A 36-month-old girl had a 3-week history of proptosis of the right eye. Computed tomography showed an ill-defined homogeneous mass filling the intraconal space. Histopathologic examination and immunohistochemistry findings of an incisional biopsy specimen were consistent with malignant undifferentiated tumor with rhabdoid features. Despite chemotherapy (a combination of vincristine sulfate and dactinomycin) and radiotherapy, massive orbital recurrence occurred 6 months later and orbital exenteration was performed. The recurrent tumor was composed entirely of pleomorphic epithelial cells with prominent nucleoli and many filamentous cytoplasmic inclusions. Immunohistochemical staining showed positive immunoreactivity for vimentin, cytokeratin, and epithelial membrane antigen, and negative immunoreactivity for muscle-specific antigen, melanoma, neural, and histiocytic markers. Electron microscopy excluded myogenic differentiation and showed that the filamentous cytoplasmic inclusions were composed of whorls of intermediate filaments. Aggressive chemotherapy with a combination of vincristine, doxorubicin, cyclophosphamide, ifosfamide, and etoposide phosphate was continued after exenteration. At 17 months' follow-up, orbital debulking surgery with externalization of the maxillary sinus was performed because of massive tumor recurrence in the right orbit and growth into the maxillary sinus. The child died 23 months after initial diagnosis from tumor invasion into the central nervous system. Extrarenal rhabdoid tumor is a rare orbital mass that carries a poor prognosis.

First recognized in 1978, malignant rhabdoid tumor of the infant kidney initially was thought to be an aggressive “rhabdomyosarcomatoid” variant of Wilms tumor. Subsequent studies suggested that this pediatric tumor was a distinct entity. Because it resembled rhabdomyosarcoma under the light microscope but lacked rhabdomyoblastic findings ultrastructurally, it was referred to as a “rhabdoid” tumor.

Malignant rhabdoid tumor of the kidney occurs most commonly in infants (mean age, 16.8 months), and preponderantly in males. This tumor is associated with an 80% mortality rate and can metastasize to liver, lung, brain, bone, and soft tissues. It is associated with central nervous system tumors, commonly in the cerebellum or brainstem, in 14% of cases. Most of these central nervous system tumors are medulloblastomas but some are primitive neuroectodermal tumors, ependymomas, or gliomas. Malignant rhabdoid tumor of the kidney is one of the least common and most deadly neoplasms of early life.

Extrarenal rhabdoid tumors have been reported that resemble malignant rhabdoid tumor of the kidney cytologically. They occur in children and adults and can be found in many different ana-

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tomic sites such as the liver, brain, soft tissues, skin, orbit, mediastinum, and retroperitoneum. There seems to be no age or site predilection for extrarenal rhabdoid tumors. We report herein an unusual case of extrarenal rhabdoid tumor of the orbit in a 36-month-old girl.

**REPORT OF A CASE**

A 36-month-old girl had a 3-week history of progressive proptosis and dilated pupil of the right eye. She had a 4-mm proptosis and could neither fix nor follow with the right eye. The right pupil was 6 mm in diameter and did not react to light. The fundus was normal except for slight optic disc hyperemia. Orbital computed tomography showed an ill-defined, homogeneous, ovoid intracanal mass filling the middle and the posterior orbit on the right side (Figure 1). The left eye and orbit were normal. The differential diagnosis included rhabdomyosarcoma, granulocytic sarcoma, lymphoma, Wilms tumor, Ewing sarcoma, and metastatic neuroblastoma.

The child had a history of Hirschsprung disease that had been diagnosed at birth and treated by partial colectomy. Physical examination revealed normal findings and no evidence of a primary nonocular tumor, metastatic disease, or leukemia. An incisional orbital biopsy was performed via a superotemporal eyelid crease approach. Histopathologic findings disclosed that most of the tumor was composed largely of sheets of undifferentiated cells. However, a smaller focus of pleomorphic epithelioid cells with abundant cytoplasm, filamentous cytoplasmic inclusions, and vesicular nuclei with large nucleoli was found in one of the sections. The latter cells showed positive immunoreactivity for vimentin, cytokeratin, and epithelial membrane antigen, and negative immunoreactivity for muscle-specific antigen, myoglobin, desmin, neuron-specific enolase, S100 protein, HMB-45, and macrophage marker LN3. The histopathologic features and pattern of immunoreactivity were consistent with a malignant undifferentiated tumor with rhabdoid features. The remaining undifferentiated cells, making up most of the tumor, did not show immunoreactivity for the above markers.

