

# Classical Malignant Rhabdoid Tumor of Central Nervous System in 9-year-old Korean

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A Malignant rhabdoid tumor (MRT) arising in the right temporoparietal lobe of a 9-year-old boy is described along with the results of an immunohistochemical study. The patient initially sought medical attention for a ptosis and right sided headache. The child underwent a subtotal resection of the tumor, followed by radiotherapy and systemic chemotherapy, but died three years after surgery. A MRT, a primary neoplasm of the central nervous system (CNS), is an entity of unknown histogenesis with a dismal prognosis, which only occurs in early childhood. Histologically similar tumors with more varied morphological features have been designated as an atypical teratoid/rhabdoid tumor. However, a classical MRT is extremely rare in the CNS and our case represents a classical CNS MRT.

**Key Words:** Malignant rhabdoid tumor, atypical teratoid/rhabdoid tumor, central nervous system, immunohistochemistry, 9-year-old boy

## INTRODUCTION

A malignant rhabdoid tumor (MRT) is a rare and highly aggressive tumor that occurs in children. Originally, a group of renal neoplasms with unique histological features were described among tumors collected for the National Wilms' Tumor Study in 1978.<sup>1</sup> The tumor was considered as a type of Wilms' tumor with rhabdomyosarcomatoid features because of the abundant eosinophilic cytoplasm of the individual tumor

cells and its virulent biological behavior. Despite their similarities to rhabdomyosarcoma in optical microscopy, the tumor failed to show the rhabdomyoblastic features by electron microscopy, and was designated as a "malignant rhabdoid tumor of the kidney".<sup>2</sup> In later reports, the tumor was reported to occur in various extrarenal regions, including the central nervous system (CNS).<sup>3,4</sup>

A MRT is histologically characterized by sheets of polygonal cells, which show abundant eosinophilic cytoplasm with a large vesicular nucleus with a prominent nucleolus. Mitotic figures are frequently observed, and necrosis may also be present. One of interesting histological features of a MRT by electron microscopy is the presence of an eosinophilic intracytoplasmic inclusion, which represents aggregates of intermediate filaments.<sup>2,5,6</sup> The inclusions are strongly immunopositive for vimentin. Tumors sharing these histological findings intermixed with teratoid features have also been categorized as atypical teratoid tumors (ATT)<sup>7</sup> or atypical teratoid/rhabdoid tumors (AT/RT).<sup>8</sup>

A MRT of the CNS occurs exclusively in children and invariably carries a poor prognosis with belligerent local recurrences and frequent dissemination through the CSF pathway.<sup>3,4</sup>

Differentiation from other tumors is based on histopathologic evaluation, since the clinical and imaging features of a MRT are similar to other primary CNS tumors including ATT.<sup>6</sup> However there is a paucity of reported cases of pure MRT

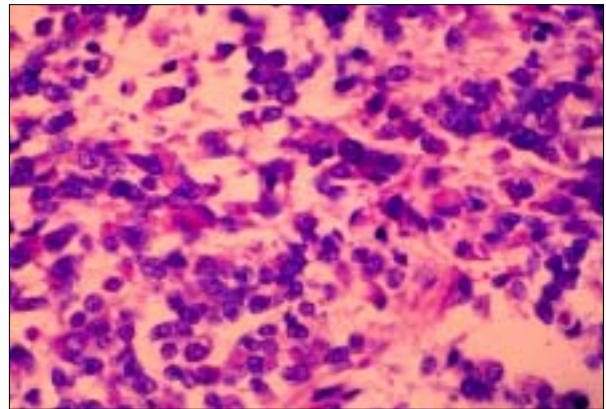
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which make precise statements regarding their epidemiological and clinical aspects difficult.

## CASE REPORT

A 9-year-old boy was admitted to a hospital for a right-sided headache, a ptosis of several months duration and he also experienced vomiting from time to time. A computerized tomography (Fig. 1) showed a poorly circumscribed, slightly enhanced, inhomogeneous mass in the right temporoparietal region, which measured approximately  $9 \times 9 \times 7$  cm in size. A subtotal resection of the tumor was performed, which showed typical pathological features of a malignant rhabdoid tumor as described below. Grossly, the specimen consisted of multiple fragments of gray-white to brown soft tissue, weighing approximately 8 gm. Microscopically, the tumor was composed of sheets of neoplastic cells with ovoid to slightly elongated vesicular nuclei and a scanty to a moderate amount of eosinophilic cytoplasm (Fig. 2). The prominent centrally located nucleoli were easily noted in their nuclei. Some of the cells showed well-circumscribed eosinophilic inclusions (Fig. 2). The tumor cells were somewhat loosely arranged, but failed to show any specific pattern of arrangement. Mitotic figures were frequently encountered and the tumor cells were diffusely immunopositive for vimentin (Fig. 3) and EMA (Fig. 4). However, they failed to dem-

