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

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
extension of this mass. Following the CT, the patient
came 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 cmH₂O. 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 postero-inferiorly (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, X 100); and (b) positive immunohistochemical stain for epithelial membrane antigen (EMA) using the Envision method (X 100).

Invasion 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 methicillin-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. This differs from medulloblastoma which has a peak occurrence at seven years of age. 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. 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. Other sites of occurrence include the pineal region (5%) and the spinal cord (2%). 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. 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. 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, 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. 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. 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. ATRT also shows increased density on non-enhanced CT and heterogeneous contrast enhancement, which were demonstrated in our patient. Unfortunately, this feature is shared with medulloblastoma which has characteristic hyperattenuation on unenhanced CT that reflects the high

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nuclear-cytoplasmic ratio seen at histologic analysis. On MR imaging, ATRTs have decreased signal intensity on T1-weighted images which again share the same feature as medulloblastoma. 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.

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. 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. 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.

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. It is not surprising that ATRTs in the posterior fossa are often misdiagnosed as medulloblastoma, as in our case, during the frozen section intraoperatively. 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. This is important as their management and prognosis are different.

REFERENCES