

Peritoneal metastasis of third ventricular atypical teratoid/rhabdoid tumor after VP shunt implantation for unexplained hydrocephalus

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Background: Atypical teratoid/rhabdoid tumor (AT/RT) of the central nervous system (CNS) is a highly malignant neoplasm seen frequently in infancy and early childhood. This report presents a 9-year-old girl of primary third ventricular AT/RT with peritoneal metastasis after ventriculoperitoneal (VP) shunt catheter implantation for hydrocephalus before the identification of the CNS tumor.

Methods: The data of clinical course, laboratory and imaging studies were obtained and carefully reviewed. Serial imaging studies including enhanced CT and MRI were performed at the first admission, during which the patient was diagnosed with a non-malignant communicating hydrocephalus. Secondary radiological studies were carried out 5 months after VP shunt, during which the patient demonstrated worsening clinical signs of intracranial hypertension. An imaging study identified a tumor in the third ventricle.

Results: The patient was treated by a surgical resection, showing the specimen was pathologically consistent with AT/RT 5 months after VP shunt. Systematic chemotherapy and radiotherapy were prescribed for the patient. After 6 months, PET/CT revealed peritoneal metastasis but negative findings in the CNS. The parents of the patient refused further intervention, and she died one month later.

Conclusion: VP shunt in a patient with AT/RT may cause distant seeding of the tumor in unrelated areas of

the body, even after intensive multimodality treatment. Further studies on shunt related metastases are needed.

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Key words: atypical teratoid/rhabdoid tumor; central nervous system; shunt metastasis; ventriculoperitoneal shunt

Introduction

Atypical teratoid/rhabdoid tumor (AT/RT) is a high-grade malignant embryonal tumor (WHO grade IV) usually seen in children below the age of 3 years.^[1] Though rare, the incidence of AT/RT is increasing in adults; more than 35 cases have been reported so far.^[2-5] According to recent epidemiology data for the pediatric population below the age of 14, AT/RT now is the sixth most common pediatric central nervous system (CNS) tumor (6.1%), with an age-standardized incidence rate of 1.38 per 1 000 000 persons.^[6] The presenting symptoms are related to tumor location since AT/RT can occur as isolated or multifocal lesions.^[3] The tumor can be found in the cerebral hemispheres, suprasellar, pineal, cerebellar, and cerebellopontine angles, or rarely in the spinal cord,^[1] or even only in the cerebral leptomeninges.^[7] A multimodal approach including surgery, chemotherapy, and radiotherapy is recommended to treat this disease,^[8] however, the outcome of AT/RT is dismal. The overall survival of AT/RT in children younger than 3 years ranges from 11 to 24 months.^[1]

We describe herewith a case of a 9-year-old girl initially diagnosed with non malignancy related hydrocephalus, who was discovered with AT/RT in her third ventricle 5 months after treatment with a ventriculoperitoneal (VP) shunt catheter. Following tumor resection, diffuse peritoneal metastasis along the VP shunt catheter were confirmed 6 months after the diagnosis despite aggressive chemotherapy and radiation therapy.

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Case report

This girl was admitted to our hospital at 8 years of age for 2 months of intermittent headache and vomiting. During her first visit, she complained of headache predominantly localized to the left temporal region and accompanied by intermittent non-projectile vomiting. She denied any fever or recent malaise. Physical examination was nothing abnormal. She had a diagnostic lumbar puncture at another hospital, with cerebral spinal fluid (CSF) profile showing high lymphocyte predominance, low glucose and high protein content (white blood cell [WBC] $18/\mu\text{L}$, lymphocytes 63%, monocytes 37%, protein 2191.98 mg/dL, glucose 10.10 mmol/L). The patient was suspected to have viral encephalitis with signs of intracranial hypertension. She was treated with mannitol, glycerin-fructose, latamoxef and ganciclovir before transferring to our hospital. On admission, the patient underwent diagnostic lumbar puncture and MRI of the brain. Repeat CSF analysis showed scant WBC but high protein content (WBC $2/\mu\text{l}$, protein 1391.30 mg/dL, glucose 3.40 mmol/L, lactate dehydrogenase 13 U/L, positive for Pandy's test). CSF culture revealed no infection. Enhanced CT scan revealed dilated ventricles with periventricular edema or intraventricular obstruction (Fig. 1A). MRI revealed no obvious evidence of intraparenchymal mass effect (Fig. 1B). Digital subtraction angiography was used to rule out venous sinus thrombosis or visible tumor vascularization. A presumptive diagnosis of communicating hydrocephalus was made. CST tests showed no abnormalities, and

the patient was treated with a VP shunt catheter with adjustable valve. Post-operative course was uneventful, and the symptoms of the patient resolved rapidly. She was subsequently discharged from the hospital.

