CASE REPORT

Primary atypical teratoid/rhabdoid tumor of the spine in an infant

Stabouli S[1], Sdougka M[1], Tsitspoulos P[2], Violaki A[1], Anagnostopoulos I[2], Tsonidis Ch[2], Koliouskas D[3]

[1]Pediatric Intensive Care Unit, Hippokration General Hospital, Thessaloniki, Greece
[2]Department of Neurosurgery, Hippokration General Hospital, Thessaloniki, Greece
[3]Pediatric Oncology Department, Hippokration General Hospital, Thessaloniki, Greece

Abstract

Atypical teratoid/rhabdoid tumor of the spine is a rare pediatric neoplasm with poor prognosis. We report a case of an atypical teratoid/rhabdoid tumor of the cervical spine in a 2-months-old infant. The patient presented with rapidly progressing tetraparesis and respiratory failure. Magnetic resonance imaging of the spinal cord revealed an intradural, extramedullary mass occupying the spinal canal on the right at the level of C1-C5. Tumor cells were immunohistochemically positive for epithelial membrane antigen, vimentin, cytokeratins, S-100 protein, and CD57/Leu-7 antigen. Despite chemotherapy, the infant presented with progressive neurological deterioration and died 6 months after initial diagnosis. We review the literature on spinal malignant rhabdoid tumor and discuss the pathology, treatment, and outcome of these rare neoplasms. Hippokratia 2010; 14 (4): 286-288

Key words: atypical teratoid tumor, rhabdoid tumor, hydrocephalous, chromosome 22q, spine, chemotherapy

Corresponding author: Stella Stabouli, 49 Konstantinoupoleos Street, 546 42, Thessaloniki, Greece, Tel +30-6976433767, e-mail: sstaboul@med.uoa.gr

Atypical teratoid/rharbdoid tumor (AT/RT) is a rare, highly aggressive and frequently lethal malignancy that usually affects young children and infants. First described in 1978 as a variant of Wilms tumor with rabdomyosarcomatus features, it was not recognized as a distinct entity until the 80s[1]. AT/RT may occur in various anatomic sites, such as the central nervous system (CNS), liver, abdomen or soft tissues. Renal and CNS are the most frequent and well-studied locations, while extrarenal, extracranial AT/RTs are extremely rare, mainly described as isolated case reports with poor prognosis. Most AT/RTs have deletions or mutations of the hSNF5/INI1 gene on chromosome 22q11, providing evidence of common origin and enabling the distinction of these neoplasms[3,4].

Although reports on AT/RT have been increasing in frequency during the past few years, the exact incidence of AT/RT has been difficult to determine. Data from a Children's Cancer group study for children with malignant brain tumors younger than 3 years of age, suggested that 10 to 15% of the children had AT/RT ([2]). We report a case of a 2-months-old infant with primary spinal AT/RT and we review the literature with regard to the pathology, treatment and outcome of this rare entity.

Case Report

A previously healthy 2-month-old boy presented with a 3-day history of worsening weakness and food refusal. The hypotonia rapidly progressed to tetraparesis over a 4-days period. Clinical examination revealed loss of muscle tone, increased reflexes of lower extremities, positive Babinski sign and a unilateral, solid mass of 3.5 cm diameter, located supraclavicularly in the an-

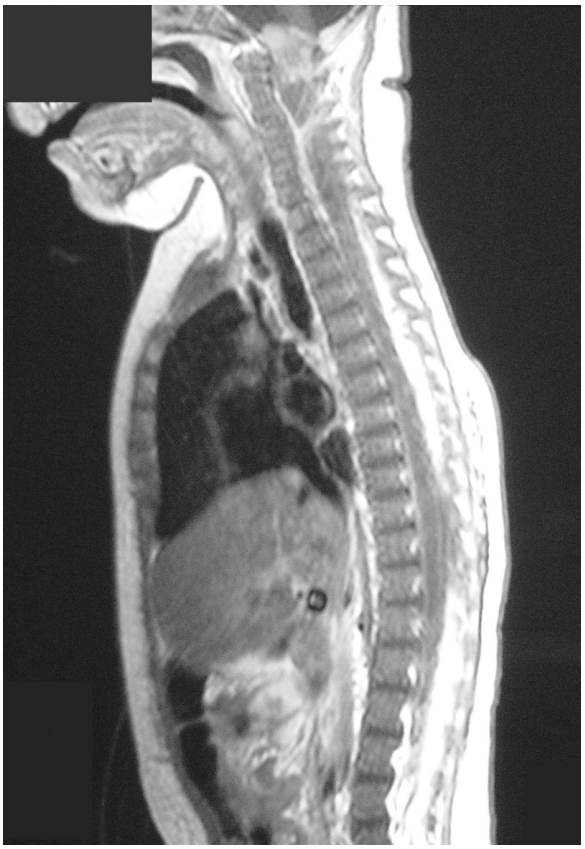

Figure 1: Initial Magnetic Resonance Imaging of the spinal cord. Sagittal T1-weighted image show an intradural, extramedullary mass occupying the spinal canal at the level of C1-C5.

