

## REPORTS

# The Ultrastructural Localization of IgA Deposits in Chronic Bullous Disease of Childhood (CBDC)

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**A case of bullous disease in a child with linear IgA immune deposits at the basement membrane zone and with some clinical, histological, and electron microscopic characteristics both of dermatitis herpetiformis and bullous pemphigoid, is described.**

The bulla formed between the basal lamina and basal cell membranes as in bullous pemphigoid, but at the same time there were numerous inflammatory cells in the dermis just below the partly destroyed basal lamina and also abundant fibrin deposits in very recent bulla and in the skin, all of which is rather characteristic of dermatitis herpetiformis.

Ultrastructurally, the IgA deposits were located chiefly below the lamina basalis (the dermal type) but also, though less abundantly, in the lamina lucida, very much as we have seen them to be in adult cases with linear IgA immune deposits at the basement membrane zone. The investigations have supplied further evidence showing the chronic bullous disease of childhood to be actually a counterpart of the form in adults with the same linear localization of IgA deposits.

The classification of subepidermal bullous diseases in children is still a matter of controversy. Cases undoubtedly do exist which in clinical, histological, and immunopathological respects correspond fully to dermatitis herpetiformis (DH) of adults [1-3] or to bullous pemphigoid (BP) [1-7]. There is no agreement, however, concerning cases with large blisters distributed chiefly over the lower parts of the trunk, genital regions, thighs, and face. The histological picture shows subepidermal blisters with numerous eosinophils as in BP, in some cases together with polymorphonuclear microabscesses—characteristic of DH. Such cases usually respond to sulfapyridine and sulfones, but more often than not the controlling doses can be toxic and full remission is obtained only by combined treatment with small doses of corticoids. We have described cases of this kind as a mixed DH-BP form [3]—a complete counterpart to the DH-BP form of adults [8,9]. Cases of the same kind have been described as juvenile pemphigoid [10,11] or as juvenile DH [1,12]: they have also been recorded as chronic bullous disease of childhood [13-17], although this name was originally given to subepidermal

bullous disease of children in which no immunological phenomena could be demonstrated in the skin [2,18,19].

In immunofluorescence (IF) studies the characteristic finding is linear deposits of IgA, occasionally with some IgG. Circulating antibodies against the basement membrane zone (BMZ) are not seen in the IgG class, whereas they were found in the IgA class in one of our patients (Chorzelski et al, unpublished data), as they are also in adults with the same localization of linear IgA deposits [20,21].

We now present the electron microscopic and immunoelectron microscopic data of a case of typical bullous disease in a child with linear IgA deposits in the BMZ. The case is to our knowledge the first one ever investigated by immunoelectron microscopy. It is our further object in the present paper to compare the results with those obtained in bullous disease of adults with linear IgA deposits at the BMZ.

## MATERIALS AND METHODS

### *Case Report*

In a boy aged 5 years, the disease began at age 2. Blisters varying in size were present occasionally in herpetiform arrangement and distributed chiefly over the lower part of the trunk, genital region, and inner aspects of thighs. There was pronounced itching. Histologically subepidermal bulla without polymorphonuclear microabscesses in the dermal papillae and with numerous polymorphs and eosinophils in infiltrations were present. Intestinal biopsy revealed no abnormalities. Gluten-free diet administered for several months gave no results. Direct immunofluorescence studies (DIF) showed linear IgA deposits at the BMZ. Sulfapyridine and sulfones failed to bring about full remission in dosages as high as 330 mg daily, and corticosteroids alone were ineffective in dosages up to 50 mg daily. Combined treatment with Diazone 80 mg and prednisone 20 mg daily for several days produced a remarkable improvement, and the daily dosages of Diazone and prednisone were gradually reduced to 40 mg and 10-5 mg respectively. Eventually the treatment was discontinued, and the child is at present in a full remission.

### *Tissue Processing*

For electron microscope studies the skin specimen was taken from the site of an early bullous lesion and fixed in 5% glutaraldehyde.

For immunoelectron microscope studies biopsy specimens were taken from the unchanged skin on the margin of bullous lesions. They were placed in O.C.T., kept up to 24 hr at -20°C in a cryostat, and then sectioned for examination. Sections 30-50 μm thick were investigated with the aid of the peroxidase-antiperoxidase multistep method [21,23], with proper controls.

The material for electron microscopy and immunoelectron microscopy, postfixed in 1% osmium tetroxide, dehydrated in alcohol and propylene oxide, was embedded in Epon 812, sectioned in a Porter-Blum MT2 ultramicrotome, and examined in a JEM-7 electron microscope.

