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Electron Microscopic Features of Malignant Dyskeratosis in Human Oral Squamous Cell Carcinoma

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SUMMARY

The ultrastructural morphology of dyskeratotic cancer cells in human oral squamous cell carcinoma was investigated by transmission electron microscopy. Dyskeratotic cells showed a considerable variation in their shapes and structures according to the stage of the dyskeratotic changes, such as aggregations of tonofilaments and decrease in desmosomes. However, these cells could be divided into two types: (1) cells with marked aggregations of Tfs packed in the whole cytoplasm and (2) cells with partial aggregations of Tfs as masses in the cytoplasm, which occasionally appeared to phagocytize them. The morphogenesis of the dyskeratotic cells in squamous cell carcinoma is discussed.

Key words: Dyskeratosis, Electron microscopy, Squamous cell carcinoma

INTRODUCTION

In general, dyskeratosis may be defined as abnormal, premature keratinization. Under light microscopy, malignant dyskeratosis in squamous cell carcinoma is characterized by the presence of individual cell keratinization, in contrast to benign dyskeratiosis such as in the formation of corps rond in Darier's disease (1). Histologically, such dyskeratotic cells are round and homogeneously eosinophilic. However, the ultrastructural features and the pathogenesis of malignant dyskeratotic cells remain obscure (2).

This paper describes the electron microscopic features of malignant dyskeratosis in human oral squamous cell carcinoma (SCC).

MATERIALS AND METHODS

Biopsy specimens were taken from the oral lesions of five patients with oral SCC. One half of the specimens were fixed in 10% buffered formalin and embedded in paraffin. Sections were stained with hematoxilin and eosin. The remaining specimens were fixed in 2.5% phosphate-buffered glutaraldehyde and postfixed in 1% buffered osmium tetroxide for electron microscopic observation. The specimens were then dehydrated with a series of graded alcohol, and embedded in Epon. Semithin sections from Epon blocks were stained with 1% toluidine blue for orientation. Ultrathin sections were stained with uranyle acetate and lead citrate, and examined under a JEM-100C electron microscope.

RESULTS

Light microscopic findings

Light microscopically, all specimens examined showed the histology of well to moderately differentiated SCC with the sparse presence of single cell keratinization in the cancer cell nests (Fig. 1).

Electron microscopic findings

Cancer cells were somewhat pleomorphic with large nuclei, and were attached to each other by their desmosomes in the widened intercelluar spaces. Basal lamina tended to be relatively intact with hemidesmosomes. However, occasional disruption or duplication of the basal lamina occurred, and pseudopods of the cytoplasm were seen protruding into the underlying connective tissue.

Nuclear envelopes of cancer cells were irregular, and nuclear chromatin granules were loosely scattered in the nucleus. Nucleoli tended to be enlarged, increased in number, marginated, and composed of granular components. Occasional nuclear bodies were also found. Numerous clusters of free ribosomes were seen in abundance throughout the cytoplasm. Mitochondria were tended to be swollen and occasionally degenerated. Moderate number of lysosomes were also obeserved.

Each cancer cell varied considerably according to the development of tonofilaments (Tfs), although generally a few small swirling bundles of Tfs were seen scattered in the cytoplasm of the cancer cells. Dyskeratotic cancer cells were found as cells with numerous aggregated bundles of Tfs in the cytoplasm. Densely aggregated bands of Tfs were observed in the perinuclear or peripheral locations within the cytoplasm (Figs. 2 and 3). In these cancer cells intercellular desmosomes (DES) tended to be reduced (Fig. 2). Occasionally, degenerated nuclei were found with heavily aggregated bundles of Tfs in the cytoplasm and with