terior cervical fossa. On the 4th day of illness the patient presented clinical deterioration with decreased level of consciousness and respiratory failure, was intubated and transferred to the Pediatric Intensive Care Unit. Magnetic resonance imaging of the spinal cord revealed an intradural, extramedullary mass occupying the spinal canal on the right at the level of C1-C5, extending to the ipsilateral brachial plexus through the C1-C2 intervertrebal foramen (Figure 1). Imaging findings of the brain, chest and abdomen were normal. An open biopsy of the tumor was performed. Surgical resection of the tumor could not be performed, as access to the tumor which adhered to the spinal cord and nerve root, would deteriorate the infant's condition. Histologically, the tumor specimen was composed of round or atractoid cells with diffuse growth and necrotic areas. The cells had increased nuclear/cytoplasmic ratio and nucleic polymorphism. Many nuclei had prominent nucleoli, indented by eosinophilic cytoplasmic inclusions. Tumor cells were immunohistochemically positive for epithelial membrane antigen, vimentin, cytokeratin (AE1/AE3), S-100 protein, and CD57/Leu-7 antigen. The results were consistent with the diagnosis of AT/RT. Chromosome 22q and Xp11 impairment was demonstrated on genetic analysis.

The patient was treated with chemotherapy consisting of vincristine, etoposide, doxorubicin, mesna, and ifosfamide. Further chemotherapy included mesna, ifosfamide, etoposide, carboplatin and vincristine, mesna, cyclofosphamide, epirubicin, etoposide with poor response. 1 month after admission the infant developed hydrocephalus and a subdural hygroma on the right fronto-temporal region. An external ventricular drain was placed. During the following months the patient presented with inability of weaning from mechanical ventilation, hemodynamic instability and progressive neurological deterioration. He died 6 months after the initial diagnosis.

Discussion

AT/RT is a highly malignant CNS neoplasm. Location in the spine is rare. Tekautz et al reported only one case of AT/RT of the spine out of 31 patients diagnosed with CNS AT/RT, during a 19-year period[3]. In a meta-analysis of 133 cases of CNS AT/RT in children (median age 2.1 years), 61% of the tumors were located in the spinal cord[4].

Review of the documented cases of spine AT/RT in the literature revealed an age range from 2 months to 9 years (table 1)[5-8]. Outcome was dismal in the majority

Table 1: Published cases of spinal AT/RT.

Case	Author	Year	Age (mo)	Sex	Location	Therapy	Outcome/ mo after diagnosis
1	Roseberg et al	1994	24	F	C6-T1	CMT	DOD/2mo
2	Howlett et al	1997	9	M	T5-T10	Surg/CMT/RT	DOD/4mo
3	Tamiya et al	2000	7	F	T7	Surg	DOD/2mo
4	Cheng et al	2005	24	F	T12	NS	DOD/2mo
5	Tanizaki et al	2006	10	F	T10	Surg/CMT/RT	DOD/3mo
6	Bannykh et al	2006	48	M	T9-L1	NS	NED
7	Kodama et al	2007	9	M	C4-T6	Surg/CMT/RT	DOD/20mo
8	Moeller et al	2007	108	M	T11-L2	Surg/RT	NED
9	Yang et al	2007	84	M	L spine	Surg	NS
10	Seno et al	2008	5	F	C4-T3	Surg/CMT	DOD/2mo
11	Yano et al	2008	21	F	Cerv spi	Surg/CMT/ABMT	NED
12	Tinsa et al	2008	48	F	T1	NS	DOD/2mo
13	Niwa et al	2009	72	M	C3-C6	Surg	NS
14	Fridley et al	2009	13	F	C spine	Surg/CMT	DOD/4mo

Abbreviations: F: female, M:male, Surg:surgery, CMT:chemotherapy, RT:radiation therapy, ABMT: autologous bone marrow transplantation, NS: not specified, DOD: died of disease, mo:months, NED: no evidence of disease.

of cases (disease related death within 2-20 months from diagnosis). Only 3 patients were reported as long-term survivors.

Imaging findings may include isointensity with hypertintense foci due to intratumoral hemorrhage on T1-weighted images, and heterogeneity (a mix of hypo-, iso-, and hyperintense foci) on T2-weighted images[21].

Histologically, AT/RTs consist of nests or sheets of rhabdoid cells, which typically have eccentric round nuclei with a prominent nucleolus, a plump cell body with characteristic cytoplosmic filament inclusions and are characteristically positive for epithelial membrane antigen (EMA), vimentin, smooth-muscle antigen and negative for germ cell markers[20]. Chromosome 22q11 abnormalities are frequently seen in AT/RTs and have been proved valuable for diagnostic purposes[2].

Therapeutic approaches includee surgery and a variety of postoperative chemotherapy regimens with or without radiation therapy[1,3,21]. There is only limited data from occasional survivors with spinal AT/RT. Published series on CNS AT/RTs report an overall 2-year survival rate of less than 15% for children younger than 3 years at diagnosis[1,2]. Tekautz et al found that high doses of alkylator-based chemotherapy and radiation therapy resulted in prolonged survival of patients older than 3 years old[4]. High dose chemotherapy with autologous hematopoietic progenitor cell rescue might improve survival in patients with CNS AT/RT[21].

In conclusion, spinal AT/RT carries a poor prognosis should. Prospective studies and further understanding of the biology of the disease are necessary to develop optimal treatment approaches for children with AT/RT.

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