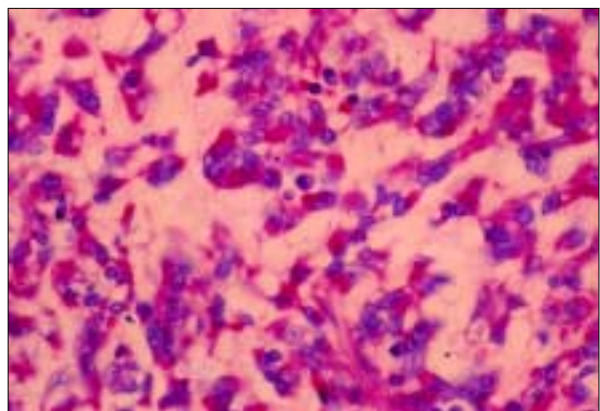
onstrate any immunoreactivity to GFAP, synaptophysin, myoglobin, HMB-45, factor VIII or smooth muscle actin. A mild focal immunoreactivity was observed for keratin (Fig. 5), and S-100 was questionably immunopositive. The strongest immunoreactivity was seen for vimentin, and the cytoplasmic inclusions, if present, were better delineated with vimentin immunohistochemistry. A PHA stimulated lymphocyte culture showed a normal 46, XY chromosomal complement. The patient was treated with radiotherapy and systemic chemotherapy, but died three years after surgery.



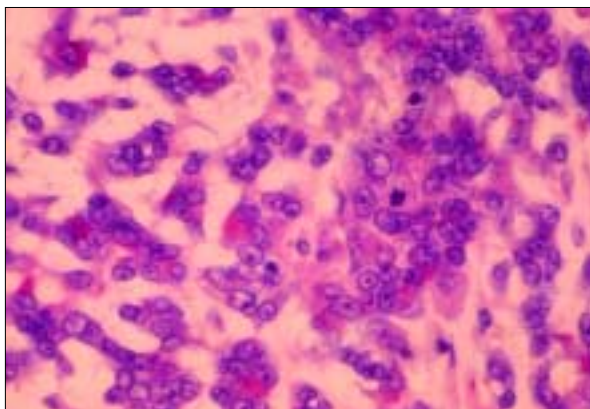
**Fig. 2.** The tumor is composed of neoplastic cells with ovoid to slightly elongated nuclei and scanty to moderate amount of pale eosinophilic cytoplasm with frequent mitotic figures. Prominent centrally located nucleoli are easily noted in several tumor cells. In some cells, one can sometimes observe poorly defined pale globular inclusion-like structures.



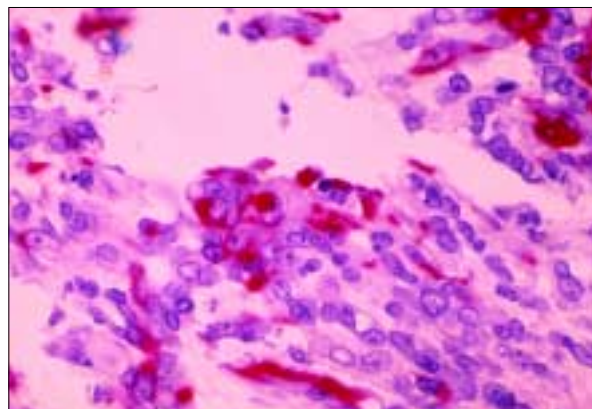
**Fig. 1.** The CT revealed a gadolinium-enhanced inhomogeneous mass, which measured  $9 \times 9 \times 7$  cm in size on the right temporoparietal region.



**Fig. 3.** The diffuse immunoreactivity for vimentin is seen in the cytoplasm of tumor cells (ABC,  $\times 142$ ).



**Fig. 4.** The immunoreactivity for EMA is seen in the cytoplasm of tumor cells (ABC,  $\times 142$ ).



**Fig. 5.** In some cells, immunoreactivity for cytokeratin (cytokeratin) is observed in the cytoplasm (ABC,  $\times 160$ ).

## DISCUSSION

Malignant rhabdoid tumors of the CNS by definition, consist entirely of monomorphic neoplastic cells with rhabdoid features, as originally described for renal MRT.<sup>1</sup> The rhabdoid features include sheets of polygonal cells with eosinophilic cytoplasm, large vesicular nuclei and prominent nucleoli, revealing occasional cytoplasmic inclusions,<sup>3</sup> as shown in the current case. However, recently cases with a mixed population of neoplastic cells have also been considered to be within the spectrum of a rhabdoid tumor as long as part of the tumor is composed of tumor cells with rhabdoid features. For instance, tumors composed of a combined population of neuroepithelial, epithelial and mesenchymal elements partially mixed with rhabdoid tumor cells were called atypical teratoid tumors, which differed from pure malignant rhabdoid tumors.<sup>7</sup> Subsequently, tumors composed entirely or partially of rhabdoid-like cells were named all-inclusively as atypical teratoid/rhabdoid tumors (AT/RT),<sup>8</sup> which blurred the histological differences between an AT/RT and a MRT.

