Rare posterior fossa EWSR1-PATZ1 gene fusion glioneuronal tumour-mimicking ependymoma in an adolescent successfully treated with surgery alone

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DESCRIPTION

An adolescent patient presented with a several week history of gait imbalance and headaches. Neurological examination revealed left-sided weakness, dysmetria and wide-based ataxic gait. MRI demonstrated a large cystic and solid contrast-enhancing tumour (figure 1) centred around the left cerebellopontine angle without reduced diffusivity or craniospinal leptomeningeal disease (not shown). The neuroradiographic differential diagnosis included pilocytic astrocytoma, ganglioglioma and ependymoma. Neuropathology from near total resection demonstrated numerous perivascular pseudorosettes without necrosis and numerous Rosenthal fibres (figure 2A). Immunohistochemistry revealed a diffusely positive Glial fibrillary acidic protein (GFAP) (figure 2B), positive S-100, weak staining EMA and few cells positive for Ki-67. Together, the histologic findings were most consistent with a diagnosis of ependymoma WHO grade 2. Next-generation sequencing revealed an EWSR1 exon 8-PATZ1 exon 1 fusion and microarray testing revealed two small deletions, a 804 kB loss at 22q12.1 and a 1.06 Mb loss at 22q12.3 of unclear significance with no known cancer genes encompassed within these regions consistent with an integrated diagnosis of EWSR1-PATZ1 gene fusion

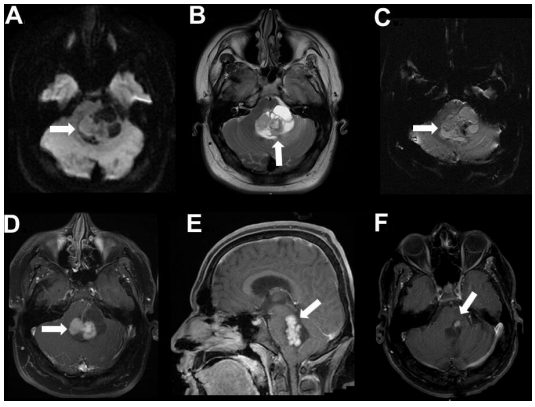

Figure 1 Neuroimaging of a glioneuronal tumour with EWSR1-PATZ gene fusion. The neuroimaging features reveal a fourth ventricular tumour (arrows) without reduced diffusivity on diffusion-weighted sequences (A) with solid/cystic features on T2-weighted sequences (B), without artifact on susceptibility-weighted sequences (C) and homogenous solid enhancement on T1-post gadolinium sequences (D–E). Five years post resection there is minimal residual enhancing tumour at the dorsum of the pons (F).

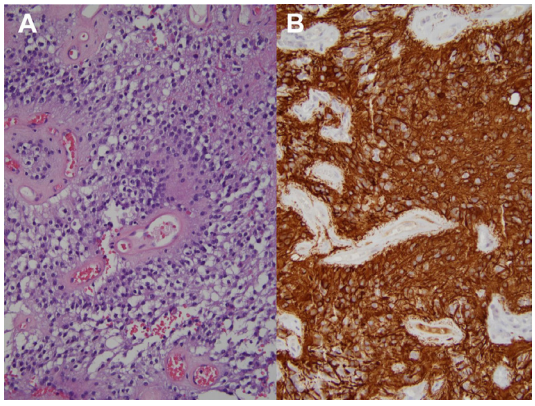

Figure 2 Neuropathological features of a glioneuronal tumour with EWSR1-PATZ gene fusion. H&E-stained section showed copious perivascular pseudorosettes with moderately hypercellular proliferation of uniform, monomorphic cells with round nuclei and clumped chromatin with scant Rosenthal fibres (A) and positive staining for GFAP (B).

glioneuronal tumour. The patient had significant postsurgical complications, including hemiplegia and lower cranial neuropathies that required extensive inpatient rehabilitation for several months and the decision was made to treat with observation alone. More than 5 years postsurgery, the patient showed remarkable neurological recovery with residual mild left-sided weakness and the MRI reveals stable minimal enhancing residual tumour at the dorsum of the pons and undergoes yearly MRI monitoring.

The EWSR1-PATZ1 fusion has been identified in a few cases of glial/glioneuronal tumours as well as extracranial sarcomas.[1–5] Translocations of the EWSR1 are typically found in intracranial Ewing sarcomas as well as primitive neuroectodermal tumours.[6] Other paediatric tumours with an EWSR-PATZ1 fusion occurring with additional mutations such as an MN1-GTSE1 fusion and a concurrent tyrosine kinase mutation have been reported that require more aggressive therapies.[7 8] PATZ1 is a transcription factor that inhibits p53 binding to its response elements and helps inhibit neural differentiation in embryonic stem cells. Dysregulation of the PATZ1 gene subsequently results in promotion of unrestricted growth in neuronal cells.[4] Due to the rarity of this entity, data are limited regarding their optimal treatment, level of aggressiveness and long-term prognosis.[5 9] At this time, EWSR1-PATZ1 gene fusion glioneuronal tumour is not

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specifically recognised in the new WHO classification of central nervous system (CNS) tumours.[10] Our case highlights the importance of molecular characterisation of tumours, as this patient may have been treated with radiation therapy with/without adjuvant chemotherapy as is the standard therapy for posterior fossa ependymoma. In summary, we present a case of a rare posterior fossa EWSR1-PATZ1 tumour with histological features of ependymoma treated successfully with surgery alone. These findings expand our understanding of this rare glioneuronal tumour with EWSR-PATZ1 fusion and highlights the importance of molecular characterisation of paediatric brain tumours in clinical decision-making.

Learning points

- EWSR1-PATZ1 fusions have been identified in glioneuronal tumours and extracranial sarcomas and rarely may be located in the posterior fossa with histologic features of ependymoma.
- EWSR1-PATZ1 fusion glioneuronal tumours of the posterior fossa may represent a unique subset of tumours treatable with surgery alone.
- Our case of an unusual posterior fossa EWSR1-PATZ1 glioneuronal tumour highlights the importance of an integrated molecular analysis in the diagnosis and management of paediatric brain tumours.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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