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## CASE REPORT

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# Disseminated Atypical Teratoid/Rhabdoid Tumour in a Boy: Uncommon Presentation of a Rare and Highly Aggressive Tumour of the Central Nervous System

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### ABSTRACT

*Atypical teratoid/rhabdoid tumour is a rare, highly aggressive tumour of the central nervous system, usually encountered in paediatric patients, and at presentation it is seldom disseminated. This report describes such a case in a 21-month-old boy.*

*Key Words: Brain neoplasms; Neuroectodermal tumors, primitive; Rhabdoid tumor*

## 中文摘要

### 散播型非典型畸胎瘤 / 橫紋肌樣瘤： 一名男童中樞神經系統內高度惡性罕見腫瘤

朱惠邦、蕭廣樂

非典型畸胎瘤 / 橫紋肌樣瘤是中樞神經系統一個罕見及高度惡性的腫瘤，通常在孩童出現，出現症狀時一般沒有散播。本文報告一名21月齡的男孩患有散播型非典型畸胎瘤 / 橫紋肌樣瘤。

### CASE REPORT

The patient was a 21-month-old boy who enjoyed good past health. The antenatal and perinatal history was unremarkable. He experienced vomiting on and off for six months; his symptoms became increasingly frequent in the week before presentation in June 2010. On admission, he had no feverishness, abdominal pain, or diarrhoea. On physical examination he had no neurological deficit, but there was macrocephaly; his head circumference was greater than the 97% percentile for his age-matched reference range. Urgent computed

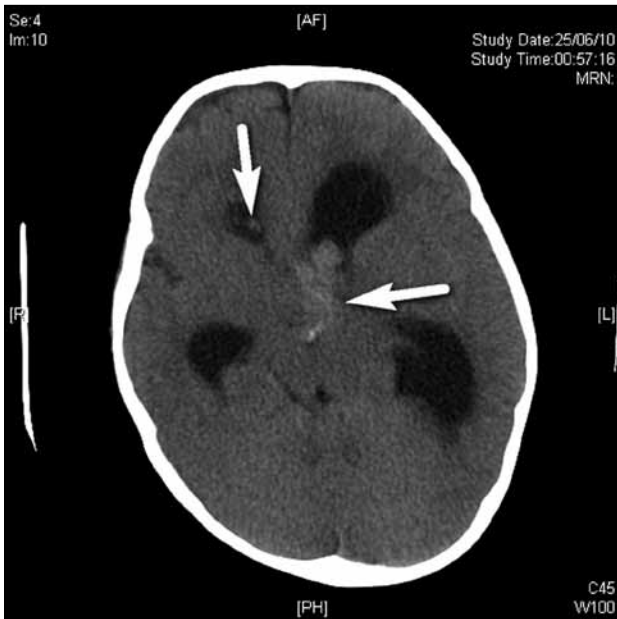
tomography (CT) of the brain performed for suspected increase of intracranial pressure yielded multifocal calcification within masses in the frontal horn of the left lateral ventricle, the foramen of Monroe and third ventricle (Figure 1). Tumours were also found over the suprasellar cistern and pineal region. Smaller nodules were attached to the walls of both lateral ventricles (Figure 2). Rightward subfalcial herniation and extensive obstructive hydrocephalus were evident. The provisional CT diagnosis was germ cell tumour with extensive intraventricular metastases.

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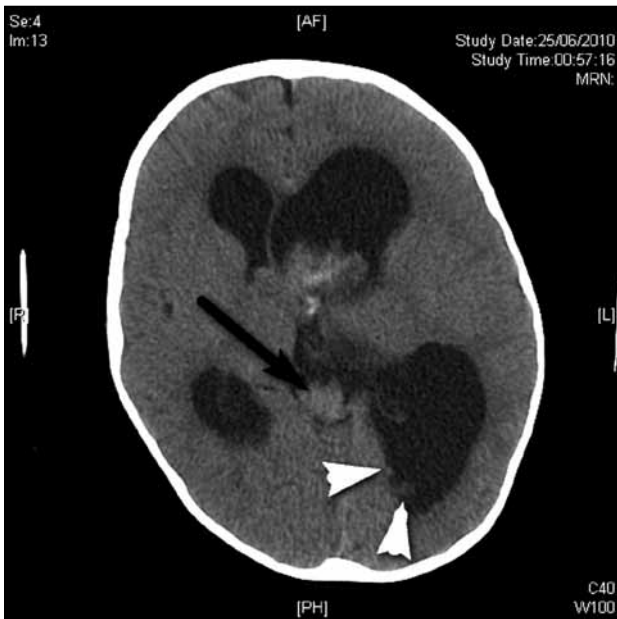
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**Figure 1.** An axial computed tomographic image shows calcification containing masses within the frontal horn of the left lateral ventricle, foramen of Monroe and the third ventricle (white arrows). Both lateral ventricles were markedly dilated.



