Acquired autoimmune bullous diseases of childhood: Analysis of 22 cases

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Abstract

Acquired auto immune bullous diseases in children are a relatively rare group of conditions, with overlapping clinical features difficult to differentiate clinically. Hardly any previous studies of acquired autoimmune bullous diseases in children had been reported in Sri Lanka. 22 cases of acquired autoimmune bullous were studied at the skin clinic of Lady Ridgeway hospital for children over a period of 3 years from May 2004 to May 2007. Based on the clinical presentation, inclusion and exclusion criteria 22 cases were included in the study. With regards to investigations and treatment no alterations were made to the existing protocols of the unit. Investigations included a skin biopsy and whenever possible direct immunofluorescence and relevant haematological investigations. Of the 22, 20 were diagnosed as chronic bullous disease of child hood. and rest as bullous pemphigoid. With regards to diagnosis there was excellent clinico-pathological correlation. Most affected children were below 5 years of age, and a male preponderance was noted. Significant hypo-albuminaemia was noted in few of the severely affected. Haemolysis was the most significant side effect of dapsone monotherapy. The combination of dapsone and predni-solone given to severely affected while reducing haemolysis seems to shorten the duration of therapy. No serious side effects of dapsone was noted.

Introduction

Acquired autoimmune bullous diseases of childhood has a world wide distribution and affects all races and both sexes.

The main type of acquired autoimmune bullous disease of childhood is chronic bullous disease of childhood (CBDC). Other types described include juvenile pemphigoid (JP), pemphigus, cicatritial pemphigoid (CP) and dermatitis herpetiformis (DH). Among the subepidermal bullous diseases (CBDC, JP and CP) there is considerable clinical overlap. However on immunohistological studies chronic bullous disease of childhood is characterized by linear deposition of Ig A along the basement membrane zone, while deposition of Ig G in a linear manner is seen in bullous pemphigoid. Both commonly involves the skin and less commonly the mucus membrane.

At the skin clinic of Lady Ridgeway Hospital in Colombo we undertook this study in order to obtain details of autoimmune bullous diseases of childhood in Sri Lanka and to study the treatment outcome.

Materials and methods

22 patients were included in the study during a period of 3 years (May 2004 – May 2007) children were referred from the out patient department of the LRH or referred from other hospitals. They were seen by the consultant dermatologist on the first visit, and a detailed history obtained from each including age, sex, symptoms, duration of the illness, possible triggers and concomitant drug therapy. Examination included noting the type of the blister,distribution, changes in the surrounding skin and a general examination. They were subjected to routine investigations which included a skin biopsy of a fresh bulla for histology and whenever possible non lesional skin direct immuno-fluorescence. The other investigations included UFR FBC, LFT, and a G6PD assay prior to treatment with dapsone. Those who required prednisolone were asked for a past history of Tuberculosis, or for a possible contact history with Pulmonary Tuberculosis. Those who had extensive blistering had their serum proteins measured.

The criteria for inclusion were

1. Clinical symptoms and signs compatible with an auto immune blistering disorder.
2. Presence of subepidermal blister or an intra epidermal blister and neutrophil or eosinophil rich inflammatory infiltrate in the skin biopsy.

Exclusion criteria were

1. Evidence of a Mechano-bullous disease.
2. Acquired non-autoimmune bullous disease.

All patients were admitted to the ward for control of the disease and followed up in the clinic initially every fortnight and subsequently monthly. Treatment was based on the clinical diagnosis, age and weight of the child, G6PD assay and disease severerity. Less than 10 blistering sites were considered as mild and more than 10 or extensive as severe. Mild cases were given dapsone monotherapy (1mg/kg/day) and severe cases with dapsone (1mg/kg/day) and 2 consecutive days of prednisolone (0.5 mg/kg)

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patients with evidence of sepsis was treated with an appropriate antibiotic. On follow up special attention was paid to the development of new symptoms, presence of blistering, and for the presence of side effects. Follow up also included a FBC, Reticulocyte count and a liver profile.

Results

Among 22 children 20 (92%) were boys, and 2 were girls (8%) and 15 (68%) of them belonged to the age group below 5 years and 7 patients were more than 5 years of age (32%). Itching and fever were the commonest symptoms encountered.

All our patients had tense blisters in the acute stage indicative of a sub epidermal blistering. 20 of the patients showed rosette formation suggestive of chronic bullous disease of childhood clinically. All patients had limb involvement, 5 had in addition trunk involvement, and extensive blistering was noted in 5 with facial involvement, and one had visible oral involvement. In children with clinical evidence of chronic bullous disease of childhood blistering occurred in otherwise healthy skin in comparison to children with Bullous Pemphigoid who had an urticarial base.

None of our patients had any significant haematological changes prior to commencement of therapy. 2 out of 5 severely affected patients showed a significant reduction in the serum albumin levels and both had pitting ankle oedema requiring transfusion of fresh frozen plasma as human albumin was not available.

