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Case Reports

Electron Microscopic Study on the So-Called Malignant Medullo-Epithelioma (Ciliary Epithelial Carcinoma)

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Summary. A pigeon's-egg-sized tumor arising in the right eye of a 63-year-old man was subjected to light and electron microscopic investigation.

The histopathological features were those of medullo-epithelioma, adult type, with tumor cells arranged in alveoli, tubules and papillary projections, and with bone formation. The tumor cells usually had round or ovoid nuclei with prominent nucleoli and a comparatively light cytoplasm. The basement membrane was mostly clear and partly indistinct. Electron microscopically, the tumor cells were partly connected with intermediate junctions; some were light cells, others dark. The light cells, in a younger stage of development, were surrounded by the dark cells with condensed cytoplasm. The tumor cells showed a slight differentiation toward a ciliary epithelium.

These findings support the hypothesis that this kind of tumor originates in the ciliary epithelium. We therefore propose calling it a poorly differentiated ciliary epithelial carcinoma.

Medullo-epithelioma, adult type, first set up by Fuchs (1908), is thought to be derived from ciliary epithelium of the optic vesicle (Nordmann, 1941). Ultrastructural details of this tumor has not been reported so far. This report is about light and electron microscopic investigation of a case of so-called malignant medullo-epithelioma, which might histogenetically be a ciliary epithelial carcinoma.

A Case Report. A sixty three year old male had been troubled with a weak eyesight of his right eye from childhood. In July 1969, he visited an ophthalmologist (co-author: F.H.), because he had been having trouble with his right exophthalmus for several months. He was treated by an enucleation of his right eye in combination with the tumor extirpation. About half a year later, he suffered from local recurrence of the tumor, severe headache and loss of the sight of his another eye. Cerebral angiography revealed an intracranial invasion of the tumor.

Gross Findings. The tumor mass, elastic soft in consistency, was the size of a pigeon's egg including his right eyeball. The cut surface of the tumor was greyish white and parenchymatous. The tumor occupied the entire eyeball including the ciliary body, posterior chamber and most inner surface of the retina. There were some localized areas of heavy brown pigment deposition. Procedures for making specimens: The specimens for light microscopy were taken from both original and recurrent tumors. These were fixed in 10% formalin solution, dehydrated in graded ethanol, embedded in paraffin and sectioned with a microtome at 6 μ. Besides routine staining with hematoxylin and eosin (H.E.), the specimens were stained with silver impregnation (Gomori's method and Bodian's method) and periodic acid Schiff's reaction (P.A.S.).

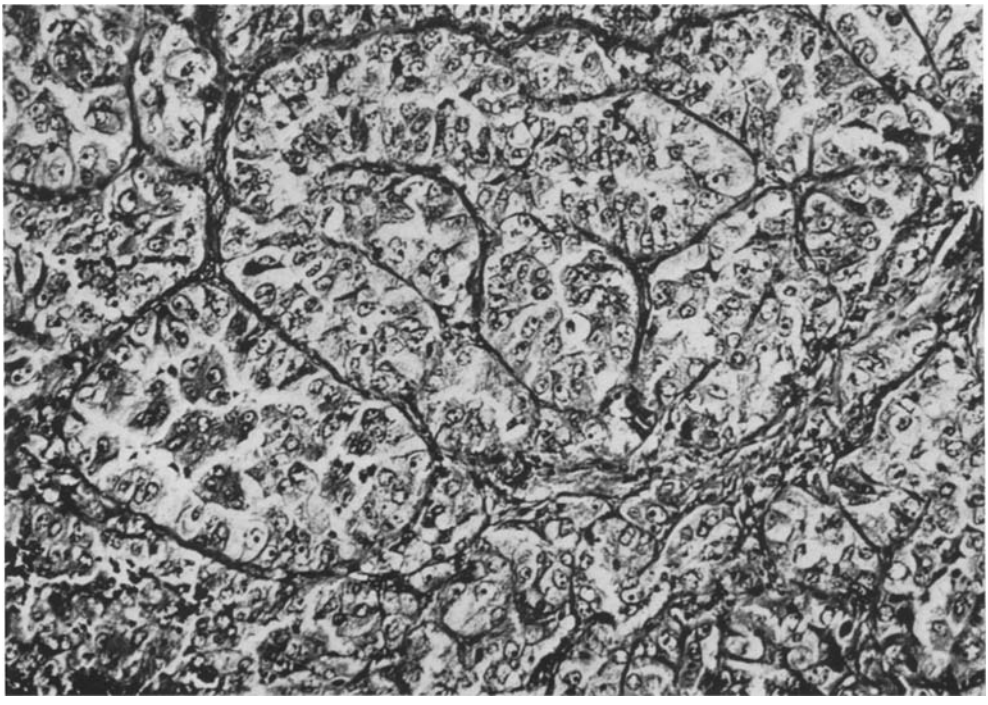


Fig. 1. The tumor cells, ovoid nucleated and rich in cytoplasm, arranged in an alveolar structure. H.E. ×200

