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Case Report

Giant Cell Glioblastoma - A Rare Pediatric Cerebral Neoplasm

Indranil Chakrabarti[1], Nilanjana Ghosh[2]

1. Dept. of Pathology, North Bengal Medical College, Siliguri, India
2. Dept. of Community Medicine, North Bengal Medical College, Siliguri, India

ABSTRACT

Giant cell glioblastoma is an extremely rare variant of Glioblastoma (WHO grade IV) which is characterized by a predominance of bizarre, multinucleated giant cells. These tumors comprise of 0.8% of brain tumors and up to 5% of glioblastomas. In pediatric age group, these tumors are still uncommon with only around 53 published cases since 1952. Here, we report a case of a 12- year old female patient who presented in outpatient clinic with a short period history of headache and seizures. A CT scan showed a large right sided frontal space occupying lesion with areas of calcification. The patient was operated and subsequent histopathology revealed a high-grade astrocytic tumor with increased cellularity, atypical mitosis, bizarre multinucleated giant cells along with large areas of ischemic necrosis and calcification. A diagnosis of Giant cell glioblastoma (WHO Grade IV) was made. The patient was symptomatically well at 3-month follow-up.

Keywords: Giant Cell Glioblastomas; Children

Introduction

Giant cell glioblastomas are rare tumors of the central nervous system, which have warranted a special mention under Glioblastoma multiforme. They are characterized a predominance of grotesque, multinucleated giant cells and comprise of 0.8% of brain tumors and up to 5% of glioblastomas (1). Giant cell glioblastomas predominate in the cerebral hemispheres but have also been described in the cerebellum, lateral ventricles, the optic chiasm and spinal cord, the mean age of presentation being 42 years and a male/female ratio of 1.6:1 (2). Here, we report a case of a Giant cell glioblastoma in a pediatric patient. In pediatric age group, this type of tumor is extremely rare with only around 53 such cases described since 1952 (3). The prognosis of this type of tumor is believed to be better than conventional

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Address communications to: Dr Indranil Chakrabarti, Dept. of Pathology, North Bengal Medical College, Siliguri, India
Email: dr.inch@yahoo.co.in

glioblastomas although this view has been challenged by some authors.

Case report

A 12-year-old female patient presented to the Outpatient Clinic of North Bengal Medical College in 2010 with complains of headache and few episodes of projectile vomiting for the last three and a half months. The patient also suffered from two episodes of seizures in the last two days. However, on neurological examination, there was no evidence of any sensory or motor deficit. A computerized tomography (CT scan) revealed a large, irregular attenuated mass lesion in the right frontal region going to deep basal ganglia area, corpus callosum and crossing the midline with areas of internal necrosis and calcification. There was evidence of post-contrast heterogenous enhancement. Frontal horns of lateral and third ventricle were compressed (Fig. 1). A provisional radiological diagnosis of anaplastic astrocytoma was made. The mass was surgically removed and the specimen was submitted for histopathological examination. Gross examination showed a 5.0 X 4.0 X 4.0 cm mass, grayish in color with areas of necrosis, congestion, and hemorrhage. Histopathology revealed a highly malignant glial tumor containing large, grotesque looking multinucleated giant cells, some containing up to 10 nuclei. Some of the nuclei contained prominent nucleoli and atypical mitotic figures (Fig. 2). There was presence of few small, fusiform syncitial cells. Areas of hemorrhage, ischaemic necrosis, and calcification were noted. An isolated focus showed the presence of foamy, xanthoma-like cells (Fig. 3). A morphological diagnosis of giant cell glioblastoma was made. The patient was further treated with adjuvant chemotherapy (with temozolomide) and radiotherapy. The patient symptomatically improved at 3-month follow-up.

