Relapsing cerebral atypical teratoid/rhabdoid tumor after trimodality therapy
A case report
Linlin Meng, MD, Linlin Wang, MD, Guangrui Shao, PhD*

Abstract
Introduction: Atypical teratoid rhabdoid tumor (AT/RT) is a high-grade embryonal malignant neoplasm of the central nervous system. It is rare and most often diagnosed in children <4 years of age. The biological manifestations of AT/RTs are highly malignant and have a very poor prognosis. Here, we present the case of a 16-year-old boy with AT/RT in the right parietal lobe and with a dismal outcome.

Patient concerns: A 16-year-old male boy presented with a headache after waking up for 1 year without obvious cause. The pain was persistent and dull, mainly in the right orbital, and was slightly relieved after pressing the orbital. Occasionally, nausea and vomiting occurred, and the vomiting was gastric contents. Examination and head computed tomography performed at a local hospital revealed a space-occupying lesion in the right parietal lobe. The patient was then transferred to our hospital for further diagnosis and treatment.

Diagnosis: The patient underwent craniotomy and gross total excision of the tumor. Further histologic examination of the tumor was identified (space-occupying lesion in the right parietal lobe) AT/RT, World Health Organization grade IV.

Interventions: The patient was transferred to the oncology department for radiotherapy and chemotherapy after surgery recovery.

Outcomes: The patient did not comply with the advice for adjuvant chemotherapy regularly and the tumor recurred rapidly. Finally, the patient died after 18 months after the definitive surgery.

Conclusion: In conclusion, in the presence of a tumor with peripheral cystic components or hemorrhage in young children, a diagnosis of AT/RT must always be considered. Patients must follow the doctor’s advice for active treatment. All relevant data are within the paper and its Supporting Information files.

Abbreviations: AT/RT = atypical teratoid rhabdoid tumor, MRI = magnetic resonance imaging.

Keywords: adolescent, atypical teratoid/rhabdoid tumor, MRI, recurrence

1. Introduction
Atypical teratoid rhabdoid tumor (AT/RT) is an aggressive malignancy that occurs predominantly in infants. It can occur in any part of the nervous system, and approximately 50% of cases occur in the posterior fossa.[1-3] It was first described by Rorke et al[4] and was defined as a grade IV tumor according to the 2016 World Health Organization classification of central nervous system tumors.[5] AT/RTs are associated with the deletion of chromosome 22q and inactivation of INtegrase Interactor 1 tumor suppressor gene located on chromosome 22q11.2.[6,7] Most AT/RTs are predominantly characterized by rhabdoid cells, with additional epithelial, neuroepithelial, and mesenchymal constituents.[8,9] The clinical presentations and neuroimaging features of patients with AT/RT often lack specificity.[10] The aim of this case report was to focus on the imaging findings and poor prognosis of AT/RT in adolescent patients.

2. Case presentation
2.1. Patient history
A 16-year-old boy presented with a headache after waking up for 1 year without obvious cause. The pain was persistent and dull, mainly in the right orbital, and was slightly relieved after pressing the orbital. Occasionally, nausea and vomiting occurred, and the vomiting was gastric contents. He was admitted to a community hospital, where he was considered to have “cervical spondylosis” and was administered local massage treatment, but the condition did not improve significantly. Examination and head computed tomography performed...
at a local hospital revealed a space-occupying lesion in the right parietal lobe. The specific diagnosis and treatment processes at the local hospital are unknown. The patient was then transferred to our hospital for further diagnosis and treatment. This study was approved by the Institutional Review Board of The Second Hospital, Cheeloo College of Medicine, Shandong University.

2.2. Neurological examination findings

Physical examination revealed no sensory or motor disorders. His hearing response was normal. Pupillary reflex and eye movements were normal. The patient denied having a personal or family history of cancer, specifically brain tumors. Cerebrospinal fluid was negative for alpha-fetoprotein and placental alkaline phosphatase.

2.3. Neuroimaging findings

Magnetic resonance imaging (MRI) of the brain demonstrated a 3.0 cm × 2.0 cm × 1.8 cm well-circumscribed solid-cystic mass located in the right parietal lobe, with hypointense and patchy hyperintense on T1-weighted images, mixed hyperintense on T2-weighted images, iso- to hypointense on FLAIR images, and hypointense on diffusion-weighted images. There was edema of the white matter around the tumor. Contrast-enhanced imaging of the lesions showed strong enhancements of the solid part and cyst wall. However, the cystic components were not enhanced. The posterior horn of the right lateral ventricle and sulci around the lesion were deformed due to tumor compression. The midline was shifted to the left side (Fig. 1).

