UC Irvine
UC Irvine Previously Published Works

Title

Results of Trabectome Surgery Following Failed Glaucoma Tube Shunt Implantation

Permalink

https://escholarship.org/uc/item/23m0k9c6

Journal

Medicine, 94(30)

ISSN

0025-7974

Authors

Mosaed, Sameh
Chak, Garrick
Haider, Asghar
et al.

Publication Date

2015-07-01

DOI

10.1097/md.0000000000001045

Peer reviewed

Malignant teratoid medulloepithelioma with retinoblastic and rhabdomyoblastic differentiation

James B. Earl, MD, PhD,[a] Don S. Minckler, MD, MS,[a] Thomas C. Lee, MD,[b,c] and A. Linn Murphree, MD[b,c]

We describe an unusual case of malignant teratoid medulloepithelioma in which distinct populations of tumor cells with different immunohistochemical staining patterns existed within the same eye. A neuroblastic population exhibited atypical features of retinoblastoma, including organization into pseudo-Flexner-Wintersteiner and Homer-Wright rosettes. Other populations evolved in strikingly different patterns, with large fields of cells resembling astrocytes and intervening streams of spindle cells that suggested smooth muscle. The spindle cell population was negative for smooth muscle antigen but stained positively for desmin, myoglobin, and myogenin. Under high magnification, the desmin, myoglobin, and myogenin-staining cells exhibited striations consistent with skeletal muscle differentiation.

Case Report

A 1-month-old girl born at 31 weeks' gestation (birth weight 2.19 kg) was found during a retinopathy of prematurity screening to have a stalk extending from the posterior pole to the lens, clinically consistent with persistent hyperplastic primary vitreous (PHPV) and confirmed by ultrasound imaging. A follow-up examination 2 weeks later revealed enlargement of a vascularized plaque on the posterior surface of the lens that blocked the view to the posterior pole.

The patient was referred to the Vision Center at Children's Hospital Los Angles, where at clinical examination PHPV also was suspected. Findings on ultrasonography revealed a large intraocular mass without calcification. Computed tomography also revealed no calcifications. The patient underwent examination under anesthesia the next day (Figure 1A). At that time, the clinical diagnosis was possible retinoblastoma. A fine-needle aspiration biopsy of the vitreous mass through peripheral clear cornea inferior nasally was performed.

Histopathologic evaluation of cell block sections from the biopsy revealed myriad clusters of small neuroblastic cells, with densely basophilic nuclei and scanty cytoplasm, some with poorly organized cell layers suggestive of retina or poorly organized rosettes (Figure 1B). Small vessels, hemorrhage, and clumps of pigment also were present. Other fields contained faintly eosinophilic material suggestive of neuropil (brain tissue). The right eye was enucleated at 3 months of age because of high suspicion of retinoblastoma.

Microscopic evaluation of the specimen revealed several distinct populations of abnormal cells filling the vitreous cavity (Figure 2). The anterior portion contained loosely arranged cells resembling astrocytes interspersed with streams of smooth muscle-like cells with central elongated elliptical nuclei and tapering or strap-like cytoplasm (Figure 2).

The cell population posteriorly (Figure 2) had compressed and invaded the optic disk and choroid temporal to the disk but had not invaded the lamina cribrosa or intraocular or orbital optic nerve (Figure 3). The posterior tumor was suggestive of retinoblastoma, including numerous Flexner-Wintersteiner–like rosettes with well-defined lumens and also many Homer-Wright rosettes, all embedded in sheets of small neuroblastic cells (Figure 4A). Necrosis and calcification, typical of retinoblastoma, were not noted. Nasally in the equatorial region a (±4 mm) colobomatous gap in the retinal pigment epithelium (RPE) and choroid was present, into which the tumor expanded to contact the long posterior ciliary nerve exposed by thinned sclera (Figures 2 and 4B). The RPE on both sides of the coloboma recurved anteriorly and posteriorly under adjacent dysplastic tissues (Figure 4B).