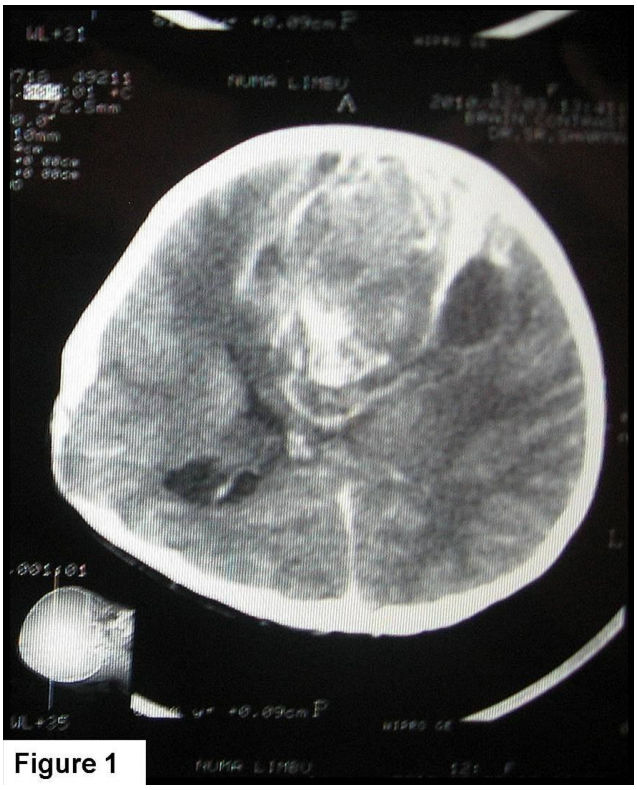

Fig. 1- Photograph of CT scan showing the bifrontoparietal Space Occupying Lesion (SOL)

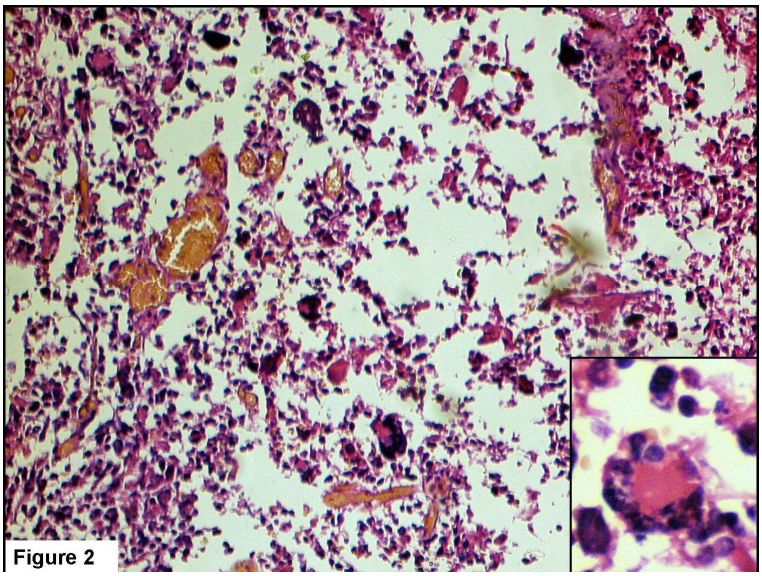

Fig. 2- Microphotograph showing the highly malignant glial tumor with plenty of multinucleated giant cells. (X100 H&E stain). Inset shows a multinucleated giant cell in higher power (X400 H&E stain)

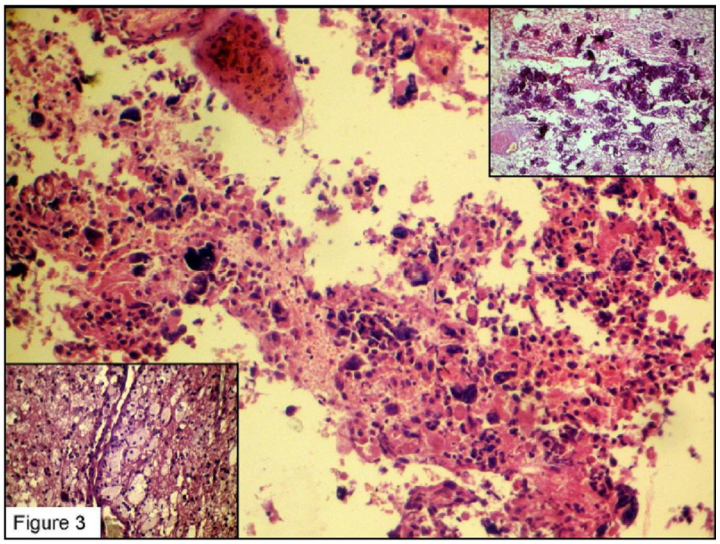

Fig. 3- Microphotograph showing another area of the tumor (X100 H&E stain) Inset in the upper right shows foci of calcification while inset in lower left shows presence of a focus of xanthoastrocytoma (X100 H&E stain)

