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Corpus callosum giant cell glioblastoma in a young girl: a case report

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ABSTRACT

Glioblastoma (GBM) is the most common and most malignant among the glial tumours. Giant cell glioblastoma (GCG) is one of rare subgroup which constitutes around 5% of all GBMs. Histologically it is characterized by the presence of abundant bizarre, multinucleated giant cells along with abundant reticulin stroma and high frequency of p53 mutations. GCG more commonly involve the temporal and frontal lobe of brain. It portends a better prognosis than the usual GBM which were depicted in few case reports and studies. Treatment approaches in cases of GCG includes surgery followed by radiotherapy and chemotherapy.The aim of surgical intervention is to achieve maximal tumour excision with minimal morbidity leading to better quality of life.A total or subtotal resection can be achieved in greater percentage of patients (pts.) when advanced magnetic resonance imaging (MRI) techniques and intraoperative MRI techniques are used simultaneously. A newer concept about two types of GBM has been recently developed combining clinical, morphological and genetic data i.e. “primary” and “secondary” glioblastoma.

Here we are sharing a case report of 27 year old lady who presented in our outpatient department (OPD) as a post-operative (post-op) case of GBM of corpus callosum for adjuvant radiotherapy. We evaluated the patient. and started radiotherapy with proper medical decompression and symptomatic management on OPD basis. After receiving 5th fraction of radiotherapy, patient.. condition deteriorated and in-spite of all resuscitative measures patient. expired on 3rd day of management in the Oncology ward.

INTRODUCTION

GBM is by far the most common and most malignant of the glial tumours. It is also one of the most lethal central nervous system (CNS) primary tumours. GCG is a rare subgroup which constitutes around 5% of all GBMs. It is characterized by the presence of abundant bizarre, multinucleated giant cells along with abundant reticulin stroma and high frequency of p53 mutations on histopathological examination. GCG more commonly involve the temporal and frontal lobe but can occur at any site and portends better prognoses than the usual GBM [1] which were depicted in few case reports and long term studies. On the contrary, in a study including 7 cases, all patients died within 14 months despite aggressive treatment. [2]

Here we are presenting a case report of 27 year old lady who reported in the department of Radiation Oncology as a post-op case of GBM of corpus callosum for adjuvant radiotherapy. We evaluated the pt.and started radiotherapy with proper medical decompression and symptomatic management. After receiving 5th fraction of radiotherapy patient. condition deteriorated and in-spite of all resuscitative measures pt. expired on 3rd day of management in the Oncology ward.

CASE REPORT

A 27 year-old young girl presented with a history of holocranial headache which was on & off in nature, associated with nausea and projectile vomiting for 20 days duration. There was no history of fever,trauma,loose motion or any major systemic illness in the past. Shewas evaluated and all related investigations were done. Her pre-operative (pre-op)MRIreveal poorly marginated and mixed signal intensity intra-axial and supratentorial soft tissue mass seen in relation with white matter

of both frontal lobe and genu of corpus callosum with moderate surrounding oedema.[Figure 1 A & B]Post contrast study of same scan shows heterogeneous peripheral and nodular enhancement with interspersed non-enhancing cystic component. [Figure 2]

After proper evaluation, she got operated outside on 05/12/13 with left pterional craniotomy and decompression. Her post-operative histopathology report, which was again done outside reveal corpus callosum GCG grade IV.

She was referred to Radiation Oncology department on 7/12/13. Her general and systemic examination was unremarkable. On neurological examination, she was well oriented to time place and person. Her motor and sensory system along with reflexes was within normal limits. Her only complaint was holocranial headache with nausea.After complete workup she was advised one course of adjuvant chemotherapy (tab temozolamide 250 mg once a day for 5 days) after which she had 60% subjective improvement in symptoms. Twenty days after shewas started on radiotherapyas per plan (phase one 45 Gy in 25# @1.8 Gy/ #,five fractions per week on Linear Accelerator,Elekta synergy with 6X photon energy). She tolerated well till five fractions which she received in morning but in afternoon, she again got headache of holocranial naturewith nausea & vomiting. She was given symptomatic treatment but the severity of symptoms increased within 2 days and she got admitted in in-patient wardwith neurological deterioration. Neurology consultation was opted and on examination it was found that she was drowsy, her pupils were nonreactive to light bilaterally,and all deep tendon reflexes were absent. All emergency measures were taken but in-spite of all efforts, pt. could not revive and died on third day of admission. Since pt. was on respiratory support and her general condition was not good, no further active intervention taken and no radiological scans were done but possibility of brain herniation was made at that time of examination by the neurologist.To delineate one of the causes of death in adults with supratentorial GBM ismost likely due to brain herniation. It is the most common side effect of a brain tumour. It may be axial, transtentorial, subfalcine, tonsillar. It can be caused by the intracranial pressure brought by surgery to remove the tumour. It is also caused when brain tissue, cerebrospinal fluid, and blood vessels are moved or pressed away from their usual position in the head.

