Primary giant cell tumor of the skull base with HMGA::NCOR2 fusion, an ultra-rare entity in the young pediatric patient

Kelly Shaftel, MD[1]; Smruti K. Patel, MD[2,3]

[1]Henry Ford Health,

[2]Cincinnati Children's Hospital Medical Center,

[3]University of Cincinnati College of Medicine

INTRODUCTION

Giant cell tumors (GCTs) are rare, benign but osteolytic neoplasms that typically arise from the epiphyses of long bones; fewer than 1% have been found to involve the skull or skull base, most of which involve the sphenoid and temporal bones, less commonly the occipital bone.[1] These tumors are primarily diagnosed in young adulthood,[2,3] with very few documented cases in childhood, and only two publications to date involving infants.

Further, there is a paucity of literature regarding the subset of GCTs with the HMGA::NOCR2 mutation.[4] These authors discuss an extremely rare case of a neonate diagnosed with a primary skull base HMGA::NCOR2 fusion GCT treated with surgical management.

CASE REPORT

An 8-day-old female, who failed her newborn hearing screen with her left ear, initially presented to an outside hospital for progressive difficulty breathing and vomiting. Medical workup was negative for structural or infectious etiologies. CT Head was performed, showing a large, left occipital enhancing extra-axial mass with associated erosion of the occipital and temporal bones, destruction of the mastoid air cells, semi-circular canals, and widening of the jugular foramen at the skull base with severe mass effect on the cerebellum. Subsequent MRI demonstrated a T1 isointense, T2 hypointense, enhancing, hypervascular extra-axial lesion with central necrotic core (Figure 1).

At 16-days-old, the patient underwent lesional biopsy, with initial pathology suggestive of juvenile xanthogranuloma, however, final pathology and updated gene sequencing demonstrated a HMGA-NCOR2 mutation, consistent with giant cell neoplasm. Given the very young age of the patient, she was initially treated with chemotherapy including prednisone, vincristine and cytarabine, with no response. Rather, progression of the tumor was noted, and the patient underwent two subtotal surgical debulking procedures at ages 3 and 4 months (Figure 2).

The patient was subsequently transferred to our pediatric institution for a higher level of care and additional management. After optimization of nutrition and weight, the patient underwent definitive resection of the tumor at 6-months of age. Surgical treatment resulted in near total resection with residual tumor notably left on CN VII where additional tumor removal threatened cranial nerve dysfunction (Figure 3).

Upon further follow up imaging of the lesion, it appears to continue to involute with minimal residual lesional tissue (Figure 4). Clinically, patient is also doing very well and neurologically stable and making progress with developmental milestones.

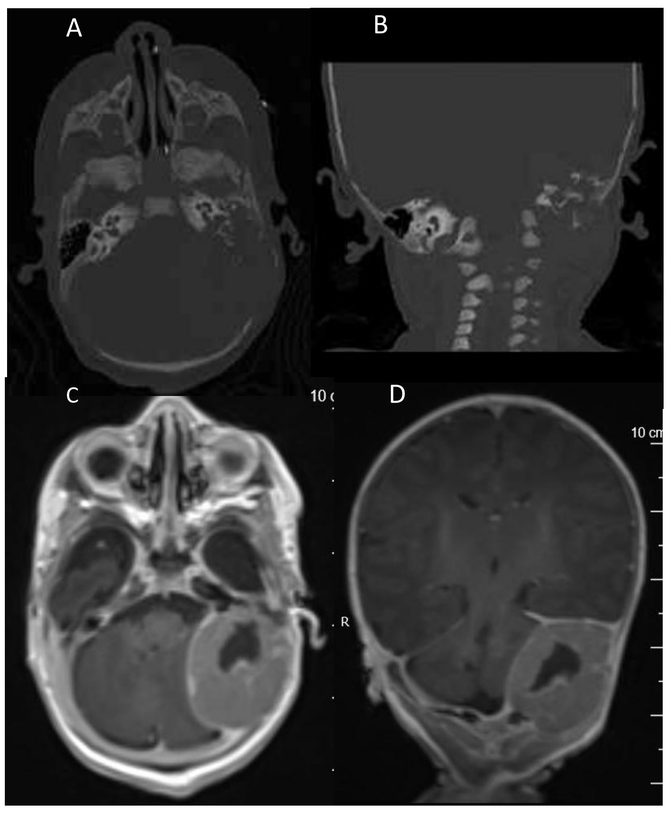

Figure 1: Initial CT head bone window axial (A) and coronal (B) views showing extensive bony erosion of the left occipital and temporal bones and mastoid air cells. Initial MRI brain with and without contrast axial (C) and coronal (D) views shows the enhancing lesion with necrotic core causing significant mass effect on the left cerebellum.