The only relatively well-differentiated retina was noted on the far periphery of the temporal side of the anterior mass. Here, middle and outer nuclear layers were present and nubbins of eosinophilic material resembling photoreceptor inner segments protruded through a distinct external limiting membrane, suggesting normal retinal differentiation through at least 6 months' gestation. We did not detect anterior chamber seeding or tumor spread to the cornea after the transcorneal biopsy. The surgeon did not believe the lens had been injured, and multiple sections did not reveal lens injury or pathologic cataract. Periodic acid Schiff preparations demonstrated an intact lens capsule. The angles were open and there was no neovascularization on the iris. Mild entropion was apparent, with infolding of the iris sphincter. One section revealed a defect in the iris nasally, correlating with the needle biopsy. There was no
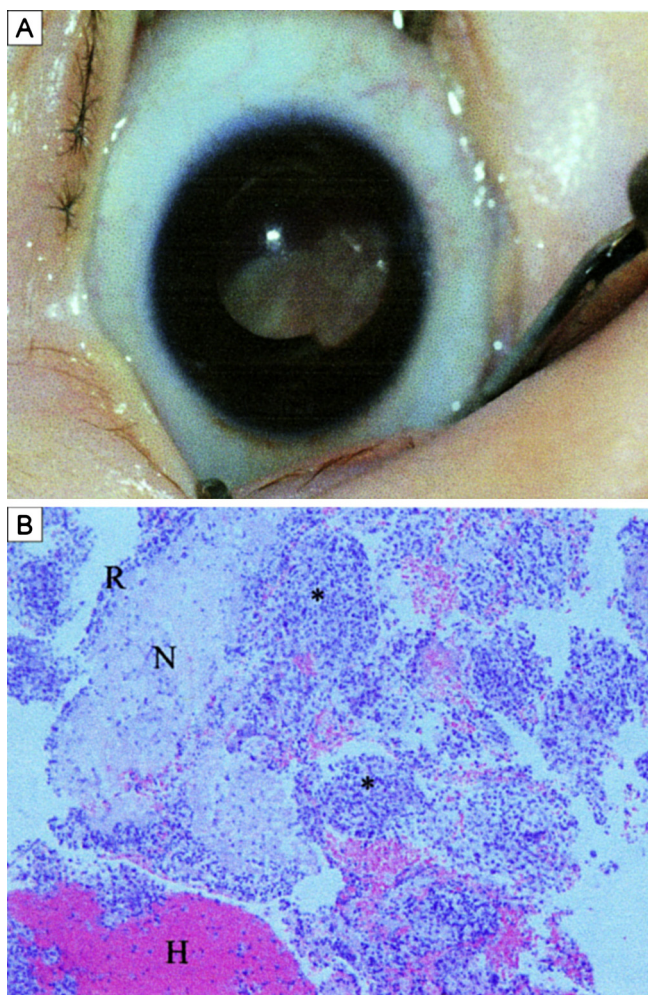
FIG 1. A, External view of right eye. Inferior nasal mass measures about 12 mm basal diameter by ultrasound. Nasal pupil distortion was probably caused by posterior synechiae. B, Hematoxylin and eosin–stained section from biopsy. Retina (R), brainlike tissue or neuropil (N), hemorrhage (H), and poorly organized rosettes (asterisks) are all highly suggestive of retinoblastoma.

FIG 2. Section of the globe demonstrating 2 populations of tumor cells labeled α (anterior) and β (posterior). Numerous pseudo Flexner-Wintersteiner rosettes and Homer-Wright rosettes were present in part β. The arrow indicates the area of a coloboma nasally with thinned inner sclera, absent choroid, and tumor intruding into or possibly arising from its edges (hematoxylin and eosin, original magnification 1:1).
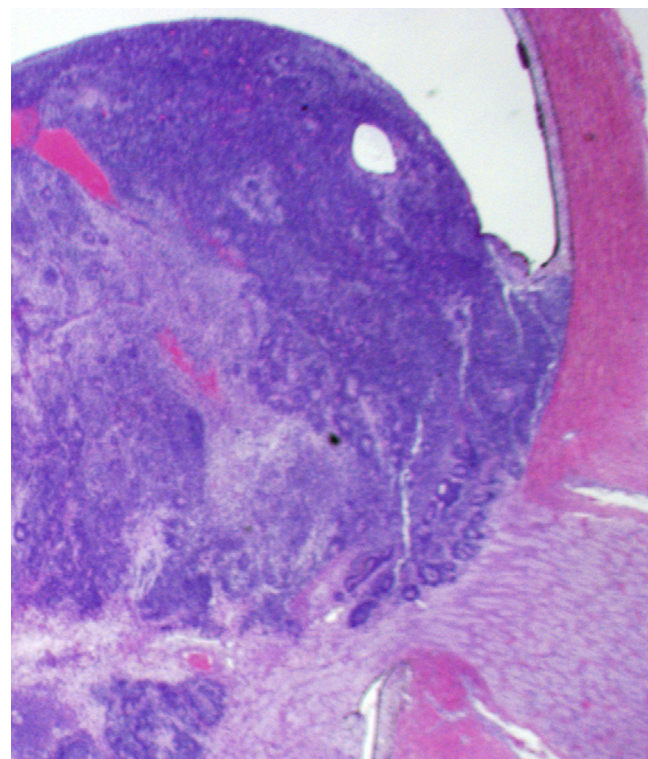
FIG 3. Optic nerve with choroidal invasion temporally and tumor intruding into disk tissues (hematoxylin and eosin, original magnification ×50).

