

DISSEMINATED EPIDERMOLYTIC ACANTHOMA

Nonsystematized Multiple Verrucoid Lesions Showing Granular Degeneration

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Abstract. This is a case report of a patient with non-systematized multiple verrucoid lesions showing the light microscopic feature of granular degeneration. The disease was identified as disseminated epidermolytic acanthoma. It is not congenital and seems to be non-heritable. Electron-microscopic observation revealed that the essential change in the lesions is the premature cornification of epidermal cells with anomaly in the formation of tonofilament bundles.

Three dermatologic conditions are recognized which show the histologically characteristic feature of granular degeneration described by Lapière (9). The first, bullous congenital ichthyosiform erythroderma, has a generalized hyperkeratosis on a background of varying degrees of diffuse erythema. It is inherited by autosomal dominant transmission (11, 13). The second, systematized nevus verrucosus, has uni- or bilaterally distributed, systematized lesions consisting of verrucous papules. It is generally considered to be a localized form of bullous congenital ichthyosiform erythroderma (2, 17). Hereditary palmo-plantar keratoderma of Vörner (14) is also regarded as a localized form of bullous congenital ichthyosiform erythroderma. The third, isolated epidermolytic acanthoma usually occurs as a solitary localized lesion, and has the characteristic feature of granular degeneration (12). This condition is not familial.

This paper presents another entity which is histologically similar, but clinically different, from these three established conditions.

CASE REPORT

A 26-year-old male visited the dermatology clinic because of verrucoid papules on the shoulders, chest, back and

upper arms. There were no subjective symptoms. He stated that he had first noted the skin lesions 9 months previously, and that at first they occurred on the shoulders, increased in number with time, and later extended down the chest, back and upper arms. There was no family history of similar or other skin disease.

Physical examination

The general examination was normal except for skin lesions. There was a randomly distributed eruption consisting of multiple oval, pin-head- to pea-sized, slightly elevated, skin-colored verrucoid papules, many smooth-surfaced and others slightly scaly, on the shoulders, chest, back and upper arms (Fig. 1). The lesions were discrete and well-defined. No lesions consistent with ichthyosis or epidermal nevus were present. Clinical diagnosis was verruca plana.

Light microscopic examination

The materials examined were as follows: a pin-head-sized smooth-surfaced papule, a pea-sized smooth-surfaced papule, and a pea-sized scaly papule. For light microscopy, the biopsy specimens were fixed in 10% neutral formalin and stained with hematoxylin and eosin.

Light microscopy of these three specimens showed similar patterns, and characteristic changes were more prominent in the large papules than in the small papule. The following features have been distinguished: The horny layer, which varies from dense to loosely laminated, shows a moderate degree of hyperkeratosis with occasional areas of parakeratosis (Fig. 2). The epidermis, which varies from slightly to moderately acanthotic, shows three characteristic changes. One is thickening of the granular cell layer accompanied by clumping of coarse keratohyalin granules (Figs. 2, 3). Extraordinarily large keratohyalin granules are noted in the uppermost cells of the granular layer. The second is eosinophilic granular change in the granular and squamous cell layers (Fig. 3). Eosinophilic fine granules and strands are seen in the cytoplasm of the cells in the lower portion of the squamous layer. As cells ascend in the epidermis, both granules and strands tend to become larger. In granular cells, they are often associated with keratohyalin granules, and sometimes they show a ribbon-like arrangement around the nuclei. The third is a varying degree of vacuolar change in the

