Ultrastructural study of the formation of psammoma bodies in fibroblastic meningioma

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The fine structure of psammoma bodies was examined in four cases of fibroblastic meningioma. In general, large numbers of various-sized calcified bodies (psammoma bodies) were scattered among the interstitial fibers. In these bodies, the smallest calcific site was found in the extracellular membrane-bound matrix vesicles, which measured approximately 0.1 to 0.2 μ in diameter. In addition, extracellular “matrix giant bodies,” with or without hydroxyapatite aggregates and measuring up to 3 μ in diameter, were frequently encountered. These bodies were apparently invested with single, double, or multiple concentric walls averaging nearly 0.1 μ thick. They presumably originated from the neoplastic cells as a consequence of cytoplasmic residues associated with cellular degeneration or necrotic cell processes. Hydroxyapatite crystals precipitated repeatedly within the bodies. The precipitate may gradually aggregate within the bodies, and gather in clusters, resulting in a large psammoma body. Finally, collagen fibers around the calcified giant bodies accrued deposits of apatite crystals to make a huge psammoma body. These findings suggest that both matrix giant bodies and matrix vesicles may serve as initial nidus of calcification of psammoma bodies in fibroblastic meningioma. Consequently, this mineralization process may represent a certain dystrophic calcification of meningocytic cells.

KEY WORDS • fibroblastic meningioma • psammoma body • matrix vesicle • matrix giant body • collagen fiber • calcification

Materials and Methods

Four surgically removed meningiomas were investigated for this study. These tumors included a convexity meningioma from a 53-year-old woman, a cerebellopontine angle meningioma from a 51-year-old woman, a falk meningioma from a 37-year-old man, and a suprasellar meningioma from a 56-year-old woman. Samples of each tumor were minced into 1- to 2-mm pieces immediately after surgical removal, fixed in cacodylate-buffered 2.5% glutaraldehyde solution for 2 hours, postfixed in 1% osmium tetroxide for 1 hour, dehydrated in increasing concentrations of alcohol, and embedded in Epon-Araldite. For orientation purposes, thick 1-μ sections of epoxy-embedded tissue were stained with toluidine blue and observed by light microscopy. Ultra-thin sections were stained with lead citrate and uranyl acetate, and examined by electron microscopy. The remaining tissues were fixed in 10% formalin; some pieces were embedded in paraffin, and stained with hematoxylin and eosin, reticulin, and Masson trichrome stains, for light microscopic study.

Results

Light Microscopic Findings

The specimens taken from the four patients exhibited multiple psammoma bodies (Fig. 1). The tumors con-
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FIG. 1. Photomicrograph of an area of fibroblastic meningioma showing a stream-like arrangement of neoplastic cells containing numerous psammoma bodies. H & E, × 200.

consisted of interlacing bundles of long narrow spindle cells with an occasional whorl formation characteristic of fibroblastic meningioma. A distinctive feature was the marked tendency to form reticulin and collagen fibers between the tumor cells.

Electron Microscopic Findings

The representative tumor tissues were grossly discerned between the cellular parts and the areas of interstitial fibers. The neoplastic cells comprising the cellular portions showed the distinctive ultrastructural features of meningocytic cells, with elongated cell processes and occasional interconnection of neighboring cells by junctional complexes. On the other hand, a majority of the extracellular spaces were closely packed by abundant collagen fibers. In some specimens elastic fibers were also present among the collagen fibers, and scarce neoplastic cells were distributed among these fibers as well. Within the fibrous area, various sizes and shapes of membrane-invested structures, presumably immature psammoma bodies, were frequently encountered (Fig. 2). Highly electron-dense materials, namely hydroxyapatite aggregates, were usually recognized within these structures. In some specimens, the most minute membrane-bound vesicles, with apatite deposits averaging 0.1 to 0.2 μ in diameter, were noted (Fig. 3). These vesicles appeared to be morphologically identical to the matrix vesicles reported in calcifying tissue. In addition to the presence of matrix vesicles, larger round or oval structures measuring up to 3 μ in diameter were frequently revealed (Figs. 4, 5, 6, and 7A). Some of them were intimately associated with degenerated cells, suggesting that these bodies were produced by degenerated cells or necrotic cell processes (Fig. 4). These giant bodies were commonly invested with thickened walls averaging 0.1 μ in width. In general, they were nearly round to oval, but some showed a wavy contour. These bodies frequently had apatite aggregates deposited within them in varying degrees (Fig. 5). Further-

more, other large bodies with various amounts of apatite aggregates were seen in some specimens (Fig. 6A). Apatite precipitations were sometimes copiously deposited within the bodies (Fig. 6B). It is assumed that these bodies become mature psammoma bodies after apatite crystals fill up the cavity of the body (Fig. 7A). These

FIG. 2. Electron micrograph of a fibrous portion of a fibroblastic meningioma demonstrating several thick membrane-bound structures with hydroxyapatite aggregates among the interstitial fibers. × 10,000.