As several series of AT/RT cases failed to treat classical MRT separately, the exact incidence or clinical aspect of a pure CNS MRT cannot be determined by reviewing the published series of AT/RT cases. However, a classical MRT appears to be extremely rare.

In general, the majority of AT/RT patients are below two years of age, and there is male preponderance.<sup>8-11</sup> The current case was a 9-year old boy,

but the oldest age reported thus far is 12 years.<sup>11</sup> Although any part of the brain may be involved, the tumor occurs most commonly in the posterior fossa. Therefore an AT/RT is clinically difficult to differentiate from a medulloblastoma. AT/RTs frequently show cystic portions visible on a CT and may be enhanced with gadolinium on MRI. Rhabdoid tumors of the kidney may rarely be associated with extrarenal rhabdoid tumors but unless there are other typical signs of rhabdoid tumors of the kidney such as young age and hypercalcemia, a search for a primary kidney tumor is probably unnecessary.<sup>12</sup> An AT/RT often shows chromosome 22 abnormalities, and a commonly found chromosomal aberration is a monosomy.<sup>13</sup> However, no chromosomal abnormality was found in the current case.

MRTs carry a poor prognosis. Two features, vimentin expression and aggressive biologic behavior, are of particular interest in light of recent studies indicating an association between vimentin expression and increased tumor cell invasion of the basement membranes.<sup>14</sup> Furthermore, their aggressive biologic behavior can also be explained by the fact that MRTs usually reveal enhanced mitotic activity as well as foci of necrosis.<sup>8</sup>

Because the tumor tends to recur with widespread dissemination throughout the CSF pathway,<sup>4</sup> children with a CNS AT/RT should receive intensive systemic chemotherapy and craniospinal radiation therapy.<sup>12,15</sup> Despite a combination of chemo- and radiotherapy the patient died of a meningeal spread 3 years after tumor.

The origin of CNS-MRT development is unknown. A MRT is potentially derived from meningoepithelial precursor cells, which are embryonically equal to the serosal mesothelial precursor cells that surround the kidney and other organs. Hence it tends to occur at the location of abundant meningeal infoldings such as the cerebellar cortex. Its meningeal involvement may be diffuse or multicentric.<sup>13</sup> However, AT/RTs can develop in any CNS sites as in our case whose tumor was mainly located in the temporoparietal region. In addition, Bergmann<sup>9</sup> et al have speculated that a similar rhabdoid phenotypic expression in different tissues may be due to a similar modulation or metaplasia of differing primitive substrate cells during oncogenesis and differentiation.

The most salient immunohistochemical feature of a pure MRT is the strong vimentin immunopositivity of the intracytoplasmic inclusion body, as originally described for malignant rhabdoid tumors of the kidney. The same immunohistochemical finding was noted in our case. However, it has been reported that in some MRT as well as for AT/RT case, the presence of vimentin and immunopositive intracytoplasmic inclusions is not a necessary morphological requirement. Because of this perplexing heterogeneous immunohistochemical as well as morphological definition of MRTs, Bergmann et al suggested that MRTs may be a collection of different tumors with a similar appearance, and some of the MRTs may represent primitive neuroectodermal tumors.<sup>9</sup> For instance, GFAP immunopositivity was shown in 35%,<sup>9</sup> 61%,<sup>8</sup> 91%<sup>16</sup> and 100%<sup>10</sup> of AT/RT cases. Synaptophysin was immunoreactive in approximately 20 to 25% of cases.<sup>8,10</sup> Parham et al.<sup>17</sup> critically re-evaluated cases with so-called extrarenal rhabdoid tumors, and only 2 of 11 CNS cases were found to satisfy the criteria of a classic malignant rhabdoid tumor without any neuronal or glial immunoreexpression. It is also agreed that the "so-called" CNS rhabdoid tumors that are immunopositive for specific glial or neuronal markers (like GFAP or synaptophysin) should be re-classified as a poorly differentiated glial or neuronal tumor with rhabdoid features instead of a malignant rhabdoid tumor. In the current tumor, several attempts to

obtain an immunopositive reaction for GFAP or synaptophysin were unsuccessful, which appears to satisfy the criteria of a classical malignant rhabdoid tumor, as originally defined by Haas et al.<sup>2</sup>

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