A child with atypical teratoid/rhabdoid tumour of the posterior cranial fossa

Rahmat K, Kua C H, Ramli N

ABSTRACT

Primary central nervous system (CNS) atypical teratoid/rhabdoid tumours (ATRT) are highly malignant neoplasms which usually present in infancy or early childhood. Although ATRT may arise anywhere within the CNS, the majority (approximately two-thirds) arise in the cerebellum or posterior fossa, and the remainder in the cerebrum. We described the imaging characteristics of CNS ATRT in the posterior cranial fossa of a 14-month-old boy.

Keywords: atypical teratoid/rhabdoid tumour, central nervous system neoplasm, paediatric brain tumour, rhabdoid tumour

Singapore Med J 2008; 49(12): e365-e368

INTRODUCTION

Central nervous system (CNS) neoplasms in infants and children consist of a spectrum of both glial and nonglial tumours that differ significantly in location and biological behaviour from those of adults. Paediatric brain tumours most often arise from central neuroepithelial tissue, whereas a significant number of adult tumours arise from CNS coverings (e.g. meningioma), adjacent tissue (e.g. pituitary adenoma), or metastases. The most common brain tumours in adults are supratentorial malignant gliomas, whereas primitive neuroectodermal tumour (PNET)/medulloblastoma represents the most common malignant paediatric brain tumour. There is an entity called the CNS atypical teratoid/rhabdoid tumour (ATRT) that displays similar clinical and radiological features as PNETs/medulloblastomas.[1] However, this entity is associated with significantly worse prognosis than the classic medulloblastomas.[2]

CASE REPORT

A previously-healthy 14-month-old boy with no past medical history presented to the casualty department with a ten-day history of vomiting and poor oral intake. The vomiting was non-projectile and occurred after feeding. The vomitus contained food particles with no bile or coffee-ground stain. The patient had not passed motion for the past six days prior to presentation. Otherwise, there was no fever, respiratory tract symptoms or urinary tract symptoms. On examination, the patient appeared lethargic and mildly dehydrated. He was afebrile, pink and not jaundiced. Both pupils were equal and reactive to light. The vital signs were normal and other examinations were unremarkable except for a palpable faecal mass per abdomen. Abdominal radiograph showed only faecal-laden large bowels with no evidence of bowel obstruction. The patient was subsequently investigated for vomiting and treated for constipation.

On admission, the patient developed a generalised tonic seizure which lasted for about ten minutes. Intravenous diazepam 2 mg was given. There was post-ictal drowsiness but the vital signs were stable. Subsequently, urgent computed tomography (CT) of the brain was performed and showed a poorly-enhanced ill-defined posterior fossa midline mass causing obliteration of the fourth ventricle with resultant acute obstructive hydrocephalus (Fig. 1). There was also supratentorial

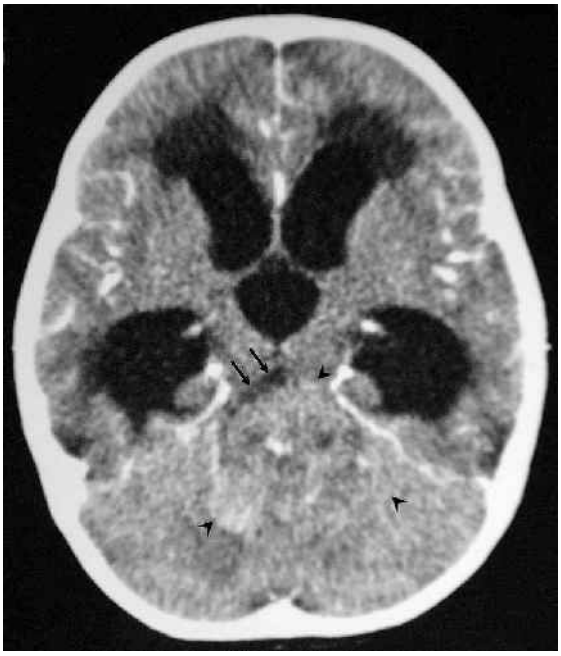

Fig. 1 Contrast-enhanced axial CT image of the brain shows an ill-defined heterogeneously-enhancing mass in the midline of the posterior fossa (arrowheads). The brainstem is compressed anteriorly (arrows) and the fourth ventricle is not seen. There are dilatations of the third and lateral ventricles with CSF seepage in keeping with acute obstructive hydrocephalus.

