BULLOUS ACRODERMATITIS DUE TO ZINC DEFICIENCY DURING TOTAL PARENTERAL NUTRITION: AN ULTRASTRUCTURAL STUDY OF THE EPIDERMAL CHANGES

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Abstract. A 5½-year-old girl with idiopathic intestinal pseudo-obstruction became severely depleted of zinc during total parenteral nutrition and developed a vesico-bullous rash on face, hands and feet such as is seen in acrodermatitis enteropathica. Light and electron microscopy of a bullous lesion on one foot revealed a pronounced extracellular edema with cyst and cleft formation in the deep part of the epidermis. A few acantholytic cells were seen. In the electron microscope degenerate keratinocytes showed multiple vacuoles in the dark cytoplasm and slender, finger-like protrusions. Desmosomes were few. The basal lamina was well-preserved forming deep invaginations, which may serve to distinguish the condition from other bullous diseases of the skin.

Key words: Acrodermatitis enteropathica; Electron microscopy; Extracellular edema; Pemphigus-like; Total parenteral nutrition; Zinc deficiency

Skin changes are important clinical markers of acute and chronic zinc deficiency in man and animals (9). Earlier histopathological studies have dealt mainly with the changes of scaly, infiltrated skin lesions characteristic of a chronic zinc deficiency, as observed in acrodermatitis enteropathica (AEP) (2, 6, 9) and in acquired zinc deficiency syndromes (3, 8). Few studies have dealt with the acute vesico-bullous skin lesions of AEP (1, 6, 7) and acquired zinc deficiency (4, 9). In the present investigation we concentrated on the ultrastructural changes of the epidermis in a case of acquired zinc deficiency presenting with bullous acrodermatitis.

CASE REPORT

The patient was a 5½-year-old girl who had suffered from intestinal pseudo-obstruction since early childhood. Biopsies had revealed the presence of normal ganglion cells in the rectal wall. At the age of 5 years she developed paralytic ileus and underwent a hemicolectomy. Subsequently she was reoperated on twice because of intestinal adhesions causing ileus.

She was then started on total parenteral nutrition (TPN) which supplied about 0.5 mg zinc daily. The recommended daily dietary allowance at her age is about 10 mg zinc by mouth, of which approximately 2 or 3 mg is absorbed (9). After 2 months her condition deteriorated; she became febrile and soon a bullous rash appeared on her hands and feet, and a crusty eczema appeared around her mouth, nostrils, eyes and on her ears. She was then transferred to this hospital.

On admission, she was chronically ill, peevish, withdrawn and showed signs of photophobia. Bullae standing on a redbrown erythema were present on the volar aspects...
Large intra-epidermal cysts and clefts are seen. In the dermal papillary layer there is a moderate perivascular infiltration of lymphocytes, neutrophilic granulocytes and histiocytes (A). Pronounced extracellular oedema is present at the level of the basal cells which appear degenerate. A few acantholytic cells are seen (B). H. E., ×106 and ×900.

MATERIAL AND METHODS

Skin specimen. Before zinc therapy was initiated, a 4-mm punch biopsy was obtained from the edge of a bulla on her left big toe (Fig. 1). The specimen was prepared routinely for conventional light microscopy and for transmission electron microscopy (for details see (10)). Hematoxylin-eosin, uranyl acetate and lead citrate were used for staining. A JEOL electron microscope was used for the ultrastructural study.

RESULTS

Light microscopy. The epidermis was dominated by a pronounced extracellular edema, large cysts and cleft formation low in the epidermal cell layers (Fig. 2A and B). The roof of the cysts was edematous, being formed of degenerate keratinocytes; the floor was degenerate basal cells. The dermal papillary layer showed perivascular infiltrates of lymphocytes, neutrophils and a few histiocytes.

