Mesectodermal Leiomyoma of the Ciliary Body: New Evidence for Neural Crest Origin

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ABSTRACT
An 8-year-old white boy had a mass of the ciliary body in his left eye. Both the translucent characteristics and the magnetic resonance imaging findings suggested that this lesion was cystic. Fluid aspiration biopsy and iridocyclectomy were performed. By light microscopy the neoplasm showed the characteristic appearance of a neuroendocrine tumor; however, on electron microscopic examination, the tumor exhibited characteristic features of a smooth muscle neoplasm and was diagnosed as a mesectodermal leiomyoma. Observation of melanin granules in scattered tumor cells further confirmed that the tumor had the same origin as uveal melanocytes, which also derive from the neural crest.

INTRODUCTION
Several cases of hybrid neurogenic- myogenic tumors of the ciliary body, termed "mesectodermal leiomyoma" by Jakobiec et al 1 in 1977, have been reported. 2-7 Jakobiec and Iwamoto, 2 in 1978, described a case of mesectodermal leiomyoma of the ciliary body associated with a nevus; and in 1985, Takagi et al, 6 reported a case in which the melanocytes were observed among the tumor cells, adding evidence for the neural crest origin of this tumor.

We herein report a case of mesectodermal leiomyoma in which melanin granules observed in scattered tumor cells further confirm that these tumors have the same origin as uveal melanocytes, which derive from the neural crest. The mesectodermal leiomyoma had some unique clinical and electron microscopic features that, to our knowledge, have not previously been described.

CASE REPORT
An 8-year-old white boy was seen during a school vision screening by an ophthalmologist, who noted a tumor in the left eye and referred the patient to us for further clinical management. The patient gave no family history of visual disorders and had enjoyed excellent health. He denied history of previous trauma and was the product of a full-term, spontaneous, normal delivery. On ophthalmic examination, visual acuity in the right eye was 20/20 and in the left eye was 20/40 best corrected. By applanation tonometry, the intraocular pressure was 12 mm Hg in both eyes. A tumor occupied the inferior temporal quadrant of the left ciliary body and the anterior chamber angle. The iris was atrophic and hypopigmented. The tumor appeared pinkish and richly vascularized and had displaced the peripheral iris anteriorly and centrally, resulting in a shallow anterior chamber and an iridocorneal touch. The tumor could also be seen through the dilated pupil in the posterior chamber as a brownish mass displacing the subluxated lens superonasally (Fig 1). The pupils of both eyes remained reactive. On gonioscopy, the inferotemporal chamber angle appeared to be occluded by the anteriorly bulging iris and tumor. On transillumination, the mass extended posteriorly at the 2:00 to 6:30 position, and was translucent and cystic.

Systemic findings of the physical examination were unremarkable. Ultrasound examination showed that the

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mass at the inferotemporal quadrant of the iris and ciliary body had mixed high and low internal reflectivity, which was not diagnostic but was suggestive of a solid lesion. Magnetic resonance imaging (MRI) was performed using the orbital surface coil. A lesion with a smooth surface was seen, and it was hyperintense in both T₁ and T₂ weighted images (Fig 2), suggesting that it was composed of proteinaceous fluid.

Because of the clinical impression of a cystic lesion of the iris and the ciliary body, supported by interpretation of the MRI findings, the patient was taken to the operating room for an aspiration biopsy of the fluid. During the procedure, the lesion bled excessively and the aspirated fluid consisted only of blood. The patient then underwent iridocyclectomy, lensectomy, and vitrectomy of the left eye; an oval lesion was removed. The surrounding ciliary body and iris were treated with the contact Nd:YAG laser with a sapphire-tip probe. Retinal photocoagulation was performed posterior to the region of resection and on the resection site by endolaser. No complications occurred in the postoperative course.

PATHOLOGIC FINDINGS

On gross examination, the specimen consisted of a 10 × 13 × 12-mm nodule of brownish tissue containing iris and ciliary body. The tumor was cut along the anteroposterior axis, and the cut surface was yellowish with a rubbery consistency. On microscopic examination, the specimen consisted of iris, ciliary body, and fragments of sclera and lens capsule. A tumor in the ciliary body extended anteriorly to the root of the iris and bulged into the vitreous cavity behind the iris into the pupillary region. The ciliary processes were atrophic. The inner surface of the tumor was lined by pigmented and nonpigmented ciliary epithelium. A piece of lens capsule with lens epithelium was tightly adhered to the ciliary epithelium on the inner surface of the tumor. At the base of the tumor, a piece of necrotic sclera was seen (Fig 3).

By light microscopy, the tumor cells had large oval nuclei with occasional nucleoli. The cells had abundant cosinophilic cytoplasm, and slender cellular processes blended into a fibrillar background (Fig 4A). Some of the tumor cells, particularly toward the base of the tumor, were spindle-shaped (Fig 4B). Focal cystoid degeneration with a myxoid background was also seen. The tumor was highly vascularized. Some of the vessels appeared dilated with thin vascular walls (Fig 4C). Moderate cellular pleomorphism was noted, but no mitotic figures were observed. Occasional tumor giant cells with hyperchromatic nuclei were seen. A fibrovascular membrane was noted on the anterior surface of the iris resulting in the ectropion uveae. The tumor cells extended in close approximation to the pigmented and
nonpigmented ciliary epithelium.

Masson’s trichrome stains demonstrated fuchsinophilia of the tumor cell and cell processes. Phosphotungstic acid hematoxylin and Wilder’s reticulin stains showed purple fibers and reticulin around the tumor cells. Fontana’s stain failed to show melanin granules in the tumor cells, but dendritic melanocytes were seen at the base of the tumor around the more normal ciliary muscle fibers. Glial fibrillary acidic protein did not demonstrate any glial elements, but S-100 protein showed positive staining in the ciliary muscle at the base of the tumor and focal areas throughout the tumor.

