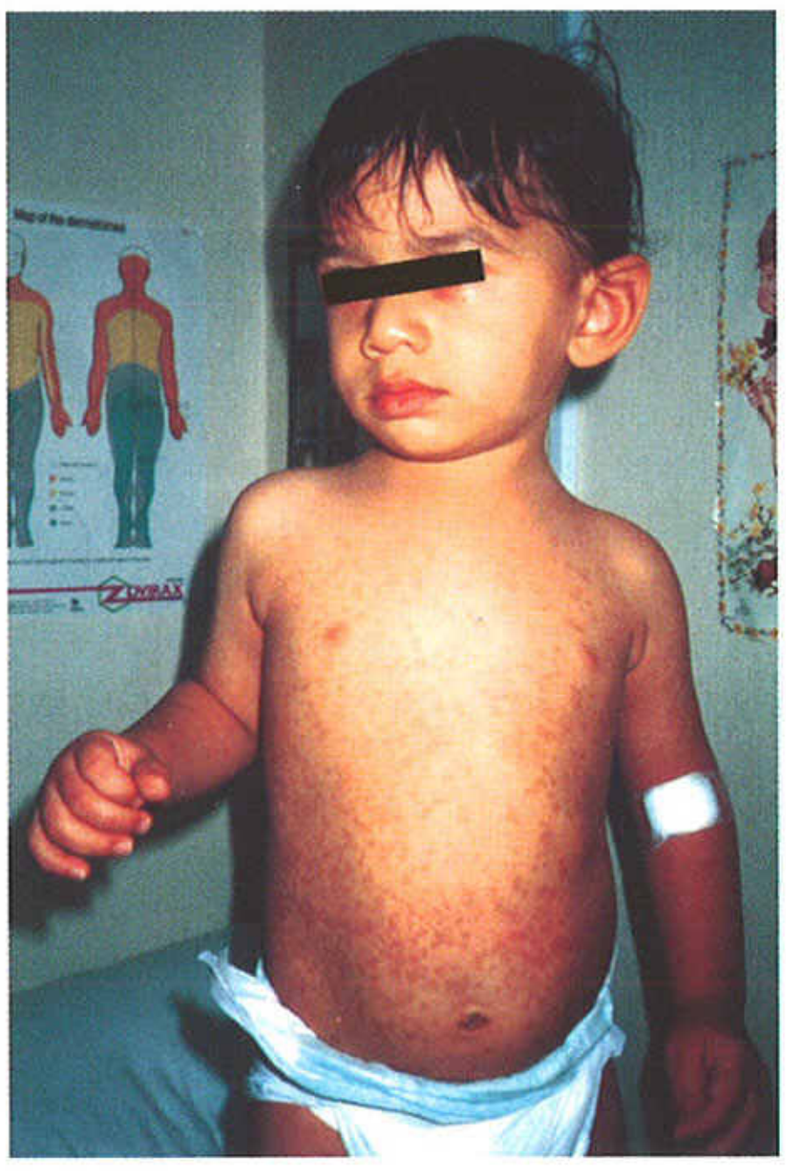

Figure 5: Healed lesions with only hyperpigmentation.

DISCUSSION

Linear IgA disease of childhood (LADC) (chronic bullous dermatosis of childhood) (CBDC) is a rare acquired ,self-limiting subepidermal vesiculobullous disorder of childhood ,with unknown prevalence . It is characterized histopathologically by the presence of a linear band of IgA at the dermoepidermal junction [1,2]. The disease usually starts before the age of 5 years [2,3,4]. It is more common in males, and the precipitating factors include post vaccination [5], upper respiratory tract infection , drug ingestion or idiopathic [2,6] . The onset is usually abrupt with blisters typically localized to the lower abdomen and anogenital areas. The blisters gradually involve other body areas like feet, hands and face, particularly the perioral area [3,4,7,8]. Pruritis is not usually a predominant feature. The bullae are clear and / or hemorrhagic and usually arise on normal- looking skin [2,7,8].

Jewel like clustering, with fresh vesicles arising around the edge of an old or healing blister is seen in many patients, but cannot be regarded as diagnostic as it may occur in other skin disorders like bullous pemphigiod [8,9,10].

Healing may result in hyperpigmentaion but not scarring . Mouth ulcers occur in 50% of the patients [2]. Ocular symptoms such as grittiness, burning or discharge has been reported but it appears to be more common in those with long- standing disease and in those who are HLA- B8 negative[11,12]. As in dermatitis herpetiformis ,LADC has been reported in association with HLA-B8 ,but there have been no reports of association with gluten-sensitive enteropathey [8,13] . HLA-B8 is present in 82% of the patients who are in remission, compared with 40% of patients who have active disease, the significance of this finding is unknown [11,12].

The differential diagnosis of LADC includes bullous impetigo, erythema multiforme ,childhood bullous pemphigoid , dermatitis herpetiformis, epidermolysis bullosa simplex (particulary Dowling Meara type) and cicatricial pemphigoid [4,14,15,16]. These may have similar clinical and histopathologic features as in our case it was misdiagnosed as erythema multiforme clinically and as DH histologically. Differentation of LADC from these bullous disorders rests on the direct immunofluorescence which shows linear deposits of IgA at the basement membrane and this will eliminate any diagnostic uncertainty [4,17,18].

Although the majority of cases remit in months or years [8,19], in a small proportion of patients it may persist into adult life [12,20].

