The Ultrastructure of Bowen's Disease: Nuclear and Nucleolar Lesions

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SUMMARY

Histologically typical skin lesions of 10 patients with Bowen's disease were examined by means of the usual electron microscopic procedures to provide more information on the fine structure of nuclei and nucleoli in giant cells.

Nuclei of giant cells were characterized by the presence of an increased number of interchromatinic and perichromatinic granules. In addition, dense globular structures about 500 to 1500 Å in diameter were noted in association with chromatin. The spherical clusters observed in interchromatinic areas at the condensed chromatin were composed of particles about 300 Å in diameter.

Most nucleoli in giant cells were either small and compact or with nucleolonemas. Some small nucleoli of spherical shape were characterized by segregation of fibrillar and granular ribonucleoprotein components. Ring-shaped nucleoli as well as nucleoli with unusual organization of nucleoprotein structures were found only in small numbers.

The ultrastructural appearance of nucleoli in some giant cells suggested a low rate or inhibition of the synthesis of nucleolar RNA in these cells.

INTRODUCTION

The presence of giant cells in the altered epidermis is one of the main histopathological and diagnostic features of Bowen's disease. The nuclei of these cells are usually very large, irregularly shaped and hyperchromatic (1). Their fine structure, however, is less known (7, 11, 14).

For more information on the fine structure of nuclei including nucleoli in giant cells of altered epidermis of Bowen's disease, these structures were studied electron microscopically. The results have shown that nuclei of giant cells contained numerous interchromatinic and perichromatinic granules as well as atypical spherical and globular structures. In addition, only a relatively low number of nucleoli in giant cells seemed to be of usual ultrastructural appearance compared with the cells of normal epidermis.

MATERIALS AND METHODS

Skin biopsy specimens from 10 untreated patients with clinical and histological lesions typical of Bowen's disease were used for electron microscopic studies. The lesions were excised under minimal local procaine anesthesia. Small blocks cut from each sample were fixed immediately in 2.5% glutaraldehyde at 4° for 2 hr. Then the blocks were washed twice in 0.15 M phosphate buffer at room temperature for 1 to 2 hr. After embedding in Epon, areas for ultrathin sectioning were chosen after previous examination of "thick" sections stained with toluidine blue and Azur II. Ultrathin sections stained with uranyl acetate followed by lead citrate were observed with a Siemens-Elmiskop IA electron microscope.

RESULTS

The cytoplasmic structural appearance of giant cells of Bowen's disease did not differ in general from that described in previous studies (11, 14).

The ultrastructural morphology of nuclei and nucleoli was very similar in both mononucleated and multinucleated giant cells.

The Nuclear Ultrastructure of Giant Cells. The nuclear size in ultrathin sections was variable. The shape of the nuclei appeared irregular, and numerous deep cytoplasmic invaginations into nuclei were observed (Fig. 1). As in normal epidermal cells (10), the nuclear chromatin structure in giant cells was composed of fibrils which were present in large amounts ("condensed chromatin") along the nuclear membrane, around nucleoli, and in chromocenters (Fig. 2). At the margin of chromatin structures including nucleolus-associated chromatin, perichromatinic granules were more frequent in the nuclei of giant cells (Figs. 2 and 3), in comparison with normal epidermal cells (10). The size of perichromatinic granules varied considerably between 300 and 600 Å. Intercromatinic areas contained numerous "dense" interchromatinic granules which occasionally formed clusters (Fig. 4). Nuclear bodies were frequent; their ultrastructure in giant cells of epidermal lesions of Bowen's disease has been described in the previous study (7). In addition to the structures mentioned above, unusual spherical and globular structures were found in the nuclei of a few giant cells. Spherical structures were represented by clusters of particles, about 300 Å in diameter, which were usually observed at the margin of condensed chromatin (Fig. 2). Globular structures (formations) 500 to 1500 Å in diameter were located in clumps of condensed chromatin (Fig. 5).

The Nucleolar Ultrastructure in Giant Cells. In ultrathin sections, the number of nucleoli ranged between 1 and 5...
The ultrastructural morphology of nucleoli varied not only in various nuclei but also in the same nucleus (Fig. 1).

