THE FINE STRUCTURE OF HYALINE INCLUSIONS (PSEUDOPSAMMOMA BODIES) IN MENINGIOMAS

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ABSTRACT

"Hyaline inclusions" of a meningotheelial meningioma were examined under the electron microscope. These eosinophilic, PAS-positive proteinaceous structures, which under the light microscope are seen in both extra- and intracellular location, were found by electron microscopy to consist of granular masses surrounded by cell membranes with microvilli. The "intracellular" bodies were also surrounded by similar microvilli in a space within the cells. Such spaces, variously known as intracellular ductules and "neolumen formation", have been previously described in mammmary cancer, bronchiolar carcinoma and pleural mesotheliomas, among others, and have been, in the latter instances, regarded as signs of secretory differentiation. Thus, hyaline inclusions of meningiomas are different from truly intracellular hyaline bodies of neoplastic astrocytes (found by Rubinstein and Herman to be bodies within autophagic vacuoles) and may be regarded as a possible factor in ultrastructural differential diagnosis between meningiomas and gliomas.

INTRODUCTION

Hyaline inclusions in meningiomas were first described by Cushing and Eisenhardt (2) in a meningotheelial meningioma. According to these authors the tumor was "exceptionally rich in whorls and had numerous peculiar cellular inclusions of highly refractive glassy hyalinoid material". The authors did not further elaborate on the nature of these inclusions, but did include two photomicrographs of them stained by the phosphotungstic acid hematoxylin stain.

Kepes (5) described five additional cases of meningiomas with hyaline inclusions and found that the inclusions ranged in size from 3 to 100 micra. The smaller bodies were seen in the cytoplasm of meningotheial tumor cells, whereas the larger ones appeared to lie free in the tissue spaces. The various staining reactions characteristic of these bodies were discussed.

Recently, a surgically removed meningioma containing these inclusions, was obtained for electron microscopic examination.

MATERIALS AND METHODS

A convexity meningioma was removed from the right frontal lobe of a 69-year-old Caucasian male at the Veterans' Administration Hospital in Kansas City. Pieces of the tumor were diced and submerged in 2% phosphate buffered glutaraldehyde solution in the operating

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This paper has been presented in part at the 50th Annual Meeting of the American Association of Neuropathologists, Boston, Mass., June 9, 1974.
room. Subsequently the tissues were postfixed in 1% Veronal buffered osmium tetroxide, dehydrated and embedded in Epon-Araldite. Thin sections were cut on an LKB Ultratome III, mounted on copper grids and examined with a Hitachi HU 11-C electron microscope. The rest of the tumor was fixed in 10% formaldehyde and sections were prepared for light microscopy. These were stained with H.E., PAS, Gomori's trichrome stain and Weigert's fibrin stain.

RESULTS

Light Microscopy. Sections stained with hematoxylin and eosin showed a meningotheial meningioma with numerous cellular whorls, some of which had undergone hyalinization, and others early calcification. Throughout the tumor large numbers of hyaline inclusions were encountered; the small ones appeared to be intracellular, the large ones extracellular (Figs. 1, 2). Their staining reactions conformed to those previously described (5).

By electron microscopy the inclusions were seen both individually and in clusters (Figs. 3, 4, 5). They were composed of moderately electron dense material, mostly finely granular (Figs. 5, 7), although in some of the larger inclusions globular aggregates of more osmophilic particles could be observed (Fig. 6). As to the location of the inclusions, the larger ones were clearly extracellular, surrounded by one or more meningotheial cells. At the interphase between cells and hyaline bodies, the cell membranes displayed numerous microvilli (Figs. 7, 8). No certain clues were evident as to the genesis of the granular material of the bodies, except that morphologically similar granules could be observed on the inner side of the cell membrane as well as within the microvilli themselves (Fig. 7) but the actual process of extrusion of this material into the extracellular space could only be surmised.

One surprising finding was that the hyaline inclusions contained within cells also occupied a space lined by microvilli. These spaces corresponded to the structures variously described in other tumors as intracellular ductules (1) or “intracellular neolumen formation” (10) (Fig. 5). Some of the cells contained more than one inclusion.