For electron microscopical examination, the specimens from recurrent tumor of the right orbit, soaked in 5% glutaraldehyde s-collidin buffer, pH 7.4, were cut into small pieces, 1 mm cube in size. These tissue blocks were fixed in this solution for one hour, rinsed in s-collidin buffer three times at intervals of 15 min and kept overnight in the refigerator. The specimens were postfixed in s-collidin buffered osmium tetroxide for one hour, dehydrated with graded ethanol, rinsed two times in propylene oxide for 30 min and embedded in epon (Luft, 1961).

These tissue blocks, cut with an LKB ultrotome, were selected by toluidine blue staining of the thick sections. The ultrathin sections, stained with uranyl acetate and lead citrate, were observed and photographed with a JEM 7A electron microscope (Japan Electron Optics Laboratory Co., Ltd) at direct magnifications of 1500 to 10000.

Microscopical Findings. The tumor showed conspicuous alveolar structures with papillomatous and tubular arrangement (Fig. 1). The interstitium in and around the sclera had a heterotopic bone formation. The nuclei of these tumor cells were large and had prominent acidophilic nucleoli. Some of the tumor cells were multinucleated and frequently showed mitotic figures. The tumor cells had clear and slightly eosinophilic cytoplasm. The basement membrane demonstrated by silver impregnation was mostly clear and partly indistinct around the cylindrical tumor cells. P.A.S. staining of the tumor cells was negative, except for tiny granules in some tumor cells. The brown pigment identified macroscopically, showed partly a feature of hemosiderin and partly of pigmented retina. Toluidine blue staining

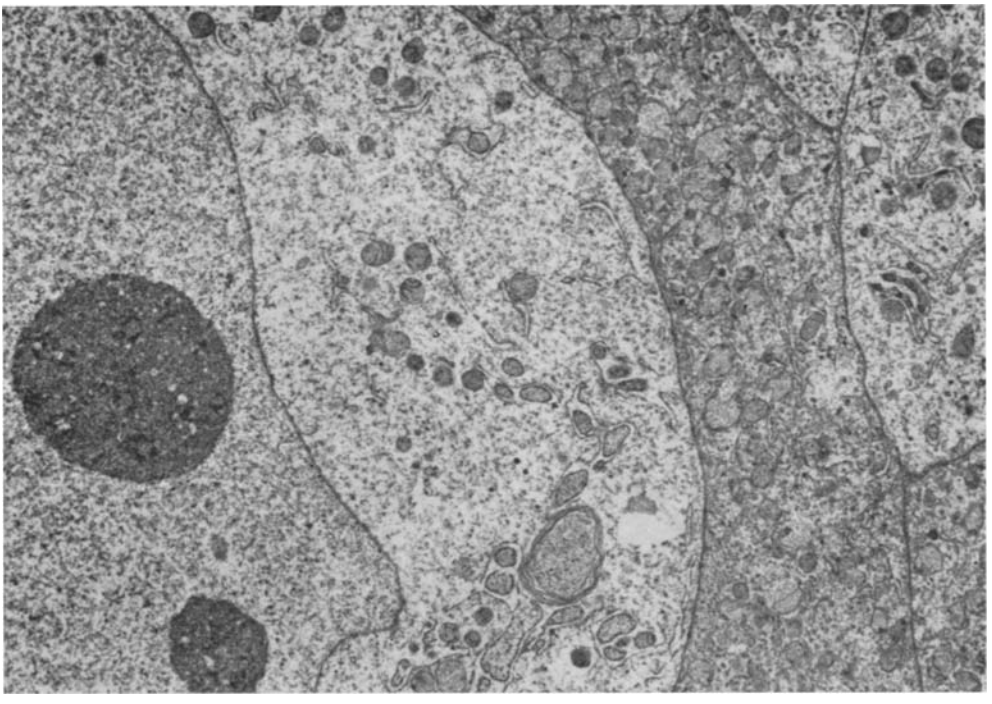


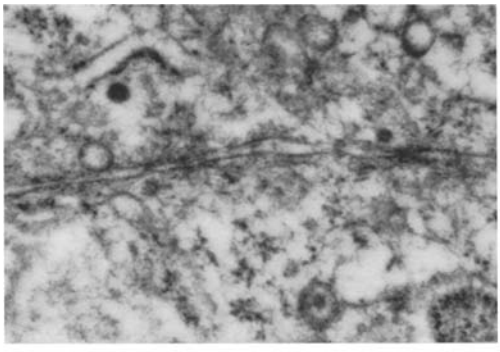
Fig. 2. The tumor cell with light cytoplasm contained ill-developed endoplasmic reticulum and an oval mass of granular matrix surrounded by concentric lamellar arrangement of the smooth membrane. The adjacent dark cells with compact organellae encircled the light cell smoothly. × 3900