## RESULTS

### *Electron Microscopy*

On the whole, no ultrastructural abnormalities were seen in the dermis, basement membrane zone, and epidermis of areas

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#### Abbreviations:

- BL: basal lamina
- BMZ: basement membrane zone
- BP: bullous pemphigoid
- DH: dermatitis herpetiformis
- DIF: direct immunofluorescence studies
- IF: immunofluorescence

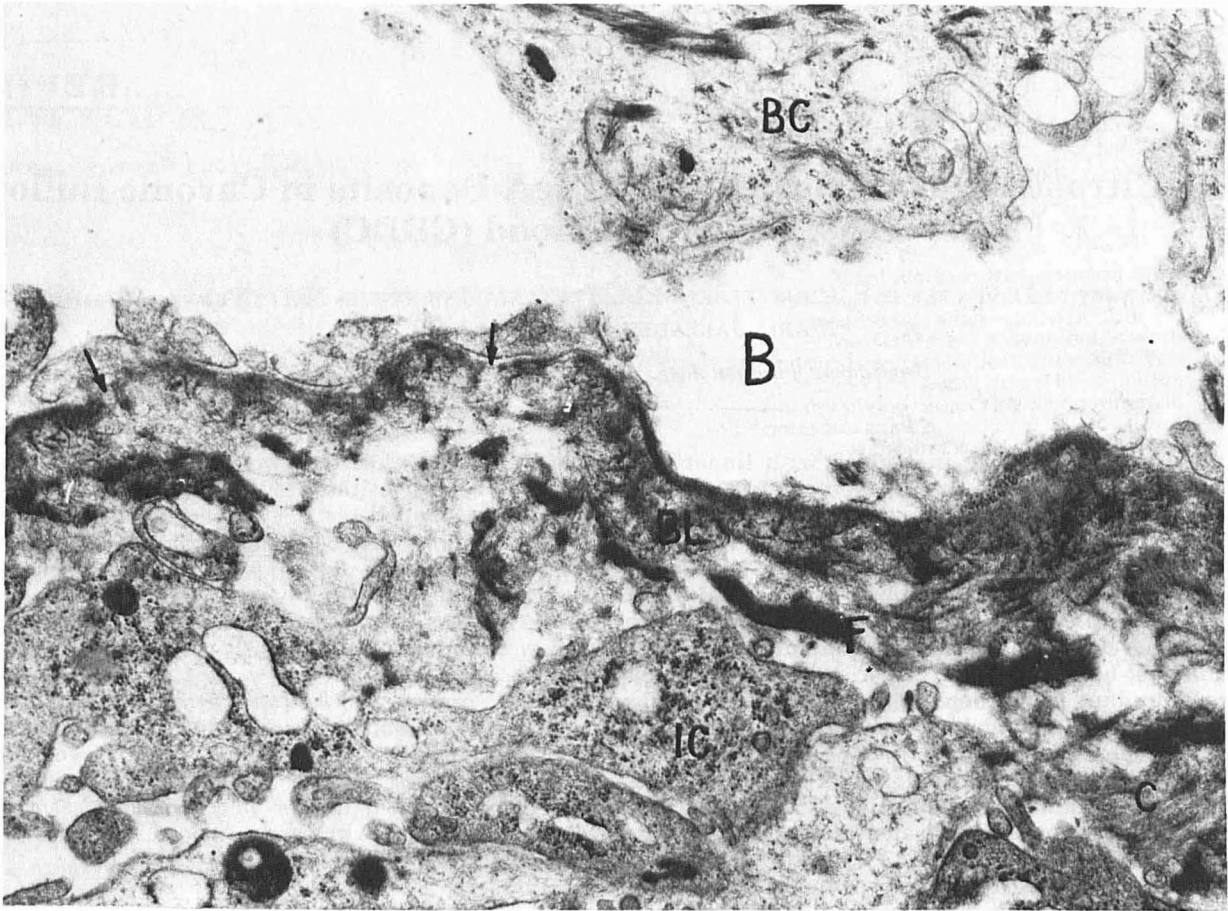


FIG 1. Area of lesion. Bulla (*B*) above basal lamina (*BL*). Basal lamina partly preserved, and destroyed in parts / → /. Infiltration cell (*IC*) and fibrine (*F*) in the corium. Collagen (*C*). Basal cell of epidermis (*BC*) ( $\times 17\ 000$ ).