The patient received chemotherapy (a combination of vincristine and dactinomycin) and external beam radiotherapy (500 Gy) to the right orbit. After an initial response to treatment, massive orbital recurrence occurred 6 months later despite continuing chemotherapy. An eyelid-splitting exenteration was performed. Marginal bone biopsy specimens were negative for tumor. The recurrent tumor was composed entirely of the poorly differentiated epithelioid cells that had a pattern of immunoreactivity identical to that of the portion of the original biopsy specimen that showed rhabdoid tumor features. Filamentous cytoplasmic inclusions were noted in many cells (Figure 2). Transmission electron microscopic examination showed that the inclusions com-
prised whorls of intermediate filaments (Figure 3). No ultrastructural or immunohistochemical evidence of muscle differentiation was noted.

Aggressive chemotherapy with a combination of vincristine, doxorubicin, cyclophosphamide, ifosfamide, and etoposide was continued after exenteration. At 14 months’ follow-up, the tumor had recurred in the right socket despite maximum chemotherapy. The recurrent tumor was excised but invasion into the orbital floor was noted. Orbital debulking surgery with externalization of the maxillary sinus was performed at 17 months’ follow-up because of massive tumor growth in the orbit and the maxillary sinus. The child died 6 months later of local invasion of the tumor into the central nervous system, 23 months after the initial diagnosis.

COMMENT

Extrarenal rhabdoid tumor of the orbit is rare. We are aware of only 4 previously published cases\(^5\)\(^-\)\(^8\) (Table). Orbital extrarenal rhabdoid tumor can occur in children and adults and can be seen as an intraconal or extracanal mass. One patient had a tumor involving the lacrimal gland that was initially thought to be a pleomorphic adenoma on histopathologic examination.\(^7\) Two other patients and the one described herein had intraconal tumors.\(^3\)\(^,\)\(^4\) Another orbital rhabdoid tumor was diagnosed in the anophthalmic socket of a child 27 months after enucleation and radiotherapy for retinoblastoma.\(^6\)

The histopathologic diagnosis of extrarenal rhabdoid tumor is based on the presence of characteristic cytologic features similar to those found in malignant rhabdoid tumor of the kidney. These include large oval to polygonal cells with abundant eosinophilic cytoplasm, large vesicular nuclei with prominent nucleoli, and conspicuous filamentous cytoplasmic inclusions. Ultrastructurally, filamentous cytoplasmic inclusions are composed of concentric whorled arrays of parallel intermediate filaments of 6 to 9 nm in diameter.\(^2\) The filamentous cytoplasmic inclusions are not membrane bound and occasionally incorporate lipid droplets or mitochondria. Although filamentous cytoplasmic inclusions are the characteristic feature of extrarenal rhabdoid tumors and are the primary basis for most diagnoses, they are known to be nonspecific and have been reported in other tumors such as melanoma, rhabdomyosarcoma, malignant peripheral nerve sheath, colonic adenocarcinoma, endometrial sarcoma, and many benign conditions.\(^4\) One of us (R.C.E.) has observed similar inclusions in several uveal melanomas and eyelid basal cell carcinomas. These light-microscopic and ultrastructural findings of rhabdoid tumor were present in our patient.

Immunohistochemistry is helpful in establishing the diagnosis of rhabdoid tumor. Many tumors such as that of the patient described herein have a characteristic pattern of positive immunoreactivity for vimentin, cytokeratin, and epithelial membrane antigen. Vimentin usually is positive in rhabdoid tumor, but immunoreactivity for cytokeratin and epithelial membrane antigen is more variable.\(^4\)\(^,\)\(^5\)\(^,\)\(^7\) Negative staining for muscle markers, histiocytic markers, HMB-45, and S100 protein serves to exclude myogenic and histiocytic neoplasms and malignant melanoma.\(^3\)\(^,\)\(^5\)\(^,\)\(^7\)

