Turkish Neurosurgery 2008, Vol: 18, No: 1, 30-34

Atypical Teratoid/Rhabdoid Tumors: Imaging Findings of Two Cases and Review of the Literature

Atipik Teratoid Rabdoid Tümör: İki Olguda Radyolojik Bulgular ve Literatürün Gözden Geçirilmesi

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ABSTRACT

Atypical teratoid/rhabdoid tumor (AT/RT) is a malignant embryonal central nervous system (CNS) tumor, manifesting in children, and composed of rhabdoid cells, with or without fields resembling a classical primitive neuroectodermal tumor (PNET), epithelial tissue and neoplastic mesenchyme. Around 200 cases of CNS AT/RT have been documented in the literature. Although the clinical and pathological findings have been defined in large series previously, and AT/RT has become increasingly recognized, awareness of typical AT/RT is important in making the correct diagnosis of this uncommon but probably underdiagnosed entity. Neuroradiologists rarely mention AT/RT in their differential diagnosis and this paper presents two additional cases in which clinical and pathological findings are combined with neuroradiological presentation.

KEY WORDS: Atypical teratoid /rhabdoid tumor, Computerized tomography, Magnetic rezonance imaging

ÖZ

Atipik teratoid/rabdoid tümör (AT/RT), genellikle çocukluk çağında görülen malign bir merkezi sinir sistemi (MSS) tümörüdür. Histopatolojik olarak rabdoid hücrelerden oluşur ve içinde klasik primitif nöroektodermal tümör (PNET), epitelyal doku ve neoplastik mezenşimi düşündüren alanlar görülebilir. Literatürde 200 dolayında merkezi sinir sistemi AT/RT'ü bildirilmiştir. Daha önce büyük serilerde klinik ve patolojik bulgularının geniş olarak tariflenmesine ve AT/RT'lerin tanınma sıklığının gittikçe artmasına rağmen, AT/RT'leri akılda tutmak, bu nadir görülen tümörlere tanı koyabilmenin en önemli kriterlerinden biridir. Halen daha nöroradyologların ayırıcı tanıda AT/RT'lerden nadiren bahsetmekte olmaları nedeniyle bu yazıda 2 AT/RT olgusu klinik, patolojik ve nöroradyolojik bulguları ile birlikte sunulmuştur.

ANAHTAR SÖZCÜKLER: Atipik teratoid /rabdoid tümör, Bilgisayarlı tomografi, Manyetik rezonans görüntüleme

Received: 25.08.2007
Accepted: 20.11.2007

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INTRODUCTION

Atypical teratoid rhabdoid tumor (AT/RT) of the brain is a highly malignant central nervous system neoplasm described as a unique entity in the late 1980s. It usually affects very young children although it has been reported in adults as well (11), but the true incidence of the disease is not yet known. The differential diagnosis includes primitive neuroectodermal tumor, medulloblastoma, ependymoma and choroid plexus carcinoma because of their similar histologic features (4,15). AT/RT is the first pediatric brain tumor for which a candidate tumor suppressor gene has been identified. A mutation or deletion in the INI1 gene occurs in the majority of AT/RT tumors.

AT/RT behaves in a very aggressive manner and, while cure is possible for a small minority of patients based on the data from small and retrospective series, no standard or effective therapy has been defined for most of the patients. Sasani et al (16) reported a child with favorable outcome following radical surgery and aggressive chemotherapy, whereas another study supported the evidence that manipulation of the epigenetic structure of DNA may offer new treatment options for embryonal tumors (8).

Several authors have described the radiologic properties of AT/RT (1,2,5,7,9,10,17,18) that showed some agressive features such as hydrocephalus, invasion of the adjacent brain and dura, and marked mass effect reflecting the histopathologic complexity of these tumors. We describe the imaging and histopathological features of AT/RT in two cases.

CASE REPORT

Case-1: A previously healthy 9-year-old boy presented with sudden onset of severe headache, vomiting and right sided fasciculations around the mouth. Precontrast computerized tomography (CT) (Figure 1A) showed a large, solid mass located in the left frontotemporal lobe with surrounding edema. The mass was slightly hyperdense compared to gray matter and contained some hemorrhagic regions. There were no calcified areas and contrast enhancement of the lesion (Figure 1A,B). An angiography performed in an other medical center showed avascular nature of the tumor The patient underwent surgery and the tumor was removed partially. Postoperative CT scans revealed left frontoparietal infarct and edema. The patient died on the first day following the operation.

