Primary Intraocular Malignant Extrarenal Rhabdoid Tumor: A Clinicopathological Correlation

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ABSTRACT

Malignant extrarenal rhabdoid tumor is a rare and highly aggressive tumor of childhood. Intraocular involvement by malignant extrarenal rhabdoid tumor has only been described once as a metastasis. No report exists in published literature describing a primary intraocular malignant extrarenal rhabdoid tumor. The authors report the first such case along with its clinico-radiological features and histopathologic and electron microscopic characteristics. **[J Pediatr Ophthalmology Strabismus 2013;50:e18-e20.]**

INTRODUCTION

Malignant rhabdoid tumor of the kidney was first described in 1978 as a variant of Wilm's tumor.[1] In the central nervous system, it is also referred to as "atypical teratoid-rhabdoid tumor."[2] Malignant extrarenal rhabdoid tumors (MERTs) have been described at several anatomical locations, including the orbit, which is an extremely rare location.[3-5] Intraocular MERT is even more rare and has been described as metastases in a case report.[6] No report of a primary intraocular MERT exists in literature and we describe one such case with its clinico-radiological and histopathologic features.

CASE REPORT

A 1-month-old male infant had a history of reddish discoloration of the left eye for 3 days associated with bulging of the cornea and an increase in size of the eye. A fungating, tan to dark brown colored mass was seen protruding through a limbal tear from the 12- to 3-o'clock positions (**Figure 1A**). Scan of the left eye demonstrated a mass lesion filling the entire vitreous cavity with moderate to low reflectivity (**Figure 1B**). Hematological examination and systemic work-up was negative for any primary tumor. Due to suspected intraocular malignancy and no visual potential, the globe was enucleated. A small extraocular spread in contiguity to the intraocular tumor was noted intraoperatively.

Gross examination revealed an intraocular tumor with a variegated appearance composed of solid hemorrhagic and necrotic foci (**Figure 1C**). In the region of the limbus, the tumor was seen infiltrating the extraocular tissues (**Figures 1C** and **1D**). Microscopic examination showed a cellular tumor composed of sheets of discohesive, polygonal to epithelioid cells with abundant eosinophilic, glassy to amphophilic cytoplasm (**Figure 1E**). The nuclei were large, round to horseshoe shaped, and vesicular, with prominent nucleoli. Many cells displayed pale eosinophilic, intracytoplasmic inclusions characteristic of a rhabdoid morphology (**Figure 1F**). Mesenchymal differentiation with spindle cells was seen in some foci. Mitotic activity was moderate with presence of few abnormal mitoses. The tumor involved the optic nerve with a retrolaminar spread of approximately 2 mm. Rhabdomyosarcoma, epithelioid sarcoma, and MERT were considered in the differential diagnosis.

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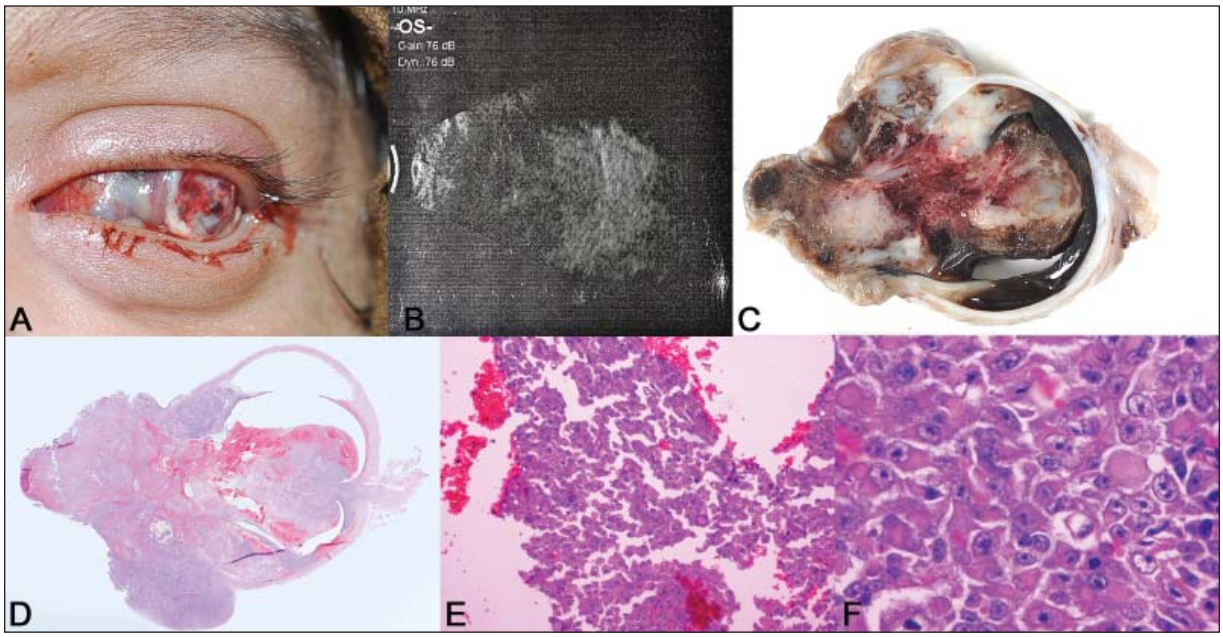