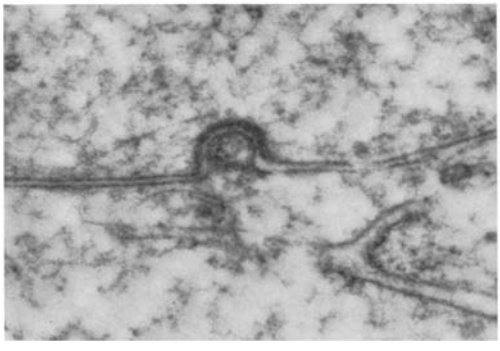
for the plastic section disclosed light cells with oval transparent cytoplasm and comparatively narrow dark cells with dense cytoplasm. In general, dark cells were arranged around light cells.

Electron Microscopical Findings. Lower magnification of electron micrographs showed that dark cells with oval nuclei surrounded light cells with round nuclei containing prominent nucleoli (Fig. 2).

A cell surface contact among both types of the tumor cells was mostly smooth. Their intermediate junctions were observed especially in the basal portion of the glandular structures (Fig. 3). In either type cell, there were found localized interdigitations and buddings of the plasma membranes, 0.1–0.3 μ in diameter, associated with the adjacent dense cell membranes (Fig. 4). Fine filaments were dispersed within the cytoplasm of these tumor cells. The basement membrane was not always distinct between the tumor cells and the stromal cells.

The light cells contained comparatively round or oval nuclei with large distinct nucleoli (Figs. 2 and 6). The nucleoli sometimes showed a fine granular round chromatin mass (pars amorpha) with clear hof. The transparent cytoplasm contained ill-developed Golgi apparatus, sparse cytoplasmic organellae (Figs. 2 and 6) and a few lipid granules. The cytoplasm of the light cells occasionally contained slightly dense granular mass, 1–3 μ in diameter, which were sometimes surrounded by concentric arrangement of smooth membrane (Fig. 2). There was sometimes





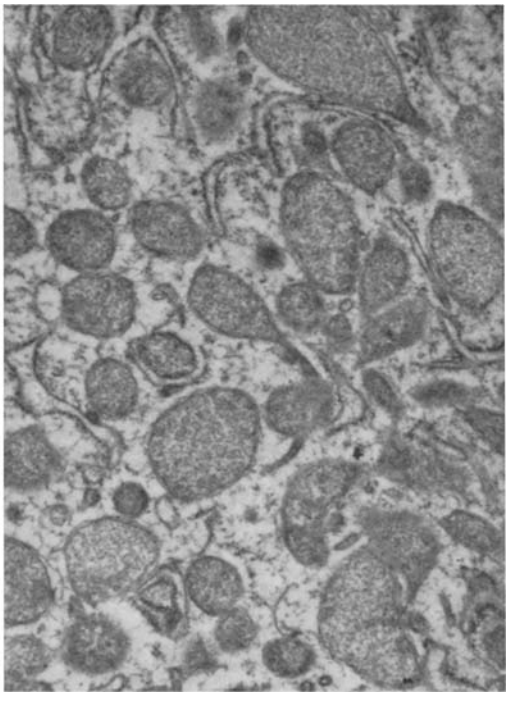


Fig. 3. Intermediate junctions between the adjacent plasma membranes of the tumor cells. ×26000

Fig. 4. A budding of plasma membrane, associated with concaved adjacent cell membrane of electron density. ×26000

Fig. 5. Round or ovoid mitochondria mostly without cristae connected partly with endoplasmic reticulum. ×14000

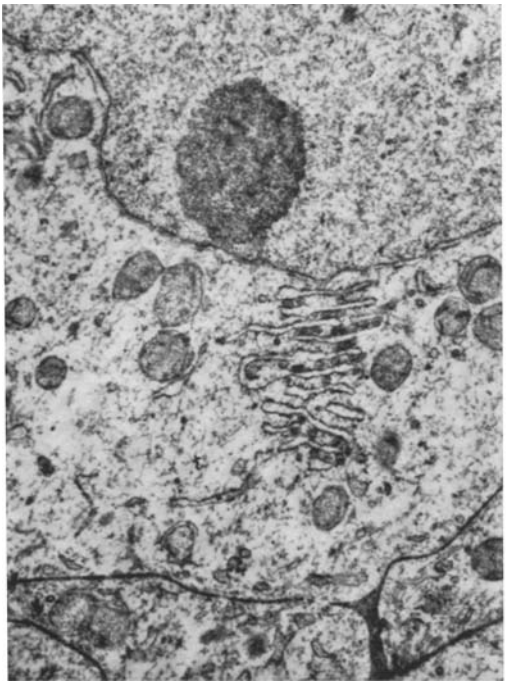
observed a spiral-like structure of ergastoplasmic membrane associated with outer nuclear membrane (Fig. 6). The mitochondria were comparatively round or oval in shape, having few cristae and frequently associated with endoplasmic reticulum (Fig. 5). There was no pigment granule comparable to melanin in these cells.