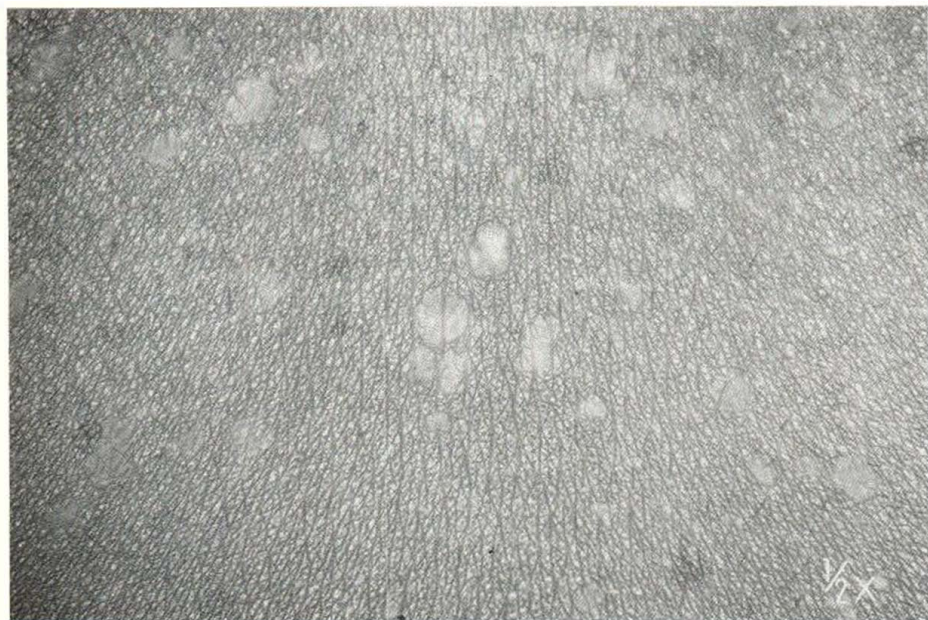


Fig. 1. Multiple, discrete, verrucoid papules on the lower part of the back of a patient with disseminated epidermolytic acanthoma.

granular and squamous cell layers (Figs. 2, 3). This usually occurs in groups or islands of cells. The early stage of vacuolar change is recognized as a clear perinuclear zone, with a corresponding enlargement of the cell. In the portions with advanced change, there are reticulated changes with occasional pyknosis. The basal cells have a normal appearance and contain a small amount of melanin granules. A mild lymphocytic perivascular infiltrate is present in the upper dermis.

Electron-microscopic examination

A portion of the biopsy specimen of the pea-sized smooth-surfaced papule taken for light microscopy was used as the material. For electron microscopy, small blocks of the tissue specimen were fixed in 2.5% glutaraldehyde buffered to pH 7.4 with cold cacodylate for 2 hours and then postfixed in cold 2% osmium tetroxide buffered to pH 7.4 with sucrose-added cold Veronal-acetate. After dehydration in a graded series of acetone, it was embedded in Epon 812. Sections were cut with glass knives on a Porter-Blum MT-2 ultramicrotome, stained with uranyl acetate followed by lead citrate, and examined in a Hitachi HU-11E electron microscope.

Electron microscopic features of the verrucoid papules are as follows: Basal cells appear morphologically normal. Three striking changes are seen in the squamous and granular cell layers. One is abnormal aggregation of tonofilaments (Fig. 4). It occurs in the lowermost cells of the squamous layer: the cells contain a few small aggregates of tonofilaments in the cytoplasm. As cells ascend, the aggregates tend to become larger and more numerous. They consist of filamentous or homogeneous material of mod-

erate electron density. These aggregates are often associated with normal-appearing desmosomes (Fig. 5). This finding strongly suggests that they are formed by clumping of tonofilament bundles. In addition to formation of aggregates, tonofilament bundles become thicker and fail to keep their regular orientation in upper squamous and granular cells. They are often arranged in a whorl configuration or in a perinuclear orientation (Figs. 6, 7, 8). Tonofilament bundles extending outward from the whorls are often anchored in normal-appearing desmosomes. The second is a formation of extraordinarily large keratohyalin granules (Fig. 6). In the lower cells of the granular layer, keratohyalin granules appear as extremely electron-dense, homogeneous deposits in parts of tonofilament bundles. As cells ascend, they become larger and more elongated. In the cells with abnormal tonofilament configuration, keratohyalin substances are deposited on the whorls of tonofilament bundles and perinuclear thickened bundles of tonofilaments (Figs. 6, 8). The third is intracellular edema which occurs in areas from the upper squamous layer to the granular layer (Fig. 9). It can be recognized by the pale appearance of cytoplasmic matrix. As the process advances, the cells become swollen and the cytoplasmic organelles become smaller. However, both aggregates of tonofilaments and thickened bundles of tonofilaments are persistent.