Comment. There are very few tumors that display as many histological variations as meningiomas do. Meningothelial, fibroblastic, lipomatous, chondroblastic, osteoblastic variants, to name just a few, make this one of the most colorful of human neoplasms. The presence of proteinaceous material in microvilli-lined extracellular spaces suggests the possibility of still another variant: meningioma with secretory differentiation. This is further underlined by the presence of intracellular spaces also lined by microvilli and filled with the proteinaceous “inclusions”. Such intracellular vacuoles with microvilli have been described in human breast cancer by Buerger and Scarpelli (1) who referred to them as intracellular ductule formation and considered the possibility that they were extensions of intercellular ducts, but did not rule out the possibility that they were independent intracellular structures. Wang (10) observed such spaces in the cytoplasm of pleural mesothelioma cells as well as in bronchioloalveolar carcinomas. Bronchial and mammary gland epithelium are of course normally engaged in secretory activity and therefore such manifestations in
neoplasms originating from these epithelia should not be surprising. Pleural mesothelium on the other hand does not form "glands" under normal circumstances but may do so in proliferative states and as one phase of the "biphasic" mesotheliomas. (An even more "glandular" differentiation of mesothelial cells is seen in the so-called adenomatoid tumors of fallopian tubes and other locations (6)).
Fig. 3. A cluster of 8 inclusions (center) and part of a single inclusion (bottom) are seen. They are composed of granular, moderately electron dense material. (× 11,000)

For meningotheelial cells such "glandular metaplasia" must be even more uncommon, since we do not usually encounter it in normal arachnoidal cap cells or in Pachionian granulations, and as stated above, only in a small minority of meningiomas. Nevertheless in undergoing these changes the meningotheelial cells perhaps demonstrate a structural analogy to mesothelial cells which are
Fig. 4. Four inclusions composed of light granular material. Even at this low power microvilli are seen at interphase between cytoplasm and inclusions. (× 12,500)

Fig. 5. This inclusion appears to be entirely surrounded by the cytoplasm of one tumor cell. Condensations of tonofibrils are seen in the area surrounding the inclusion. (× 10,000)
also non-epithelial cells performing a function normally delegated to epithelium, that of lining the walls of cavities. It should be pointed out however that the material thus secreted in mesotheliomas contains stainable acid mucopolysaccharides, whereas the hyaline inclusions of meningiomas are free of these substances.

By light microscopy hyaline inclusions, particularly the intracellular ones, are similar to eosinophile hyaline globules seen in other neoplasms. Dekker and Krause (3) recently examined the fine structure of intracytoplasmic hyaline globules of three patients with various carcinomas and found them to be essentially identical to each other and to hyaline globules seen in non-neoplastic liver and in the adrenal medulla. These globules, however, differed from the hyaline inclusions of meningiomas, in that the former were always found to be truly intracytoplasmic, closely related to, and perhaps derived from, endoplasmic reticulum, whereas, as demonstrated above, the hyaline inclusions of meningiomas were always found within microvilli-lined ductal structures, both extra- and intracellularly.

In the field of neuropathology "hyaline inclusions" have been described in non-neoplastic cells, such as neurons (particularly motor neurons of the hypo-
**Fig. 7.** Interphase between tumor cell cytoplasm and granular inclusion. Single and branching microvilli are seen. Within the microvilli granular material similar to that of the inclusions is seen. ($\times 51,000$)

**Fig. 8.** Another area of interphase. Microvilli are seen near the fine granular material (left) and the larger round clusters (right). ($\times 23,000$).
glossal nuclei) (7) and were found to be truly intracytoplasmic. The same is true for the cosinophilic granules or globules of astrocytes described by Russell and Rubinstein (9), Hossmann and Wechsler (4), and Zülich (11). Rubinstein and Herman (8) examined these structures, found in the astrocytic component of a cerebral ganglioglioma, under the electron microscope and found them to consist of membrane-bound bodies within autophagic vacuoles, thus essentially different from the hyaline inclusions of meningiomas.

Acknowledgements. The author wishes to express his sincere gratitude to Drs. S. Rengachari and I. Watanabe for making tissue available for this study and to Mrs. Kay Pierce and Mr. Charles Sittler for their valuable technical help.

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