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Original Article

Light microscopic findings in Pakistani children with chronic bullous disease of childhood

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Abstract

Background Autoimmune blistering diseases, though uncommon in children, often pose a diagnostic dilemma in the absence of immunofluorescence techniques. Light microscopic histopathological features for chronic bullous diseases of childhood CBDC have been adequately recorded in the literature but not for the Pakistani population.

Objective This study aims at recording the histopathological features of children with CBDC in our population.

Methods Light microscopic changes were recorded in 22 children with CBDC, diagnosed on the basis of direct immunofluorescence findings.

Results Of the 22 children that presented with CBDC, Strong linear IgA with or without other immunoglobulins deposition at the basement membrane zone was seen in 19 patients. Histopathology could be performed on 13 biopsy specimens of which 11 were suitable for reporting. Sections revealed a subepidermal blister in 81.8% specimens and papillary tip micro abscesses in 45.5%. A predominantly neutrophilic infiltrate was also present in 54.6% of the specimen

Conclusion These findings show a strong overlap between the histological findings of most patients with CBDC and dermatitis herpetiformis, while the remaining CBDC patients resemble those of bullous pemphigoid as far as the histology is concerned.

Key words
Chronic bullous dermatosis of childhood, immunofluorescence, dermatopathology, IgA bullous diseases.

Introduction

Autoimmune blistering diseases are not very common in children, but often pose a diagnostic dilemma when they do occur. Immunofluorescence studies and immunoblot analysis help delineate the various categories of childhood blistering disorders. Autoimmune blistering diseases of the children were initially grouped into a rather descriptive term of chronic bullous diseases of childhood (CBDC). Later on it was shown that most of these patients had linear deposition of IgA at the basement membrane zone (BMZ) similar to that of the adults and that the circulating IgA antibodies bound to the same 97-kd antigen as in the adults, and therefore, this group of diseases was labeled as linear IgA bullous disease

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(LABD) of children.[1] The objective of this paper is to highlight the light microscopic histopathological features of CBDC, in Pakistani children with a view to see any distinguishing histology.

CBDC is generally characterized by eruption of annular and configurate erythema and jewel string blisters over the skin, preferentially affecting the pelvic and perioral areas in preschool-age children. Histologically, the lesional skin shows a subepidermal blister along with a predominantly neutrophilic (with or without eosinophils) infiltrate and sometimes even papillary tip microabscesses.[2] Immunofluorescence is, however, diagnostic in most cases showing linear deposition of IgA at the basement membrane zone on direct immunofluorescence (DIF). In some cases though, DIF may be negative[3,4,5] despite the classical clinical presentation along with supportive histological features and excellent response to dapsone therapy. As mentioned earlier, this disease is generally considered to be the same as the adult LABD but affecting a younger age group.[1]

Patients and methodology

A total of 22 patients over a six year period were recorded. They were all children under the age of 10 years, suffering from CBDC. For diagnosis the perilesional skin was generally biopsied, including the blister where ever possible. The specimens were cut in half, submitting the blister part for histopathology and the perilesional part for direct immunofluorescence. In some patients, however, the blister was either too infected, old or ruptured forming scabs, especially, in partially treated patients. Routine histopathology could not be performed on such patients. Key histological features like the level of blister, type of infiltrate and papillary tip changes were recorded whereever available. Diagnosis was based on the presence of a strong deposition of IgA at the BMZ with or without deposition of other immunoglobulins. In three patients, however, DIF was negative but they otherwise had a classical presentation of clustered vesicles at a young age all over the body including face along with a very good response to dapsone and so were included in the study as it is known that DIF may be negative in some patients with CBDC.[3,4,5]

Results

Patient's ages ranged between 5 months to 10 years (mean 4.5 yrs). Routine histopathology could be performed in 13 (59%) patients, as shown in **Table 1**, of whom, the report was inconclusive in 2 patients because of heavy infection in 1 patient, while, an old healing blister was biopsied in the second patient, so a total of 11 (50%) biopsy specimens were useful enough for routine histopathology.