Most nucleoli in giant cells were either small and compact (about 30% of nucleoli (Figs. 2 and 6)) or they were large and composed of nucleolonemas (about 40% of nucleoli). Some small and compact nucleoli of spherical shape were characterized by a distinct segregation of nucleolar components (Fig. 6). Some nucleoli with nucleolonemas contained large filamentous areas (Fig. 7). The density of these structures was lower than in nucleolar fibrillar ribonucleoprotein components.

Ring-shaped nucleoli (16) were present only in limited numbers of nuclei. They were characterized by the presence of ribonucleoprotein structures in the nucleolar peripheral part which formed a shell surrounding a central light core. In a few nuclei, nucleoli with unusual organization of ribonucleoprotein structures were observed (Fig. 8). Such nucleoli were composed of a central mass containing mainly fibrillar components, which was surrounded by a light circular zone and peripheral ribonucleoprotein shell. It is evident that the section across the top of such a nucleolus would present an appearance similar to that of the ring-shaped one. Lacking serial sections, we cannot ascertain whether each of both last-mentioned nucleoli represents a different type of nucleolus.

DISCUSSION

This study provides additional information on the ultrastructural morphology of giant cells in the epidermal lesions of patients with Bowen's disease. However, in contrast to the previous studies (7, 11, 14), the present observations deal with nuclear and nucleolar ultrastructural morphology.

The results of the present study have shown that the ultrastructural morphology of many nucleoli in giant cells of Bowen's disease is greatly similar to the nucleolar changes produced by the inhibition of the RNA synthesis. The segregation of ribonucleoprotein components observed in small and compact nucleoli of giant cells resembled the nucleolar segregation induced by inhibition by some antimetabolites of DNA-directed RNA synthesis (3, 5, 15, 17). In addition, ring-shaped nucleoli found in some giant cells were similar to those observed in cells with a very low rate of RNA synthesis, which was produced either by the cell maturation or by some inhibitors of RNA synthesis (12, 13, 16). Thus, the ultrastructural morphology of nucleoli in numerous giant cells of Bowen's disease seems to indicate an inhibition or a low rate of nucleolar RNA synthesis in these cells. On the other hand, the synthesis of extranucleolar RNA in such cells does not appear to be altered since the number of perichromatinic granules was very high and increased, in comparison with normal epidermal cells. A similar high number of perichromatinic granules was observed in various cells after the treatment with actinomycin D (16), aflatoxin, and lasiocarpine (9) at doses which presumably block nucleolar RNA synthesis but do not inhibit the synthesis of other species of RNA (8, 9).

Other nuclear as well as nucleolar characteristics and abnormalities cannot be explained, although it cannot be excluded that they belong to the category of nonspecific changes observed in tumor cells (3, 4, 6). However, giant cells of Bowen's disease are also considered as degenerative cell forms (2). The nucleolar ultrastructure in numerous giant cells indicating a low rate or inhibition of RNA synthesis in nucleoli, as mentioned above, does not exclude such a possibility and may indicate the beginning of regressive changes connected with cell degeneration.

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REFERENCES


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Fig. 1. Skin lesion of Bowen’s disease with giant cells. N, nuclei; arrows, nucleoli. X 5,600.
Fig. 2. Nucleus of a giant cell with a large number of perichromatinic granules (arrows) and a spherical structure (pointer) composed of small particles. C, chromocenter; N, nucleolus. X 30,000.
Fig. 3. Perichromatinic granules (arrows) in the nucleolus-associated chromatin (pointer). N, nucleolus. X 33,000.
Fig. 4. Nuclear interchromatinic granules (pointer). N, nucleolus. X 30,000.
Fig. 5. Nuclear globular formations (pointer). N, nucleolus. X 50,000.
Fig. 6. Small compact nucleolus with segregation of fibrillar (F) and granular (G) components. C, cytoplasm. X 40,000.
Fig. 7. A large and round nucleolus with nucleolonemas and large filamentous areas (f). X 23,000.
Fig. 8. Nucleolus with zonal distribution of nucleolar ribonucleoprotein components, A, central area with ribonucleoprotein components; C, cytoplasmic invagination into the nucleus. X 40,000.
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5

6

G
F
C

7

A

8

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