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CASE REPORT

Leiomyoma of The Ciliary Body and Hemangiopericytoma of the Choroid

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Two unusual uveal tumors occurring in eyes enucleated for presumed malignant melanoma are discussed. One was a leiomyoma of the ciliary body, affecting a 22-year-old female, the other a hemangiopericytoma of the choroid in an 84-year-old male patient. The latter case is the fourth intraocular hemangiopericytoma reported in the literature to date. The histopathologic diagnosis was confirmed by immunohistochemistry and electron microscopy. (Pathology Oncology Research Vol 2, No1–2, 89–93, 1996)

Key words: intraocular non-melanocytic tumors, leiomyoma, hemangiopericytoma

Introduction

The clinical differential diagnosis of uveal tumors deals with two main problems: the distinction between benign and malignant melanocytic tumors,[4,5] and the differentiation of melanocytic from non-melanocytic tumors.[3,5] The purpose is to avoid under- or over-treatment and to preserve visual function, whenever possible, without endangering the patient's life. Non-melanocytic primary tumors of the uvea are rather rare, therefore not only the clinical, but the histopathologic diagnosis may be challenging, as well. This paper calls attention to two kinds of tumors that occur mostly in the soft tissues but can also develop in the eye.

Materials and Methods

Light microscopy

One of the enucleated globes was fixed in 10% buffered formalin and the other, referred for consultation, was fixed in Bouin fixative. Both were routinely processed and embedded in paraffin wax. Sections were stained with HE (hematoxilin-eosine), Masson trichrome, PAS (periodic acid-Schiff) and reticulin. Immunohistochemistry was performed on the paraffin-embedded material.

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Electron microscopy

In both cases small blocks were cut from the formaldehyde or Bouin-fixed samples, postfixed with 2% phosphate-buffered glutaraldehyde and processed for Epon embedding.

Case 1

A 22-year-old female had a two-year lasting complaint of "ocular inflammation" in the left eye before a mass was noted in the ciliary body. The tumor, a smooth rounded lesion, occupied the 7 to 11 o'clock position and extended backwards to the choroid. An A-scan ultrasonography revealed high to medium internal reflectivity of the mass. Color Doppler imaging disclosed a well developed arterial and venous vascular network. The tumor was clinically considered a malignant melanoma and the eye was enucleated after a negative checkout for possible tumor dissemination. After a 30 month follow-up, there is still no evidence of recurrence.

Pathology

Gross findings

The globe was opened horizontally. On the nasal side, a pinkish fleshy tumor was found, measuring 14×12×7 mm. The tumor expanded within the ciliary body and supraciliary space causing a slight bulge of the sclera *(Fig. 1)*.

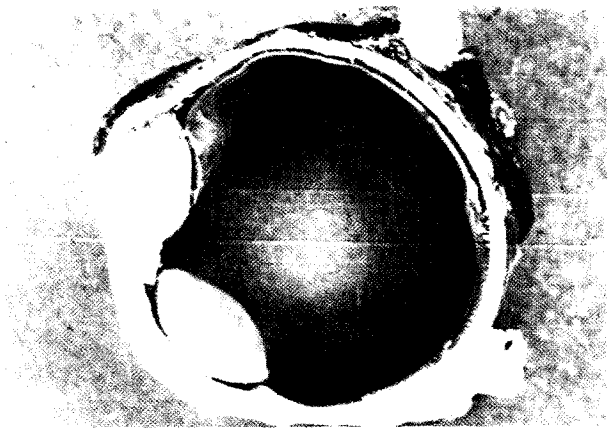

Figure 1. Leiomyoma of the ciliary body. A smooth-surfaced, sharply circumscribed fleshy tumor is present in the ciliary body with extension into the suprachoroidal space toward the equator of the globe.