Table 2 shows the summary of histopathological changes in the 11 biopsy specimens. A subepidermal blister was seen in only 9 (81.8%) specimens. Papillary tip changes were seen in 6 (54.6%) specimens of which frank microabscesses were present in 5 and papillary tip oedema in just 1. A neutrophilic infiltrate was seen in 6 (54.6%) specimens, while a mixed infiltrate comprising neutrophils, eosinophils and

Table 1 Histopathological and direct immunofluorescence data of 22 patients suffering from CBDC

Patient No.	*Age (years)*	*Histopathological features*	*Immunofluorescence findings*
1.	5	Neutrophilic infiltrate with papillary tip microabscesses	Strong linear IgA & weak IgG deposition at the BMZ
2.	5	-	Strong linear IgA deposition at the BMZ
3.	4	-	
4.	4	-	"
5.	12	Subepidermal blister with neutrophils & eosinophils	"
6.	5	-	"
7.	5	-	Strong linear IgA and weak IgM deposition at the BMZ
8.	8	Subepidermal blister with neutrophils	Negative*
9.	3	Subepidermal blister with neutrophils & papillary tip microabscesses	Strong linear IgA and weak IgM deposition at the BMZ
10.	4	Subepidermal blister with neutrophils eosinophils & papillary edema	"
11.	5	-	"
12.	5	-	"
13.	0.5	Subepidermal blister with neutrophils	Negative*
14.	2	Subepidermal blister, insignificant infiltrate	Strong linear IgA and weak IgM deposition at the BMZ
15.	10	Infected blister. Not fit for reporting	Strong linear IgA deposition at the BMZ
16.	6	-	"
17.	3	Subepidermal blister with neutrophils & papillary tip microabscesses	Negative*
18.	2	Intraepidermal blister with spongiosis and neutrophils (a healing blister)	Strong linear IgA and weak IgM deposition at the BMZ
19.	4	Neutrophilic infiltrate with papillary tip microabscesses	"
20.	5	Subepidermal blister with neutrophils & papillary tip microabscesses	"
21.	6	Subepidermal blister with mixed infiltrate	Strong linear IgA deposition at the BMZ
22.	6	-	"

* No immunofluorescence was detected, but the children had otherwise a classical presentation of CBDC

Table 2 Key histopathological features of 11 patients with CBDC

Histopathological feature	*n (%)*
Subepidermal blister	9 (81.8%)
Papillary tip microabscesses	5 (45.5%)
Neutrophilic infiltrate	6 (54.6%)
Mixed infiltrate	3 (27.3%)
Papillary tip edema	1 (9.1%)

lymphocytes in only three.

Discussion

In this study routine histopathology of biopsy specimens of children with CBDC/LABD show a lot of overlap with other autoimmune bullous diseases like dermatitis herpetiformis (DH) and bullous pemphigoid (BP). Papillary tip microabscesses and a neutrophilic infiltrate with or without eosinophils are a predominant feature of DH, whereas the type and quantity of infiltrate is very

variable in BP. A subepidermal blister is common to all the three.

This study does not show any histopathologic features characteristic of LABD/CBDC in our population, and therefore, leaves us only with immunofluorescence studies as a diagnostic tool. On histopathology alone most of these patients would have most likely been diagnosed to be suffering from DH because of the presence of papillary tip microabscesses and a neutrophilic infiltrate along with a subepidermal blister.

Moreover, in about half of the patients in our setting, histopathology may not even be possible because a fresh, non infected, intact blister may not be available at the site selected for a biopsy, or may be missed while sectioning the specimen. We generally prefer a non-facial and a non-pressure bearing site to avoid scarring and discomfort to the patient. This makes the utility of routine light microscopic histopathology very limited in LABD/CBDC in our population.

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