

Intramedullary spinal cord and intraventricular astrocytoma of varied pathology and molecular features in a teenager

Yan Yuen Lo,¹ Denise Malicki,² Michael Levy,³ John Ross Crawford⁴

¹Neurosciences, University of California San Diego, La Jolla, California, USA

²Pathology, Rady Children's Hospital University of California San Diego, San Diego, California, USA

³Neurosurgery, University of California San Diego, San Diego, California, USA

⁴Neurosciences and Pediatrics, University of California San Diego, La Jolla, California, USA

Correspondence to

Dr John Ross Crawford; jrcrawford@ucsd.edu

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DESCRIPTION

A 16-year-old male adolescent with a medical history of autism and kyphosis presented following 2 years of worsening back pain. Neurological examination revealed a wide-based gait with diminished lower extremity reflexes and abnormal joint position/vibratory sense. MRI of the spine showed a large solid and cystic heterogeneous haemorrhagic contrast-enhancing mass in the lower thoracic spinal cord and conus between T10 and L2 (figure 1A,B). The patient underwent a near total surgical resection where pathology revealed moderately cellular proliferation of glial process-forming cells with nuclear pleomorphism, mitotic activity (four mitosis per high-powered field), eosinophilic granular bodies, myxoid background and mildly hyalinised blood vessels consistent with a histopathological diagnosis of a high-grade glioma (figure 2A). An MRI of the brain was performed to assess for disseminated disease revealing a non-enhancing cystic mass in the left foramen of Monro concerning

for metastatic disease (figure 1C,D). The neuroradiographical differential diagnosis included an area of metastasis versus an unusual low-grade glioma or atypical neurocytoma. He underwent endoscopic biopsy of the intraventricular mass where pathology demonstrated a moderately cellular proliferation of small cells with round nuclei, perinuclear halos and few mitotic figures, few scattered admixed mature neurons and microcyst formations with myxoid background (figure 2B). Immunohistochemistry was diffusely positive for synaptophysin and glial fibrillar acid protein (not shown), consistent with a histological diagnosis of low-grade glioneuronal tumour (figure 2B).

Next-generation sequencing of the spinal cord tumour revealed a *KIAA1549-BRAF* fusion and microarray showed a gain of chromosome 7 with high copy gain (5×) 7q34 (*KIAA1549*), gains of chromosome 5,6,14, 16p13.13-p13.12 and a loss of 22q11.21 (*CLTCL1*, *SEPT5*). Next-generation sequencing of the brain tumour detected no somatic variants of clinical significance and

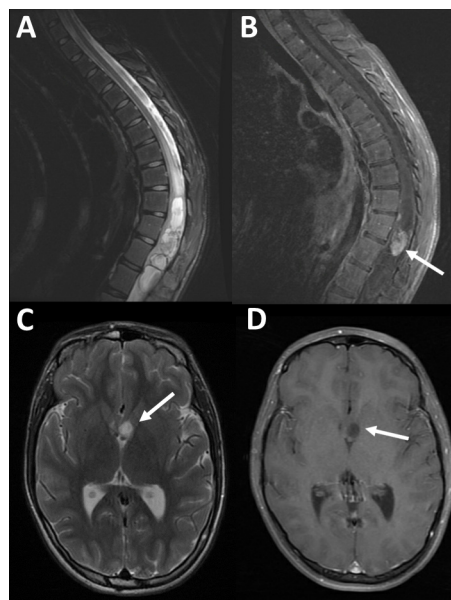


Figure 1 Neuro-radiographical features of spinal cord and intraventricular low-grade glioma. Sagittal T2-weighted MRI of the spine (A) reveals a large cystic intramedullary thoracic tumour that demonstrates focal enhancement on postcontrast T1-weighted sequences (arrow) (B). MRI of the brain revealed a cystic tumour (arrow) in the region of the foramen of Monro on T2-weighted sequences (C) without contrast enhancement (arrow) (D).

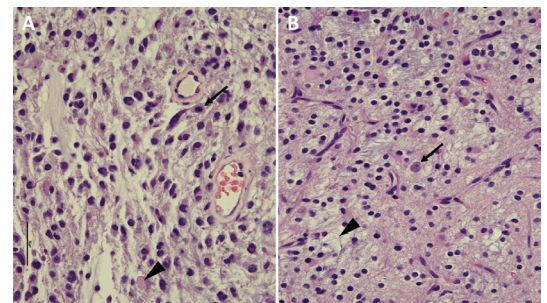


Figure 2 Pathological features of spinal cord and intraventricular low-grade glioma. Pathology of the spinal cord tumour (A) demonstrated a moderately cellular proliferation of glial process-forming cells with nuclear pleomorphism, mitotic activity (long arrow) eosinophilic granular bodies (short arrow), myxoid background and mildly hyalinised blood vessels consistent with a diagnosis of pilocytic astrocytoma with increased mitotic activity. Pathology of the intraventricular tumour (B) showed a moderately cellular proliferation of small cells with round nuclei, perinuclear halos, few mitotic figures (1 mitosis in 10 high-powered fields, not shown), few scattered admixed mature neurons (long arrow), and microcyst formation with myxoid background (short arrow). The tumour was strongly and diffusely positive for both synaptophysin and glial fibrillar acidic protein (not shown) consistent with a diagnosis of a low-grade glioneuronal tumour.



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variants of unknown significance in *PDGFRA*, *FGFR3* and *BRIP1*. Microarray showed no copy number alterations. To exclude a tumour predisposition syndrome that might explain the presence of two distinct tumours, whole-genome germline testing was performed and was normal. Based on the favourable molecular features of the spinal cord tumour, an integrated molecular diagnosis of juvenile pilocytic astrocytoma with anaplastic features was rendered, and the patient underwent observation only without evidence of recurrent disease of either the spinal or intraventricular tumour more than 5 years postsurgery.

The BRAF activating mutation of *KIAA1549-BRAF* fusion is typically associated with paediatric low-grade glioma, and duplication of 7q34 has been reported as specific to juvenile pilocytic astrocytoma.¹ More recently, however, *KIAA1549-BRAF* fusion has been reported to occur in other paediatric gliomas, including anaplastic astrocytoma.² Furthermore, even in pilocytic astrocytoma, gain of chromosome 7, as seen in the spinal cord tumour, can be associated with more aggressive disease.^{3 4} The histological features and genomic features support the classification of the lesion as juvenile pilocytic astrocytoma with anaplastic

features. The origin of the low-grade glioneuronal tumour is not entirely known. The distinct molecular and histological features compared with the spinal cord tumour do not entirely exclude the possibility of a metastatic lesion since germline sequencing did not reveal findings of a known tumour predisposition syndrome. The lack of progression of either the spinal cord or intraventricular tumour following 5 years in the absence of chemotherapy or radiation therapy confirms the lower-grade integrated diagnosis.

Our rare case of two distinct tumours of the brain and spinal cord with varied histological and molecular features treated with surgery alone associated with prolonged remission adds to the genetic diversity of paediatric low-grade glioma.

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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.

Learning points

- ▶ *KIAA1549-BRAF* fusion is commonly associated with juvenile pilocytic astrocytoma but has been reported to occur in other paediatric gliomas, including anaplastic astrocytoma.
- ▶ Delayed diagnosis of spinal cord intramedullary tumours has been reported and longer duration of symptoms is often associated with lower-grade tumours.
- ▶ We report two distinct tumours of the brain and spinal cord with varied histological and molecular features treated with surgery alone associated with prolonged remission adding to the genetic diversity of paediatric low-grade glioma.

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