Light microscopy

The tumor was covered by the pigmented and non-pigmented ciliary epithelium. The remaining ciliary processes were distorted. Markedly compressed, preserved bundles of the ciliary muscle were recognized. The sclera was not invaded, but slightly thinned over the mass. A long ciliary nerve crossed the tumor unaffected. Retinal pigment epithelium proliferation and a partial retinal detachment with subretinal exudate was observed. The tumor cells were organized into bundles. The cells themselves were polygonal in shape with an abundant eosinophilic or clear cytoplasm, large oval nuclei showing a fine dispersed chromatin and occasional nucleoli. The cells had slender cytoplasmic processes which tapered into a fibrillary background. The tumor was highly vascular. The vessels were lined by a flattened endothelium, some of which were dilated and sometimes surrounded by a clear space. Slender tumor cell processes straddled this space and reached the thin vascular wall *(Fig.2)*. A slight cellular pleomorphism was noted throughout the tumor, however only one mitosis was found. The Masson stain demonstrated longitudinal intracytoplasmic fibrils and the reticulin stain a moderately well developed reticular network. The histologic picture suggested a neoplasm of smooth-muscle origin.

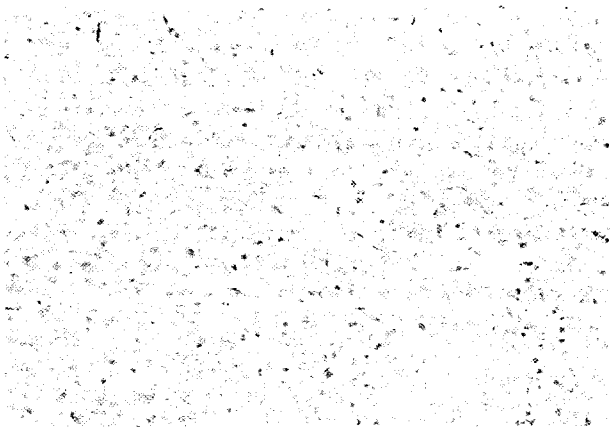

Figure 2. *The tumor is cellular and markedly fibrillar. Tumor cells are arranged in tightly packed bundles around thin-walled, compressed or dilated vessels. Some vessels are surrounded by a clear space which is straddled by slender tumor cell processes. The tumor cells are plump, polygonal in shape. The cytoplasm is acidophilic or sometimes clear. (lens 20×)*

Electron microscopy

Unfortunately, the ultrastructure of tumor cells was poorly preserved. Nevertheless their characteristics were unequivocal. The cells were elongated or irregular in shape owing to the presence of long cellular processes. The latter contained bundles of parallel cytoplasmic filaments showing fusiform densities *(Fig.4)* which identified them as smooth muscle cells. The tumor cells were partly surrounded by a basement membrane. Plasmalemmal densities and a few cellular junctions made intercellular contacts.

Figure 3. *Intracytoplasmic filaments of tumor cells show extensive smooth-muscle actin reactivity. (lens 40×)*

Immunohistochemistry

Smooth-muscle actin, vimentin, NSE, GFAP and S-100 were used as markers. The cytoskeletal filaments showed extensive positivity for smooth-muscle actin *(Fig.3)* and vimentin. S-100 reaction was noted in melanocytes and in the ciliary nerve crossing the tumor, but not in tumor cells. GFAP or NSE were negative.

Case 2

The right enucleated globe of an 84-year-old male was referred to our ophthalmic pathology laboratory for evaluation. 28 months before enucleation the patient underwent an uncomplicated right-side cataract extraction and pos-