Department of Biomedical Imaging, Faculty of Medicine, University of Malaya Medical Centre, Kuala Lumpur 50603, Malaysia

Rahmat K, FRCR
Clinical Radiologist

Kua CH, MRad
Clinical Radiologist

Ramli N, FRCR
Associate Professor and Consultant

Correspondence to:
Dr Kartini Rahmat
Tel: (60) 3 7949 2069
Fax: (60) 3 7958 1973
Email: katt_xr2000@yahoo.com

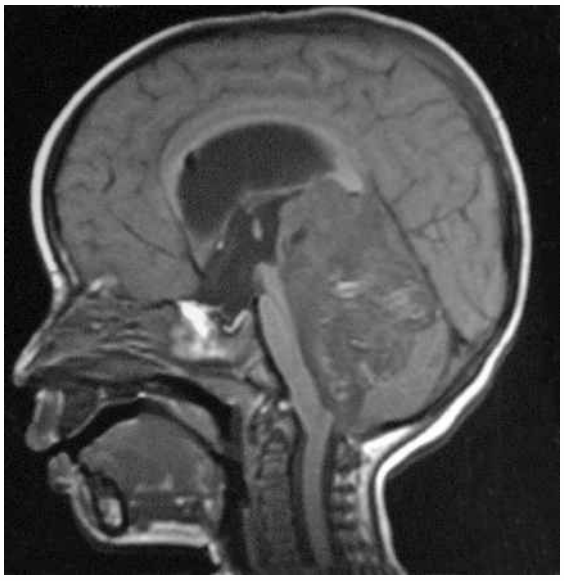

Fig. 2 Contrast-enhanced sagittal T1-W MR image of the brain shows complete filling of the fourth ventricle and upward extension of the predominantly hypointense posterior fossa mass through the cerebral aqueduct into the third ventricle. The brainstem is compressed anteriorly and the cerebellum is displaced posteroinferiorly. There is inferior extension of the mass through the cisterna magna into the foramen magnum.

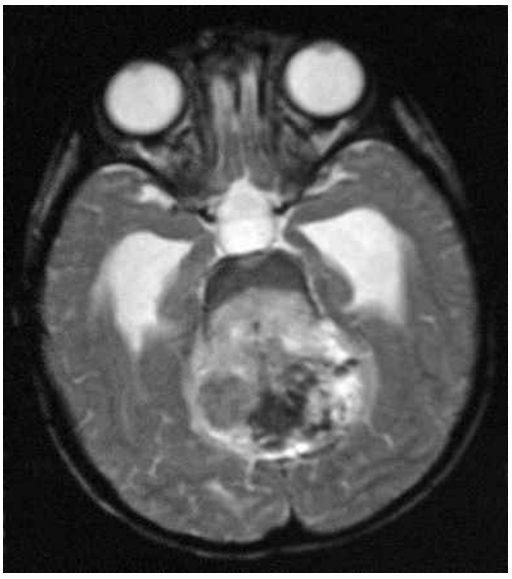

Fig. 3 Axial T2-W MR image of the brain shows marked hypointensity areas within the mass, which are slightly hyperintense on the T1-W image at the corresponding areas. These features are consistent with intracellular methaemoglobin. There was acute dilatation of the third and lateral ventricles with CSF seepage.

extension of this mass. Following the CT, the patient became bradycardic (pulse rate 69/min) and his Glasgow coma scale dropped. He was then intubated and stabilised. An urgent external ventricular drainage was performed on the patient the same night and found to have a high opening pressure of more than 15 cmH_2O. Clear cerebrospinal fluid (CSF) was obtained. The patient's vital signs returned to normal after the procedure, but he remained intubated.