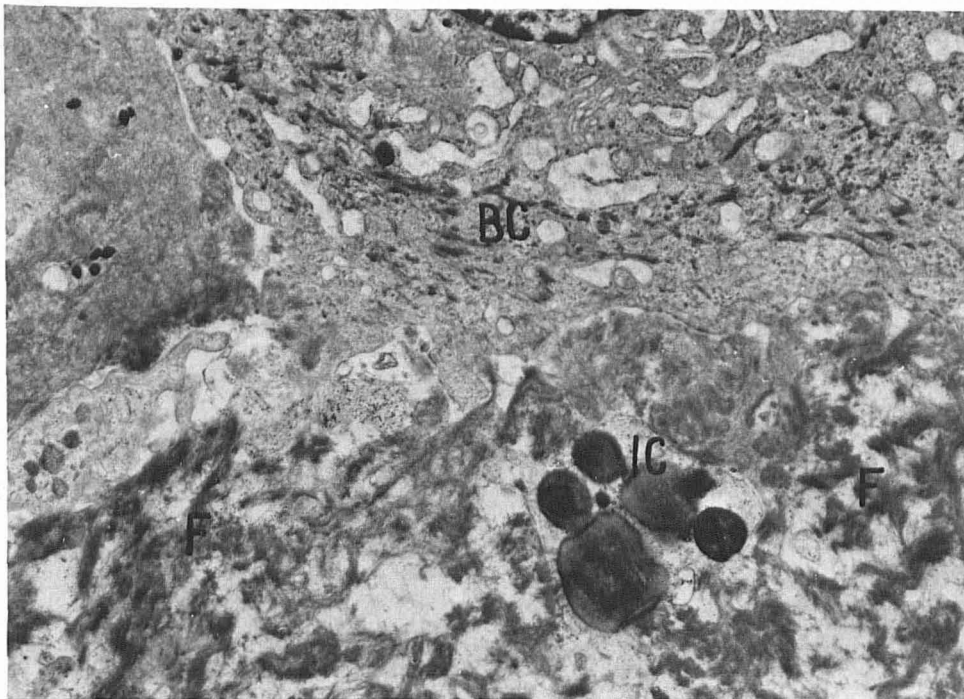


FIG 2. Area of lesion. Fibrine (*F*) in the bulla. Infiltration cell (*IC*). Basal cell (*BC*) ( $\times 6\ 250$ ).

outside the bullous lesions. At some points, however, there were inflammatory cells just underneath the basal lamina (*BL*) or slightly deeper in the corium. The bullous lesions were the result chiefly of the separation of basal cell membranes from

the *BL*, which remained connected with the corium and formed the floor of the blister (Fig 1). Developing blisters contained large amounts of fibrin and inflammatory cells (Fig 2). Less abundant fibrin deposits were seen also in the dermis next to

inflammatory cells just below the BL, which was destroyed in parts (Fig 1).

*Immunoelectron Microscopy*

The ultrastructure of the tissues investigated was intact and was not found to have suffered injury in the region of the basement membrane.

Suitably treated sections showed granular peroxidase deposits, chiefly in the corium just below the BL, which they either touched or were distributed parallel to, in very close proximity. Sometimes the deposits were associated with collagen fibers or

anchoring fibers (Fig 3,4). Occasional peroxidase granules were in evidence in the lamina lucida between the BL and basal cell membranes, which together with the hemidesmosomes had the electron-density of peroxidase (Fig 3,4).

No peroxidase deposits were seen in the control preparations (Fig 5).

DISCUSSION

Bulla forming above the BL in the electronmicroscopic picture is characteristic rather of BP [24-29]. However, the inflammatory cells in the corium where the bulla had not yet formed

