NEUROPATHOLOGY

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Neuropathology Education

A nine-year-old boy with temporal lobe enhancing mass

Sassan Keshavarzi,[1] Sharona Ben-Haim,[1] Denise Malicki,[2] Katayoon Shayan,[2] Hunter Volk,[3] and Michael L. Levy[1,3]

[1]Department of Surgery, Division of Neurosurgery, University of California, San Diego, [2]Department of Pathology, and [3]Division of Pediatric Neurosurgery, Rady's Children's Hospital of San Diego, San Diego, California, USA

CLINICAL HISTORY

The patient was a neurologically intact 9-year-old boy who presented to the emergency room complaining of a 1-week history of headaches. He had no significant past medical, surgical or family history. His head CT scan and MRI demonstrated a 4 cm × 5.5 cm left temporal lobe enhancing mass (Fig. 1). The patient was taken to the operating room and underwent a resection, leaving a small residual tumor seen on his post-operative MRI (Fig. 2A). The tumor was atypically firm and had a distinct border that allowed blunt dissection and resection as a single mass. This atypically well-circumscribed border was also appreciated microscopically by the pathologist (Fig. 3). Neurologically intact, the patient was discharged home only to return 4 weeks later for a second resection after undergoing MRI for the planning his stereotactic radiosurgery, which demonstrated the alarming rate of tumor growth and new tumor burden (Fig. 2B).

PATHOLOGIC FINDINGS

The HE-stained sections (Fig. 3) demonstrated a well-circumscribed high-grade glial neoplasm (Fig. 3A) containing large, bizarre cells with a markedly high mitotic rate. Giant tumor cells have vesicular nuclei with prominent nucleoli and abundant eosinophilic cytoplasm. In general there is a sharp border demarcating the tumor from the surrounding cortex, with focal evidence of tumor invasion into the brain parenchyma (Fig. 3B). Geographic necrosis was present (Fig. 3C). The reticulin stain was negative in the majority of the specimen with focal areas of minimal deposition around large groups or nests of cells (not shown). Although the vast majority of the specimen was negative for GFAP immunostaining, there were areas that were focally positive (Fig. 4A), with Ki-67 immunostaining showing an approximately 70% nuclear labeling index (Fig. 4B).

DIAGNOSIS

Giant cell glioblastoma (GCG).

DISCUSSION

Giant cell glioblastoma is an histological variant of glioblastoma with a high number of multinucleated giant cells, smaller fusiform cells and a reticulin network.[1] GCG is rare and makes up less than 5% of glioblastomas.[2–4] The mean age at presentation is 41 but the age distribution covers a wide range, including pediatrics.[2,5,6] Because of the small incidence of GCG in the pediatric population it has not been well characterized.

Typically glioblastomas spread by rapid infiltration of neighboring brain tissue and do not have a well-circumscribed border, invade the subarachnoid space or spread through the cerebrospinal fluid. A number of molecules described in the infiltration by glioblastoma multiforme (GBM) include TGF-β and AKT pathway. Another protein involved in advancing the tumor infiltration is hypoxia-inducible factor (HIF)-1α, which is up-regulated when the tumor becomes hypoxic. Typically, infiltrating borders histologically characterize glioblastoma; however, here we report on a case of pediatric GCG with a relatively well-circumscribed border. Unlike other glioblastomas, GCGs grossly appear well-circumscribed and firm to the touch, most likely secondary to their marked production of tumor stroma.[1] This was appreciated not only on histological slides but also radiographically and during our intraoperative dissection.

Correspondence: Sassan Keshavarzi, MD, Division of Neurosurgery, University of California, San Diego, 200 W. Arbor Drive, Suite 8893, San Diego, CA 92103-8893, USA. Email: skeshavarzi@ucsd.edu