**Clinical Features of Orbital Rhabdoid Tumor Cases**

<table>
<thead>
<tr>
<th>Source, y</th>
<th>Age of Patient</th>
<th>Location of Tumor</th>
<th>Treatment*</th>
<th>Duration of Follow-up, mo</th>
<th>Status of Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rootman et al,(^5) 1989</td>
<td>6 wk</td>
<td>Intraconal</td>
<td>Inc+RT+chemo</td>
<td>24</td>
<td>Alive</td>
</tr>
<tr>
<td>Johnson et al,(^6) 1991</td>
<td>47 y</td>
<td>Intraconal</td>
<td>Exc+RT+chemo</td>
<td>24</td>
<td>Alive</td>
</tr>
<tr>
<td>Niffenegger et al,(^7) 1992</td>
<td>50 y</td>
<td>Lacrimal gland</td>
<td>Exc+RT+chemo</td>
<td>16</td>
<td>Alive</td>
</tr>
<tr>
<td>Walford et al,(^8) 1992</td>
<td>29 mo</td>
<td>Anophthalmic socket</td>
<td>Inc+RT+chemo</td>
<td>N/A</td>
<td>Alive</td>
</tr>
<tr>
<td>Gündüz et al (current case)</td>
<td>36 mo</td>
<td>Intraconal</td>
<td>Exc+RT+chemo</td>
<td>23</td>
<td>Dead</td>
</tr>
</tbody>
</table>

* Inc indicates incisional biopsy; exc, excisional biopsy; exc, exenteration; RT, radiotherapy; chemo, chemotherapy; and N/A, not available.
The histogenesis of extrarenal rhabdoid tumor is controversial. It currently is uncertain whether extrarenal rhabdoid tumor is a discrete entity that is histogenically related to malignant rhabdoid tumor of the kidney or merely a biologic expression or phenotype that can be assumed by many unrelated neoplasms. After reviewing 42 extrarenal rhabdoid tumors retrospectively, Parham et al concluded that extrarenal rhabdoid tumor is a heterogeneous group of neoplasms comprising unrelated tumors with rhabdoid cells, tumors of apparent neuroectodermal derivation with polyphenotypic features, and a small group of primitive neoplasms that cannot be categorized. Based on the results of their study, these authors were unable to prove or disprove the existence of an extrarenal neoplasm identical to malignant rhabdoid tumor of the kidney. For this reason they advocate the designation “malignant undifferentiated neoplasm with rhabdoid features” for “pseudorhabdoid tumor” not proven to represent gliomas, epithelioid sarcomas, rhabdomyosarcomas, or other neoplastic entities. They stress that those extrarenal lesions with aggressive, invasive behavior and rhabdoid cytomorphicologic features tend to have the same aggressive behavior, resistance to therapy, and grim prognosis attached to rhabdoid tumor of the pediatric kidney.

The latter aggressive pediatric variant of malignant rhabdoid tumor tends to be resistant to multimodal chemotherapy and is almost invariably fatal. Thirteen infants were treated for malignant rhabdoid tumors at the St Jude Children’s Research Hospital between 1981 and 1990. Ifosfamide alone or in combination with carboplatin and etoposide was recommended as front-line therapy for malignant rhabdoid tumor because this chemotherapeutic agent produced partial responses in a few cases. Despite intensive chemotherapy, however, all patients died at a median period of 5 months after diagnosis (range, 0.5–30 months). Our patient’s fulminant clinical course is consistent with that experience.

In contrast to our patient’s clinical course, other well-documented cases of orbital rhabdoid tumor have had good short-term responses without local invasion or systemic metastasis at follow-ups ranging from 16 to 24 months. However, 2 of these patients were middle-aged adults. Given the heterogeneity of extrarenal rhabdoid tumors, it is possible that these adults had less aggressive lesions with rhabdoid phenotypes rather than the aggressive pediatric variant. Only 1 patient with orbital rhabdoid tumor had been treated with exenteration. Therefore, it is unclear whether early exenteration prolongs survival.

In a series of 42 cases of extrarenal rhabdoid tumors, the most frequent cause of death was metastasis to the lung followed by local invasion from intra-abdominal tumors. Our patient had no clinical or imaging evidence of systemic metastasis when she died of central nervous system invasion.

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REFERENCES