By electron microscopy, the tumor cells appeared to be ovoid and polyhedral, with an occasional aggregation of mitochondria around the perikaryon (Fig 5). Abundant cell processes containing fine filaments with focal density were seen. The cell processes were interwoven and formed the tumor matrix. Under higher power, pinocytotic vesicles, segments of poorly formed basement membrane, and desmosomal-like cell junctions were also seen (Fig 6). Melanin granules were observed in the scattered tumor cells, and had an irregular shape. They were homogeneously dense granules and did not show filamentous internal structure (Fig 7). In focal areas, intracellular edema was seen in the cell processes. The blood vessels in the tumor had mature smooth muscle cells in the vessel wall, some of which were degenerated, and contrasted sharply with smooth muscle tumor fibers. At the base of the tumor, normal ciliary muscle fibers could be seen (Fig 8).

FIGURE 4: (A) Tumor cells (arrowheads) showed large oval nuclei with occasional nucleoli, abundant eosinophilic cytoplasm, and cellular processes blended into fibrillary background (hematoxylin-eosin, original magnification x 120). (B) Tumor was highly vascularized. Some vessels (V) appeared dilated with thin vascular walls. Abundant neuroid tumor cells (arrowheads) and focal cystoid degeneration with a myxoid background were seen (hematoxylin-eosin, original magnification x 480). (C) Spindle-shaped tumor cells (arrowheads) were found mostly in the tumor base, adjacent to the sclera (S), and blended with some normal smooth muscle cells (arrows) (hematoxylin-eosin, original magnification x 120).
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FIGURE 5: Tumor cell nuclei appealing to be ovoid and polyhedral, with occasional aggregation of mitochondria (arrows) around perikaryon. Abundant cell processes containing fine filaments with their associated densities (arrowheads) were noted. Cell processes were interwoven and formed the tumor matrix (original magnification × 3720).

FIGURE 6: Pinocytotic vesicles (arrows), segments of poorly formed basement membrane and desmosomal-like cell junctions (arrowheads), were seen in tumor cells (original magnification × 11900).

COMMENT

Since the term "mesectodermal leiomyoma" was coined in 1977,¹ several case reports have appeared in the medical literature.¹⁷ Our 8-year-old patient is younger than the other patients described in the literature, and the patient's tumor shows some unique clinical and electron microscopic features not described previously.

Mesectodermal leiomyoma has a characteristic appearance on light microscopy, suggestive of neuropil tumors¹² and compatible with ganglionic, astrocytic, and even peripheral nerve tumors. These tumors consist of large polyhedral cells with ovoid nuclei and prominent nucleoli, abundant eosinophilic cytoplasm, and a fine fibrillary background reminiscent of a neuropil of cell processes. Pleomorphic nuclei, the orientation of some of the cell processes toward the capillaries, and the rich vascular network all suggest a glial tumor. A leiomyoma classically comprises intertwining bundles of spindle-shaped cells with elongated nuclei, which may be absent, except at the base of the tumor. Since phosphotungstic acid-hematoxylin stains both neurofibrils and myofilaments, it is not helpful to differentiate neuropil tumors from myogenic tumors. However, electron microscopic characteristics are diagnostic. The occasional clusters of mitochondria near the perikaryon, abundant fine filaments with fusiform densities, basement membrane, and small caveolae of plasmalemma betray the leiomyomatous characteristics of this tumor.

The term "mesectodermal" refers to the connective tissue of the head and neck derived from the neural crest. While the connective tissues of the body and smooth muscles are derived from the mesoderm, the connective tissues of the head and neck are derived from the neural crest. Uveal cells, pericytes, and the smooth muscle fibers of the ciliary body originate from the neural crest. The smooth muscle of the iris is derived directly from the neuroectodermal iris pigment epithelium.

The mesectodermal origin of the ciliary muscle may explain the neuroid histologic characteristics of these unusual tumors. Furthermore, observation of melanin granules in scattered tumor cells further confirms that these tumors have the same origin as uveal melanocytes, which are derived from the neural crest. Some of the melanin granules were of an irregular shape and suggested malformation. However, the granules were fully mature, homogeneously dense, and showed filaments or rodlets. Jakobiec and Iwamoto² described a mesectodermal leiomyoma associated with a nevus, a lesion that also originates from the neural crest. Takagi et al⁶ reported a case of mesectodermal leiomyoma in which melanocytes

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were scattered throughout the tumor, thus providing additional evidence for the neural crest theory.

The clinical presentation of this tumor in our patient was also unusual. The translucent characteristics of this lesion and the MRI findings suggested a cystic lesion.\textsuperscript{10} Oscar-Croxatto and Malbran\textsuperscript{4} also reported a case of mesectodermal leiomyoma of the ciliary body, which appeared to transilluminate when observed with indirect illumination. There is a possibility that the tumor in our case was highly vascularized, and showed cystic degeneration. However, variable ultrasound internal reflectivity suggested a more solid lesion. These features misled the clinician to believe that this was a cystic lesion that could be diagnosed by aspiration.

Finally, mesectodermal leiomyoma is believed to be benign, but its forward extension to the root of the iris, resulting in atrophic iris and rubecosis iridis, suggests that this tumor may be locally aggressive.

\textbf{REFERENCES}
\begin{enumerate}
\item Orsini JG, Daicker B, Cardillo-Piccolino T. Mesectodermal leiomyoma of the ciliary body extending into the anterior chamber. \textit{Ophthalmologica}. 1987;191:127-129.
\end{enumerate}