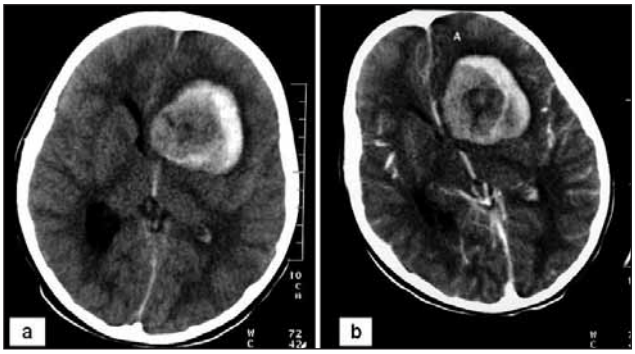

Figure 1: *9-year-old boy with left frontotemporal AT/RT (Case-1).* ***A****, Precontrast CT scan shows slightly hyperdense large tumor causing midline shift with peripheral hemorrage, and minimal intraventricular bleeding in the 3rd ventricle.* ***B****, Postcontrast CT scan at the same level shows no enhancement of the mass.*

Microscopic examination (Figure 2) showed avascular nature of the tumor; heterogenous tumor tissue with hemorrhage. The patient underwent operation, and adjacent brain parenchyma was hemorrhagic and ischemic. The tumor was composed mainly of spindle cells showing high mitotic activity. Besides mesenchymal areas, there was a rhabdoid component characterised by eccentrically located vesicular nuclei, prominent nucleoli, and eosinophilic cytoplasm. Immunohistological studies (Figure 3) revealed vimentin positivity in the neoplastic mesenchymal component. The rhabdoid cells showed smooth muscle actin (SMA), epithelial membrane antigen (EMA), and vimentin immunoreactivity whereas desmin was negative. Histomorphological and immunohistochemical features supported the diagnosis of AT/RT.

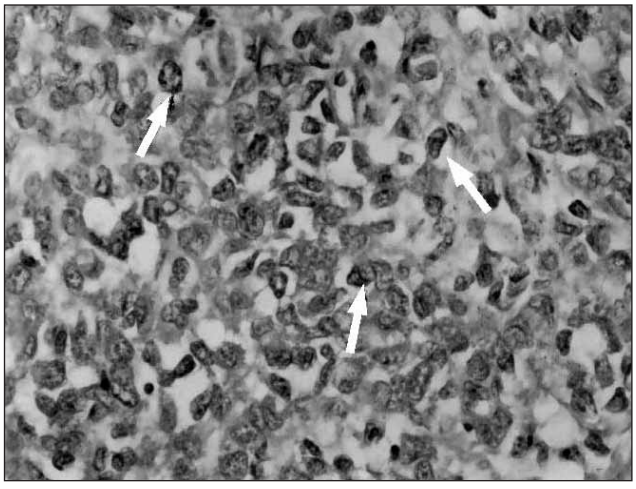

Figure 2: *Rhabdoid cells with eccentric nuclei (arrows) and eosinophilic cytoplasm were diagnostic for AT/RT (H&E, X400)*

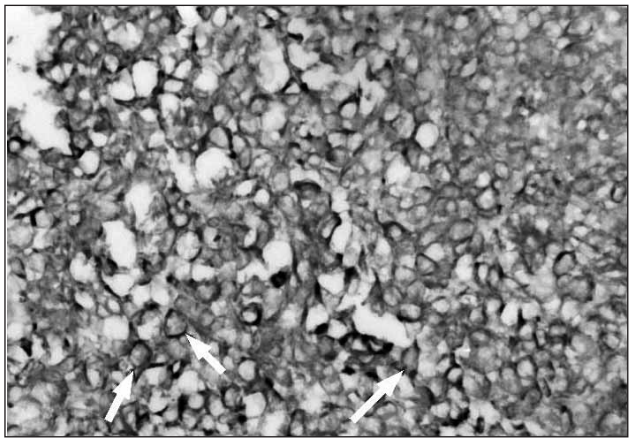

Figure 3: *Immunohistochemical expression of SMA (arrows) in the rhabdoid cell cytoplasm (SMA, X200).*

