Case Report

Atypical Teratoid Rhabdoid Tumor of the Right Cerebellopontine Angle in a 2-Year-Old Girl: A Case Report

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Abstract

ATT/RhTs of the central nervous system have been wrongly diagnosed in the past as medulloblastoma due to some similarity between these tumors. The differentiation between ATT/RhT and medulloblastoma is important owing to their different treatment regimes. Medulloblastomas have recently been separated into 2 subgroups regarding INI 1 positivity and negativity, which contrasts with ATT/RhT cases that have always been associated with INI 1 negativity. INI 1 negative medulloblastoma and ATT/RhT require different treatment regimes; INI 1 negative medulloblastomas also have a worse prognosis than INI 1 positive medulloblastomas. It is important to be conservative and preserve the current clinical condition of the patients during surgical excision of these tumors due to the short survival period of INI 1 negative medulloblastoma and ATT/RhT.

Keywords: ATT/RhT, cerebellopontine angle, medulloblastoma, surgery

2 Yaşındaki Bir Çocukta Serebellopontin Açığı Yerleşmiş Atıpk Teratoid Rhabdoid Tümör: Vaka Sunumu

Özet

Atıpk teratoid rhabdoid tümörler medulloblastomalara benzerlikleri nedeni ile geçmişte yanlış olarak medulloblastoma olarak tanılmışlardır. Her iki tümörün birbirinden ayırmanın yapılması değişik teadavi rejimlerinin olması nedeni ile önemlidir. Medulloblastomalara son zamanlarda iki ayrı alt gruba ayrılmaktadır. Bu ayrıntı INI 1’in pozitif ya da negatif olması göre yapılmaktadır. INI1 negatif medulloblastomalara, INI1 pozitif medulloblastomalardan daha kötü prognoza sahiptirler. INI1 negatif medulloblastomalara ve atıpk teratoid rhabdoid tümörler INI1 pozitif medulloblastomalardan farklı teadavi rejimleri ile teadavi edilmektedir. Özellikle çocuklarda serbellopontin yerleşim gösteren tümörlerde INI 1 negatif medulloblastoma ve atıpk teratoid rhabdoid tümör arayıcı tanida düşünülerek, hastaların mevcut kliniğini koruyucu cerrahi işlem uygulanması hastaların cerrahi sonrası hayat kalitesini olumlu ölçüde etkileyecektir.

Anahtar Kelimeler: Atıpk teratoid rhabdoid tümör, cerrahi, medulloblastoma, serbellopontin köşe
INTRODUCTION
Beckwith and Palmer identified the first rhabdoid tumor, a highly malignant lesion of the kidney, in 1978(1). Biggs and colleagues(4) were the first to describe an intracranial malignant rhabdoid tumor, and Rorke and colleagues referred to a primary malignant rhabdoid tumor of the central nervous system as an “atypical teratoid / rhabdoid tumor” (ATT/RhT) because it consisted of a unique combination of neuroepithelial, peripheral epithelial, and mesenchymal elements(6,12). Molecular and cytogenetic analyses have frequently shown partial or complete deletion of chromosome 22 in both renal and extrarenal rhabdoid tumors, and these findings confirm the common origin of these lesions. Immunohistological findings such as the presence of epithelial membrane antigen, smooth muscle actin and vimentin, a pleomorphic structure similar to that of ATT/RhTs; the identification of typical rhabdoid cells; and a lack of immunopositivity for nuclear INI 1 can be used to differentiate ATT/RhTs from medulloblastomas and other tumors of the cranium(3,6,7,14). The presence of the above factors is diagnostic for ATT/RhT if it not possible to use a method that demonstrates INI 1 positivity. INI 1 should be studied in suspicious cases where these features have not been shown but we made a diagnosis of ATT/RhT without the need for an INI 1 study as we showed these histological features in our case.