DISCUSSION

GBM is the most common and most malignant primary brain tumour in adult pt. The 2007 WHO classification of tumours of the CNS codifies 3 main variant of GBM: pleomorphic cell GBM (PCG), gliosarcoma, and GCG. [3] Previously termed as monstrocellular tumour due to the macro size of its cells, the glial origin of these tumours has now been confirmed on electron microscopy and immunohistochemistry (IHC).

GCG, defined as GBM with predominance of giant cells, is a rare subgroup and is often considered as a variant of GBM, classified as grade 4 tumour of WHO classification, although they might be considered as midway between grade 3 and 4 glioma, as they are prognostically better in terms of survival than the grade 4 GBM. [4] The mean age at presentation has been calculated to be 51 years with male predominance. About 9% of the cases were under 20 years of age and 6% of cases were under 10 years of age, 35% occurring in people under 40 years. The duration of symptoms is usually short and clinical presentation is similar to GBM.GCG predominates in the cerebral hemispheres, mainly sub-cortically in the temporal and parietal lobes. [5] Other possible primary locations include the cerebellum, the lateral ventricles, the optic chiasm, and the spinal cord. The lesion can be multifocal. [6] MRImay reveal a contrast enhancing heterogeneous mass with solid and cystic areas, hypo-intense on T1 weighted sequences and hyperintense T2 weighted sequences

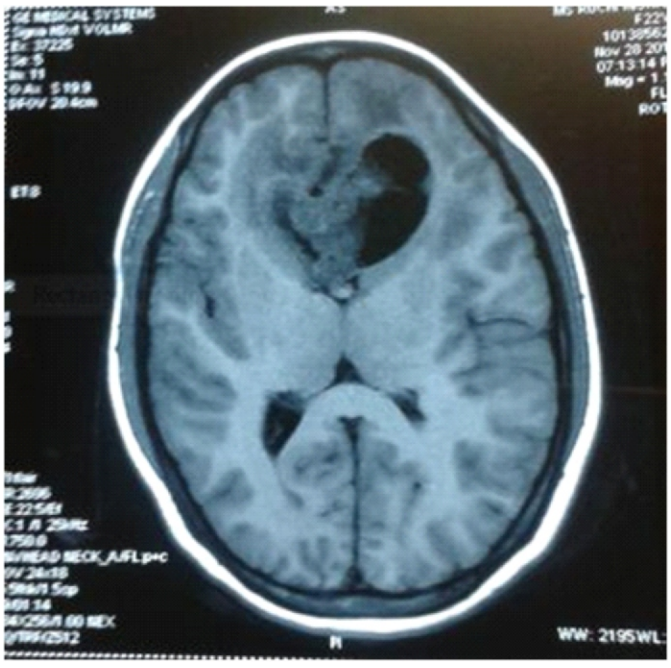

Fig. 1A : Preoperative MRI without contrast T1 flair axial view showing poorly marginated and mixed signal intensity intraaxial and supratentorial soft tissue mass lesion with white matter of both frontal lobes and genu of corpus calosum with moderate surrounding oedema.

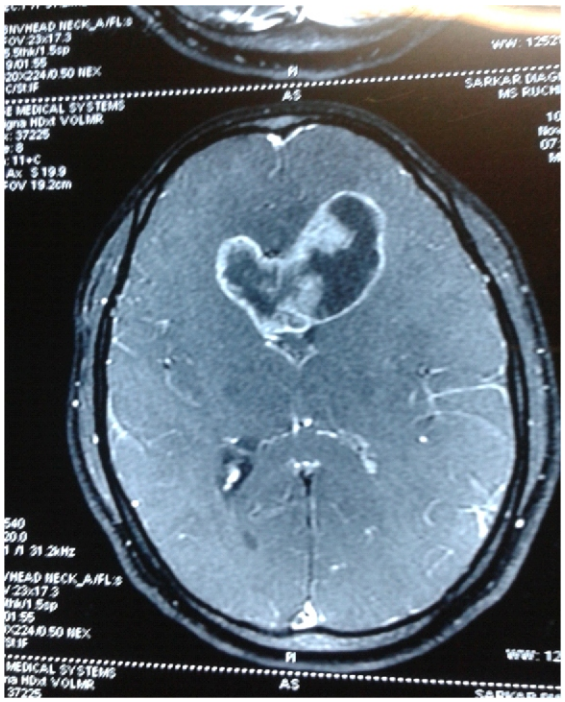

Fig. 1B : Preoperative MRI post contrast axial viewshowing heterogenous peripheral andnodular enhancement with interspersed non enhancing cystic component.