The granular cell layer also demonstrates numerous membrane-coating granules in the intercellular space as well as in the cytoplasm of the cells, although the granules show varying degrees of degradation in the extracellular space. Occasional images are encountered which show that the uppermost cells of the granular layer and the cells just

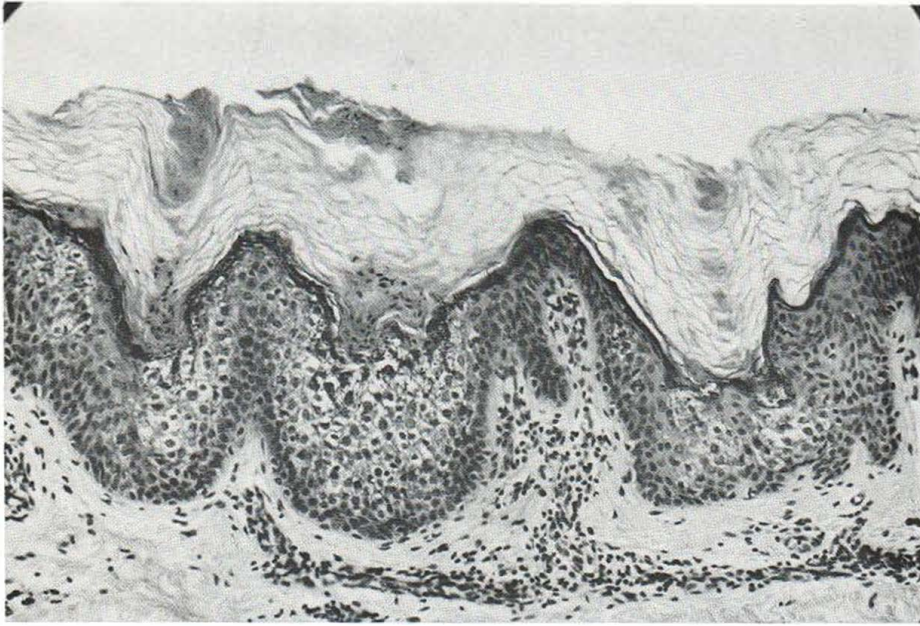


Fig. 2. Histologic appearance of a papule from the left shoulder. Hyperkeratosis with focal parakeratosis, acanthosis, thickening of the granular layer, and vacuolization

of the granular and squamous cell layers are noted. Hematoxylin-eosin, $\times 140$.