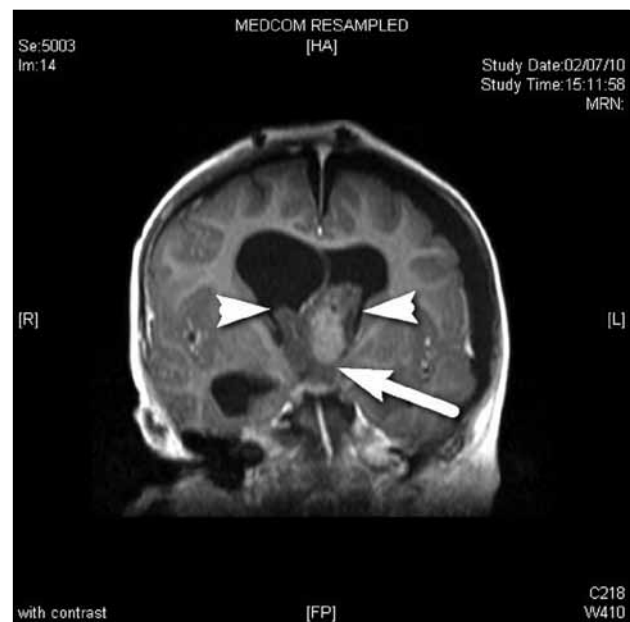
**Figure 2.** An axial computed tomographic image shows the tumour mass over the pineal region (black arrow) and smaller intraventricular nodules over the occipital horn of the left lateral ventricle (white arrowheads).

The patient's serum alpha-fetoprotein and human gonadotrophin levels were normal however. Bilaterally, external ventricular drainage catheters were inserted and an emergency endoscopic biopsy of the ventricular tumour was performed. A whitish friable and frond-like tumour was noted in the frontal horn of the left lateral ventricle.

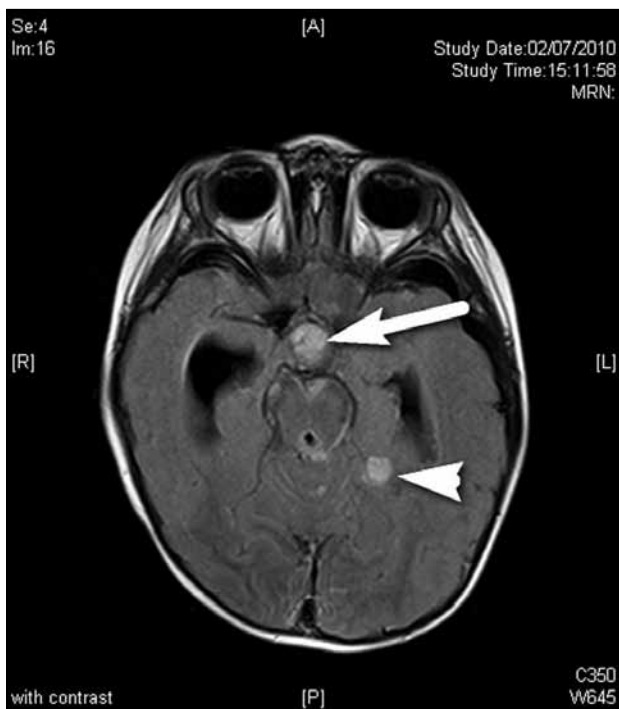
Cytological examination of the cerebrospinal fluid (CSF) revealed atypical cells suggestive of seeding. Magnetic resonance imaging (MRI) of the brain demonstrated multiple heterogeneously enhancing masses within the third and both lateral ventricles (Figure 3). Extra-axial lesions of similar signal characteristics were also present over the pineal region and suprasellar cistern.

MRI more clearly delineated the multifocal supra- and infra-tentorial leptomeningeal deposits (Figure 4) with contrast-enhancing tumours filling both internal acoustic meati.