Magnetic resonance (MR) imaging of the brain showed a large predominantly hypointense mass on the T1-weighted image occupying the fourth ventricle, with an upward extension through the cerebral aqueduct into the third ventricle and inferior extension through the cisterna magna into the foramen magnum. It was compressing the brainstem anteriorly and infiltrating the cerebellum posteroinferiorly (Fig. 2). Hypointense areas on the T2-weighted image were noted within the mass with a corresponding slightly hyperintense mass on the T1-weighted image, consistent with intracellular methaemoglobin. This mass caused acute obstructive hydrocephalus, as evidenced by the gross dilatation of the third and lateral ventricles associated with CSF seepage (Fig. 3). There were two small enhancing lesions which were hypointense on T1-weighted and hyperintense on T2-weighted images in the right basal ganglia and right occipital lobe, respectively, consistent with leptomeningeal dissemination. The impression at the time was a medulloblastoma or an ependymoma.

The patient was operated via the posterior fossa approach four days later. Intraoperatively, an intraventricular vascular tumour was encountered within the fourth ventricle with invasion of the cerebellum. A near-total excision was performed. The third ventricle and aqueduct of Sylvius were free of tumour. The frozen section of the tumour was reported as medulloblastoma. Histopathological examination showed tumour infiltration of the cerebellar folia. The tumour was arranged in solid sheets of malignant cells with abundant cytoplasm and large vesicular to hyperchromatic pleomorphic nuclei with prominent nucleoli. In some areas, there was presence of rhabdoid cells with eosinophilic cytoplasm and eccentric nuclei. In yet other areas, there were small round cells. There were frequent aberrant mitotic activity and extensive areas of necrosis. There was no well- differentiated epithelial structure. The malignant cells expressed vimentin, epithelial membrane antigen (EMA), glial fibrillary acid protein (GFAP), neurofilament and actin, but were negative for synaptophysin (Fig. 4). The features were consistent with atypical teratoid rhabdoid tumour (WHO grade IV).

Contrast-enhanced MR imaging of the brain and spine was done on the following day postoperatively. The previously-noted tumour bulk in the posterior fossa was now replaced with a haematoma. Leptomeningeal