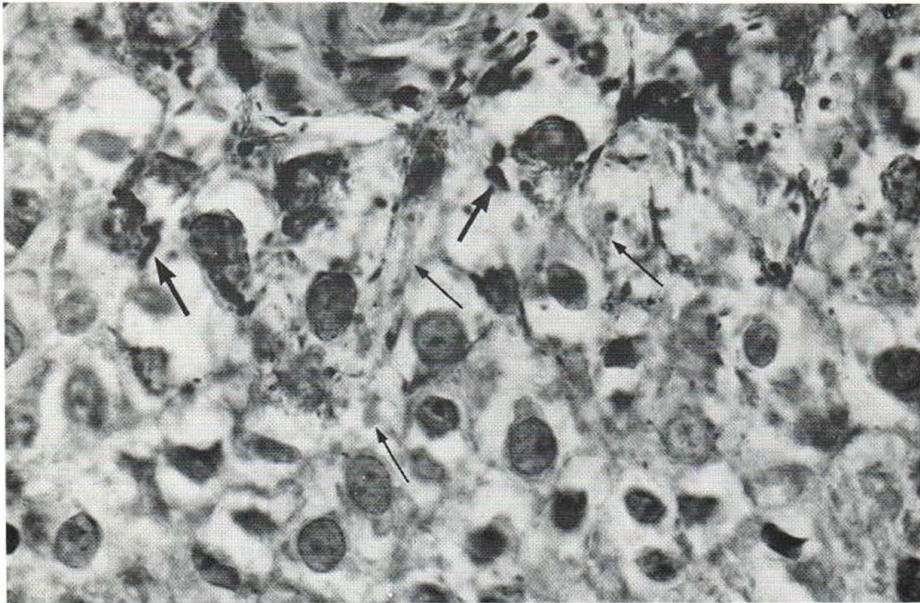


Fig. 3. Enlargement of part of Fig. 2. Coarse keratohyalin granules (thick arrows) and eosinophilic fine granules and strands (thin arrows) are seen. Hematoxylin-eosin, $\times 875$.

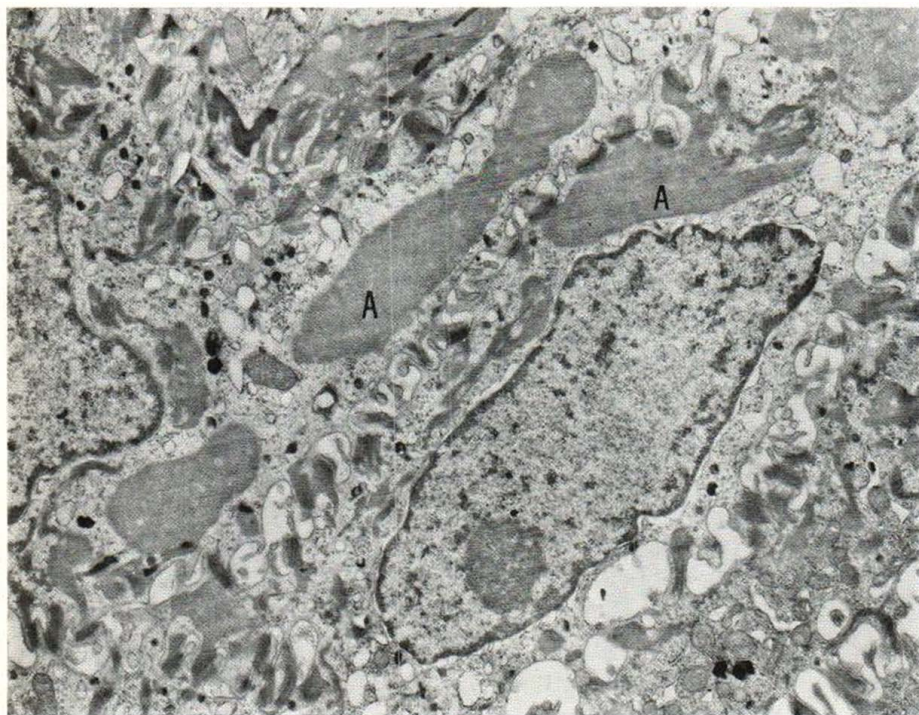


Fig. 4. Upper cells of the squamous layer. Abnormal aggregates of tonofilaments (A) are seen in the cytoplasm. $\times 9\,000$.