2.4. Diagnosis and treatment

The patient underwent craniotomy and gross total excision of the tumor. The tumor was grayish–white, soft, friable, mildly vascular, with areas of multifocal hemorrhage/necrosis. Further histologic examination of the tumor was identified (space-occupying lesion in the right parietal lobe) AT/RT, World Health Organization grade IV.

The patient had a stable postoperative course and was discharged after a week with a scheduled follow-up appointment. About 8 months after the operation, the brain MR showed no

---

Figure 1. Preoperative magnetic resonance imaging. A, Axial T1-weighted images demonstrated a well-circumscribed solid-cystic mass measuring 3 cm in the right parietal lobe. The mass displayed hypointensity for the most part with a cystic component showing very low intensity. Prominent peritumoral edema and midline shift were seen. B, On axial T2-weighted images, the mass showed heterogeneous high intermediate intensity. C, On axial T2 flair-weighted images, the mass showed heterogeneous low intermediate intensity. D, On diffusion-weighted images, the mass showed low and slightly high intensity. E, F, Axial and coronal T1-weighted images with administration of the contrast medium demonstrated a well-demarcated lobular mass with heterogeneous enhancement. A cystic component with no enhancement was seen in the mass.
signs of residual or recurrence of the tumor on January 6, 2019 (Fig. 2A). Subsequently, the patient was transferred to the oncology department for radiotherapy and chemotherapy after surgery recovery. The patient tolerated the adjuvant radiotherapy and chemotherapy regimen well and without complications. On March 18, 2019, the patient was admitted to the neurosurgery department again, and cerebral MRI showed that part of right parietal lobe was missing after surgery, with patch long T1 and long T2 signal areas, and the surrounding signals were not homogeneous. A small ring enhancement was observed on enhanced imaging (Fig. 2B). On April 15, 2019, the patient was admitted to the neurosurgery department. The patient relatives refused chemotherapy and were not compliant with the advice of adjuvant therapy. The patient experienced occasional dizziness and no other apparent discomfort on September 15, 2019. Brain MRI showed a contrast-enhancing mass composed of both cystic and solid areas in the right occipital lobe, with unclear boundaries (Fig. 2C). The lesion showed significant heterogeneous enhancement with obvious marginal enhancement. Tumor recurrence was considered, and the patient was recommended to be transferred to oncology department. Doctors explained the condition to the patient’s family repeatedly, and the patient’s family said that they informed consent and would make a decision after consultation. One week before March 23, 2020, he experienced headache, accompanied by vomiting, no blurred objects and no dizziness, which made him readmitted to the our hospital. MRI revealed enlargement of the tumor, 4.2 × 2.3 × 2.5 cm in size (Fig. 2D), showed evidence of progress of tumor. Finally, the patient died after 18 months after the definitive surgery. Table 1 shows the patient’s medical history.

2.5. Pathological findings

On pathological sectioning, microscopic examination revealed histological evidence of rhabdoid cells, with abundant eosinophilic cytoplasm, and large and eccentrically placed nuclei. Tumor cell atypia was evident, and mitosis was common. Immunohistochemical analysis of the neoplastic cells revealed positive reactions of antibodies to epithelial membrane antigen, vimentin, glial fibrillary acidic protein, Friend leukemia virus integration 1, oligodendrocyte lineage transcription factor 2, and vimentin (Fig. 3).

3. Discussion

AT/RTs are rare and aggressive neoplasms that account for approximately 6% of the central nervous system tumors in pediatric population.[11] Tumor diagnosis is ultimately dependent on the pathology. The clinical manifestations of AT/RT are related to tumor location and are, therefore, not specific. Because of its malignancy, AT/RTs have a high rate of local relapse and subarachnoid dissemination in the early stages,