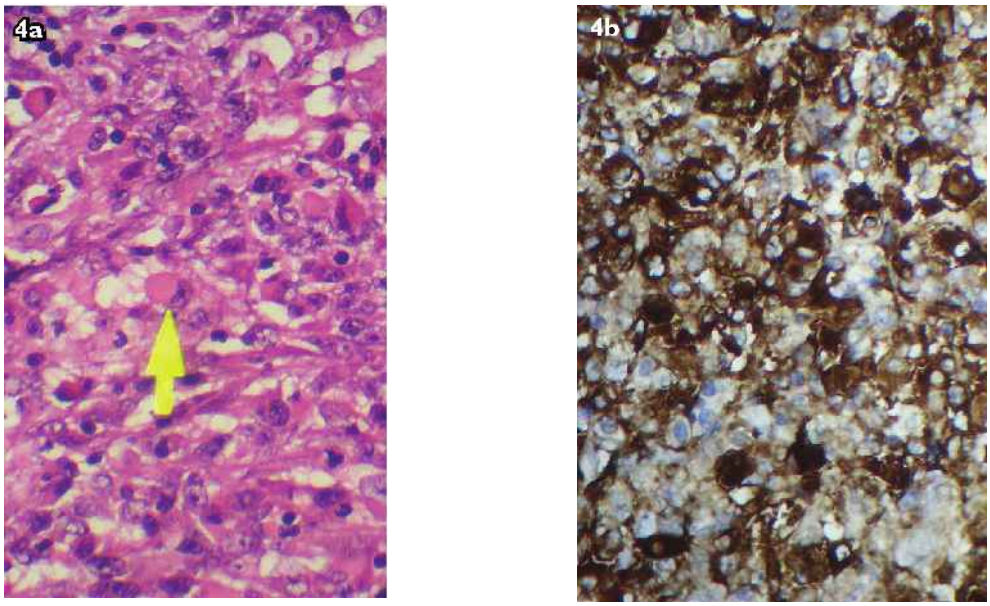

Fig. 4 Histology of the tumour mass. Photomicrographs show (a) typical large rhabdoid cells with eosinophilic cytoplasm and eccentric nuclei (arrow) (Haematoxylin & eosin, × 100); and (b) positive immunohistochemical stain for epithelial membrane antigen (EMA) using the Envision method (× 100).

enhancement of the spinal cord within the thecal sac from the level of T5 vertebra downwards was demonstrated, in keeping with drop metastases. Chemotherapy was commenced for the patient one month postoperatively. The patient developed several complications, such as persistent ventriculitis in which his CSF grew methicilin-resistant *Staphylococcus epidermidis* (MRSE), despite being on multiple intravenous and intraventricular antibiotics. He also developed neutropenic enterocolitis. Finally, the patient developed sepsis leading to septic shock, and he succumbed to his disease four months after his initial presentation.

DISCUSSION

Primary CNS atypical ATRTs are highly malignant neoplasms of infancy and childhood. The tumour usually presents in infancy or early childhood, with a mean age at diagnosis of 29 months.[2] This differs from medulloblastoma which has a peak occurrence at seven years of age.[3] Koral et al described that the mean age of presentation of ATRT was lower than that of medulloblastoma, i.e. 1.32 years vs. 6.52 years.[1] Our patient was 14 months of age, which favoured the diagnosis of ATRT. Although ATRT may arise anywhere within the CNS, the majority (approximately two-thirds) arise in the cerebellum or posterior fossa, and the remainder in the cerebrum.[3] Other sites of occurrence include the pineal region (5%) and the spinal cord (2%).[4] Our patient's tumour arose in the posterior fossa, centring at the region of the fourth ventricle.

ATRT is an aggressive tumour, and malignant local invasion is typical.[3] Intraoperative findings in our patient revealed an intraventricular vascular tumour with infiltration of the cerebellum and incomplete excision of the tumour. Apart from malignant local invasion, up to one-third of patients have CSF dissemination at the time of diagnosis.[3] This was again demonstrated in our patient in the postoperative MR imaging of the spine. ATRT carries a dismal prognosis. The death rate from the disease is 84%, with a median survival of only six months,[5] despite aggressive therapy including chemotherapy and radiotherapy. It was also reported that patients with subarachnoid tumour spread and a primary infratentorial tumour location survive only 2.5 months on average.[4] On the contrary, the five-year survival rates for PNET/medulloblastoma have achieved 90% or greater with advances in neurosurgery, chemotherapy and radiotherapy. Our patient succumbed to his disease four months after his first presentation despite aggressive management with neurosurgery and chemotherapy.

The MR imaging and CT features of ATRT consist of multiple prominent cystic / necrotic areas associated with an inhomogeneous contrast-enhanced solid component.[5,6] These MR imaging and CT features were present in our patient, and there were also areas suggestive of haemorrhage. However, these features are non-specific and the differential diagnoses include PNET/medulloblastoma, teratoma, choroid plexus papilloma and ependymoma.[5] ATRT also shows increased density on non-enhanced CT and heterogeneous contrast enhancement,[4] which were demonstrated in our patient. Unfortunately, this feature is shared with medulloblastoma which has characteristic hyperattenuation on unenhanced CT that reflects the high

nuclear-cytoplasmic ratio seen at histologic analysis.[7] On MR imaging, ATRT has decreased signal intensity on T1-weighted images which again share the same feature as medulloblastoma.[7] On T2-weighted images, they both show variable signal intensities. The other most likely alternative consideration for a hyperattenuated midline cerebellar mass in a child is ependymoma. In contrast to medulloblastoma and ATRT, an ependymoma is typically calcified and often extends from its common fourth ventricular origin through the foramen of Luschka into the adjacent cerebellopontine cistern.[7]