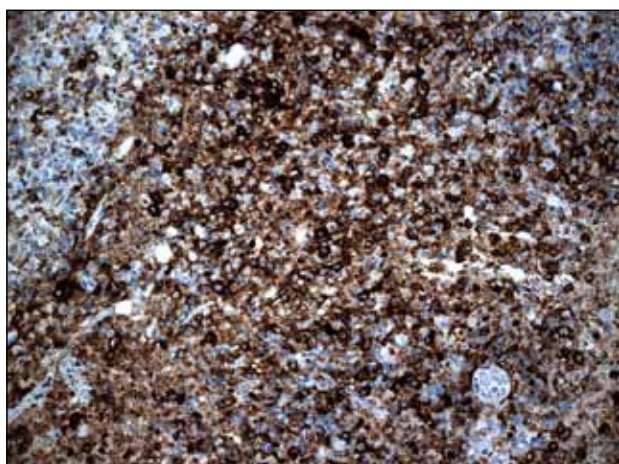
Histological examination of the biopsied tumour yielded sheets of tumour cells with prominent necrosis. The tumour comprised intermixed small and large cells; each small cell had hyperchromatic and irregular nucleus and a scanty nucleolus with abundant clear-to-eosinophilic cytoplasm (Figure 5). Rhabdoid cells were noted focally (Figure 6). Immunohistochemistry showed the tumour cells were strongly positive for epithelial membrane antigen (Figure 7), glial fibrillary acidic protein, and smooth muscle actin. Diffuse loss of nuclear INI1 immunostain in the tumour cells was evident (Figure 8). Histopathology was compatible with atypical teratoid/rhabdoid tumour with extensive intra- and extra-ventricular involvement. Supra- and infra-tentorial CSF seedlings were demonstrated by imaging.



**Figure 3.** A coronal T1-weighted magnetic resonance image obtained after injection of gadolinium shows heterogeneously enhanced masses within both dilated lateral ventricles (white arrowheads) and the third ventricle (white arrow).

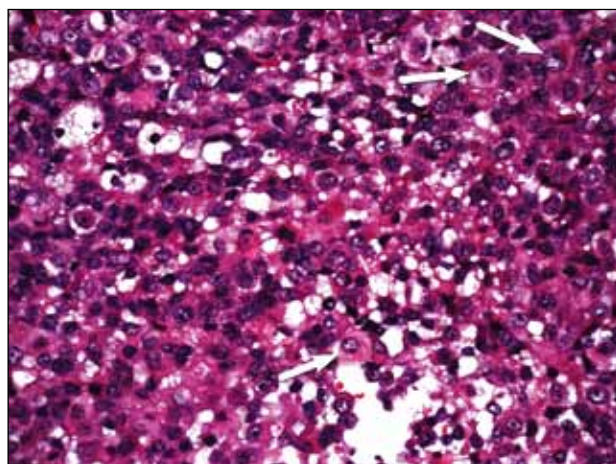


**Figure 4.** An axial fluid-attenuated inversion recovery (FLAIR) magnetic resonance image shows a hyperintense suprasellar tumour (arrow) and leptomeningeal deposit along the left tentorium (arrowhead). The temporal horns of both lateral ventricles are also dilated.

