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A Case of Infant-Type Hemispheric Glioma with *NTRK1* Fusion

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Abstract

The incidence of childhood central nervous system tumors in infants is about 6 per 100 000 children. Recent studies have showed recurrent fusion of the neurotrophic tyrosine receptor kinase *(NTRK)* gene in 10% of non-brainstem high grade glioma in very young children suggesting an oncogenic effect of the *NTRK* fusion genes. In this report, we present a rare, severe case of a full-term neonate who was noted to have widely splayed sutures and a bulging fontanelle at birth who was found to have infant-type hemispheric glioma with *NTRK1* fusion with course complicated by seizures refractory to medical treatment. Patient was deemed a poor surgical candidate due to the size of the mass and thus parents opted for comfort care.

Keywords

Brain tumor, brain, children, epilepsy, magnetic resonance imaging, neonate, neuroimaging, neurooncology

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Introduction

The incidence of childhood central nervous system tumors in infants is about 6 per 100 000 children with glioma having the highest incidence at 1.38 per 100 000.[1,2] Recent studies have showed recurrent fusion of the neurotrophic tyrosine receptor kinase *(NTRK)* gene in 10% of non-brainstem high grade glioma in very young children suggesting an oncogenic effect of the *NTRK* fusion genes.[3,4]

Here we present a rare, severe case of a full-term neonate who was noted to have widely splayed sutures and a bulging fontanelle at birth who was found to have infant-type hemispheric glioma with *NTRK1* fusion.

Case

A full-term infant with normal prenatal course, including a 20-week anatomy scan, was born with widely splayed sutures, bulging anterior fontanelle and head circumference >99th percentile (40 cm). Head ultrasound showed severe hydrocephalus and a large intracranial mixed echogenicity lesion in the left cerebral hemisphere with hemorrhage. He had sustained leftward gaze, and video EEG revealed seizures that were refractory to medical treatment. MRI demonstrated a large 6 × 7cm lesion, hydrocephalus with subfalcine herniation and mass effect on the brainstem (Figure 1A-B). He underwent biopsy and ventriculoperitoneal shunt placement. MRI 2 weeks later showed tumor enlargement, obstructive hydrocephalus and severe brainstem compression (Figure 1C-D). Pathology was consistent with infant-type hemispheric glioma with *NTRK1* fusion. Neurosurgery evaluated patient, who was deemed a poor surgical candidate due to the size of the mass and very young age. In the setting of this assessment, the patient's severe refractory seizures, and the resulting dismal prognosis, parents opted for comfort care.

Discussion

Infant-type hemispheric glioma, previously termed glioblastoma (GBM), is a rare, rapidly-growing congenital tumor, and prenatal imaging is often normal. Mixed-age hemorrhages and diffusion restriction is suggestive of the diagnosis.[5] Our patient represents an unusual presentation of this rare disorder due to the size of the tumor and diagnosis made at birth.

As seen in our patient, the *NTRK* genes *NTRK1, NTRK2,* and *NTRK3* are involved in infant-type hemispheric gliomas, which

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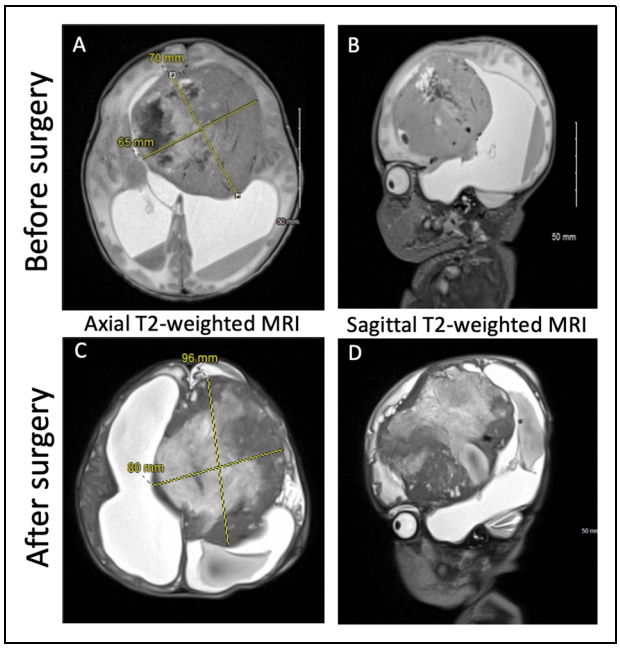

Figure 1. (A-B) Preoperative imaging. (C-D) Postoperative imaging 3 weeks after shunt placement and biopsy demonstrates a progressively enlarging mass and severe hydrocephalus.

are typically high grade in histology. A recent study by Torre *et al* showed most *NTRK*-fused gliomas were hemispheric and had a higher prevalence in non-brainstem high grade gliomas in patients younger than 3 years old. Although historically associated with high mortality and/or recurrence due to their high grade histology and aggressive nature, the prognosis of *NTRK*-fused gliomas may change with the recent FDA approval of selective pan-TRK inhibitors, larotrectinib and entrectinib.[6]

Declaration of Conflicting Interests

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Informed Consent

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