The dark cells were packed with cytoplasmic organellae (Figs. 2 and 7). The cytoplasm were filled with granular endoplasmic reticulum showing a network pattern, vesicles and a few lipid granules. The radiating projections of the cytoplasm with bundles of intracytoplasmic filaments were sometimes observed in the dark cells (Fig. 7).

The stromal cells occasionally contained some membrane-bound granules, globose in shape, filled with fine electron-dense granular matrix.

Discussion

The tumor reported here showed poorly differentiated carcinomatous character, showing alveolar arrangement, mostly smooth intercellular attachment with intermediate junctions and prominent nucleoli. Heterotopic bone formation seen



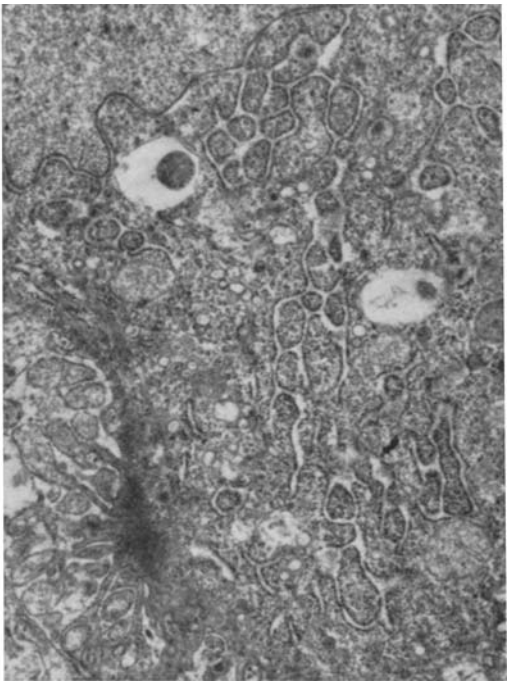


Fig. 6. A localized area of tortuous endoplasmic reticulum associated with the outer nuclear membrane of a light cell. ×5200

Fig. 7. A dark cell showed dense cytoplasmic matrix, a network pattern of endoplasmic reticulum and cytoplasmic processes associated with intracytoplasmic filaments. ×9500

in this tumor might be comparable to cartilaginous tissue in Böck's case (Böck, 1929).

The tumor cells were classified as light and dark cells. Transitional cells were occasionally found between these cells. The light cells, the tumor cells in the younger stage, might transform into the dark cells, the ones in the advanced stage of development or in the degenerative condensation.

The extraordinary prominent nucleoli and the proliferation of intracellular membranous system might represent high activity of cellular growth. Ovoid mitochondria with few cristae, partly associated with endoplasmic reticulum, might be young mitochondria or the ones engaged in anaerobic glycolysis (Linnane *et al.*, 1962; Wallace and Linnane, 1964). A network pattern of the endoplasmic reticulum (Fig. 7) might represent underdeveloped cell type (Yamamoto, 1971).

Electron microscopic studies of the ciliary epithelium (Holmberg, 1955; Pappas *et al.*, 1958, 1959; Urayama *et al.*, 1959; Tormy, 1963; Kozart, 1968) revealed infolded plasma membranes as a feature of special differentiation. Though the plasma membranes of this tumor cells were usually smooth, occasional infoldings and cytoplasmic processes might imply the differentiation toward ciliary epithelium (Fig. 7).

A budding of plasma membrane, a kind of intercellular junction, and intermediate junctions (Fig. 3) intensified the characteristic epithelial natures of this tumor.

Andersen (1948) and Reese (1956) pointed out that many tumors reported as medullo-epithelioma were really atypical malignant melanoma with epithelioid arrangement. The fact that no pigment being comparable to melanin was found in these tumor cells, might serve to exclude melanoma from the lesion. The pigment occasionally seen in some stromal cells, was identified as hemosiderinlike granules, because the fine electron-dense matrix was thought to be iron particles.

Based on the above-mentioned findings, histogenesis of the so-called medullo-epithelioma, adult type, might be set on the ciliary epithelium as Fuchs (1908) postulated. Thus, the tumor in this study should be diagnosed as poorly differentiated ciliary epithelial carcinoma.

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