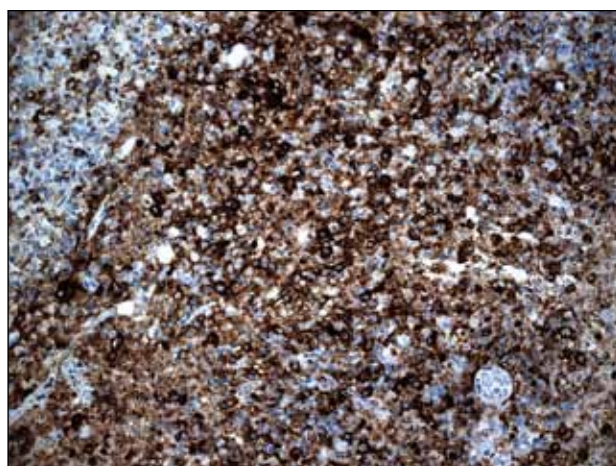


**Figure 5.** Light microscopic image with haematoxylin and eosin staining shows areas with small cells (x 100).

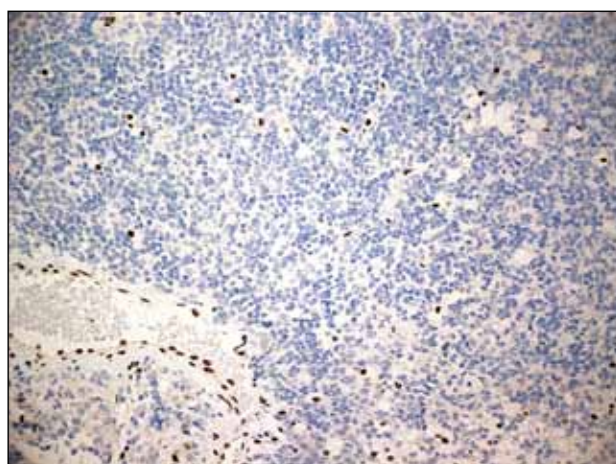
Excision of the intra-ventricular tumours was contemplated 10 days after admission. However, the patient's intracranial pressure remained elevated despite tumour excision and repeated revision of the external ventricular drainage catheters. The boy's clinical condition was always critical in the paediatric intensive care unit.



**Figure 6.** Light microscopy with haematoxylin and eosin staining shows the large cell area and the presence of rhabdoid cells (some are indicated by the white arrows) (x 400).

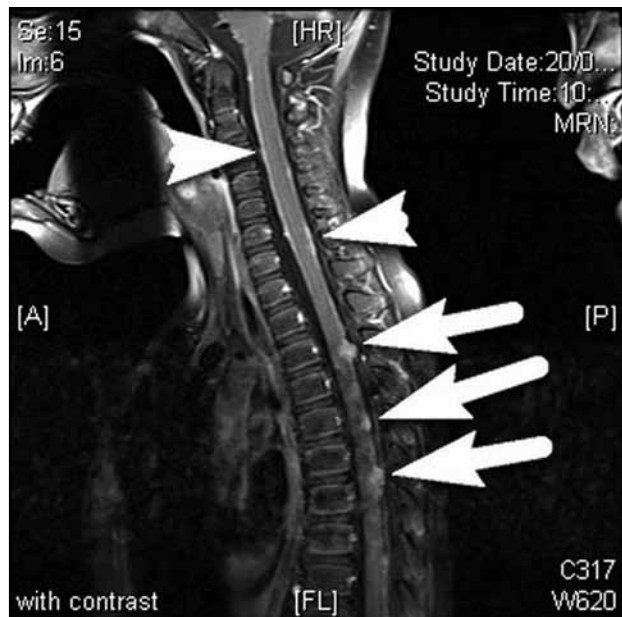


**Figure 7.** Immunohistochemical staining shows the tumour cells positive for the epithelial membrane antigen (EMA). Medulloblastoma, one of the major differential diagnoses, is typically negative for EMA (x 400).

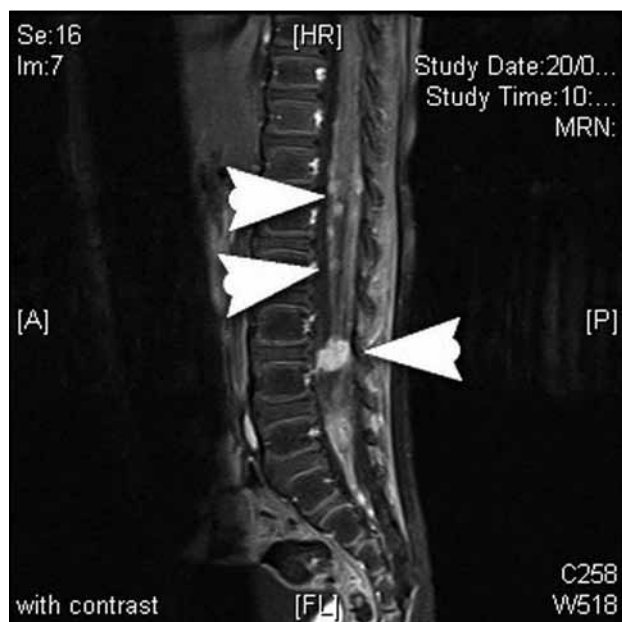


**Figure 8.** An immunohistochemical image shows the tumour cells were negative for INI1, which is a confirmatory test for atypical teratoid/rhabdoid tumour (x 100).

MRI of the spine yielded multiple drop and leptomeningeal metastases along the cervical, thoracic, and lumbar spine (Figures 9 and 10). Lesions abutting onto the cerebellum and right side of the medulla were also found.



