Primary atypical teratoid/rhabdoid tumor of the clival region

Case report

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An atypical teratoid/rhabdoid tumor of the central nervous system (CNS) is a rare, aggressive neoplasm found in infants and children that has similar characteristics to CNS primitive neuroectodermal tumors/medulloblastomas. The authors present the case of a patient with an atypical teratoid/rhabdoid tumor and discuss the imaging, histopathological, immunohistochemical, and cytogenetic findings. Tumor cells displayed positive reactions for vimentin, epithelial membrane antigen, and cytokeratin, and they displayed no reaction for glial fibrillary acidic protein, desmin, and actin. The karyotype was 46, XY. The phenotype of an atypical teratoid/rhabdoid tumor appears heterogeneous when examined by histological, immunohistochemical, and genetic analysis. The authors describe the case of a 4-year-old boy who harbored an atypical teratoid/rhabdoid tumor in the clivus, which appeared as a chordoma on neuroimages. To their knowledge, this location of an atypical teratoid/rhabdoid tumor has not been described in the literature.

KEY WORDS • atypical teratoid/rhabdoid tumor • central nervous system • clivus • pediatric neurosurgery

A n atypical teratoid/rhabdoid tumor in the CNS is an extremely rare, aggressive neoplasm that occurs in infants. This tumor of uncertain origin is most commonly located in the posterior fossa in children younger than 2 years old; its morphological and imaging characteristics are similar to those of primitive neuroectodermal tumors and medulloblastomas in the CNS. In 1978, Beckwith and Palmer first described a rhabdoid tumor as a variant of Wilms tumor in the kidney. The occurrence of rhabdoid tumors in other locations was later reported, and in 1987 a malignant CNS tumor—known as an atypical teratoid/rhabdoid tumor—was identified. Recently, not only histopathological and immunohistochemical but also molecular cytogenetic features of this tumor have been well understood. In this report, we present the case of a 4-year-old boy harboring an atypical teratoid/rhabdoid tumor in the posterior fossa; the unusual imaging appearance mimicked that of a clival chordoma.

Case Report

Presentation and Examination. This 4-year-old boy had been having difficulty in swallowing and speech function progressively for 4 months. He was found to be malnourished on admission to our hospital; a neurological examination revealed dysphonia, disturbed palatal arch function, right ocular miosis, ptosis, and severe gait ataxia. The MR images (Fig. 1) and cranial 3D CT scan (Fig. 2) revealed a mass originating in the clival region which destroyed adjacent bone structures and exhibited a significant medullary compression effect.

Operation and Postoperative Course. Surgery was performed through a right suboccipital craniectomy and C-1 posterior arch excision. The intradural and extradural compartments of the tumor were observed, and subtotal removal was undertaken. The patient’s postoperative course was uneventful.

Pathological Examination. Histopathologically, the tumor cells had large nuclei and prominent nucleoli with a rhabdoid phenotype. Most of these cells were large and had eosinophilic cytoplasm (Fig. 3A). An immunohistochemical

Abbreviations used in this paper: CNS = central nervous system; CT = computed tomography; IGF = insulin-like growth factor; MR = magnetic resonance.
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Fig. 1. Axial (left) and sagittal (right) Gd-enhanced MR images showing heterogeneous enhancement and significant medullary compression effect. (The abbreviations ARH, LFA, PLF, and RHP are automatically generated by the MR imaging software and are not integral to the images.)

analysis revealed surface immunoreactivity for epithelial membrane antigen (Fig. 3B), cytokeratin (Fig. 3C), and vimentin. No immunoreactivity was observed for actin, desmin, and glial fibrillary acidic protein. The mass was diagnosed as an atypical teratoid/rhabdoid tumor.

Fresh tissue was cultured in RPMI-1640 (Irvine Scientific) and supplemented with HEPEMS buffer and 10% fetal calf serum (Irvine Scientific), L-glutamine, penicillin, streptomycin, epidermal growth factor (Sigma), and insulin (Sigma). After 3 to 7 days, the cultures were exposed to Colcemid (0.01 mg/ml; Gibco) for 4 hours, harvested by hypotonic treatment in 0.06 M KCl (Merck), and fixed repeatedly in methanol/acetic acid (3:1). High-resolution Giemsa banding (850-level bands) revealed the karyotype to be 46, XY.

Neither leptomeningeal nor systemic dissemination was detected. The patient was referred to our pediatric oncology clinic for adjuvant therapy, which his parents refused. Unfortunately he died 6 months after admission.