ATRTs are histologically-mixed tumours that contain a "rhabdoid" element plus a variable amount of PNET-like areas. Recognition of the rhabdoid element by the pathologist is critical because this phenotype correlates with a significantly worse prognosis than the classic PNET/medulloblastoma. The tumour is characterised by the presence of a distinct cell type which is called the rhabdoid cell. The cell contains a large, vesicular (i.e. lightly staining chromatin) nucleus, prominent nucleolus, and a concentration of whorled cytoplasmic intermediate filaments.[2] The rhabdoid cells of ATRTs are always immunopositive for vimentin, which is highlighted in the cytoplasmic filamentous inclusions. The large majority of tumours (95%) are also positive for EMA and 75% are positive for smooth muscle actin. Variable immunopositivity is seen for a variety of other epithelial markers (cytokeratins) and neuroectodermal markers, e.g. GFAP.[3] In our patient, the malignant cells were stained positively for all the markers mentioned above, i.e. vimentin, EMA, actin and GFAP, consistent with rhabdoid cells. The primitive neuroectodermal components of ATRTs are generally larger and more pleomorphic than those of a typical medulloblastoma, and more epithelioid than a typical malignant astrocytoma; thus the overall morphological impression is that of a clearly malignant neoplasm that doesn't quite fit with either medulloblastoma or glioblastoma.[3]

The majority of ATRTs (approximately 70%) contain areas of both rhabdoid and PNET (i.e. small blue cells) histology. However, only a few of the ATRTs contain a pure population of rhabdoid cells.[2] It is not surprising that ATRTs in the posterior fossa are often misdiagnosed as medulloblastoma, as in our case, during the frozen section intraoperatively.[8] In conclusion, ATRT is an aggressive intracranial tumour with non-specific imaging characteristics, which should be included in the differential diagnosis of a posterior cranial fossa mass in young children. As it shares many similar imaging features with medulloblastoma, immunohistochemical investigation is most helpful to differentiate the two entities.[8] This is important as their management and prognosis are different.

REFERENCES

1. Koral K, Gargan L, Bowers DC, et al. Imaging characteristics of atypical teratoid-rhabdoid tumor in children compared with medulloblastoma. Am J Roentgenol 2008; 190:809-14.
2. Yachnis AT. Neuropathology of pediatric brain tumors. Semin Pediatr Neurol 1997; 4:282-91.
3. Vogel H, Fuller GN. Primitive neuroectodermal tumors, embryonal tumors, and other small cell and poorly differentiated malignant neoplasms of the central and peripheral nervous systems. Ann Diagn Pathol 2003; 7:387-98.
4. Oh YM, Koh EJ, Choi HY. Atypical teratoid rhabdoid tumors in adult patient with multiple lesions. J Korean Neurosurg Soc 2005; 38:387-9.
5. Zuccoli G, Izzi G, Bacchini E, et al. Central nervous system atypical teratoid / rhabdoid tumour of infancy: CT and MR findings. Clin Imaging 1999; 23:356-60.
6. Parmar H, Hawkins C, Bouffet E, Rutka J, Shroff M. Imaging findings in primary intracranial atypical teratoid/ rhabdoid tumors. Pediatr Radiol 2006; 36:126-32.
7. Koeller KK, Rushing EJ. Medulloblastoma: a comprehensive review with radiologic-pathologic correlation. Radiographics 2003; 23:1613-37.
8. Arslanoglu A, Aygun N, Tekhtani D, et al. Imaging findings of CNS atypical teratoid/rhabdoid tumors. Am J Neuroradiol 2004; 25:476-80.