**Figure 9.** A sagittal T1-weighted magnetic resonance image with fat suppression and obtained after injection of gadolinium showing leptomeningeal enhancement along the cervical spine (arrowheads) and multiple enhancing intradural extramedullary nodules along the cervical and upper thoracic spine (arrows).



**Figure 10.** A sagittal T1-weighted magnetic resonance image with fat suppression obtained after injection of gadolinium, showing irregular leptomeningeal enhancement and multiple enhancing intradural extramedullary nodules along the lower lumbar spine and cauda equina (arrowheads).

The pros and cons of chemotherapy and radiotherapy were discussed by the neurosurgeon and paediatric oncologists and the patient’s parents. Conservative treatment was opted for owing to the patient’s poor general condition and high risk from treatment in view of the patient’s brainstem involvement. Serial CT examinations of the brain showed persistent hydrocephalus and extensive intra-ventricular and extra-ventricular tumours. The general condition of the patient continued to deteriorate despite intensive medical and neurosurgical support. The boy passed away two months after admission.

## DISCUSSION

Atypical teratoid/rhabdoid tumour is a rare, highly aggressive tumour of the central nervous system which is usually diagnosed in childhood. The exact incidence of this disease entity is not yet established. Atypical teratoid/rhabdoid tumour was first defined as a distinct disease entity in 1987<sup>1</sup> and first included in the World Health Organization classification of tumours of the central nervous system (CNS) in 2000.

Clinical symptoms depend on the location of tumour and its associated mass effects. Common presentations are related to increased intracranial pressure and include vomiting, increased head circumference and lethargy.

Usually CT is the first-line imaging study in patients with acute neurological symptoms in emergency settings. Concerning the location, atypical teratoid/rhabdoid tumours can occur at any sites within the CNS. Extra-axial involvement, like that in our patient, has not been described commonly. Around 50% of the tumours are infra-tentorial<sup>2</sup> and can involve the cerebellopontine angles, brainstem and cerebellar hemispheres. There is a tendency for the tumours to be off midline, which is in contrast to medulloblastomas. Around 40% of them are supratentorial<sup>2</sup> and suprasellar and hemispheric involvements also occurs. As in our patient, 15 to 20% of those affected present with disseminated tumour.<sup>2</sup> Concerning its morphology, the tumour is heterogeneous in attenuation, which probably reflects the complexity of its histology. Hyperattenuating components can be found within the tumour mass and reflect increased cellularity. Intratumoural cysts and haemorrhage can also be found. Calcification is also possible, which is also present in germ cell tumours. Obstructive hydrocephalus and various mass effects are readily demonstrated. To fully delineate the extent of intracranial tumours and identify possible subarachnoid

spread along the neural axis, MRI of the brain and whole spine before and after intravenous injection of gadolinium contrast medium is the imaging modality of choice. Craniospinal radiation therapy, in addition to treatment of the primary tumour, is indicated if leptomeningeal dissemination occurs.<sup>3</sup> Concerning tumour delineation, MRI is superior to CT for demonstrating its intraventricular extent, involvement of the brainstem, and the cerebellopontine angles.

The critical step in management is to determine the correct histology, as there are no pathognomonic imaging features of this tumour. The exact diagnosis requires histological examination, usually with the aid of immunohistochemical studies. Diagnosis requires the presence of rhabdoid cells, which tend to grow in sheets. Under light microscopy, they have distinct borders, eccentrically placed nuclei and eosinophilic cytoplasm, and abundant mitotic figures and field necrosis are prominent.<sup>4</sup> However, other cell types, including mesenchymal and epithelial components, may also be found. Immunohistochemical studies have played an important role in the diagnosis. The *INI1/SNF5* gene, a tumour suppressor gene, has been localised to chromosomal band 22q.11.2, and is part of a complex protein involved in chromatin remodelling.<sup>5</sup> In paediatric patients suffering from rhabdoid tumours within and outside the CNS, inactivation of this gene has been demonstrated by lack of immunoreactivity with monoclonal antibodies against the INI1 protein.<sup>6-8</sup> It is essential to include atypical teratoid/rhabdoid tumour as a differential diagnosis when a medulloblastoma or primitive neuroectodermal tumour is considered in a child under the age of three years, as these tumours have a significantly different prognosis. Complete surgical resection of the atypical teratoid/rhabdoid

tumour appears to be the only curative treatment, but this assertion is not based on high-quality, prospective data.<sup>3</sup> The response of this tumour to radiotherapy and chemotherapy has been disappointing, median survival being about six months.<sup>9</sup>

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