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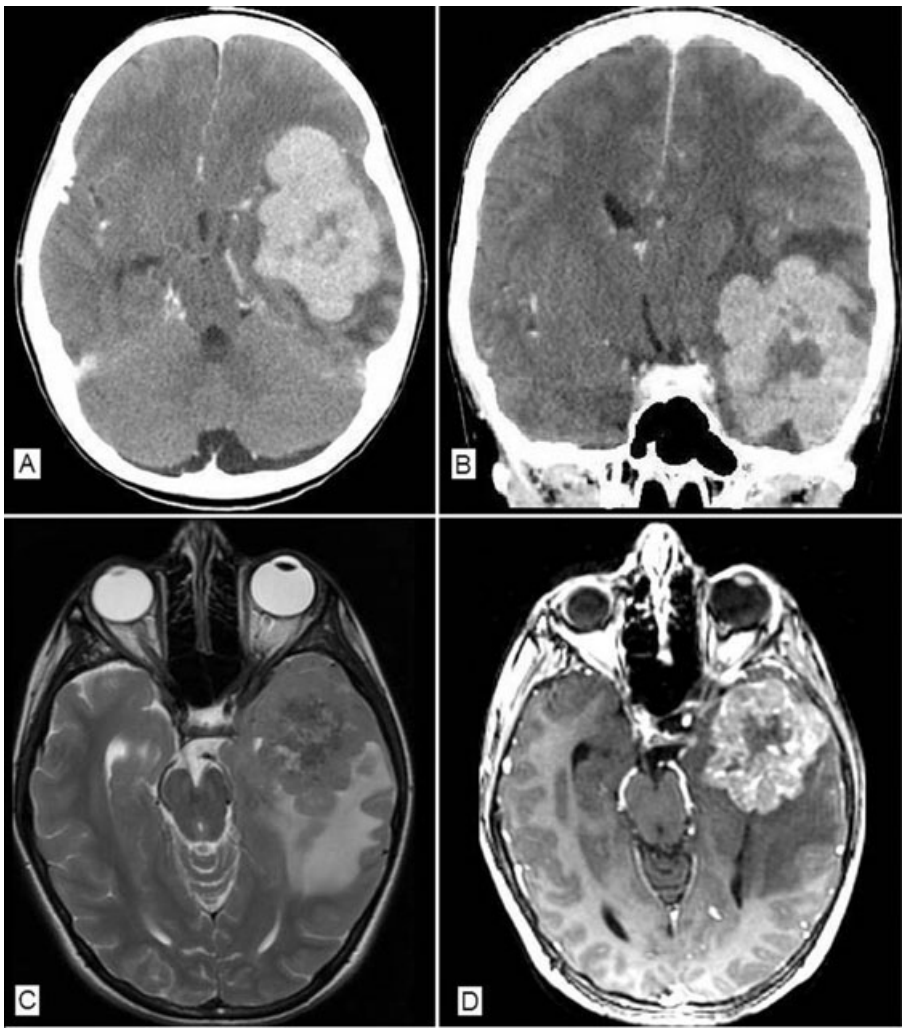

Fig. 1 (A) Axial and (B) coronal preoperative CT scan with contrast illustrating diffuse enhancement of left temporal mass with a necrotic center. (C) Preoperative axial T2 and (D) T1 MRI with contrast, demonstrating significant enhancement, mass effect and edema.

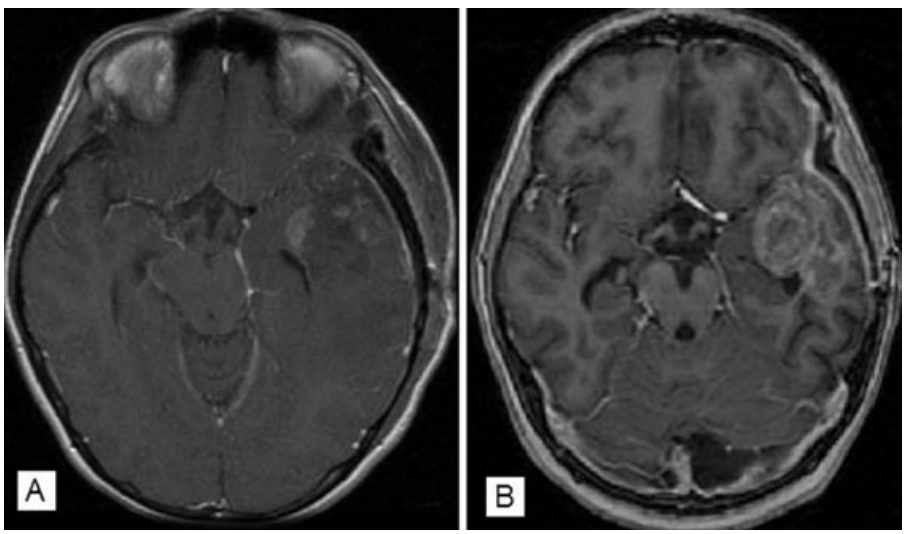

Fig. 2 (A) Axial T1 MRI with contrast demonstrating post-operative residual tumor and (B) 4 weeks post-operative axial T1 MRI with contrast demonstrating significant growth of residual tumor.