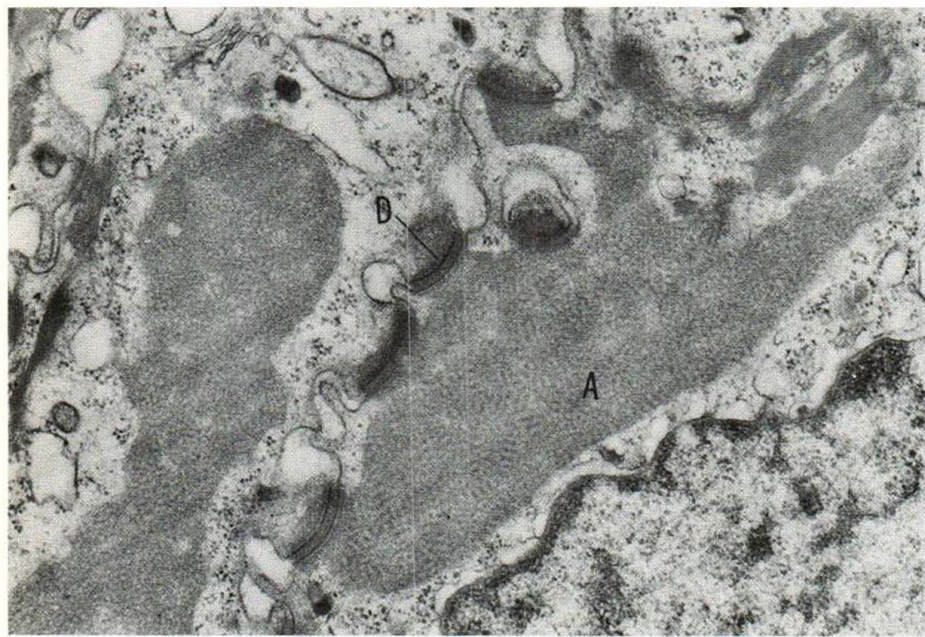


Fig. 5. Enlargement of part of Fig. 4. The aggregate (A) consisting of filamentous material is connected with normal-appearing desmosomes (D). $\times 21\,000$.

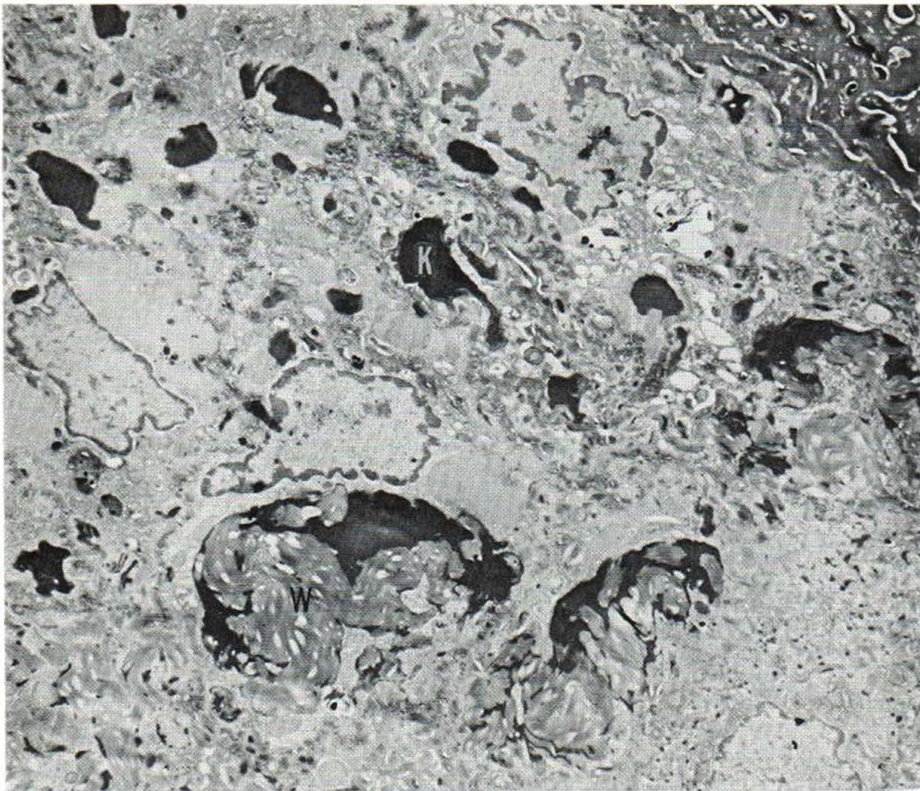


Fig. 6. Upper cells of the granular layer. Extraordinarily large keratohyalin granules (*K*) and whorls of tonofilament bundles (*W*) with partial deposition of keratohyalin substances are seen. $\times 4\,300$.