Discussion

Giant cell glioblastoma is an extremely uncommon WHO grade IV tumor which is characterized by the presence bizarre looking, multinucleated giant cells. Their rarity can well be assessed by the fact that these tumors comprise of only 0.8% of brain tumors and up to 5% of all glioblastomas (1). Giant cell glioblastomas predominates in the cerebral hemispheres but have also been described in the cerebellum, the lateral ventricles, the optic chiasma and spinal cord, the mean age of presentation being 42 years and a male/female ratio of 1.6:1 (2).

Our case was a 12-year old female patient with a giant cell glioblastoma in the frontal region.

This type of glioblastoma is extremely rare in pediatric patients. Recently, the total number of published cases in the "pediatric age group" has been estimated to be 53 since 1952 and in a large series of pediatric brain tumors, these tumors constituted 0.2% (1/364) (3). The total number of cases aged less than 10 years old have been estimated to constitute 6%, while those in patients between 10 and less than 20 years make up to 9% of the total (4). Only one case has been reported in a child of 1 year (5). The margins of these tumors are usually well delineated but may slowly evolve to tumorous masses with infiltrative margins, as was in this case. Histopathologically, giant cells with nuclei of variable number, size, and shape are the characteristic feature with some of the giant cells reaching up to 500 μm. These giant cells might have originated from multiple small tumor cells, also of astrocytic nature (6). In certain cases abundant stromal reticulin fibers can be found - the stromal fibrosis probably responsible for the firmness, good resectability and perhaps a better prognosis of these tumors (7). However, Karremann *et al* (8) in their observation in 18 cases of pediatric giant cell glioblastomas could not agree on the widely known hypothesis of better prognosis of these tumors over the "common" glioblastomas. De Prada *et al* (3) also reported the case of an 11-year-old girl diagnosed with this rare tumor where the tumor recurred in a month after apparent total removal. An important morphological differential diagnosis of giant cell glioblastoma is pleomorphic xanthoastrocytoma. However, rapid evolution of seizures, numerous great sized giant cells, numerous mitoses with atypical forms and necrosis with pseudo-palisading will favor the diagnosis of a giant cell glioblastoma over that of a pleomorphic astrocytoma (3). Immunohistochemistry also aids in differentiating these tumors. Giant cell gliobalstomas are positive for p53 but are negative for neuronal nuclear antigen, neurofilament protein, and synaptophysin. The reverse is true for pleomorphic astrocytomas. Differentiation from anaplastic astrocytomas requires the need to show a more rapid clinical course, more number of mitosis and more frequent large sized multinucleated giant cells in case of giant cell glioblastomas. A hypothesis of a possible progression of anaplastic pleomorphic xanthoastrocytoma (WHO grade III) from pleomorphic xanthoastrocytoma (WHO grade II) towards giant-cell glioblastoma (WHO grade IV) has been raised (9). In our case, after extensive sampling, we demonstrated a focus of xanthoastrocytoma like area, which is conjunction with the above theory. Deb *et al* (10) reported a case of 8-year old patient diagnosed with giant cell glioblastoma who suffered two relapses, the histopathology done during the second recurrence showing evidence of gliosarcoma.

Fortunately, for our patient, there was no evidence of spinal, leptomeningeal or extracranial dissemination of the tumor. The patient, following surgical resection, was treated with adjuvant radiotherapy and chemotherapy (with temozolomide) and was symptomatically better at three-month follow-up indicating that a combined approach of radiotherapy and chemotherapy following gross total resection of these tumors may prove to be an effective form of treatment.

Acknowledgements

The authors declare that there is no conflict of interests.

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