Discussion

An atypical teratoid/rhabdoid tumor is an uncommon tumor that occurs in infancy and childhood. The mean age of patients at diagnosis is 2.9 years, and three quarters of them are boys.9 The tumor’s incidence remains undefined, but it may be as high as one in four primitive CNS tumors in infants. These tumors develop in the posterior fossa in slightly more than half of the patients and have also been reported to occur in the cerebellar hemispheres, cerebellopontine angle, and fourth ventricle.1,10 The neuroimaging appearance of atypical teratoid/rhabdoid tumors is similar to that of primitive neuroectodermal tumors and medulloblastomas. The characteristic CT findings of these tumors include heterogeneous contrast enhancement, calcification, cyst formation, and hemorrhage. Magnetic resonance imaging usually reveals a decreased signal intensity on T1-weighted images, an isointense signal on proton images, and heterogeneous enhancement after the administration of Gd.6,11 For all these types of tumors, signs of aggressive behavior were revealed on images and included hydrocephalus, apparent invasion of the adjacent brain and dura mater, and marked mass effect. In our case, neuroimaging characteristics of the tumor such as T1 signal hypointensity, heterogeneous Gd enhancement, and adjacent bone destruction resembled those of a chordoma. The striking heterogeneity of the atypical teratoid/rhabdoid tumor shown on imaging studies reflects the histopathological complexity of these tumors.1

The origin of malignant rhabdoid tumors in the CNS is unknown. These tumors are potentially derived from meningoepitheelial precursor cells, which are embryonically comparable to the serosal mesothelial precursor cells that surround the kidney and other organs. Hence, the tumors tend to occur at the location of abundant meningeal infoldings such as the cerebellar cortex.3 Approximately one third of patients develop leptomeningeal dissemination via cerebrospinal fluid; cytological examination of cerebrospinal fluid is important in the early diagnosis, analysis of disease progression, and therapy modulation.11 An atypical teratoid/rhabdoid tumor contains rhabdoid cells and, in some instances, small cell, embryonal, and mesenchymal components. In addition some tumors may have adenomatous and squamous rests. Choroid plexus carcinomas, immature teratomas, and large cell medulloblastomas were considered in the differential diagnosis.

Deletions and mutations of the hSNFS/INI 1 locus in chromosome band 22q11.2 have been demonstrated in rhabdoid tumors of the kidney, CNS, and extrarenal sites.4 Inactivating mutations of this tumor suppressor gene locus are regarded as a crucial step in their molecular pathogenesis.15 Biegel et al.4 demonstrated chromosome 22 deletion and INI 1 mutations among 100 primary rhabdoid tumors using fluorescence in situ hybridization and polymerase chain reaction–based microsatellite, heteroduplex, and sequence analyses. The highest frequencies of INI 1 were seen in exons 5 and 9 for CNS tumors, and two potential hot-spot mutations include a cytosine-to-thymine transition in codon 201 in exon 5 and a cytosine deletion in exon 9. Except for the changes shown in 22q, several changes to other chromosomes including 1, 2, 5, 6, 7, 11, 13, 16, 17, and 19 were
also described. 10 Although monosomy or deletion of chromosome 22 is a useful diagnostic marker for this tumor, 25% of the histologically confirmed rhabdoid tumors do not show detectable chromosome 22 defects such as in our case. Also the expression of abnormal tumor suppressor genes such as pRb, p16, p53, and MMAC/PTEN indicates alteration of the G1-to-S-phase step in the cell cycle, which could be an explanation for the aggressive nature of these tumors. Another molecular-based explanation was reported by Ogino et al., 12 in which the authors demonstrated that tumor cells express both the IGF-I receptor and IGF-II, supporting the hypothesis that autocrine/paracrine stimulation of cell growth by IGF-II may be one mechanism in tumorigenesis. Cathepsin D expressed by the tumor cells may also be involved in both tumor cell invasion and growth. In our case, high-resolution Giemsa banding revealed the karyotype to be 46, XY. Therefore, tumorigenesis and progression may be explained with epigenetic factors and molecular pathological entities in a related gene or genes.

Despite multimodal therapy including surgery, systemic and intrathecal chemotherapy, radiotherapy, Gamma Knife surgery, and stem-cell rescue, the survival rate remains very poor in patients with atypical teratoid/rhabdoid tumors. Hilden et al. 7 reported a 16.7-month median survival time in 42 patients with atypical teratoid/rhabdoid tumors in the CNS. Authors have reported a few cases in which the patients have survived 5 or more years. 8,13 The majority of patients die within the 1st year of local tumor recurrence or of leptomeningeal dissemination. An atypical teratoid/rhabdoid tumor is frequently disseminated along the neuraxis at the time of disease relapse. The purpose of surgery is to make a diagnosis and reduce the tumor burden. Survival is unrelated to patient age at the time of diagnosis, the extent of resection, or the type of postoperative adjuvant therapy. 6

In summary, we have reported the case of a 4-year-old boy who presented with brainstem compression. The preoperative imaging appearance seemed to indicate a clival chordoma, but histopathological examination of the resected tissue revealed that the tumor was consistent with an atypical teratoid/rhabdoid tumor. To the best of the authors’ knowledge, this is the first reported case of an atypical teratoid/rhabdoid tumor in the clival region.

References


Fig. 3. Photomicrographs. Prominent “rhabdoid” phenotype stained with H & E (A) and displaying immunoreactivity for epithelial membrane antigen (B) and cytokeratin (C). Original magnifications × 200 (A and B) and × 400 (C).
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