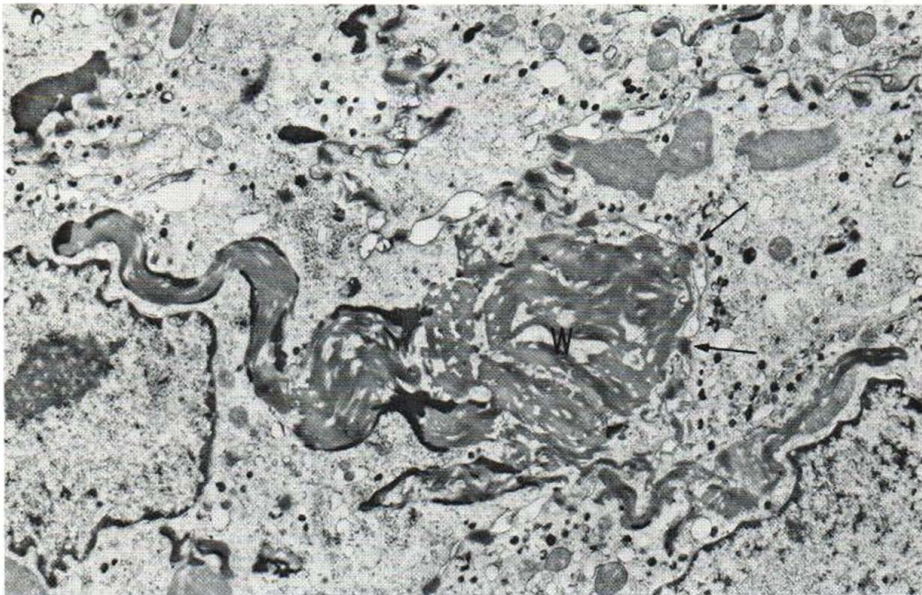


Fig. 7. Part of a granular cell. The connection of desmosomes with tonofilaments from the whorl (*W*) are observed at arrows. $\times 6\,200$.



Fig. 8. Granular cell containing perinuclear thickened bundles of tonofilaments (T) with partial deposition of keratohyalin substances (K). $\times 16\,000$.

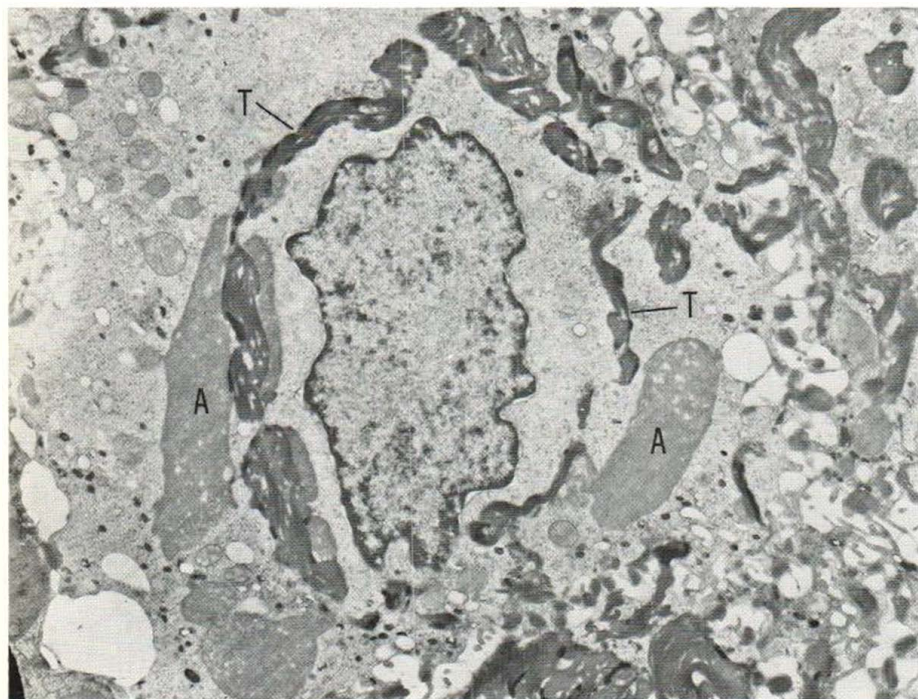


Fig. 9. Granular cell showing marked edematous change in the cytoplasm. Both aggregates (A) and perinuclear

thickened bundles of tonofilaments (T) are still unchanged. $\times 6\,200$.

