

Cure of Atypical Teratoid/Rhabdoid Tumor of the Central Nervous System: A Case Report

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Abstract

Atypical teratoid/rhabdoid tumor (AT/RT) is an embryonic central nervous system tumor. It has a low incidence with a high degree of malignancy and a poor prognosis. Five years ago, we successfully treated a child with AT/RT. Treatment comprised total tumor resection, 6 MV X 3D conformal radiotherapy (DT: 36Gy/18FX) and six courses of chemotherapy, including teniposide 25 mg (qd × 5d), ACNU 25 mg (qd × 1d), vincristine 1 mg (qd × 1d). There was no tumor recurrence after 5 years of follow-up. We adjusted the previous AT/RT regimen to make it more suitable for the individual treatment of this patient, and now the patient has achieved a cure. So we think this regimen is effective and it is worthy of recommendation.

Keywords

Atypical Teratoid/Rhabdoid Tumor, Case Report

1. Introduction

Atypical teratoid/rhabdoid tumor (AT/RT) is a rare embryonic tumor in the central nervous system. The tumor contains a mixture of rhabdoid cells, primitive neuroectoderm, epithelial tissues, and mesenchymal tissues. The incidence of AT/RT is low, but there is a high degree of malignancy and a poor prognosis. Cause of death is primarily tumor recurrence and metastasis. Imaging features of AT/RT such as bleeding, necrosis, and cystic changes can often be observed by MRI or CT. The most common cause of AT/RT is an abnormality in chromosome 22 with the deletions of 22q11.2. For the treatment of AT/RT, most scholars still advocate the combination of radiotherapy and chemotherapy after surgical resection. Five years ago, we treated one case of AT/RT. The patient underwent total tumor resection, conformal radiotherapy and chemotherapy. As there was no recurrence after 5 years of follow-up with no recurrence, we consi-

dered that she had been cured. We obtained the consent of the patient's parents to report the case. The case is reported herein for sharing with peers.

2. Case Report

The patient, a 3-year-2-month-old girl, was admitted due to “headache with weakness of the double lower limbs for 7 days”. The physical examination revealed the following: being conscious, normal myodynamia in the double upper limbs (*i.e.*, grade V), and grade IV myodynamia in the double lower limbs. CT scan showed a space-occupying lesion at the midline of the brain with a density similar to brain tissue, along with hydrocephalus (**Figure 1**). MRI revealed large space-occupying lesions in the ventricle with clear borders. Subsequent to contrast agent administration, most of the mass was enhanced, but we also observed some irregular sheet-like non-enhancing areas (**Figure 2**). We performed a total tumor resection under general anesthesia. During the operation, we discovered a large tumor (approximately $5 \times 4 \times 1.8$ cm) characterized by soft tumor tissue and dark red color, implying rich blood supply and we removed all the tumor tissue we could see in the bilateral ventricle and the third ventricle. Postoperative pathological diagnosis determined that it was an atypical teratoid/rhabdoid tumor (WHO Grade IV) in the lateral ventricle. Immunohistochemistry examination showed the following expressions: CK (+/-), EMA (+/-), vimentin (+), Syn (-/+), GFAP (+/-), Desmin(-), Olig2(-), NeuN(-), and INI-1(-). One month after operation, the patient received 6MV x 3D conformal radiotherapy. However, after radiotherapy ($1.8\text{Gy} \times 2\text{FX}$), the patient suffered from hydrocephalus and subdural effusion. Thus, a ventriculoperitoneal (VP) shunting was performed. Two months after VP shunting, the patient underwent 6MV x 3D conformal radiotherapy again (DT: $36\text{Gy}/18\text{FX}$). At the conclusion of radiotherapy, chemotherapy was administered as follows: teniposide 25 mg (qd \times 5d),

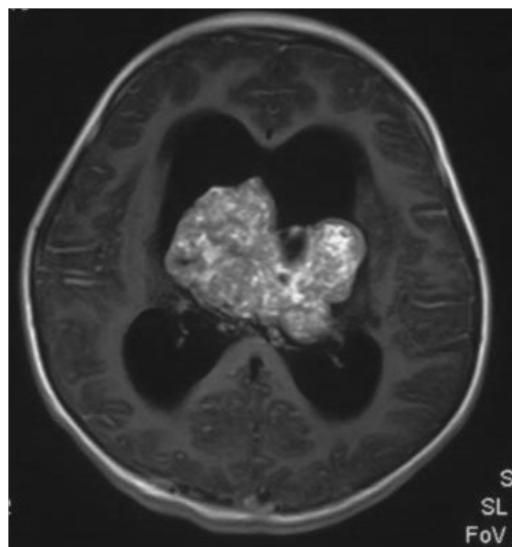


Figure 1. The preoperative CT scan shows a space occupying lesion at the midline of the brain, with a density similar to brain tissue, along with hydrocephalus.

