

Giant cell glioblastoma in a child: A rare case report

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ABSTRACT

Giant cell glioblastoma (GCG) is a subtype of Glioblastoma multiforme that is rare in incidence and distinct in features and histopathological examination. It is reported to have better prognosis than common glioblastomas. The incidence of GCG in children is even more rare. We report a case of GCG in a 10-year-old boy along with a review of the relevant literature focusing on the differentiating points from common glioblastoma.

Keywords: Giant cell glioblastoma, glioblastoma, pediatric

Introduction

Giant cell glioblastoma (GCG) is an unusual subtype of glioblastoma (GBM) that merits mention as a distinct variant of the classical glioblastoma in the current WHO classification of gliomas. It represents 1% of glioblastomas in general.^[1] Only around 53 published cases exist in the pediatric age group since 1952. Histopathological features of GCG include giant cells with nuclei of variable number shape and size among other features of GBM. p 53 positivity helps differentiate it from the closely related pleomorphic xanthoastrocytoma.

Case Report

A 10-year-old male child presented with recent onset headache and vomiting. On examination, the child was conscious and had no localizing signs. A contrast-enhanced CT scan was performed which showed an ill-defined intra axial mass in left parietal region with significant surrounding edema causing mass effect and midline shift to the right side. A contrast-enhanced MRI was performed to further evaluate the lesion. The MRI showed a large intra axial mass lesion in left parietal region with cystic and necrotic components with perifocal edema. The mass was heterogenous and hypointense on T1-weighted images and hyperintense on T2-weighted images. On administration of gadolinium as

contrast, the solid portions of the lesion showed intense contrast enhancement. A preoperative diagnosis of high-grade glioma was made and the patient was taken up for surgery. Intraoperatively, the lesion was ill-defined, highly vascular with solid and cystic components. Complete removal of the tumor was done. Histopathological study of the tumor revealed numerous giant cells, numerous and atypical mitoses were seen along with the usual features of glioblastoma. The overall picture was suggestive of GCG. An MRI was performed in the postoperative period and showed complete excision of the tumor. The patient recovered from the surgery and underwent radiotherapy. The last follow-up was at 8 months and there are no clinical or radiological signs of recurrence as yet.

Discussion

GCG is an extremely uncommon WHO grade IV tumor which is characterized by the presence of bizarre looking, multinucleated giant cells. The mean age at presentation has been calculated to be 51 years and a male predominance described.^[1] This type of glioblastoma is extremely rare in pediatric patients and in a large series of pediatric brain tumors, these tumors constituted 0.2%.^[2] About 9% of the cases were under 20 years of age and 6% of cases were under 10 years of age, 35% occur in people under 40 years.^[3,4] Microscopically, giant cells up to 500 μm in diameter with nuclei of variable number, size, and shape are the characteristic feature. In certain cases, abundant stromal fibrosis can be found—probably responsible for the firmness, good resectability and perhaps a better prognosis of these tumors. GCG predominates in the cerebral hemispheres, mainly subcortically in the temporal and parietal lobes.^[4] Other possible primary locations include the cerebellum,^[5] the lateral ventricles, the optic chiasm, and the spinal cord. The lesion can be multifocal.^[6]

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The duration of symptoms is usually short, and the clinical presentation is similar to that of “common” glioblastoma.^[4]

On imaging, GCG has no distinguishing features when compared with the “common” glioblastoma. Magnetic resonance (MR) may disclose a contrast enhancing heterogeneous mass, with solid and cystic areas, hypointense on T1-weighted sequences, and hyperintense on T2-weighted sequences, surrounded by edema.

However, the lesion can evolve from well circumscribed and homogeneous, to infiltrative and heterogeneous in a short period. Radiological differential diagnosis include Common GBM, Metastases from extracranial primary^[7] and even intra cerebral hemorrhage.^[8]

The treatment strategy has generally included surgery which by itself may offer 32 weeks of mean survival time. Radiotherapy has proven beneficial, adding 25 weeks to the total mean survival time. Use of chemotherapy has been described as well, although protocols are quite variable.

Treatment approaches in cases with GCG include surgery followed by radio and chemotherapy. The tumor has been variably described as friable, partially cystic, moderately vascularized, amenable to suction or as solid, firm, and well demarcated and with a good cleavage plane, adhesion to the dura can occur. The aim of surgical intervention is to achieve maximal tumor excision with no or with minimal patient deterioration.

The standard regimen for radio and chemotherapy includes fractionated focal irradiation in daily fractions of 2 Gy given 5 days per week for 6 weeks, for a total of 60 Gy, and continuous daily temozolomide (75 mg per m² of body-surface area per day, 7 days per week from the first to the last day of radiotherapy), followed by 6 cycles of adjuvant temozolomide (150 to 200 mg per m² for 5 days during each 28-day cycle).^[9]

A total or subtotal resection can be achieved in a greater percentage of patients when advanced MRI techniques and intraoperative MRI techniques are used.^[10]

A positive relationship has been shown between the length of survival of patients with glioblastomas and the presence of the giant cell variety. The more circumscribed radiologic and histopathologic appearance of GCG may permit more complete resection and thus improve prognosis compared with GBM.^[1]

An important morphological differential diagnosis of GCG is pleomorphic xanthoastrocytoma. GCG has numerous great-sized giant cells, numerous atypical mitoses, necrosis with pseudo-palisading and rapid evolution of seizures in comparison with pleomorphic astrocytoma.^[2] Immunohistochemistry is positive for p53 but negative for neuronal nuclear antigen, neurofilament protein, and synaptophysin in case of giant cell astrocytoma. The

reverse is true for pleomorphic astrocytomas. Anaplastic astrocytomas are differentiated from GCGs by a more rapid clinical course, more number of mitosis, and more frequent large-sized multinucleated giant cells in case of GCGs. Giant tumor cells may show lipid accumulation,^[11] and abundant microcalcifications may be present as well.^[11] Infiltration of the tumor by cells pertaining to the immune system can be prominent, namely mononuclear leukocytes and eosinophilic granulocytes.

In GCG, gene p53 (syn. TP53) has a mutation in 75 to 89% of the cases.^[12] p53 protein is involved in cell cycle arrest and apoptosis when DNA is damaged. Mutant p53 proteins are stable and can be detected by immunohistochemistry. These techniques disclose positivity for p53 protein in GCG. Approximately 30% frequency of PTEN (phosphatase and tensin homologue) gene mutations is recorded in GCG.^[13] The PTEN gene is located on chromosome 10 and it is related to cell cycle arrest, apoptosis, and inhibition of cell motility; mutation allows cell division. A chromosomal abnormality consisting of loss of 17p, 1p, and 19q has been described for GCG; the combination of 1p and 19q deletions has been associated with a better prognosis.

Conclusion

GCG is subtype of glioblastoma that has distinct pathological features that differentiate it from common glioblastoma, though often the clinical and radiological features are similar in both. Overall, analyses of survival in large series seem to agree that the prognosis is somewhat better than that of “common” glioblastoma. Incidence in children is even more rare than in adults and merits mention to spread awareness about this variant of glioblastoma that may have a slightly better prognosis.

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