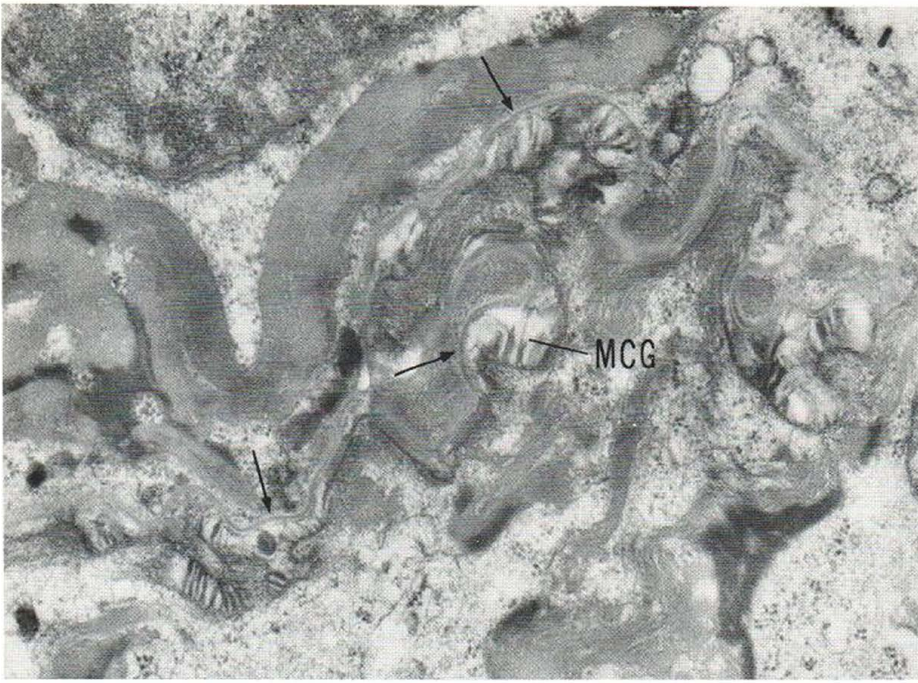


Fig. 10. Small area of two adjacent granular cells. Degrading membrane-coating granules (MCG) are observed in the intercellular space. Arrows indicate the thickened

plasma membrane of the cell beneath the uppermost granular layer. $\times 32\ 000$.