CASE PRESENTATION
A 2-year-old girl was admitted to our hospital in October 2007 with a 1-week history of a cervical tilt to the left side. The results of a blood analysis were within normal limits, and her physical examination yielded nothing remarkable except for the cervical tilt. Magnetic resonance imaging and a computed tomographic scan of the brain revealed a cystic mass of the right cerebellopontine angle (Fig. 1a, 1b). This lesion demonstrated heterogeneous enhancement with contrast infusion and had pushed the brainstem to the left. The mass was partially resected, and the cranial nerves were preserved. Tumoral tissue that had infiltrated the brainstem was not excised. The patient was mobilized on the first postoperative day. She could swallow comfortably but exhibited left-sided sixth nerve palsy and right-sided central facial paralysis. She was referred to the Department of Oncology for chemotherapy and radiotherapy to other center. The patient was treated with cisplatin (15 mg/m² intravenously per day for 5 days) and etoposide (3.3 mg/kg intravenously per day for 3 days). This regimen was given for 8 course. Afterwards, disease progressed and spinal seeding has been developed. The treatment has been changed to temozolomide 180 mg/m² peroral for five days. Additionally, She had been treated with craniospinal radiotherapy. She died with disease in 17 months after the diagnosis.

Pathological Characteristics of the Tumor
The excised tumor consisted predominantly of highly cellular sheets of small, round, undifferentiated cells and large cells with eosinophilic cytoplasm and eccentric nuclei. Low mitotic count and small foci of necrosis were noted. An immunohistochemical analysis of the tumor revealed positivity for neuron-specific enolase, smooth muscle actin, and epithelial membrane antigen. The combination of small foci of necrosis were noted. An immunohistochemical analysis of the tumor revealed positivity for neuron specific enolase, smooth muscle actin, and epithelial membrane antigen. The combination of small undifferentiated cells and large pale cells with rhabdoid characteristics and a characteristic immunohistochemical profile were consistent with a diagnosis of ATT/RhT. (Fig. 2a- c, Fig 3a-d)
DISCUSSION

Over the past 20 years, ATT/RhTs have been diagnosed by their intranuclear lack of INI 1 protein. ATT/RhTs and refractory medulloblastoma/primitive neuroectodermal tumors (MB/PNETs) exhibit similar histological, anatomic and radiographic features, but ATT/RhTs are much more aggressive than are MB/PNETs\(^2\,^5\). The mean duration of survival is 6 months after the diagnosis of an ATT/RhT in contrast to about 5 years in patients with an MB/PNET\(^9\). MB- PNETs develop at the midline of the posterior fossa and mostly present with a midline mass. They arise from the vermis and at less than 0.1% of the cases\(^1\), but Rorke and colleagues found that ATT/RhTs developed at the cerebellopontine angle in 15% of the subjects in their series\(^13\). There is no effective treatment for an ATT/RhT, and most patients with this tumor die from localized recurrence of the tumor.

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**Figure 1:** a) Axial T1 MRI scan after a contrast injection showing an extensive irregular mass at the right cerebellopontine angle and the infiltration of the tumor into the brainstem. b) Coronal T1 MRI scan after a contrast injection showing an extensive irregular mass at the right cerebellopontine angle and the infiltration of the tumor into the brainstem.

**Figure 2:** a) Immunohistochemical study showing immunopositivity for a) smooth muscle actin, b) epithelial membrane antigen, and c) neuron-specific enolase (immunoperoxidase stain, original magnification × 200).

