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An Ultrastructural Study of the Epidermis in Hyperkeratosis Lenticularis Perstans

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Abstract. A 60-year-old Japanese man contracted hyperkeratosis lenticularis perstans (Flegel). Biopsy specimens of the keratotic papules on the dorsa of the feet were studied with electron microscopy. An increase in the number of membrane coating granules, keratohyalin granules and tonofilaments was the most prominent feature of the keratinocytes underlying the keratotic papule. However, in the area just above the cone-shaped dermal infiltration, membrane coating granules were absent and keratohyalin granules and tonofilaments were poorly developed.

Key words: Electron microscopy; Membrane coating granules; Keratohyalin granules

Hyperkeratosis lenticularis perstans (HLP) is a rare dermatosis characterized by inflammatory keratotic papules involving the extremities. Since the first

report by Flegel (3), several reports have confirmed HLP as a distinct entity. In a previous paper (8), we described the ultrastructure of the infiltrating cells of HLP in which were present intracytoplasmic inclusions.

In this report, we present electron microscopical findings of the keratinocytes in HLP.

MATERIAL AND METHODS

A 60-year-old Japanese man was seen primarily because of increasing numbers of keratotic papules (Fig. 1) on the legs and forearms of 2 years' duration. The eruptions first appeared over the anterior aspects of the lower legs and dorsa of the feet.

Biopsy specimens were obtained from well-developed keratotic papules on the dorsa of the feet. All tissue was cut into two. One-half was processed for routine microscopy and sections were stained with hematoxylin-eosin. The other half was divided into small pieces for electron microscopy. They were fixed in cold 4% glutaraldehyde in 0.1 M phosphate buffer, pH 7.4, for 2 hours, rinsed overnight in several changes of the same buffer containing 10% sucrose at 4°C, post-fixed in cold 1% osmium tetroxide for 2 hours, dehydrated in graded

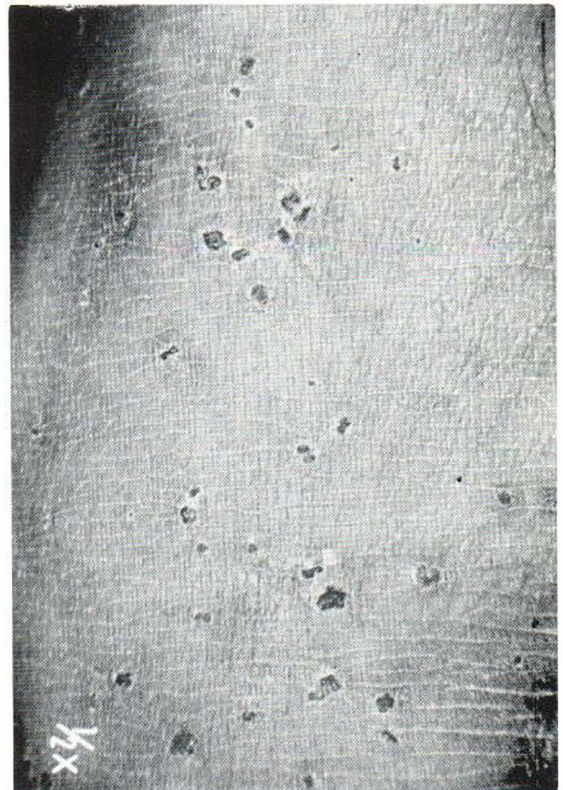


Fig. 1. Typical lesions of HLP on the dorsum of the foot.

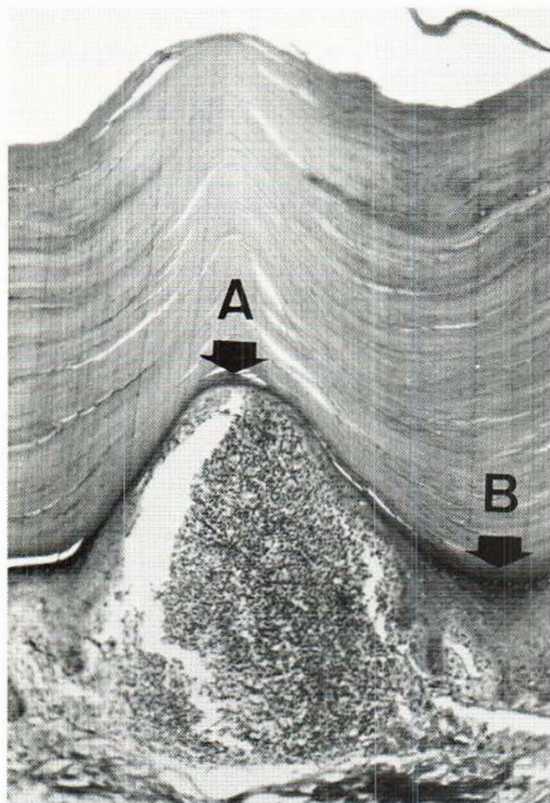


Fig. 2. Lesion of the foot, showing the thick horny layer, a cone-shaped elevation of the atrophic epidermis, and a well-circumscribed inflammatory infiltrate in the upper dermis (H-E, $\times 260$).