Table 1

| Medical history timeline. |
|---------------------------|
| September, 2018           | Symptoms of headache, nausea, vomiting, CT at a local hospital revealed a space-occupying lesion in the right parietal lobe |
| November 26, 2018         | Neurosurgery department visit with referral for further treatment |
| November 29, 2018         | Brain MRI obtained demonstrating solid-cystic mass located in the right parietal lobe (Fig. 1) |
| December 02, 2018         | Subparietal craniotomy for mass removal |
| January 06, 2019          | Brain MRI obtained demonstrating gross total resection and consistent with favorable radiotherapy treatment response (Fig. 2A) |
| January 07, 2019          | Postoperative adjuvant radiotherapy begins |
| January 14, 2019          | Postoperative adjuvant chemotherapy begins |
| January 25, 2019          | Discharged from hospital |
| March 17, 2019            | Postoperative visit—symptomatic improvement and wound healing well |
| March 18, 2019            | Follow-up brain MRI obtained and with evidence of recurrence (Fig. 2B) |
| March 19, 2019            | postoperative adjuvant chemotherapy begin |
| April 15, 2019            | Postoperative visit, rejected regular chemotherapy |
| September 15, 2019        | Brain MRI obtained demonstrating increased lesion range, indicating the progress of tumor (Fig. 2C) |
| February 25, 2020         | Symptoms of headache, vomiting |
| March 23, 2020            | Brain MRI obtained demonstrating enlargement of the tumor (Fig. 2D) |
| June 21, 2020             | Patient expired |

CT = computed tomography, MRI = magnetic resonance imaging.
with 30% to 40% of patients presenting with metastases at the time of detection. Treatment approaches are multimodal, and the widely used treatment is combination of surgical resection with systemic chemotherapy and radiation therapy. High-dose chemotherapy with stem cell rescue may have value for AT/RTs and has increasingly become a popular and mainstay of adjuvant therapy following surgery. Despite the use of adjuvant chemotherapy and/or radiotherapy, the prognosis is poor, with a mean survival time of less than 1 year. Death from tumor progression occurred very rapidly in children who were not treated at the time of diagnosis. Once progression occurred in the patients being treated, death occurred rapidly. In this report, we describe a case of primary cerebral AT/RT in a young boy. The patient underwent a gross surgical resection of the mass, followed by chemotherapy and radiotherapy with no acute sequelae and partial regression of the previous symptoms. The patient was not compliant with the advice for adjuvant therapy, which led to the tumor recurrence.

Radiological findings of AT/RTs are nonspecific. They were isointense to slightly hyperintense to the gray matter on T1-weighted images and heterogeneous intermediate hyperintense on T2-weighted images, with multiple necrotic foci, cysts at the periphery of the tumor, hemorrhage, and variable contrast enhancement. Peritumoral edema is sometimes observed around the tumor. Similar to these characteristics, necrosis, hemorrhage, cystic changes, and peritumoral edema were also observed in our case. A previous study has described an unusual pattern of band-like enhancement zones surrounding the cystic or necrotic areas. Clinically, children with AT/RTs have a much worse prognosis than children with primitive neuroectodermal tumors /medulloblastomas, with little or no response to chemotherapy or radiation therapy, and death usually occurs within a year.

4. Conclusion
In conclusion, in the presence of a tumor with peripheral cystic components or hemorrhage in young children, a diagnosis of AT/RT must always be considered. Patients must follow the doctor’s advice for active treatment.

Acknowledgment
The authors thank Lulu Zhang for preparing the pathological figure.

Author contributions
Resources: Linlin Wang.
Writing – original draft: Linlin Meng.
Writing – review & editing: Guangrui Shao.

References
[1] Leon-Bojorge BD, Rueda-Franco F, Anaya-Jara M. Central nervous system atypical teratoid rhabdoid tumor: experience at the National Institute of Pediatrics, Mexico City. Childs Nerv Syst 2008;24:307–12.
[2] Buscariollo DL, Park HS, Roberts KB, Yu JB. Survival outcomes in atypical teratoid rhabdoid tumor for patients undergoing radiotherapy in a surveillance, epidemiology, and end results analysis. Cancer 2012;118:4212.
[3] Cocce MC, Lubieniecki F, Kordes U, Alderete D, Gallego MS. A complex karyotype in an atypical teratoid/rhabdoid tumor: case report and review of the literature. J Neurooncol 2011;104:373–80.
[4] Rorke LB, Packer RJ, Biegel JA. Central nervous system atypical teratoid/rhabdoid tumors of infancy and childhood: definition of an entity. J Neurosurg 1996;85:56–65.

[5] Louis DN, Perry A, Reifenberger G, et al. The 2016 world health organization classification of tumors of the central nervous system: a summary. Acta Neuropathol 2016;131:803–20.