cyclitic membrane or any evidence of extraocular spread of tumor.

Several stains were used to determine the cell types in the tumor. Synaptophysin, a neuron-associated integral membrane glycoprotein of presynaptic vesicles, is normally concentrated in synaptic regions of the retina. Globe sections stained for synaptophysin contained focal areas of positivity throughout the posterior tumor population within the pseudo-rosette–forming regions (Figure 2), consistent with previous studies.[1,2] Glial fibrillary acidic protein (GFAP) is an intermediate filament found in astrocytes and Müller cells.[2] Globe sections stained heavily for GFAP throughout the optic nerve and plexiform layers of the retina in the temporal periphery but demonstrated only rare faint positivity in the posterior tumor population, possibly consistent with reactive gliosis from preexisting
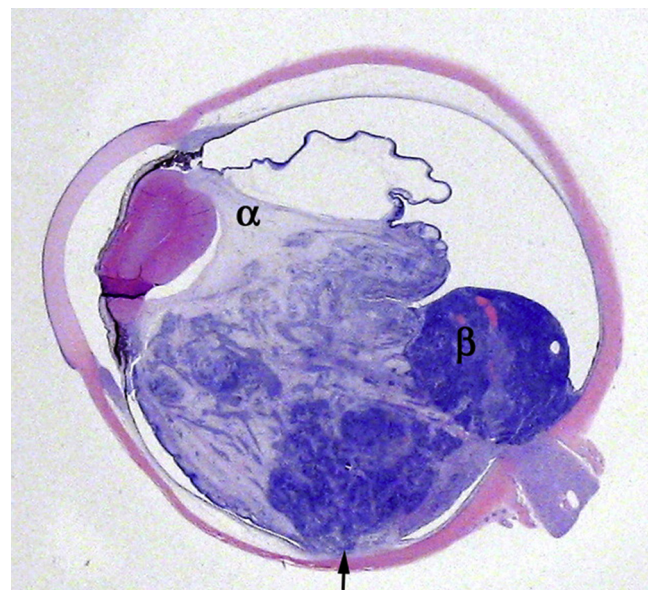
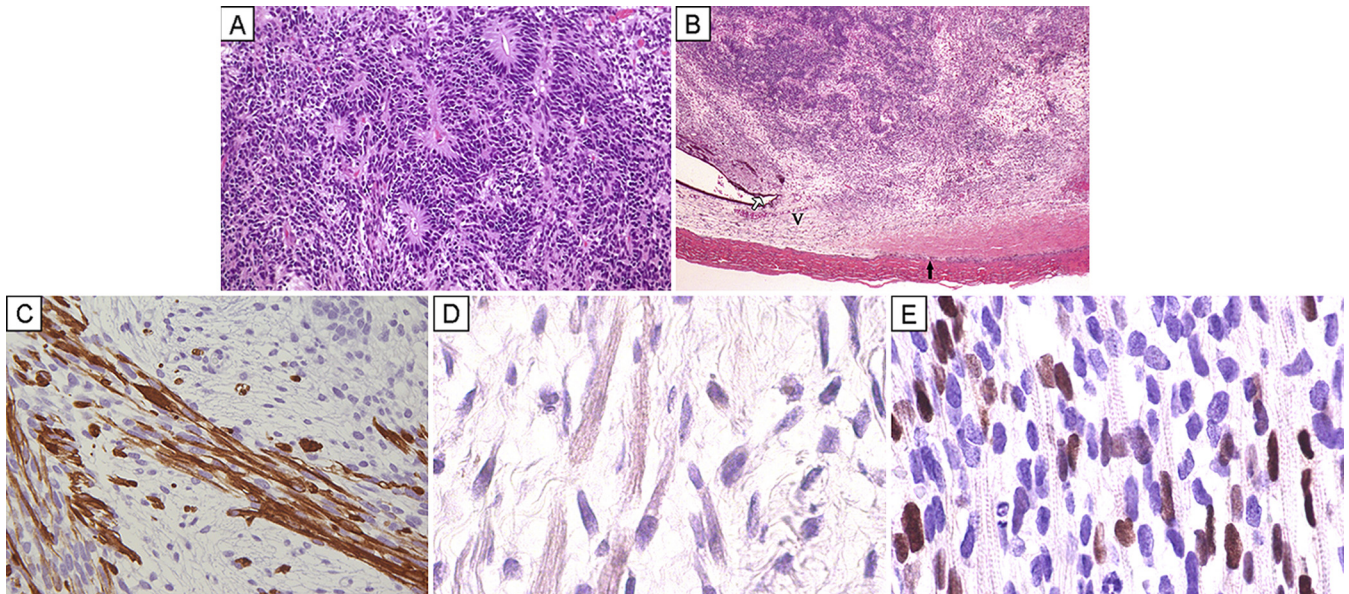**FIG 4.** A, Photomicrograph of posterior tumor (β in Figure 2) illustrating atypical Flexner-Wintersteiner rosettes which were more elliptical and multilayered than is typical for retinoblastoma embedded in sheets of neuroblastic cells. Alcian blue staining was negative in the centers of these pseudo Flexner-Winterstiner rosettes (hematoxylin and eosin, original magnification ×100). B, Photomicrograph demonstrating ±4 mm nasal coloboma with absent RPE, choroid, and thinned inner sclera. Tumor intrudes into or arises from the eye wall defect. A choroidal vein (V) extends from the tumor base into the choroid at the anterior edge of the RPE defect. Recurving of the RPE (white arrow) anteriorly under the dysplastic tumor mass is apparent. The long posterior ciliary nerve is indicated by the black arrow (hematoxylin and eosin, original magnification ×31.25). C, Photomicrograph of anterior tissues including several fusiform and strap-like cells manifesting striations (desmin immunoperoxidase, original magnification ×400). D, Photomicrograph from anterior tumor area demonstrating faint striations within strap-like cells (myoglobin immunoperoxidase, original magnification ×787.5). E, Strap-like cells from the anterior portion of the tumor demonstrating long segments of intracellular striations, although fainter than with desmin (myogenin immunoperoxidase, original magnification ×400).