Case-2: A 12-month-old girl was presented with a convulsion. The past medical history revealed a decrease in the motor skills and lack of response to external stimulations for the last three months. In the last two days, intermittent arm and leg movements with lethargy had ensued. CT scans (not shown) showed a large, hyperdense suprasellar mass. It extended into the third and lateral ventricles and caused periventricular edema secondary to obstructive hydrocephalus. On magnetic resonance imaging (MRI) scans, the solid component of the mass was hypo-isointense on T1-weighted images (Figure 4A) and iso-hyperintense on T2-weighted images in relation to the gray matter (Figure 4B). There were some necrotic areas within the tumor. Contrast enhanced CT and MR images showed a patchy pattern of enhancement of the tumor (Figure 4C). Extensive debulking of the tumor was performed.

Microscopically, a tumor containing primitive neuroectodermal and rhabdoid cells was detected. The rhabdoid component was composed of medium-sized, round to oval cells with eccentric nuclei, prominent nucleoli and eosinophilic cytoplasm. Immunohistologically, the rhabdoid cells were immunoreactive with SMA, EMA and vimentin, but negative with desmin. The small cell embryonal component expressed vimentin. Germ cell markers were negative. The morphological features were compatible with diagnosis of AT/RT.

The child was treated with two cycles of chemotherapy (cysplatin 15mg/m^2, UP-16 100mg/m^2). 3 months after the operation, status epilepticus developed and MRI showed increase in the size of residual tumor mass at the primary site (Figure 5). She died 6 months after the operation.

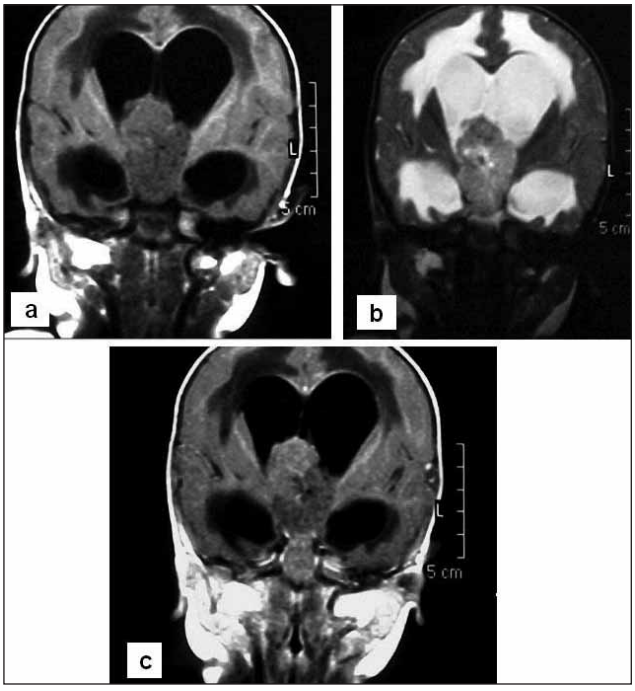

Figure 4: *12-month-old girl with suprasellar AT/RT (Case-2). **A**, coronal T1-weighted and, **B**, coronal T2-weighted MR images showing a large mass containing small central necrotic areas and, predominantly isointense with gray matter. There is intraventricular extension causing obstructive hydrocephalus and resultant periventricular edema. **C**, Post-contrast coronal T1-weighted MR image showing patchy tumor enhancement.*

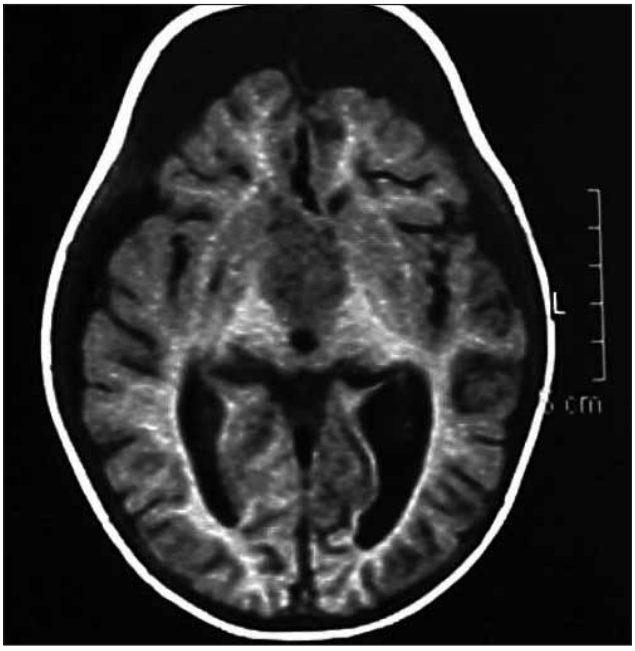

Figure 5: *Three months after the operation (Case-2). Axial T1-weighted MR image demonstrating residual tumor at the primary site with resolution of the hydrocephalus causing frontoparietal subdural cerebrospinal fluid collection.*