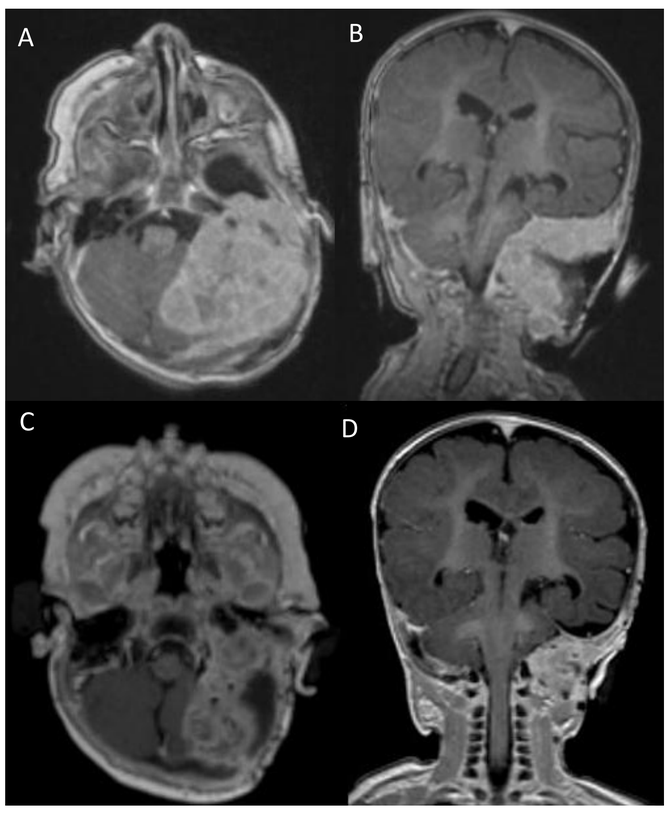

Figure 2: MRI brain post-contrast (A-D) demonstrating tumor burden after the first and second surgical debulking. Axial (A) and coronal (B) views after first subtotal surgical debulking demonstrating tumor progression and no response to chemotherapy. The patient then underwent a second surgical debulking with evidence of further subtotal resection as demonstrated in axial (C) and coronal (D) views.

DISCUSSION

Skull base GCTs are a rare entity, accounting for only 1% of all GCTs, with the majority of cases described in young adults.[3,4] Even rarer, is the incidence of pediatric skull base GCTs, particularly the subset of tumors harboring the HMGA2::NCOR2 fusion. Furthermore, prior literature describing the HMGA2::NCOR2 fusion subtype of GCTs in children demonstrate keratin-positivity on pathology, [4] which was not seen in this patient's tumor histopathology. Interestingly, tumors with this translocation have also been documented to overexpress CSF1R and thus, susceptible to pexidartinib treatment; we did not identify overexpression of CSF1R in our case.

While the clinical relevance of this is unclear, our case report further informs our understanding this unique subset of GCTs, which may behave differently in pediatric patients.

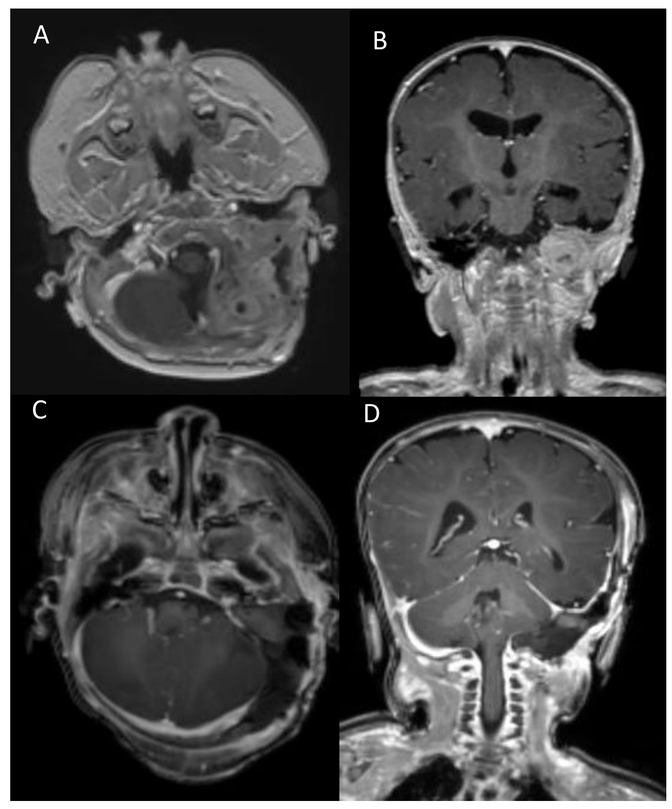

Figure 3: Further tumor progression was noted on the MRI brain post-contrast, axial (A) and coronal (B) which was completed immediately pre-operatively from planned third attempt at surgical resection. Patient underwent left sided retrosigmoid craniotomy for resection with the skull base team resulting in a near total resection (axial, C and coronal, D). Small residual of enhancing tumor surrounding CNVII and small focal area of non-enhancing presumed lesional tissue involving CN IX/X, and notably with improvement in mass effect on the cerebellum.

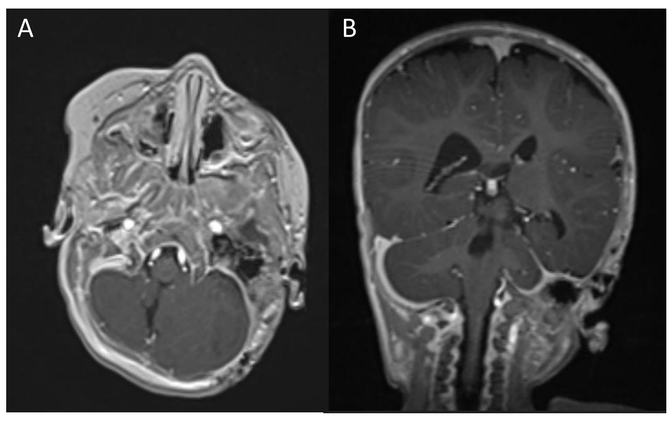

Figure 4: 16 weeks post-operative MRI with and without contrast shows decreased enhancement with no recurrence or progression of disease shown on axial (A) and coronal (B) views

CONCLUSION

To our knowledge, we present the youngest documented case to date treated primarily with surgical intervention with a promising outlook. We are also the first to describe this already rare GCT subtype with these unique pathology characteristics.

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