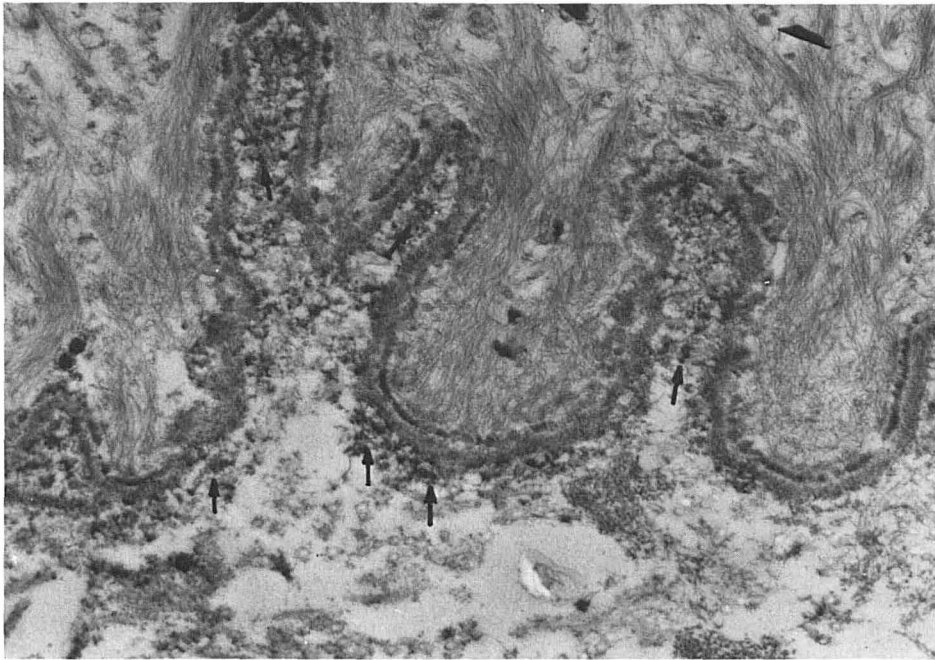


FIG 3. Immunoelectron microscopy. IgA deposits / → / mainly below basal lamina (× 16 500).

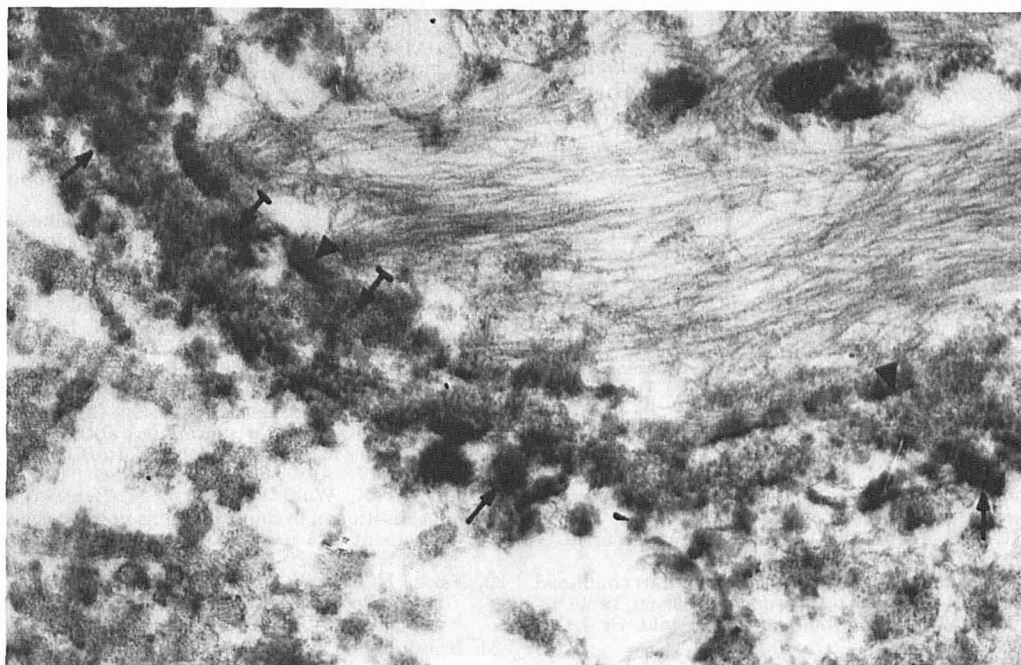


FIG 4. Immunoelectron microscopy. IgA deposits below basal lamina / → / and in lamina lucida next to the basal-cell membrane / ↔ /. Hemidesmosomes / ▶ / (× 54 000).



FIG 5. Immunoelectron microscopy—control. No reaction product deposited ( $\times 27\,600$ ).

and the abundant fibrin deposits in very recent bulla and in the corium just underneath the partly destroyed BL were atypical features and characteristic rather of DH [26,29–34].

We have seen electronmicroscopic pictures of this kind in adults with linear IgA deposits [29]. Such immunologic findings are a characteristic feature of CBDC. This name originally introduced by Jordon et al [2,18] for immunologically negative cases, has been recently applied to the cases with IgA linear deposits [14,15].

Immunoelectron microscopy showed the IgA deposits chiefly below the BL, i.e., the linear (dermal) type of Yaoita and Katz [23], and only in insignificant amounts in the lamina lucida, i.e., the linear (lamina lucida) type of Yaoita and Katz [23]. We have seen this kind of twin localization also in adults (Dąbrowski et al, in print).

The immunoelectronmicroscopic studies lend further support to our previously expressed view that the bullous disease of childhood characterized by a linear distribution of IgA deposits in the BL is in actual fact the equivalent of the linear IgA dermatosis in adults.

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