**Figure 3:** a) The tumor cells, which are relatively uniform in size, are characterized by small cells in a pseudorosette formation (hematoxylin-eosin stain, original magnification × 200). b) Large partially vacuolized cells that consist of eosinophilic cytoplasm and that exhibit atypical mitosis (hematoxylin-eosin stain, original magnification × 200). c) Elongated cells and collagen cords (hematoxylin-eosin stain, original magnification × 200). d) Typical rhabdoid cells, which are large and possess eccentric nuclei (hematoxylin-eosin stain, original magnification × 200).
tumor or from leptomeningeal dissemination within the first year after diagnosis\(^4\),\(^6\),\(^10\),\(^11\),\(^13\). Surgical resection worsens the clinical situation and increases the incidence of morbidity and mortality in patients with an ATT/RhT as these individuals have minimal reserves and because ATT/RhTs rarely respond to treatment, despite the use of aggressive chemotherapy and/or radiotherapy\(^10\),\(^11\),\(^13\). Parmar and colleagues reported that 71\% of patients with ATT/RhT had leptomeningeal disease at the time of diagnosis and that all such tumors in their study subjects were correctly diagnosed via pathology analysis\(^11\). As a general rule, maximal tumor resection with minimal neuronal damage results in a better likelihood of survival in patients with a primary malignant intracranial or spinal lesion, but those with an ATT/RhT are exceptions. In these individuals, complete or partial resection of the tumor does not alter (and may even worsen) the prognosis due to the genetic characteristics of ATT/RhTs\(^10\),\(^11\),\(^13\). Lack of INI 1, which is a ubiquitously expressed protein encoded by the hSNF/INI 1 gene on chromosome 22q11.2.10, is characteristic of ATT/RhTs. The hSNF/INI 1 gene has been implicated as a tumor suppressor gene for peripheral rhabdoid tumors and ATT/RhTs of the central nervous system\(^11\). Haberler and colleagues retrospectively investigated the cases of 306 pediatric patients diagnosed as having a malignant primary tumor of the central nervous system\(^5\). Their investigation showed that the tumors of 26 of those patients, including 6 medulloblastoma cases, lacked the INI 1 protein while all ATT/RhTs demonstrated no immunopositivity for nuclear INI 1 protein. Those authors concluded that analysis to determine INI 1 immunopositivity should be routinely performed in all embryonic tumors of the central nervous system as a lack of immunopositivity for the nuclear INI 1 protein leads to resistance to conventional chemotherapy and radiotherapy in patients with a medulloblastoma or an ATT/ RhT. They suggest that nuclear INI 1 negative tumors, including a few medulloblastomas and all ATT/RhTs, be treated with intensive chemotherapy and radiotherapy\(^5\). These findings, however, are in conflict with those of other authors who report that duration of survival in patients with an ATT/RhT is approximately 6 months after diagnosis, despite the use of aggressive chemotherapy and/or radiotherapy\(^10\),\(^11\),\(^13\).

In our opinion, the use of aggressive treatment or conventional therapy should be decided after the INI 1 negativity or positivity of a medulloblastoma or an ATT/RhT has been determined. We suggest that clinicians should carefully compare the treatment response in patients with an INI 1 positive or INI 1 negative tumor. In the past, both INI 1 negative and INI 1 positive medulloblastomas and ATT/RhTs were diagnosed incorrectly as being medulloblastomas and were treated with the same regimen\(^5\). Now, however, it is possible to differentiate between these tumors and to treat them with different regimens, which improves the survival rate of patients. We have presented this case report to emphasize that the identification of a tumor in an unusual location, such as the cerebellopontine angle, in pediatric patients should suggest the possibility of a lesion like the rarely seen ATT/RhT as in our patient. When tumoral tissue is resected, neuronal function must be preserved to decrease the mortality and morbidity associated with surgery. It is best to identify a lack of INI 1 by means of immunohistochemical methods; however, it is possible to make a correct diagnosis in some patients' specimens with characteristic features of ATT/ RhT as in our patient without demonstrating the negative nuclear staining of ATT/RhT cells with an antibody against INI 1\(^5\). Many authors have shown that it is very unlikely for tumor cells (except ATT/RhT cells) to fail to show immunohistochemical expression of epithelial membrane
Haberler and colleagues found 6 pathology tissue samples that had been identified as being of ATT/RhT origin before the use of INI 1 in their retrospective study, and showed that using an antibody against INI1 demonstrated the negative nuclear staining of the tumor cells in these 6 specimens, and also that 11 cases were diagnosed incorrectly as medulloblastoma, rhabdomyosarcoma, ependymoblastoma or as other disorders instead of ATT/ RhT prior to the use of INI1 antibody. They thought that this discrepancy originated from poor sampling during preparation of the specimens. We identified our patient's tissue samples as being of ATT/RhT origin based on histomorphological characteristics and the results of immunohistochemical analysis, except for the use of antibodies against INI 1 to demonstrate the negative nuclear staining of tumoral cells.

CONCLUSION
We suggest that malignant primary tumors of the central nervous system, especially those located at the cerebellopontine angle, in pediatric patients should be diagnosed with noninvasive methods such as cytogenetic analysis by stereotaxic sampling of tumoral tissue, or via very limited surgery due to the deleterious effects of extensive surgery on the morbidity of patients with an INI 1 negative medulloblastoma or an ATT/ RhT.

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Received by: 05 March 2009
Revised by: 14 May 2009
Accepted: 21 May 2009

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