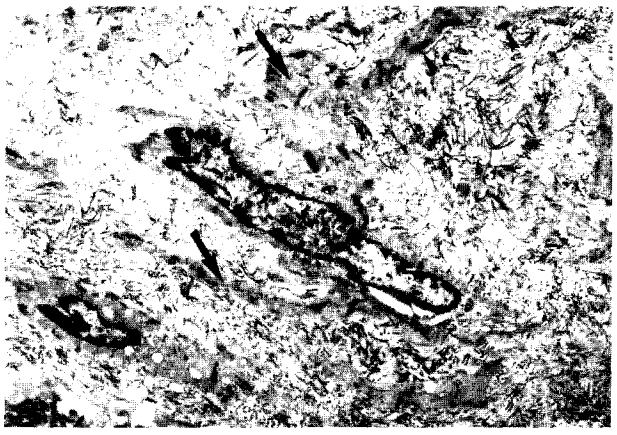

Figure 4. Tumor cells are elongated, have long wavy cellular processes (arrows) tapering into a fibrillary background. Bundles of parallelly arranged cytoplasmic filaments with fusiform densities (arrowheads) are depicted. (7600×)

terior chamber lens implantation. The cataract surgery was performed in our department and, upon discharge, the ocular fundus was normal. He complained of visual impairment. Fundus examination disclosed a choroidal tumor with markedly dilated vessels in the retina overlying the mass. An A and B scan ultrasonography confirmed the diagnosis. The enucleation was performed at the referring hospital after a limited check for metastasis: thoracic X-ray showed emphysema, and liver functions were normal.

Pathology

Gross findings

The globe was opened in an antero-posterior vertical plane. The posterior chamber was occupied by a lens implant with a whitish membrane attached to its posterior surface. Arising from the choroid, a tan-colored mass, measuring 18×12×11 mm, protruded into the vitreous. The central part of the mass gave the impression of being hemorrhagic, however this was not proved to be true at the microscopic level *(Fig.5)*.

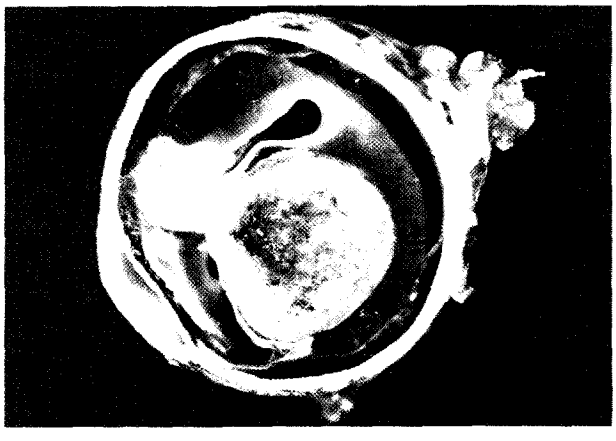

Figure 5. Hemangiopericytoma of the choroid. The tumor has a spongy structure, is tan-colored, and the center looks hemorrhagic owing to blood-filled, markedly dilated sinusoid-like spaces.

Light microscopy

The tumor arose from the choroid, was not encapsulated and ill-demarcated. The tumor invaded the Bruch's membrane and the inner scleral lamellae. The center of the tumor exhibited a conspicuous sinusoidal pattern, with markedly dilated, blood-filled vascular spaces lined by flattened endothelial cells and surrounded by tumor cells. Toward the periphery of the tumor, the vascular pattern was less evident, the proliferating tumor cells squeezing the vessels to irregular, narrow clefts *(Fig.6)*. An antler-like pattern was discernible with reticulin stain. The tumor cells were plump, spindle shaped, with indistinct cellular borders. Nuclei were vesicular, plump and mildly pleomorphic, with centrally placed, medium-sized, slightly eosinophilic nucleoli *(Fig7)*. A few scattered mitoses (one to two per 10 high power fields) were seen. A diagnosis of hemangiopericytoma was made.