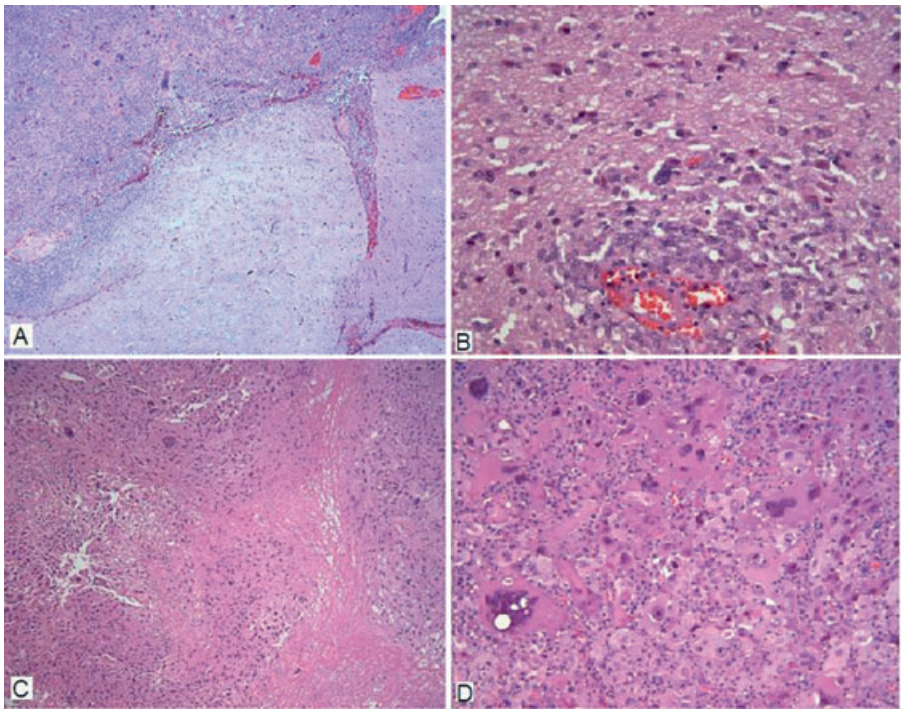

Fig. 3 (A) 40× HE stain demonstrates a sharp border between the tumor and surrounding cortex. (B) 400× HE stain which shows a few tumor cells invading the brain parenchyma. (C) 100× HE stain demonstrating geographic necrosis. (D) 200×. Large number of mitotic figures with giant cell eosinophilic cytoplasm, vesicular nuclei and large eosinophilic nucleoli.

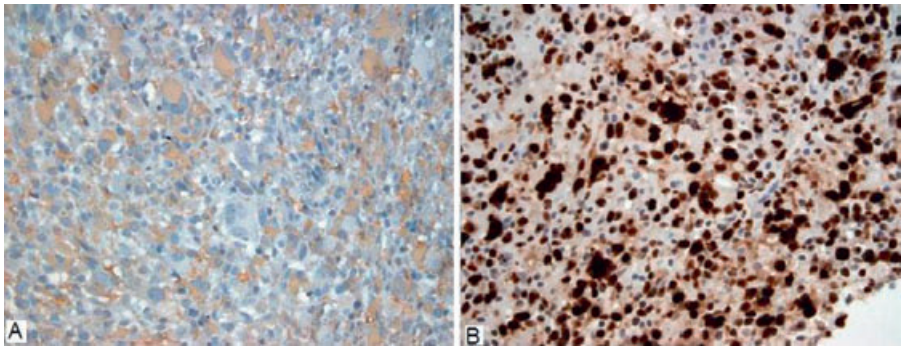

Fig. 4 (A) Focal area stained positive for GFAP (although majority of the tumor was negative). (B) Ki-67 stain with a 70% nuclear labeling index.

In evaluating a pediatric supratentorial intraparenchymal specimen with large, bizarre cells and necrosis, it is important to differentiate GCG from pleomorphic xanthoastrocytoma (PXA) with anaplastic features. Although PXA is a low-grade astrocytic tumor that typically presents in children and young adults and demonstrates benign behavior (World Health Organization grade II tumor classification), anaplastic variants and malignant potential have been described.[7] GCG and PXA both demonstrate features of gross circumscription, lymphocytic infiltrate, and prominent populations of giant tumor cells.[8] Markers such as Ki-67 and p53 do not have significant utility in discriminating the subpopulation of PXA that demonstrate malignant transformation from those that do not.[7] However, reticulin and Ki-67 help discriminate PXA with anaplastic features from GCG. Typically with a reticulin stain PXA is positive and GCG is negative. The challenge is that with malignant transformation from PXA to one with anaplastic features the reticulin deposition "may become fragmented or disappear completely",[9] and GCG can put down a reticulin network.[10] If Ki-67 labeling is positive in ~3–5% of the specimen it favors PXA with anaplastic features; if it is positive in ~20% or more it favors GCG. In this patient the reticulin stain was negative in the majority of the specimen with a minimal amount of deposition around large groups/nests of cells, and the Ki-67 labeling was positive for nearly 70% of the specimen. Both the mitotic index and reticulin stain were congruent with a diagnoses of GCG, not PXA with anaplastic features.

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