Electron microscopy. Electron microscopy revealed changes similar to those found by light microscopy. There was a pronounced extracellular edema, especially at the level of the basal cell layer. Keratinocytes were degenerate and necrotic. Few desmosomes and hemidesmosomes were seen (Fig.
3). The basal cells were partly or completely sepa­
rated from the basal lamina (Fig. 3). Slender finger­
like protrusions of the cytoplasm and multiple vac­
uoles derived from mitochondria, lysosomes and a
dilated endoplasmic reticulum were present in the
degenerate keratinocytes (Fig. 4). The basal lamina
was monolayered, forming deep invaginations in
the underlying papillary layer of dermis (Fig. 3).
Multiple thin anchoring fibrils were present (Fig.
4). At the edge of cystic lesions, normal regenerat­
ing keratinocytes were seen. They showed normal
desmosomes but no hemidesmosomes. The cysts
contained mainly fibrin coagula, a few acantholytic
keratinocytes, neutrophilic granulocytes and melano­
cytes.

DISCUSSION
Light microscopy revealed epidermal changes simi­
lar to those reported in studies dealing with the
acute vesico-bullous or erosive skin changes seen in
AEP (1, 6, 7) and in severe zinc deficiency caused

Fig. 3. A keratinocyte (K) is partly
separated from the basal lamina
(BL). The basal lamina shows deep,
multiple invaginations, is mono­
layered and has no interruptions.
There are numerous vacuoles (V) in
the dark cytoplasm of the keratino­
cytes. Finger-like, slender protru­
sions are indicated by solid arrows.
The area marked with an asterisk is
shown in Fig. 4. D with thin arrows,
desmosomes; M, mitochondria;
N, neutrophilic granulocyte; H,
histiocyte. ×4000.

Fig. 4. A degenerate keratinocyte
(K) contains vacuoles derived from
cysterna of endoplasmic reticulum
(V), mitochondria (M) and lysos­
omes (L). The monolayered basal
lamina (BL) separated from the
keratinocyte shows multiple thin
anchoring fibrils (solid arrows).
×20000.

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by TPN (4, 9). The lack of parakeratosis in the present case was probably due to acute onset and young age of the lesion studied. Focal parakeratosis is characteristically seen in subacute and chronic zinc deficiency (2, 3, 5, 6, 8). Such lesions additionally show various degrees of spongiosis and irregular acanthosis, sometimes with psoriasis-like rete ridges. The designation parakeratosis psoriasiformis could be used for this condition (9).

Electron microscopy has been performed on skin lesions of AEP infants. In the one studied by Ginsburg et al. (5) a chronic scaly lesion showed extracellular edema and cell degeneration mainly in the middle and outer part of the epidermis, whereas the basal cell layer was unaffected. Baudon et al. (1) took biopsies from an erosive skin lesion and found pronounced edema and cell degeneration in the deep part of epidermis, but with an intact basal lamina. Their findings are in agreement with the present study, indicating that the ultrastructural epidermal picture of severe acute zinc deficiency is identical in congenital and acquired states of deficiency of the element.

Zinc deficient animals never develop vesicobullous dermatitis characteristic of acute zinc deficiency in man. The changes are dominated by hyperkeratosis and parakeratosis. Rats deprived of zinc for 4 weeks were studied by electron microscopy (10). Two different types of ultrastructural changes were found. One was characterized by swollen keratinocytes with preserved desmosomes and multiple cytoplasmic protrusions of a coarser structure than the finger-like extensions observed here. The second type showed parakeratotic, severely degenerate keratinocytes with few, poorly developed desmosomes. As in man, the dermal changes were comparatively slight.

Acute zinc deficiency presenting with bullae, vesicles and erosions may be mistaken for other bullous diseases of the skin. The present finding of a deeply invaginated intact basal lamina without any interruptions may be helpful in distinguishing pemphigus vulgaris, familial pemphigoid, and epidermolysis bullosa of the junction blister type, from bullous acrodermatitis due to severe zinc deficiency.

REFERENCES


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