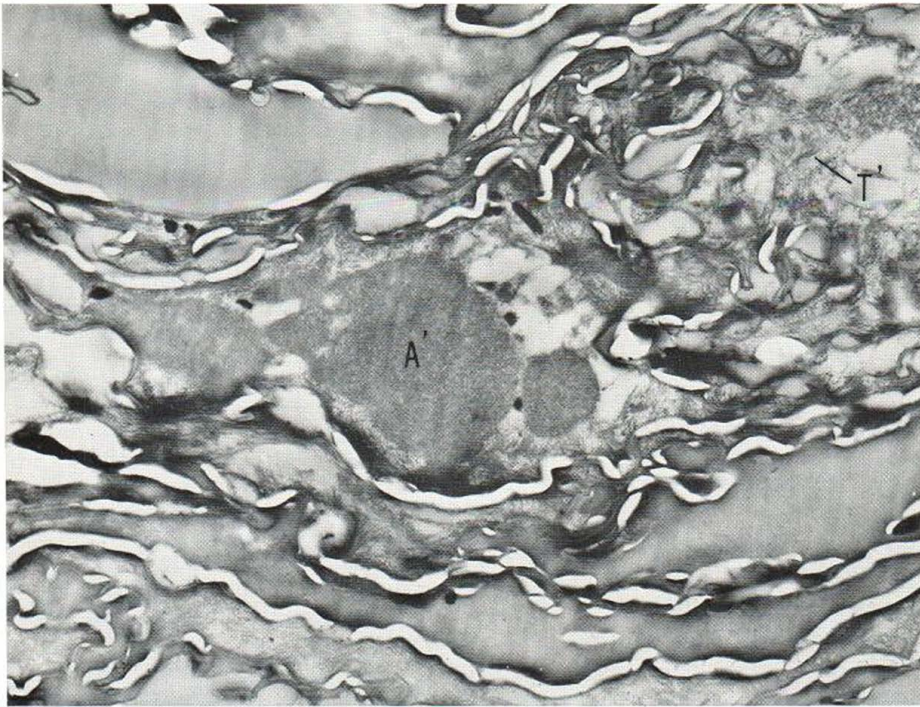


Fig. 11. Part of the horny layer. Fine filaments (T') and oval masses (A') resembling tonofilaments and their

aggregates respectively are seen within incompletely cornified cells. $\times 12\ 300$.

beneath them are enveloped by a thickened plasma membrane similar to that of the horny cell (Fig. 10).

Horny cells are not uniformly cornified (Fig. 11). Some of them are flattened and fully cornified, and others show irregular configuration and contain numerous filaments and a few oval masses which resemble tonofilaments and their aggregates respectively. Viral particles are found in neither epidermal cells nor horny cells.

DISCUSSION

Light microscopy has shown that the changes in the verrucoid lesions of the patient reported herein consist mainly of acanthosis with varying degrees of thickening of the granular cell layer and eosinophilic granular and vacuolar changes in the squamous and granular cell layers. These changes are characteristic, closely resembling those in isolated epidermolytic acanthoma as well as those in bullous congenital ichthyosiform erythroderma and systematized nevus verrucosus. In this patient, however, there was no evidence of any relation to either bullous congenital ichthyosiform erythroderma or systematized nevus verrucosus, and no family history of such conditions. The clinical manifestations in this condition consist of disseminated, randomly distributed, multiple verrucoid papules, thus differing from the above-mentioned three previously established conditions. Therefore, we consider it to be a new clinical condition, and have termed it "disseminated epidermolytic acanthoma". The name means a disseminated multiple occurrence of lesions which resemble isolated epidermolytic acanthoma in clinical and histological features.

At first glance, clinically one may mistake disseminated epidermolytic acanthoma (DEA) for verruca plana or epidermodysplasia verruciformis. Histologically one may confuse it with viral warts, especially verruca plana. However, it can usually be differentiated from these viral dermatoses by careful light microscopic observation, and conclusively differentiated by electron-microscopic observation.

Electron microscopy has revealed that the ultrastructural features in DEA are similar to those in systematized nevus verrucosus (1, 3, 10) as well as to those in bullous congenital ichthyosiform erythroderma (4, 5, 6, 7, 8, 15, 16). It has also revealed the nature of the changes in DEA. The evidence indicates that eosinophilic granules and strands correspond to abnormal aggregates of tonofilaments and whorled or unwhorled thickened

bundles of tonofilaments, and that eosinophilic strands arranged in perinuclear regions correspond to perinuclear thickened bundles of tonofilaments. It also indicates that the coarsening of keratohyalin granules is due to the deposition of keratohyalin substances on pre-existing whorled or unwhorled thickened bundles of tonofilaments. Other evidence indicates that the vacuolar appearance of cells under the light microscope is not due to an artefact but to actual intracellular edema even if it may be accentuated by shrinkage of cells during routine dehydration and embedding procedures for light microscopy. The fact that the occurrence of abnormal aggregation and abnormal configuration of tonofilaments precedes the appearance of intracellular edema in cells suggests that the former changes are not related to the latter change. In addition, the presence of the cells showing thickening of the plasma membranes in the granular layer suggests the premature cornification of epidermal cells in this condition. Therefore, it appears that the essential change in DEA consists of the premature cornification of epidermal cells with anomaly in the formation of tonofilament bundles.

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