2 patients had G6PD deficiency and required oral prednisolone for the control of blistering. Both went on to develop significant side effects including Cushingoid features and pityriasis versicolor. All patients who received dapsone showed haemolysis, in two this was severe enough to temporary withdrawal of the drug for few weeks. In order to reduce haemolysis dapsone was given for 5 days and 2 days of prednisolone. For very young children dapsone was given every other day.

On follow up identifiable triggers for disease reactivation included upper respiratory tract infection in 7 and insect bites in 2 of them.

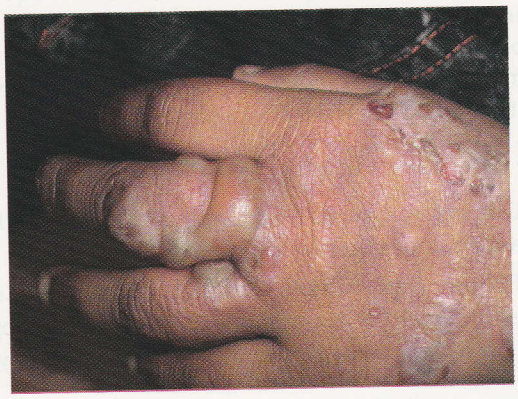

Figure 1. *Acute phase*

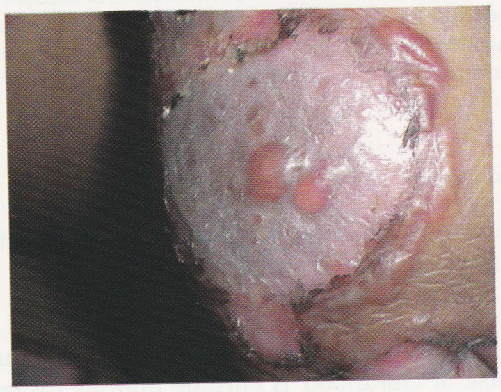

Figure 2. *Rosette formation*

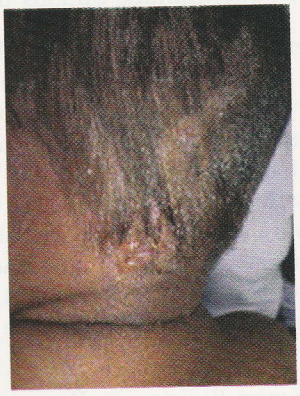

Figure 3. *Scalp involvement*

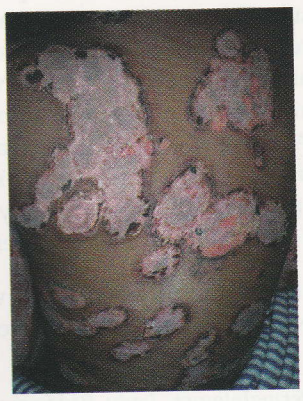

Figure 4. *Healing stage*

	Dapsone daily	*Dapsone every other day*	*Prednisolone daily (G6PD deficient)*	*Dapsone daily + prednisolone pulse*	*Dapsone every other day + prednisolone pulse*
Disease type	1. CBDC 1- JP	1. CBDC 1-JP	CBDC	CBDC	CBDC
Disease severity	Mild	Mild	Severe	Severe	Severe
Age limit	> 5years	< 5 years	< 5 years	> 5years	< 5 years
No. of patients	2	2	2	5	11
Duration of treatment	2 years (1)	2 years (1)		6 months – 1 year (3)	6 months – 1 year (5)
Average dose of prednisolone				10 mg	7.5mg

NB; from 22, 10 completed treatment, and 12 are still on treatment.

Discussion

Our study showed that autoimmune blistering mostly affects the children below 5 years of age (68%) with an average age of 2.5 and there is a marked male preponderance (90%) These findings are similar to the findings of Wojnarowska et al[1]. Among the diseases, Chronic Bullous Disease of child hood was the commonest clinical diagnosis entertained. This was based on the presence of a tense blister and rosette formation. Only one of our patients had visible mucous membrane involvement which is said to be common in CBDC (11) this may be because of difficulty in examining very young, acutely ill children with the disease. There was excellent clinico-pathological correlation. Light microscopically all 20 patients had a diagnosis compatible with CBDC. Out of 7 who underwent direct immunofloresence 5 had features of CBDC and 2 had bullous pemphigoid. 2 out of 5 children with extensive blistering had a very low albumin level necessitating the transfusion of fresh frozen plasma. We feel that this is an important finding which is relevant in the management of these children. The hypo-albuminaemia is attributed to the disease as they had normal liver functions, and a negative urine albumin test. Excessive loss of protein in the exudate is a possible explanation. We also recommend screening for G6PD prior to dapsone therapy. The use of prednisolone or dapsone as monotherapy often give rise to intolerable side effects, however the combination of dapsone with prednisolone as pulse therapy helps to reduce the side effects of both. Unfortunately we could perform direct immunofluorescence only on 7 of our patients. We see this as a draw back in our study.

Acknowledgements

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