FIG. 3. Electron micrographs, ×125,000. A: A tiny round structure, the so-called “matrix vesicle,” measuring about 0.2 μ in diameter, is visible in the extracellular space. B: One of the matrix vesicles obviously precipitates needle-like hydroxyapatite crystals within it.
giant bodies occasionally possessed more than one wall (Fig. 7B). Apatite crystals were also precipitated within concentric double- or multiple-walled bodies to make lamellated psammoma bodies (Fig. 8A), which probably coalesced to produce a large psammoma body (Fig. 8B). Furthermore, apatite depositions located alongside the collagen fibers were sometimes disclosed around the calcified giant bodies (Fig. 9A). In addition, remarkable wide areas of mineralization on the interstitial fibers were exhibited in the vicinity of the mineralized giant bodies (Fig. 9B). Calcification of interstitial fibers was confined to the areas involving the calcified giant bodies.

**Discussion**

Extracellular matrix vesicles have been repeatedly described as being the initial mineralization nidus in a number of hard tissues under both normal and pathological conditions. In this study, matrix vesicles were confirmed as a site of initial calcification in the psammoma bodies in fibroblastic meningioma as well. There seems to be little doubt that matrix vesicles are detached from cytoplasmic processes or derived from degenerated cells. The matrix vesicles in these fibroblastic meningiomas were more frequently encountered around degenerated cells and among interstitial fibers. They were rare in the vicinity of intact neoplastic cells. Therefore, many of the matrix vesicles are presumably produced during disintegrating or necrotic processes of the neoplastic cells.

A remarkable finding was the presence of extracellular matrix giant bodies, which contrasted with the aforementioned matrix vesicles. They were spheroid to oval, varied in size from 0.3 μ to several microns in diameter, and were invested by a membrane from 0.03 to 0.15 μ thick. Occasionally they had several concentric thick walls and some displayed wavy contours. Elsewhere, similar large vesicular bodies have been reported in human aortic valves and aortic media, thyroid cancer and goiter, as well as microfollicular thyroid adenoma. However, the origin of these bodies have not been substantiated ultrastructurally. To the best of our knowledge, the matrix giant bodies have not been described under physiological calcific conditions.

In this investigation, the walls of giant bodies had no trilaminar structure and were thicker than the ordinary cell and matrix vesicle membrane. We could easily find structures similar to giant bodies near the degenerated neoplastic cells. They are assumed to consist of doughnut-like profiles of cytoplasm residuals. Some of the giant bodies seemed to be comprised of material associated with degeneration of neoplastic cells under certain pathological circumstances. Moreover, the matrix vesicles were also coexistent with the giant bodies. It is

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**Fig. 4.** Electron micrograph showing the thick membrane-invested bodies dispersed among the collagen fibers. These bodies appear to arise from degenerated cells, presumably the structures of origin of matrix giant bodies. × 39,000.

**Fig. 5.** Electron micrographs (× 50,000) showing elliptical matrix giant bodies similar to those illustrated in Fig. 4. All of them are invested with thick membrane-like structures. Apatite precipitates are deposited within these bodies in varying degrees.
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interesting to note that some of the matrix vesicles and the giant bodies may be composed of the same material simultaneously derived from the degenerated or necrotic cells in some pathological conditions.

The mode of calcification was the most noteworthy feature in the giant bodies. As shown in this study, hydroxyapatite may gradually accumulate within the giant bodies and precipitate in the thick walls, eventually becoming mature psammoma bodies. The development of the psammoma bodies is presumably the result not only of single body growth, but also the fusion of small ones. On this basis, we believe that the giant bodies may play an important role in forming the psammoma body in the fibroblastic meningioma similarly to the matrix vesicles.

Meanwhile, of most interest is the mode of calcification on the collagen fibers in this investigation. Calcification located alongside the collagen fibers was not observed without it being combined with calcified giant bodies and matrix vesicles, although there is a substantial amount of collagen fibers within the tumor tissue. Collagen fibers have been proposed as one of the candidates for initial mineralization focus because of the frequent presence of collagen fibers in calcifying tissue. Conceivably, collagen fibers may not be an initial mineralization nidus, but a second calcification site subsequent to calcified matrix vesicles or matrix giant bodies in some pathological circumstances.

In conclusion, since psammoma bodies in various sizes were confined to the interstitial fibrous area, we suggest that the formation of psammoma bodies takes place as follows: At first, the neoplastic cells, surrounded by interstitial fibers, degenerate and lose their cellular configuration, then leave their cytoplasm residuals to form matrix vesicles and matrix giant bodies. Subsequently, hydroxyapatite crystals aggregate within the matrix vesicles or the matrix giant bodies. After that, the interstitial fibers adjacent to calcified bodies min-

Fig. 6. Electron micrographs. A: Several giant bodies with small amounts of apatite aggregates. × 18,000. B: One of them has remarkable apatite precipitates. × 58,000.

Fig. 7. Electron micrographs. A: Apatite aggregates fill up the area within a large body measuring about 3μ in diameter, resulting in a mature psammoma body. Vacant areas in the body show sectioning artifact. × 35,000. B: A giant body invested by a concentric double thick wall. Apatite depositions are mainly precipitated within the central portion and on the inner wall. × 47,000.
FIG. 8. Electron micrographs. A: A lamellated calcific psammoma body. Apatite precipitates are copiously deposited on the thick walls. × 54,000. B: A large psammoma body comprising three lamellated calcific giant bodies. × 22,500.

FIG. 9. Electron micrographs. A: Several calcified collagen fibers surround the mineralized giant bodies. × 14,000. B: A wide calcified area is located alongside the interstitial fibers adjacent to the mineralized giant bodies. × 9600.
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eralize. All these eventually result in a large psammoma body.

References


Manuscript received July 25, 1983.

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