The patient was asymptomatic for 5 months before she was re-admitted to the hospital due to an acute onset of headache and vomiting for 13 hours. Physical examination revealed papilledema with palsy of cranial nerve III, IV, and VI. MRI showed a $3.5 \times 3.5 \times 3$ cm mass filling the third ventricle with heterogeneous hyperintensity on enhanced T1-weighted images (Fig. 1C). There was no evidence of tumor dissemination in the cranial subarachnoid space of the spinal canal. The tumor was successfully removed by the interhemispheric transcalsal approach while preserving the VP shunt catheter. Immediate post-operative MRI showed no residual disease (Fig 1D). Pathologically, the lesion was identified as an AT/RT (Fig. 2A) and absence of integrase interactor 1 (INI1) (Fig. 2B). Chemoradiation therapy was performed for the patient in the post-operative period. The patient received one-week radiation therapy using TD8Gy/4Fx 12 days after the operation. However, the patient did not complete the therapy and left the hospital for economic problems. At another hospital, the patient received 5 cycles of chemotherapy with cisplatin ($30 \text{ mg}/\text{m}^2$) and cyclophosphamide (10 mg/kg), along with whole brain ($43\text{Gy}/24\text{Fx}+12.5\text{Gy}/5\text{Fx}$ by Intensity-modulated radiation therapy, IMRT) and spine radiation ($18\text{Gy}/10\text{Fx}+18\text{Gy}/10\text{Fx}$ by IMRT).

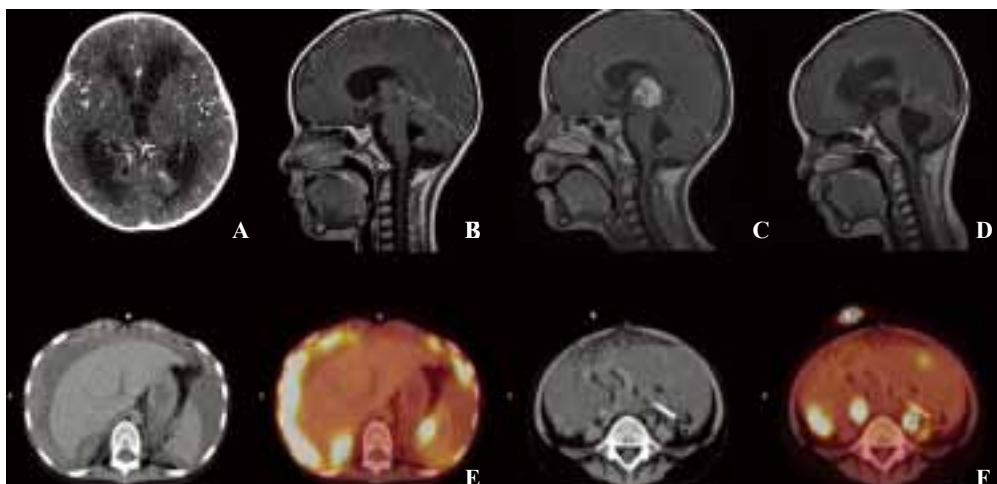


Fig. 1. A: Generalized widening of the entire ventricular system was shown by enhanced CTs before the ventriculoperitoneal (VP) shunt placement, which indicated a communicating hydrocephalus. Enhanced vascularity in the pineal region while digital subtraction angiography ruled out vascular problems and tumor; B: Enhanced MRI revealed no evidence of solid mass after VP shunt. Enhanced "C" shadow was caused by the shunt valve; C: Enhanced MRI showed a $3.5 \times 3.5 \times 3$ cm mass filling the third ventricle, which is heterogeneous hyperintense on enhanced T1-weighted images 5 months after the VP shunt; D: After tumor resection, MRI showed no tumor residue on enhanced T1 images. The enlargement of whole ventricular system without periventricular edema may be due to postoperative effect, and no symptoms of hydrocephalus were presented; E&F: PET/CT abdominal image showed severe peritoneal metastasis with high accumulation of ^{18}F -FDG and ascites with multiple metastases surrounding the peritoneal tip.