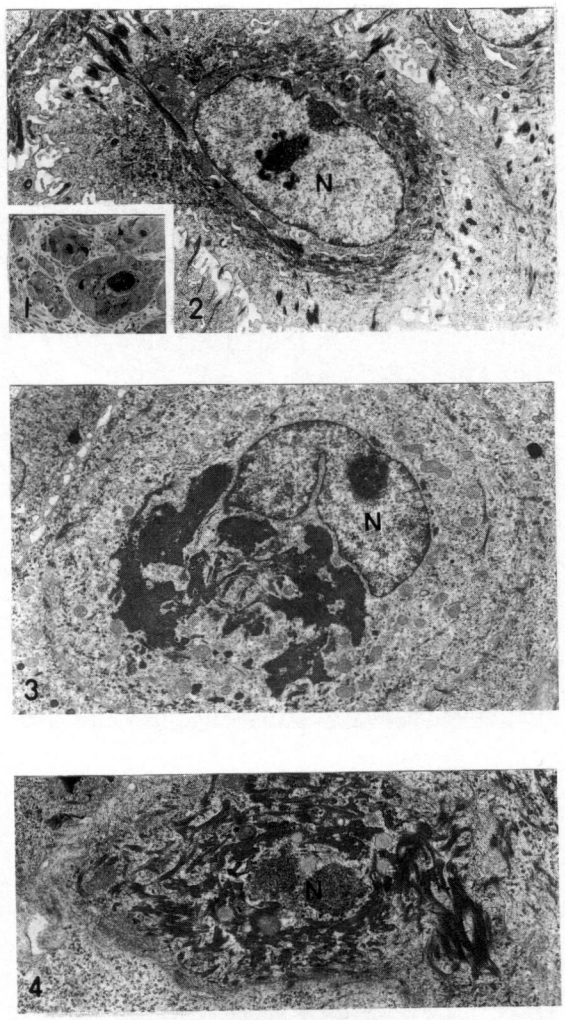
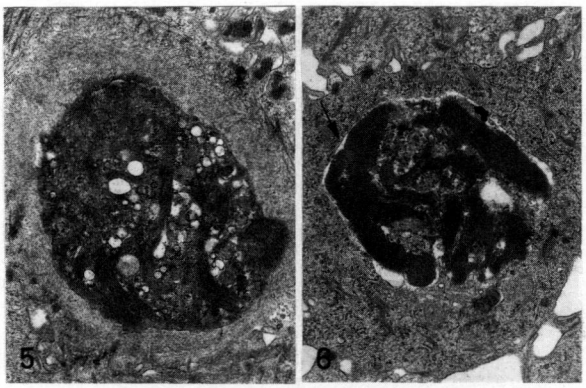


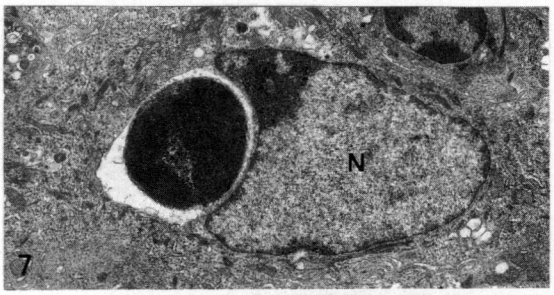
Fig. 1 Light micrograph of SCC from Epon-embedded semithin section stained with toluidine blue. ×100.

Fig. 2 Electron micrograph of a cell with perinuclear aggregation of Tfs in in the cytoplasm. N shows nucleus. ×5,300.

Fig. 3 Electron micrograph of a cell with partial aggregations of Tfs in the cytoplasm. N shows nucleus. ×5,300.

Fig. 4 Electron micrograph of a dyskeratotic cell with perinuclear aggregation of Tfs around nuclear remnant (N). ×9,500.





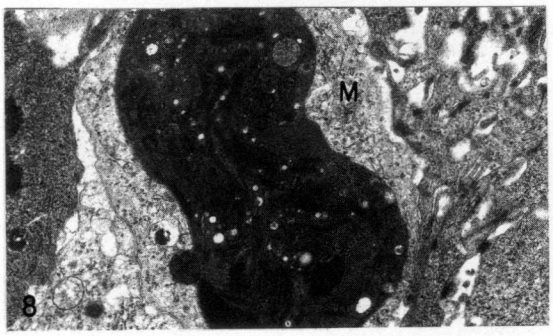


Fig. 5 Electron micrograph of a dyskeratotic cell containing centrally-located mass of aggregated Tfs and abundant vacuoles, and outer zone with abundant ribosomes in the cytoplasm. ×11,000.

Fig. 6 Electron micrograph of a dyskeratotic cell containing dyskeratotic mass with outer membrane (arrow). ×10,200.