DISCUSSION

AT/RT is a rare, highly aggressive malignant neoplasm of the CNS. Histologically it is composed entirely of rhabdoid cells or is combined with fields indistinguishable from PNET and/or with neoplastic mesenchymal and/or epithelial tissue (5). Histological features and the poor clinical outcome indicate that these tumors correspond to WHO grade IV (13). The first example affecting the CNS was reported in 1985 by Rorke et al (13) who named them AT/RT to highlight the disparate combination of rhabdoid, primitive neuroepithelial, epithelial and mesenchymal components. Although it is not clear whether the CNS rhabdoid tumor represents the same neoplasm, they share a high incidence in infancy, overlap in histological appearance, and pursue a similarly aggressive clinical course. Monosomy for chromosome 22, noted in some cases of both tumors, supports the similarity of these neoplasms (14). Molecular genetic analysis may provide supportive information. Monosomy 22 or deletions of chromosome band 22q11 with alterations of the hSNF5/INI1 gene are shown in only 25% of cases with childhood AT/RTs (4,15).

The incidence of AT/RT is not known. It occurs predominantly in infants less than 2 years of age. Lesions in adults or older children are likewise very unusual with rare case reports (1,11). Although any part of the CNS may be involved, AT/RT is mainly localized in the posterior fossa (4,6,15). Meyers et al (12) have however reported that AT/RTs were infratentorial in 47%, supratentorial in 41% and both infra- and supratentorial in 12% of their patients. Left hemispherical location is more prominently seen in older children and adults. It may be multifocal at presentation (2). Tumor may be located within or extending into the ventricles (9,17). Destruction of the overlying skull and exracranial extension have been described (7). Imaging features are nonspecific although all reported cases have similar findings. Lesions are usually large at presentation. Precontrast CT shows an iso- or slightly hyperdense mass in relation to gray matter, with associated parenchymal edema, calcification and hemorrhage (7,9,17). Multiple cystic or necrotic foci are common. When a large, sharply marginated heterogenous iso-, hyperdense hemispheric mass is seen in a child, the differential diagnosis includes ependymoma, PNET and AT/RT. These tumors cannot be differentiated from each other on the basis of imaging characteristics (3).

Although imaging features of AT/RTs have been described in multiple case reports, MRI findings of AT/RT have been very limited in larger series which mainly concentrated on the clinical and histopathologic features of the tumor (4,15). There is mixed signal intensity on T1 and T2-weighted images due to extensive necrosis and intratumoral hemorrhage (10,17). The solid component of the tumors is hypo- or isointense on T1-weighted images and iso- or hyperintense on T2 -weighted images compared to the gray matter and is also well enhanced on post-contrast CT and MRI (7,9,17). However, AT/RT still remains in the differential diagnosis of brain tumors in young children, especially those located in the cerebellar hemisphere and with eccentric cysts, as well as the solid supratentorial masses with non-specific radiological manifestations mimicking PNETs as in our cases. In the first case, the tumor was of avascular nature and was not enhanced after contrast administration. It was an unusual finding for AT/RT because all previous reports have shown that the tumors were well enhanced after contrast medium administration. Neither of our cases had eccentrically located cysts between the solid tumor and the adjacent brain.

The clinical behavior of the AT/RT is usually one of local aggressiveness, with some tumors enlarging during chemotheraphy, a feature that was prominent in the second case. Moreover AT/RT does show a strong tendency to spread with leptomeningeal involvement (9). It is therefore suggested that contrast-enhanced MR of the brain and spine should be included at presentation and during follow-up as poor prognosis is associated with MR imaging evidence of disseminated leptomeningeal tumors.

In conclusion, multicentric clinical trials that focus solely on AT/RT are needed with evaluations of aggressive surgical and medical treatment approaches. It is important to be aware of this entity and mention it in differential diagnosis for directing the immunohistochemical studies.

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