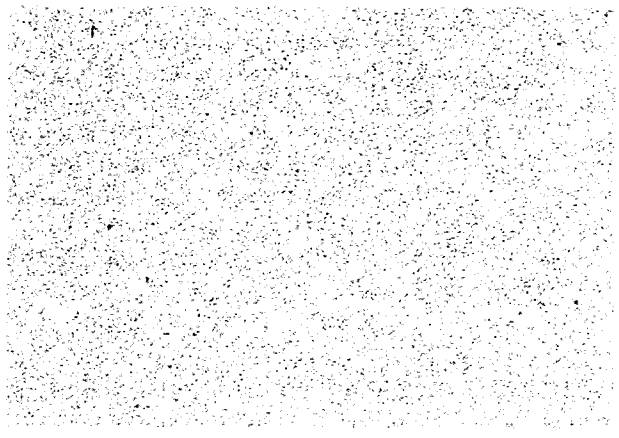

Figure 6. Typical architectural pattern of hemangiopericytoma: the tumor cells are tightly packed around vascular channels lined by a flattened endothelium. Some of the vessels are squeezed to a narrow cleft while others are dilated and filled with blood. (lens 20×)

Electron microscopy

Preservation of the material was suboptimal, nevertheless tumor cells embedded in a collagen matrix could be identified as pericytes (not shown).

Immunohistochemistry

The tumor cells evidenced overwhelming positivity for vimentin *(Fig.8)*, were negative for desmin, and F–VIII factor was demonstrated only in the endothelial cells.

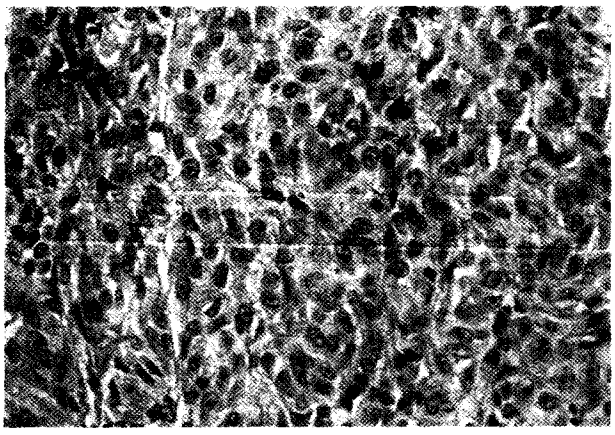

Figure 7. Solid cellular area of the tumor: cells have indistinct borders, the nuclei are round or oval with a conspicuous, centrally located nucleolus. Note the focal palisading of cell nuclei. (lens 40×)

Discussion

Leiomyoma and hemangiopericytoma are rather uncommon intraocular tumors which are frequently misdiagnosed clinically as malignant melanoma.[1,7,13,17,26] Ciliary body leiomyomas have a striking predilection for women. Of the reported cases only four have occurred in men.[23,27,28] Hemangiopericytoma of ophthalmologic interest has been reported in the orbit,[8] conjunctiva[25] and lacrimal sac.[2] Intraocular presentation has been recorded in three cases only.[1,13,19] The tumor has no sex preference,[11] however the present case is the first intraocular hemangiopericytoma being reported in a man.

Intraocular leiomyomas generally consist of fusiform cells arranged in fascicles.[11] Some of the ciliary body leiomyomas, however, as in our case, have a misleading light microscopic appearance. It is widely accepted that these leiomyomas arise from the ciliary muscle, and have been labeled "mesectodermal"[15] owing to the neural crest-origin of the ciliary muscle. They have even been referred to as hybrid myogenic-neurogenic tumors[7,16] on morphological grounds, but this has not been substantiated by immunohistochemistry or electron microscopy. In a different case,[26] electron microscopic features of the tumor cells were more consistent with pericytes than with smooth muscle cells. A vascular tumor of the choroid[14] also displayed smooth muscle and pericytic features only at the ultrastructural level. In the largest series of intraocular leiomyoma reported to date,[23] all the tumors showed intensive immunoreactivity for muscle-specific actin and smooth-muscle actin, and negative staining for S-100 protein. In previous case reports[27,28] and in our current case, the additional GFAP and/or NSE negativity demonstrates the still existing controversy concerning the histogenesis of ciliary body leiomyomas. We do not know if the morphological diversity reflects a heterogeneous, i.e. mesodermal and/or vascular origin. Demonstration of actin isoforms expressed by smooth muscle cells might answer the problem since vascular smooth muscle cells predominantly express α-isoform, while parenchymal smooth muscle cells have a large proportion of the β-isoform of actin.[21] But, whatever the histogenesis is, this intraocular neoplasm carries an excellent prognosis as no recurrence has been reported even for locally resected cases during a follow-up period extending from two to five years.