Sulfapyridine therapy is deemed to be the treatment of choice owing to the lower incidence of side effects, Dapsone and Sulfamethoxypyridazine are alternative therapies [15,21,18]. Prednisolone singly or in combination with sulfapyridine or with dapsone has been used [13,22], Colchicine as alternative for those with G6PD deficiency and also in whom first -line of treatment is contraindicated or who fail first -line of treatment or develop side effect from it [23,24]. Some recent studies find oral Flucloxacillin and Dicloxacillin to be effective [4,25], The mechanism of action is not clear but they suggest that LADC could be an immune reaction to Flucloxacillin sensitive bacteria ,most likely staph- aureus ,which is not concurrent with our finding since the antibiotic eradicate the bacteria but did not control the eruption. This report is an additional proof that Dapsone is still the first line therapy in LADC patient with normal G6PD .

REFERENCES

1. White JM,Chrisie BS,Nam D,et al. Frequency and clinical significance of erythrocyte genetic abnormalities in Omanis. J Med Genet 1993;30:396-400.

2. Marsden RA.Linear IgA disease of childhood. In: Wojnorowska F,Briggaman RA,eds. Management of blistering diseases. New York,NY:Chapman&Hall;1990:119-126.

3. Mussinovitch M,Ben-Amitai D,Finkelstein Y,Harel L and Varsano I. A boy with cutaneous bullous eeruption. Eur J Pediatr 1997 Dec;156(12):971-2.

4. Denguezli M,Ben Nejma B,Nourira R,Korbi S, Bardi R,Ayed K,Essoussi AS and Jomaa B. IgA linear bullous dermatosis in children. A series of 12 Tunisian patients. Ann Dermatol Venereol 1994;121(12):888-92.

5. Bowen JT.Dermatitis herpitiformis in children. Journal Cutaneous Disease 1905;23:79-85

6. Berlin C. Dermatitis herpitiformis in children. Brit.J.Dermatol 1952;64:281-90

7. Marsden RA,Skeete MVH and Black MM. The chronic acquired bullous disease of childhood.Clinical and Experimental Dermatology 1979;4,227.

8. Marsden RA,McKee PH,Bhogal B,Black MM and Kennedy LA. A study of benign chronic bullous dermatosis of childhood and comparison with dermatitis herpetiformis and bullous pemphigoid occurring in childhood. Clinical and Experimental Dermatology 1980;5:159-172

9. Lear JT,SmithAG.Multiple blisters in a youg boy.Archives of dermatology May 1998;134(5):625-630.

10. Tse Yand Lim HW. Chronic bullous dermatosis of childhood: Differentiation from other autoimmune blistering disease in children. Int J of Dermatol 1994;33(7) 507-509

11. Wojnarowska F,Marsden RA,Bhogal B and Black MM. Chronic bullous disease of childhood ,childhood cicatricial pemphigoid and linear IgA disease of adults, a comparative study demonstrating clinical and immunological overlape. J.Amer.Dermatol 1989;9:792-802.

12. Marsden RA,Wojnorowska F, McKee PH, Black MM.chronic bullous disease of childhood. In: HappleR,GrosshansE,eds.Pediatric Dermatology:Advances in Diagnosis and Treatment.New Yourk,NY:Springer-Verlag NY Inc;1987:75-81.

13. Aboobaker J,Wojnarowska FT,Bhogal B and Black MM. Chronic bullous dermatosis of childhood clinical and immunological features seen in African patients. Clin Exp Dermatol 1991 May;16(3):160-4.

14. Rabinowitz LG and Esterly NB. Inflammatory bullous diseases in children. Dermatol Clin 1993 July;11(3):565-81.

15. Egan CA and Zone JJ. Linear IgA bullous dermatosis. Int J Dermatol 1999 Nov;38(11):818-27.

16. Trueb RM,Didierjean L,Fellas A,Elias A and Borradori L. Childhood bullous pemphigoid:Report of a case with characterization of the targeted antigens. American Academy of Dermatology1999;40(2) 338-343.

17. Mahe A,Flagel B and Bobin P. Bullous IgA linear dermatosis of children in Mali.Ann Dermatol Venereol 1996;123(9):544-8.

18. Ajithkumar K,Kurian S, Jacob M and Pulimood S. Linear IgA bullous dermatosis in South India. Int J Dermatol 1997 March;36(3):191-3.

19. Alexander JOD. Dermatitis herpetiformis. London:WB Saunders,1975.

20. Burge S,Wojnarowska MA and Marsden A. Chronic bullous dermatosis of childhood persisting into adulthood . Pediatric Dermatology 1988;5(4) 246-249.

21. Witkampl L and Sillevis Smitt JH. Linear IgA dermatosis of childhood. Br J Dermatol 1991 Oct;125(4):395-6.

22. Jablonska S. The therapies for linear IgA bullous dermatosis of childhood. Pediatr Dermatol 1999 Sept-Oct;16(5):415.

23. Banodkar MD and Al-Suwaid AR. Colchicine as a noval therapeutic agent in chronic bullous dermatosis of childhood 1997;36:213-126.

24. Ang P, Tay Yk.Treatment of linear IgA bullous dermatosis of childhood with colchicines. Pediatr Dermatol 1999 Jan-Feb;16(1):50-2

25. Skinner BR,Rotondo CK,Schneider MA,Raby L and Rosenberg EW. Treatment of chronic bullous dermatosis of childhood with oral dicloxacillin . Paediatric Dermatol 1995 March;12(1):65-6.