Figure 1. (A) Clinical external photograph of the left eye showing a fungating, tan to dark brown colored mass protruding through the limbal area from the 12- to 3-o'clock positions. (B) Scan of the left eye demonstrated a mass lesion filling the entire vitreous cavity with moderate to low reflectivity. (C) Cut section of the specimen showing an intraocular variegated tumor perforating through the limbus into the extraocular tissues. (D) Whole mount section of the gross specimen. (E) Microphotograph showing sheets of rhabdoid tumor cells (hematoxylin–eosin, original magnification ×100). (F) Microphotograph at high magnification showing numerous rhabdoid tumor cells with eosinophilic, glass-like intra-cytoplasmic inclusions (hematoxylin–eosin, original magnification ×400).

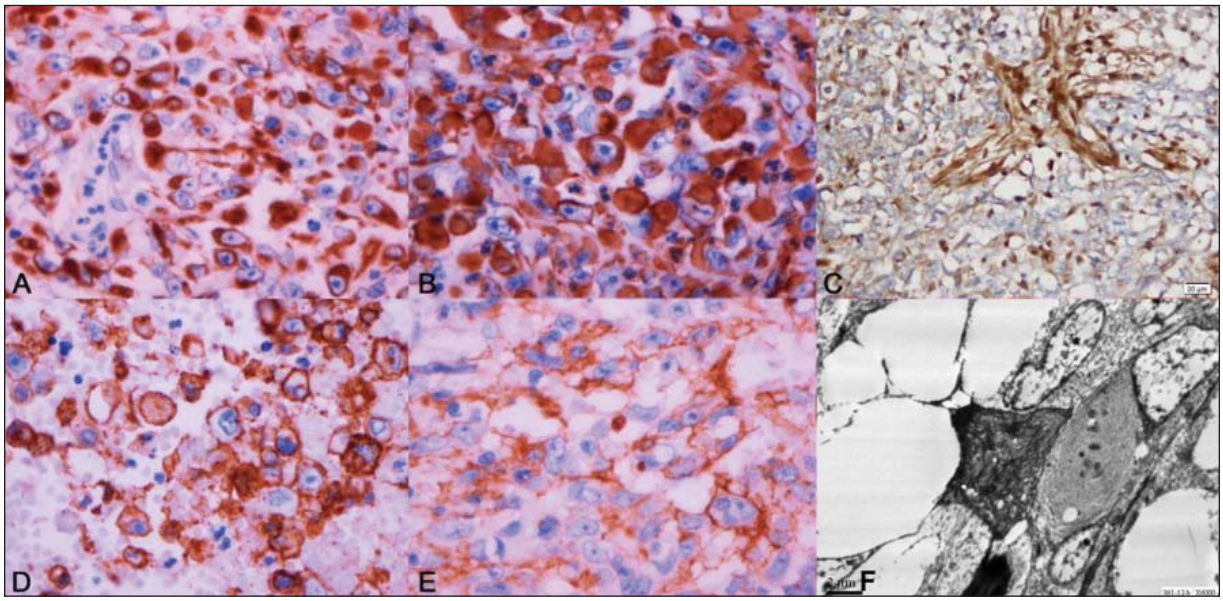

Figure 2. Immunohistochemical staining. (A) Strong immunoreactivity of tumor cells for cytokeratin (original magnification ×400) and (B) vimentin (original magnification ×400). (C) INI1 staining showing positive staining in the endothelial cells and loss of immunoreactivity in rhabdoid tumor cells (original magnification ×400). (D) CD34 immunoreactivity in tumor cells (original magnification ×400). (E) Focal immunoreactivity for epithelial membrane antigen (original magnification ×400). (F) Electron microscopic photograph showing inclusions composed of arrays and whorls of intermediate filaments amidst a few ill-defined mitochondria (original magnification ×6,000).