Fig. 7 Electron micrograph of a dyskeratotic cell containing circular dyskeratotic mass of Tfs at the opposite end of the cytoplasm from the crescent-shaped nucleus (N). ×7,300.

Fig. 8 Electron micrograph of a macrophage (M) phagocytizing aggregated mass of Tfs. ×10,500.

a paucity of desmosomes (Fig. 4). In some instances, the aggregated Tfs were found as masses with or without outer mambranes in the center of anucleated cells (Figs. 5 and 6), while in others they were locally seen as circular masses composed of condensed Tfs at the opposite end of the cytoplasm from the nuclei (Fig. 7). Occasionally, such dyskeratotic cells appeared to be phagocytized by adjacent macrophages (Fig. 8). These dyskeratotic cells were observed without special preference to locations in the cancer cell nests.

DISCUSSION

In the present electron microscopic observations, human oral SCCs contained various forms of malignant dyskeratosis, although they could be seen as individually keratinized cells which altered an otherwise monotonous histology. The common ultrastructural feature in the dyskeratotic cells was the abnormal aggregation of Tfs in the cytoplasms accompanied by decreases in cell junctional DESs. In the present study, two types of dyskeratosis were recognized in human oral SCC. One of them had aggregations of Tfs in the whole cytoplasm, and the other had partial aggregations of Tfs in the cytoplasm. The dyskeratotic cells without any limiting membrane around the aggregated masses of Tfs seemed to form the Tfs by themselves in their cytoplasms, while the aggregated masses of Tfs with outer membranes appeared to be engulfed and phagocytized by other adjacent cells, and/or autophagocytized by lysosomal organelles in thir cytoplasms. Olson et al reported the former type of dyskeratosis as primary dyskeratosis, and the latter as secondary dyskeratosis in Bowen's disease which is considered to be a precurser lesion of SCC (3). Cells with moderately-aggregated bundles of Tfs in the cytoplasms, which are seen in Figs. 2 and 3, may be those in the earliest stages of dyskeratosis. Fig. 9 shows the possible schematic presentation of the formative morphogenesis of dyskeratotic cells in human oral SCC.

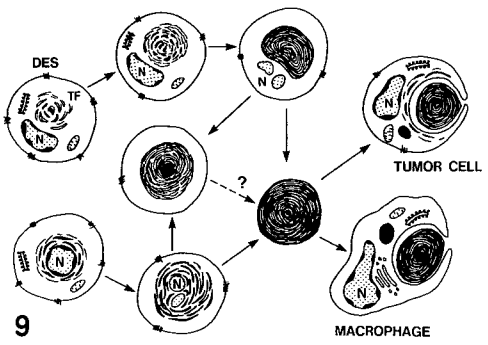


Fig. 9 Schematic presentation of morphological events in dyskeratosis.

The dyskeratotic changes observed in the the present study closely resembled those seen in Bowen's diseare (3, 4) and those in benign dyskeratosis from Darier's disease (5, 6), Hailey-Hailey disease (6), UV exposed epidermis (7), and zinc deficient epidermis (8). It is generally accepted that benign dyskeratosis originates from aggregations of Tfs which have separated from the disturbed DES-Tf complex due to acantholysis (5). On the other hand, Sato and Seiji reported that the mechanisms of dyskeratotic cell formation in Bowen's disease are assumed to differ from those in benign dyskeratosis in Darier's disease and Hailey-Hailey disease, in which the congenital or hereditary deficiency of the TF-DES complex will produce acantholytic cells followed by the formation of dyskeratotic cells (4). Moreover, they postulated that the overproduction of Tfs may disturb cell division and the formation of DES, indicating that the deficiency of DES in the dyskeratotic cells could not be the cause of the formation of the dyskeratotic cells (4). The presence of abundant free ribosomes even in the dyskeratotic cells with double zone cytoplasm of both the inner zone of markedly aggregated masses of TFs and the outer zone of scarce distribution of Tfs in the cytoplasm suggests that the cells still have the ability to produce Tfs. Therefore, there seems to be a complex pathogenesis in the formation of malignant dyskeratosis. It may be due to the fundamental characteristics of the cancer cells, the abnormal replication, the migration and infiltration. Further detailed biochemical and cell kinetic investigations are also needed to study the morphogenesis of dyskeratosis in SCC.

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