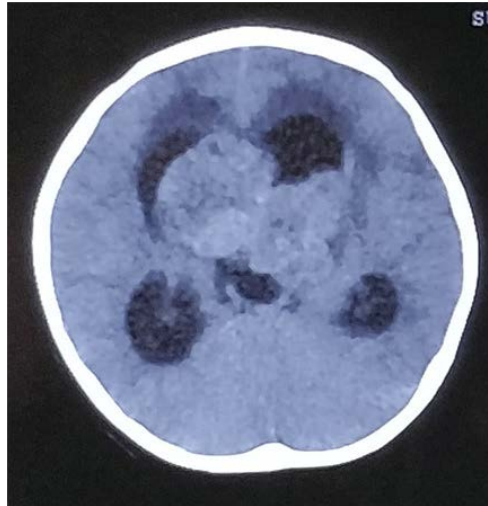


Figure 2. The MRI revealed large space-occupying lesions in the ventricle with clear borders. Most of the mass is enhanced subsequent to contrast agent administration. Some irregular sheet-like non-enhancing areas can also be observed.

ACNU 25 mg (qd \times 1d), and vincristine 1 mg (qd \times 1d) for a total of 6 courses. During chemotherapy, the patient did not have any adverse reactions to chemotherapy. In addition, the patients' general condition and cognitive activities were similar to those of children of the same age after chemotherapy. The patient was discharged home without other treatment and was advised to take valproic acid for antiepileptic action, and the patient was required to have regular reviews. At present, after 5 years of follow-up, the general condition of the patient is normal, and there is no developmental difference compared with healthy children of the same age. At the same time, we tested her neurocognition, like normal people, without being affected. MRI re-examination confirmed that there was no sign of tumor recurrence (**Figure 3**).

3. Discussion

AT/RT in the central nervous system is a rare, highly malignant embryonic tumor named by Rorke *et al.* in 1996. The tumor contains a mixture of rhabdoid cells, primitive neuroectoderm, epithelial tissues, and mesenchymal tissues [1]. In 2007, WHO classified AT/RT, embryonic neuroectodermal tumor (PNET) and medulloblastoma as Grade IV embryonic tumor. The incidence of AT/RT is approximately 1.38 per 1 million, accounting for approximately 15% of CNS tumors in children under the age of 3 [2]. This tumor has a high degree of malignancy, poor prognosis, and high mortality. Cause of death is primarily tumor recurrence and metastasis [3]. According to statistics, AT/RT occurs most often in infants or children under 3 years old, and it is rare in adults. The incidence of AT/RT is higher in males than in females, and there may be a hereditary component.

The clinical symptoms, signs, and imaging manifestations of AT/RT are varied, mainly due to factors such as the patient's age, the tumor location, and the

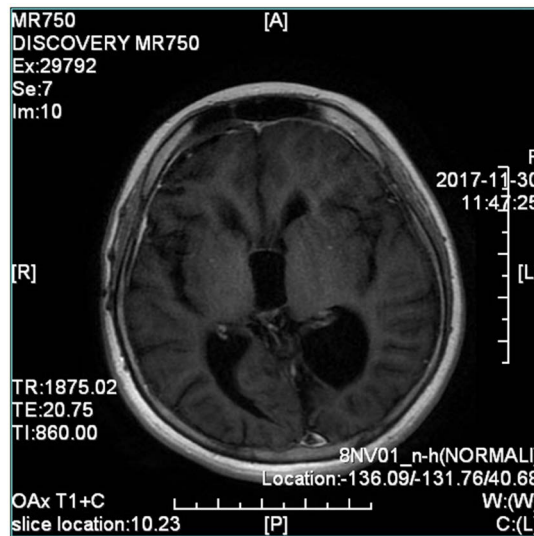


Figure 3. The MRI reexamination after five years shows no sign of tumor recurrence.

tumor size. Therefore, it often appears that different AT/RTs do not have obvious commonalities. The components of the tumor are complex. Despite similar imaging features, AT/RT needs to be differentiated from PNET and medulloblastoma. Characteristics of AT/RT include imaging features such as hemorrhage, necrosis, and cystic changes as observed through MRI or CT imaging, which are of great significance for differential diagnosis. There are also abundant vascular flow voids inside the tumor. This information can provide a certain value for differential diagnosis. Preoperative examination of the patient in this case showed significant space-occupying lesions at the midline of the brain by CT. During operation, the abundant blood supply of tumor tissues also conforms to the characteristics of AT/RT.

AT/RT has unique pathological morphology, including hemorrhage and necrosis. The physical boundary between the tumor and the surrounding brain tissue is unclear. Under light microscopy, the components of the tumor are revealed to be complex and diverse, with multiple differentiations and pleomorphisms. The morphology of the cells that make up the tumor tissue is diverse. The primitive round tumor cells are densely distributed in patches, while the epithelioid tumor cells are aggregated like nests. The primitive mesenchymal cells are distinct and have markedly deformed nuclei. The tumor is also characterized by a large number of nuclear fission phases, occasional nuclear delocalization, abundant cytoplasm, and scattered eosinophilic striated muscle (**Figure 4**). The most common histological indicators for AT/RT are cells positive for EMA, vimentin, NSE and GFAP [4]. In the case described herein, the tumor was vimentin (+) (**Figure 5**), EMA (+/-), Syn (-/+), GFAP (+/-), CK (+/-), and INI-1(-). These results are in accordance with previous studies on AT/RT.