Immunohistochemical studies revealed characteristic findings of an extrarenal rhabdoid tumor (**Figure 2**). There was strong immunoreactivity for cytokeratin, vimentin, neuron-specific enolase, and smooth muscle actin. Focal immunoreactivity for CD34 and epithelial membrane antigen were observed. The tumor cells displayed lack of immunoreactivity for desmin, myogenin, HMB-45, CD45,

synaptophysin, chromogranin, and CD117. INI1 tumor-suppressing gene was noted to be lost in the tumor cells in comparison to the endothelial lining of the capillaries. Electron microscopic photography showed inclusions composed of arrays and whorls of intermediate filaments amidst a few ill-defined mitochondria. A diagnosis of an intraocular MERT was established.

Repeat systemic evaluation was normal. The child underwent adjuvant chemotherapy with ifosfamide, carboplatin, and etoposide and is currently scheduled for adjuvant external beam radiotherapy to the left orbit.

DISCUSSION

Malignant rhabdoid tumor is a highly aggressive tumor usually affecting the kidney. It most commonly occurs in male infants. Since Rootman et al. published the first case of MERT in the orbit,[7] other reports have described its occurrence in this location.[3-5] However, only one described intraocular involvement by this tumor.[6] Although no primary tumor was found on systemic evaluation done twice in our case, there remains a remote possibility of this being a metastasis from a primary tumor elsewhere.

The histogenesis of MERT is unclear. Although MERTs share immunohistochemical and ultrastructural features with renal rhabdoid tumors, they lack uniformity in immunostaining, ultrastructural features, and cytogenetic abnormalities. The rhabdoid tumor cells are believed to be derived from a primitive pluripotent cell and hence account for the phenotypic heterogeneity observed in MERTs. These tumors characteristically express immunoreactivity for cytokeratin, vimentin, and epithelial membrane antigen.[3] Ultrastructurally, these tumors display intermediate filaments arranged in whorls or parallel arrays, thus constituting the intracytoplasmic inclusions seen on light microscopy.[3] Most of the rhabdoid tumors result from loss of function of the SMARCB1/INI1/SNF5/BAF47 tumor-suppressing gene in chromosome band 22q11.2.[8] Rhabdomyosarcoma and melanoma are intraocular tumors that may share rhabdoid morphology of tumor cells. Lack of immunoreactivity for myogenic markers (desmin and myoD1) and melanocytic markers (HMB45 and S-100) in MERTs help exclude myogenic, histiocytic, and melanocytic tumors.[3]

MERT is an aggressive tumor found to be resistant to multimodal therapy with a low disease-free survival and a grim prognosis.[5] Proximity to the central nervous system and likelihood of optic nerve involvement make an intraocular location even more fatal. The role of radiotherapy is controversial.[3-7] Non-invasive therapy in the form of stereotactic radiosurgery with a gamma-knife has been found effective.[5] Many chemotherapy drugs, such as vincristine, doxorubicin, cyclophosphamide, ifosfamide, and etoposide, have been tried for their potential role, but the results have not been encouraging.[3-7] Recent studies report the inhibitory effect of flavopiridol on tumor cells in rhabdoid tumor, suggesting that targeting the cyclin/cyclin-dependent kinase axis may be an effective therapeutic strategy in future for these tumors.[9,10]

Our case was a primary intraocular tumor with an extraocular and retrolaminar extension in a patient who did not have tumor masses elsewhere in the body. It was immunohistochemically distinct from other intraocular tumors that share rhabdoid morphology. Our report represents the first documented case of a primary intraocular MERT. The panel of immunohistochemical markers and electron microscopic features combined with demonstration of loss of INI1 helps confirm the diagnosis.

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