astrocytes.[1,2] Despite astrocytic-appearing cells in the anterior tumor, no GFAP uptake was noted.

We used 4 muscle-specific immunostains: smooth muscle actin (SMA), desmin, myoglobin, and myogenin. SMA defines myogenous differentiation when applied to tumor cells but is also present in normal eye tissue, including blood vessels, the ciliary muscle, ciliary processes, and iris muscles.[3] Staining with SMA revealed no uptake throughout the tumor, except in perivascular areas. SMA-positive capillaries were especially numerous along the plane of the RPE across the coloboma, implying that the tumor had co-opted choroidal circulation.

Desmin, however, stained the smooth muscle–like cells arranged in fascicles throughout the anterior population of tumor. Desmin is an intermediate filament characteristically found in muscle cells of both smooth and skeletal origin.[2] High magnification imaging of desmin-stained sections revealed striations within many of the smooth muscle–like cells in the anterior portion of tumor (Figure 4C).

Myoglobin and myogenin immunoperoxidase staining also demonstrated striations within similar cells in the anterior population, although not so vividly as desmin (Figure 4D–E). Both of these are considered excellent markers for muscle elements in mature and embryonal cells in formalin-fixed paraffin processed tissues.[4,5]

Less-obvious streams of similar cells also permeated the posterior tumor.

Alcian blue staining was faintly positive anteriorly and along the ciliary epithelium. The pseudo-rosette lumens did not stain positively with Alcian blue, as would be expected for Flexner-Wintersteiner retinoblastoma rosettes. Ki-67, a well-established nuclear marker of cell proliferation, was most positive among clusters of cells, including those forming pseudo-rosettes in the posterior portion of the tumor (estimated at 10% of that population). Mitoses among this population were estimated at one per high-power field. The nuclei of cells in the anterior neuropil areas were only lightly stained with this marker (estimated at <2% of the population). Consistent with Ki-67, mitoses in the anterior population were rare.