The most common cause of AT/RT is an abnormality in chromosome 22 with the deletions of 22q11.2, where the gene INI-1 (also known as hSNF5 or SMARCB1) is located [5]. Currently, it is believed that abnormal expression of

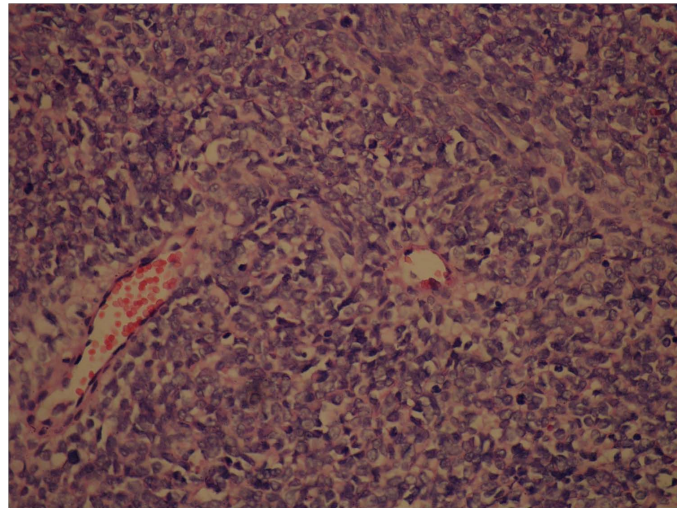


Figure 4. Hematoxylin and eosin staining of a tumor section at 400X magnification. Primitive round tumor cells are densely distributed in patches and epithelioid tumor cells are aggregated like nests. The primitive mesenchymal components between some regions are distinct, and the nucleus of tumor cell is obviously deformed. We also observed a large number of nuclear fission phases, occasional nuclear delocalization, abundant cytoplasm, and scattered eosinophilic striated muscle.

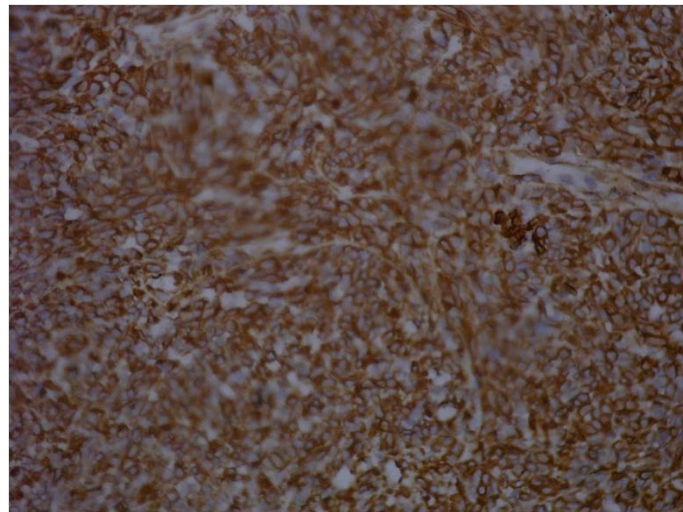


Figure 5. Vimentin is one of the most common histological indicators of AT/RT. This figure shows vimentin 400 times larger under an optical microscope.

INI-1 plays an important role in the pathogenesis of AT/RT [6]. In this case, expression of INI-1 in the tumor tissue was absent, giving further evidence that INI-1 plays an important role in the pathogenesis of AT/RT.

For the treatment of AT/RT, most scholars still advocate surgical resection followed by a combination of radiotherapy and chemotherapy. Although studies have shown that AT/RT is sensitive to chemotherapy, there are currently no clear treatment guidelines. The clinical trials conducted by research centers use a treatment protocol of cyclophosphamide, vincristine and cisplatin after surgery [7]. While the prognosis of AR/RT has improved, the overall survival time (OS)

remains approximately 11 to 24 months. In this case, we describe a modified chemotherapy plan of 25 mg (qd × 5d) of teniposide, 25 mg (qd × 1d) of ACNU and 1 mg (qd × 1d) of vincristine, for a total 6 courses of chemotherapy. After five years of follow-up, the patient was found to be in good condition with no tumor recurrence. As the follow-up time was longer than the onset age of the patient plus 9 months, the disease was considered to be cured. In previous AT/RT cases, some patients were also cured, but most patients with this disease are still prone to relapse and metastasis, and the prognosis is poor [8]. In this case, the patient's pathology was clear and provided us with a basis for improvement of the regimens, so we changed the chemotherapy regimen and dose after consulting the literature and achieved good results.

Based on our experience and knowledge of the patient's disease, we adjusted the previous AT/RT treatment regimen to make it more suitable for the individual treatment of the patient, and has obtained certain curative effect. The patient is now cured. Therefore, we believe that this program is effective and worthy of recommendation. We hope that this program can serve as the basis and reference for the treatment of this disease.

Not Published

No contents of the paper may have been presented (not published) previously.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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