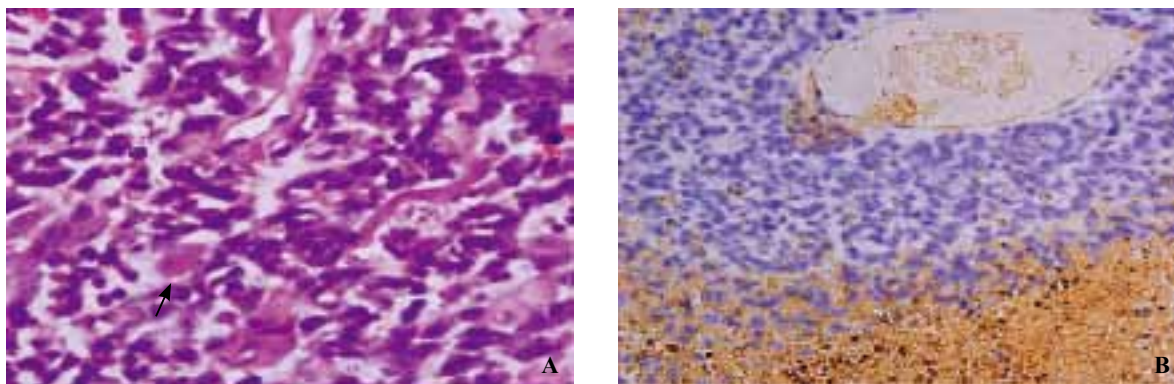


Fig. 2. A: Histology of atypical teratoid/rhabdoid tumor (AT/RT) showing multiform epithelial cells with rich tumor blood vessels. Rhabdoid cells with vesicular nuclei, prominent nucleoli and abundant, eccentric, eosinophilic cytoplasm (arrow) (HE, original magnification $\times 400$); **B:** Polyphenotypic immunoprofile of AT/RT: positive immunostaining of the nuclei in the endothelial cells and negative staining in the tumor cells (original magnification $\times 400$).

The patient was lost to follow-up 6 months after tumor resection, when she presented to our institute again for three days of abdominal pain and dyschezia. Ultrasound showed ascites with edematous bowel. Abdominal CT showed new peritoneal lesions. PET/CT revealed multiple masses with high accumulation of 18F-FDG surrounding the peritoneal tip of the VP shunt along with multiple 18F-FDG accumulating soft-tissue masses on the diaphragm and abdominal organs (Fig. 1E, F). However, MRI of the CNS provided no evidence for tumor recurrence or metastasis to the spine. Because the parents of the patient refused further test or treatment, she died because of worsening of her conditions one month later. The total time up to her death after VP shunt and tumor resection was 12 months and 7 months, respectively.

Discussion

The incidence of AT/RT is rising because of improvement in diagnostic imaging and immunohistology, specifically introduction of the marker INI1.^[9] At the time of diagnosis, patients typically present with symptoms of an advanced stage of the tumor. CT and MRI are helpful in the diagnosis of the tumor. The characteristics of this tumor on images can be one of the following: either a hyperintense or isointense solid mass with the gray matter, or, in some cases, distinct unusual patterns of a wavy band-like enhancement surrounding a central hypointensity with contrast medium on MRI.^[1,10,11] Our patient showed symptoms of hydrocephalus early without evidence of the tumor on images. Communicating hydrocephalus with a negative infectious CSF may suggest early AT/RT that can be missed by imaging study. Delayed diagnosis may influence the treatment and survival of the patient. Interestingly, we found that

VP shunt in our patient led to seeding of the tumor to the peritoneum. Our hypothesis is supported by the observation of enhanced lesions that congregate along the VP shunt catheter via PET/CT scan. A study^[12] suggested that VP shunt does not increase extracranial metastasis of pediatric primary CNS tumors, regardless of type or filter. However, there were case reports on two AT/RTs^[13,14] and other CNS tumors^[15,16] with extraneural metastases after the VP shunt. We believe that there was a correlation between VP shunt and extra CNS seeding in our patient. Further analysis with large samples is necessary to investigate the relationship between shunt and metastasis in high-grade CNS tumors. Whether VP shunt or other treatment such as third ventriculostomy for patients with tumor associated hydrocephalus remains controversial. Since there are no large studies on VP shunt-related metastases, there are no published guidelines about the methods and frequency of abdominal examinations. This case report suggests the need for abdominal examinations to rule out metastases in patients with malignant brain tumor after VP shunt. Furthermore, it is necessary to investigate lower cost alternatives for tumor diagnosis such as PET, single-photon emission computed tomography, or new test methods like plasma osteopontin^[17] for treating children with hydrocephalus in developing countries.

AT/RT is considered a highly malignant tumor, as its metastasis can occur in 13.6% of patients. Multiple therapies including tumor total resection, high-dose chemotherapy, radiotherapy, or even intrathecal chemotherapy have significantly improved the median survival time from 12 months to 46 months.^[8,18] However, the outcome of children younger than 3 years is poor with the median survival time below 12 months because of the lack of radiotherapy.^[18-20] Even in younger children, we believe that aggressive combination therapy including surgical resection along with adjuvant chemotherapy and

radiation would reduce the recurrence of primary CNS tumors. Our patient underwent total tumor resection, which was regarded as a significant prognostic factor affecting survival time.^[8,19,20] The resection was followed by chemotherapy of cisplatin and cyclophosphamide and radiotherapy with additional IMRT. Although the patient's survival time was within the predicted median survival rate for the disease, her mortality was not due to the recurrence of primary CNS tumors. The present case report suggests that aggressive use of chemotherapies^[21] and high-dose radiotherapy based on current recommendations^[19,22] decreased the recurrence of CNS tumors. Multimodality therapy might be efficacious in preventing primary CNS tumor recurrence, but it may not affect the rate of extraneural metastasis.

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