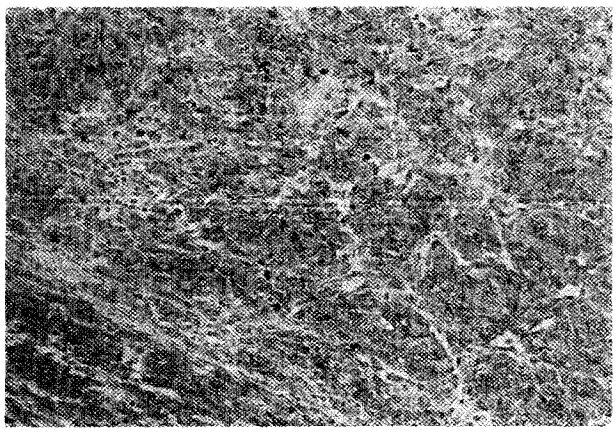

Figure 8. The cytoplasm of tumor cells shows extensive vimentin reactivity. (lens 20×)

Hemangiopericytoma is an uncommon soft-tissue tumor derived from pericytes.[24] Diagnosis is mainly based on architectural pattern, as pericytes lack individual cellular and immunohistochemical features.[11] Immunohistochemically the tumor cells express vimentin, but react also with factor XIIIa and HLA-DR.[18] The present case reacted extensively with vimentin and was negative for desmin.

The unpredictability of the biological behavior of the tumor based on morphological or clinical criteria has been emphasized in previous studies. This is also illustrated by the three reported cases of intraocular hemangiopericytoma. One[19] has remained almost unchanged for eight years after xenon arc photocoagulation with no invasion of the sclera seen on histopathological examination. In two further patients,[1,13] the presenting symptoms were noted only one to three months before diagnosis of the intraocular tumor, suggesting a rapid growth. The current case showed invasion of the inner third of the sclera, nevertheless the time elapsed since the enucleation is too short to evaluate whether this fact had any prognostic value. A prominent clinical feature caused by the rich vascularity of the tumor is teleangiectasia of the overlying structures, involving episcleral[1,13] or teleangiectasia of retinal vessels[19] as in our case. It is noteworthy that dilated episcleral vessels were important clinical signs in intraocular leiomyomas as well.[7,15,16,23]

Accumulating data on unusual uveal tumors has led to an increased awareness of clinicians and pathologists and to a steadily decreasing rate of enucleation performed as a

consequence of misdiagnosed malignant melanoma.[3,6,9] However, there is still a group of uveal neoplasms which are difficult to distinguish clinically from malignant melanoma.[5] The number of cases was 13 in 6169 enucleated eyes in a study analyzing an 11-year period,[3] and 13/369 over a 50 year period;[9] the rate was higher for tumors of the anterior uvea.[20] Fine-needle aspiration biopsy[4,5] and magnetic resonance imaging[1] was suggested to improve diagnostic accuracy.

The histopathologic differential diagnosis of intraocular soft tissue tumors is based on morphological features substantiated by electron microscopy and immunohistochemical reactions.[10,21,22] A recent retrospective study including 24 iris and 3 ciliary body tumors, previously diagnosed as leiomyomas, disclosed that, based on immunohistochemical findings, all the iris tumors were in fact, malignant melanomas.[12] Besides amelanotic melanoma, the histopathological differential diagnosis of intraocular leiomyoma includes schwannoma, neurofibroma, astrocytoma and hemangiopericytoma. Intraocular hemangiopericytoma itself should be distinguished from leiomyoma and schwannoma. Other tumors which sometimes exhibit a hemangioma-like pattern (fibrous histiocytoma, glomus tumor, synovial sarcoma and mesenchymal chondrosarcoma)[11] are not intraocular tumors.

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