Discussion

Intraocular medulloepitheliomas are rare primitive tumors thought to arise from the nonpigmented medullary epithelium lining the neural tube. They are classified as either teratoid or nonteratoid and may be either benign or malignant. Teratoid tumors contain heterotopic elements composed of cells from different embryonic germ layers, whereas nonteratoid, or simple, tumors demonstrate pure proliferation of embryonic neural tube epithelium.[3] The

histopathologic criteria for malignancy of both types are as follows: (1) poorly differentiated neuroblastic cells that resemble retinoblastoma, (2) exceptional pleomorphism and/or mitoses, (3) sarcomatous areas, and (4) invasion of the uveal stroma, sclera, and other ocular structures with or without extraocular extension.[3] We classified the neoplasm in this case as a malignant teratoid tumor because of its retinoblastic appearance, sarcomatous areas, and invasion of the optic disk and choroid.

Most intraocular medulloepitheliomas arise from the nonpigmented epithelium of ciliary body neuroectoderm; possible origins from the optic nerve or retina have also been reported.[6] Although we could not clearly identify the origin of our tumor as arising from the ciliary epithelium, its close proximity to this structure and histologic appearance with mixed cellular elements are more indicative of medulloepithelioma than retinoblastoma. Also, the lack of calcification on ultrasound and computed tomography scans is more indicative of medulloepithelioma than retinoblastoma. Other consultants concurred that the rosettes were atypical of retinoblastoma and more suggestive of medulloepithelioma.

Alternatively, this neuroblastic tumor could have arisen from persisting pluripotential medullary epithelium, perhaps related to the coloboma. The presence of a coloboma provided two additional "edges" besides the anterior lip of the optic cup and the optic groove from which persisting medulloepithelium may have proliferated.

Medulloepitheliomas are typically unilateral and unifocal and usually arise before the age of 6 years, with no hereditary pattern.[3] Treatments include local resection or enucleation if, as in this case, visual potential is deemed poor. The prognosis is good if there is no extraocular extension. At last follow-up, more than 1 year after enucleation, there was no evidence of distant metastases or recurrence in our patient.

We speculate that the coloboma arose between approximately gestational day 30, when the optic vesicle invaginates, and 7 weeks' gestational age, by which time the optic fissure has normally fused.[7] We believe that tumor growth paralleled normal retinal development until late because some mature retinal elements were present and outer retinal maturation is not complete until approximately 6 months' gestation.[7]

In conclusion, this case illustrates that medulloepitheliomas can be clinically confused with PHPV or retinoblastoma and can show retinoblastic and rhabdomyoblastic differentiation. In this case, the needle biopsy confirmed the malignant nature of the lesion.

Acknowledgments

References

1. Rodrigues MM, Wiggert B, Shields J, et al. Retinoblastoma: Immunohistochemistry and cell differentiation. Ophthalmology 1987;94:378-87.
2. Donoso LA, Shields CL, Lee EY. Immunohistochemistry of retinoblastoma. A review. Ophthal Paediatr Genet 1989;10:3-32.
3. Broughton WL, Zimmerman LE. A clinicopathologic study of 56 cases of intraocular medulloepithelioma. Am J Ophthalmol 1978;85:407-18.
4. Corson JM, Pinkuw GS. Intracellular myoglobin-a specific marker for skeletal muscle differentiation in soft tissue sarcomas: An immunoperoxidase study. Am J Pathol 1981;103:384-9.
5. Kumar S, Perlman E, Harris CA, Raffeid M, Tsokos M. Myogenin is a specific marker for rhabdomyosarcoma: An immunohistochemical study in paraffin-embedded tissues. Mod Pathol 2000;13:988-93.
6. O'Keefe M, Fulcher T, Kelly P, et al. Medulloepithelioma of the optic nerve head. Arch Ophthalmol 1997;115:1325-7.
7. Sigelman J, Ozanics V. Retina. In: Jakobiec FA, ed. Ocular Anatomy, Embryology, and Teratology. Philadelphia (PA): Harper and Row; 1982: 441-506.