[6] Valencia-Moya A, González-García L, Ros-López B, et al. Prognosis of atypical teratoid rhabdoid tumors (AT/RT) treated with multimodal therapy protocols. Report of our series. Neurocirugia 2016;27:87–94.

[7] Dardis C, Yeo J, Milton K, et al. Atypical teratoid rhabdoid tumor: two case reports and an analysis of adult cases with implications for pathophysiology and treatment. Front Neurol 2017;8:247.

[8] Raisanen J, Biegel JA, Hatanpaa KJ, et al. Chromosome 22q deletions in atypical teratoid/rhabdoid tumors in adults. Brain Pathol Zurich Switz 2005;15:23–8.

[9] Dufour C, Beauprè A, Le Deley MC, et al. Clinicopathologic prognostic factors in childhood atypical teratoid and rhabdoid tumor of the central nervous system: a multicenter study. Cancer 2012;118:3812–21.

[10] Nowak J, Nemes K, Hohm A, et al. Magnetic resonance imaging surrogates of molecular subgroups in atypical teratoid/rhabdoid tumor. Neuro Oncol 2018;20:1672–9.

[11] Rickert CH, Paulus W. Epidemiology of central nervous system tumors in childhood and adolescence based on the new WHO classification. Childs Nerv Syst 2001;17:503–11.

[12] Hoffman LM, Richardson EA, Ho B, et al. Advancing biology-based therapeutic approaches for atypical teratoid rhabdoid tumors. Neuro Oncol 2020;22:944–54.

[13] Ren YM, Wu X, You C, et al. Multimodal treatments combined with gamma knife surgery for primary atypical teratoid/rhabdoid tumor of the central nervous system: a single-institute experience of 18 patients. Childs Nerv Syst 2018;34:627–38.

[14] Slavc I, Chocholous M, Lensis U, et al. Atypical teratoid rhabdoid tumor: improved long-term survival with an intensive multimodal therapy and delayed radiotherapy. Cancer Med 2014;3:91–100.

[15] Zaky W, Dhall G, Ji L, et al. Intensive induction chemotherapy followed by myeloablative chemotherapy with autologous hematopoietic progenitor cell rescue for young children newly-diagnosed with central nervous system atypical teratoid/rhabdoid tumors: the Head Start III Experience. Pediatr Blood Cancer 2014;61:95–101.

[16] Meyers SP, Khademian ZF, Biegel JA, et al. Primary intracranial atypical teratoid/rhabdoid tumors of infancy and childhood: MRI features and patient outcomes. Am J Neuroradiol 2006;27:962–71.

[17] Biswas A, Kashyap L, Kakkar A, et al. Atypical teratoid/rhabdoid tumors: challenges and search for solutions. Cancer Manag Res 2016;8:115–25.

[18] Han L, Qu Y, Xie C, et al. Atypical teratoid/rhabdoid tumors in adult patients: CT and MR imaging features. AJNR Am J Neuroradiol 2011;32:103–8.

[19] Lee IH, Yoo SY, Kim JH, et al. Atypical teratoid/rhabdoid tumors of the central nervous system: imaging and clinical findings in 16 children. Clin Radiol 2009;64:256–64.

[20] Parmar H, Hawkins C, Bouffet E, et al. Imaging findings in primary intracranial atypical teratoid/rhabdoid tumors. Pediatr Radiol 2006;36:126–36.

[21] Warmuth-Metz M, Bion B, Dannemann-Stern E, et al. CT and MR imaging in atypical teratoid/rhabdoid tumors of the central nervous system. Neuroradiology 2008;50:447–52.

[22] Burger PC, Yu IT, Tihan T, et al. Atypical teratoid/rhabdoid tumor of the central nervous system: a highly malignant tumor of infancy and childhood frequently mistaken for medulloblastoma: a Pediatric Oncology Group study. Am J Surg Pathol 1998;22:1083–92.

[23] Zuccoli G, Izzo G, Bacchini E, et al. Central nervous system atypical teratoid/rhabdoid tumour of infancy: CT and MR findings. Clin Imaging 1999;23:356–60.

[24] Rahmat K, Kua CH, Ramli N. A child with atypical teratoid/rhabdoid tumour of the posterior cranial fossa. Singapore Med J 2008;49:365–8.

[25] Arslanoglu A, Aygun N, Tekhtani D, et al. Imaging findings of CNS atypical teratoid/rhabdoid tumors. AJNR Am J Neuroradiol 2004;25:476–80.