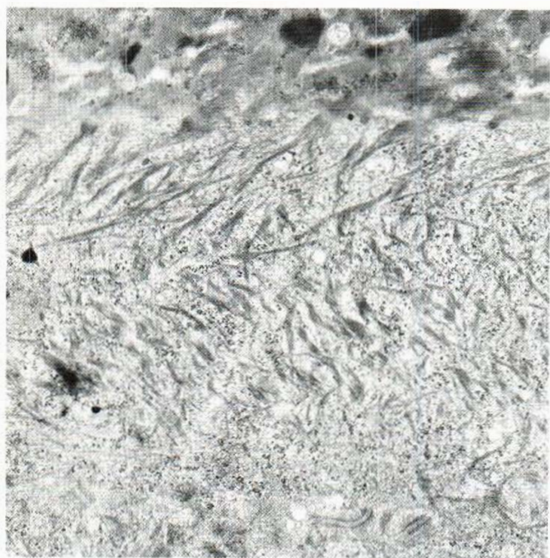


Fig. 3. Upper epidermis of area A: Keratohyalin granules and tonofilaments are reduced, and MCG are not seen ($\times 16\,000$).



Fig. 4. Border between the horny layer and the granular layer; marked aggregation of MCG is seen ($\times 5\,600$).

ethanol, and embedded in Epon 812. Thin sections were stained with methanolic uranyl acetate and lead citrate, and examined in a Hitachi HS-9 electron microscope.

RESULTS

Hematoxylin-eosin stained sections revealed marked hyperkeratosis with some degree of parakeratosis and thinning of the malpighian layer of the epidermis, and a dense dermal cellular infiltrate consisting of lymphocytes and histiocytes (Fig. 2). These histological features were identical with those reported in HLP.

We investigated the ultrastructure with special reference to the flattened epidermis just above the tent-like dermal infiltration (Fig. 2A) and the epidermis adjacent to the infiltration (Fig. 2B). Electron microscopical studies of area A showed the following features; tonofilaments were scanty, short and filamentous, and membrane coating granules (MCG) were absent in the flattened epidermis. The number of keratohyalin granules was reduced and their size was much smaller than those in normal epidermis (Fig. 3).

On the other hand, the ultrastructure of area B, i.e. the epidermis adjacent to the dermal infiltration, contrasted sharply with that of area A. The main findings were that the cytoplasm of the basal cells contained a fairly large quantity of tonofilaments. In the cells of the granular layer, the number of keratohyalin granules and tonofilaments had increased and their size was considerably larger than that of the normal epidermis (Fig. 4). There were many MCG with a lamellar inner structure.



Fig. 5. Granular layer of area B. Note the keratinization of some desmosomes (arrows) which connect to MCG ($\times 22\,750$).

In addition, they were found in the intercellular spaces in the upper granular layer. Moreover, the desmosomes, which incidentally were connected to MCG, showed marked keratinization, whereas unconnected ones did not (Fig. 5).

DISCUSSION

Hyperkeratosis lenticularis perstans appears to be a dominantly inherited condition (1, 2). However, the etiology of this disorder is, for the most part, still unknown. The present case was diagnosed as HLP on the basis of clinical and light microscopical findings, despite a lack of positive family history.

Recently, Frenk and Tapernoux (4, 5) described HLP as characterized by a unique ultrastructural alteration, lack of MCG in the epidermis underlying the keratotic papules. They suggested that HLP might be considered as an autosomal dominant in-born error of keratinization expressed by lack of MCG in small areas of the epidermis. Their interpretation depends on the theory that MCG contain hydrolytic enzymes (11, 12) and have an important function in the disintegration of desmosomal discs.

In our case, lack of MCG was observed only in area A as also described by Frenk and Tapernoux, while the epidermis adjacent to an infiltration showed increased numbers of MCG.

Hashimoto et al. (6) have reported that MCG contain polysaccharide material, and suggested that it may play a role in binding together the horny layers. Therefore, it can also be postulated that the

increase in number of MCG, which we observed in area B, causes the marked hyperkeratosis with a delayed disintegration of desmosomal discs.

In fact these changes are also observed in some hyperkeratotic diseases such as psoriasis vulgaris (9) and congenital ichthyosiform erythroderma (7). We also prefer to relate the increase in number and size of keratohyalin granules and tonofilaments to the marked hyperkeratosis. These features are seen in some ichthyosiform diseases (7).

The lack of MCG and the reduction of keratohyalin granules and tonofilaments in area A is probably a secondary event due to atrophy of epidermis which may be caused by dermal infiltrates.

Furthermore, we observed keratinized desmosomes (10) connected to MCG. This observation leads us to believe that MCG may have an important function in the keratinization process in HLP.

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