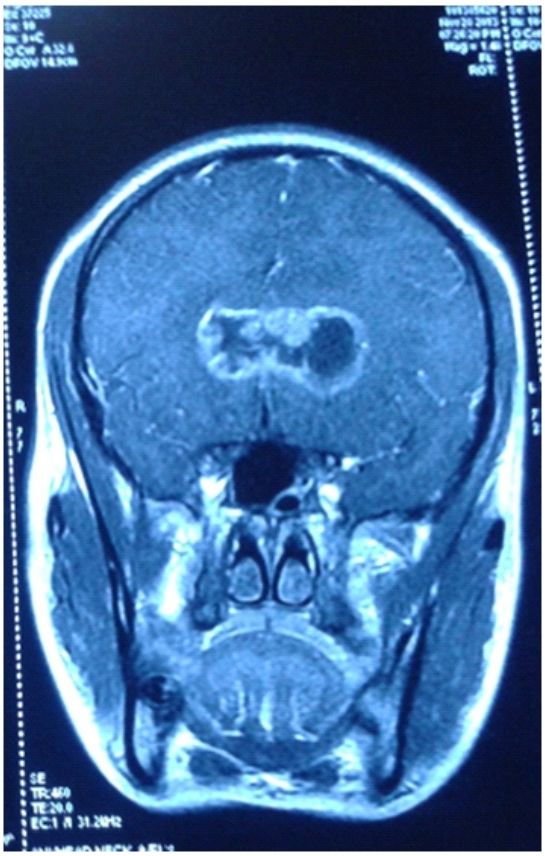

Fig. 2 : Preoperative MRI post contrast coronal view showing the mass as described in figure 1A &B.

surrounded by oedema. [7]

Microscopically, they are highly cellular lesions comprising of abundant giant cells reaching size up to 500 nm with nuclei of varying sizes, shapes, and number; abundant stromal reticulin fibres can be found in many along with necrosis, mainly in a pseudo-palisading or large ischemic forms. The correct origin and classification of these tumours have been elucidated by means of IHC profiles. The glial origin of these tumours has been supported by means of positivity for Glial Fibrillary Acidic Protein (GFAP), thus abandoning the usage of the previous term monstrocellular tumour. IHC studies have also shown positivity for S-100, vimentin, alpha 1 anti-chymotrypsin. [8] Most of molecular and genetic markers are still lacking confirmation; currently, only two markers, O^6-methylguanine-DNA methyltransferase (MGMT) promoter methylation and isocitrate dehydrogenase1 (IDH1) mutations, are commonly accepted genetic biomarkers for pts. with GBM. [9]

An important differential diagnosis both clinically and histologically to be considered is pleomorphic xanthoastrocytoma (PXA). The features which are in favour of GCG are quicker evolution of seizures, numerous great-sized giant cells, numerous mitoses, atypical mitoses, and pseudo-palisading pattern of necrosis. IHC profiles such as neuronal antigens and p53 will also aid in differentiating between the two with positivity for p53 and negativity for neuronal nuclear antigen, neurofilament protein, and synaptophysin favouring GCG. [10]

Treatment approaches in cases with GCG include surgery followed by radiotherapy and chemotherapy. The tumour 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 tumour excision with no or with minimal patient deterioration.A total or subtotal resection can be achieved in a greater percentage of pts. when advanced MRI techniques and intraoperative MRI techniques are used. [11].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.The standard regimen for radiotherapy and chemotherapy includes fractionated focal irradiation in daily fractions of 2 Gy given as 5 days per week for 6 weeks, a total of 60 Gy, and continuous daily cap temozolamide (75 mg per m^2 body-surface area per day, 7 days a week from the first to the last day of radiotherapy without any gap), followed by 6 cycles of adjuvant cap temozolamide (150 to 200 mg per m^2 for 5 days during each 28-days cycle). [12] .A positive relationship has been shown between the length of survival of patients with GBM and the presence of the giant cell variety. The more circumscribed radiologic and histopathology appearance of GCG may permit more complete resection and thus improve prognosis compared with GBM. [13]

To evaluate complication and sudden death from GBM, there are some studies seen in literature. In a study of 3 cases of sudden death with neurological symptoms due to GBM was evaluated and a new concept about two distinct type of GBM has been developed.Combining clinical, morphological, molecular and genetic data the concept has emerged of “primary” and “secondary” glioblastoma, although it is unclear how to distinguish this differentiation, or the extent to which it is therapeutically and prognostically relevant. [14].Like astrocytoma of lower grade, GBM may be discovered on evaluation for seizures or headache but unlike lower-grade lesions who's infiltrating and insinuating qualities carry the cells unobtrusively into intact parenchyma with little resultant mass effect, at least initially, GBM are often expansive and oedema generating. As a result, they are more likely to produce frank neurological deficits and sign of increased intracranial pressure: a subset present in sudden, stroke-like fashion as a consequence of intratumoral haemorrhage.

The features of intratumoral vascular proliferations, in fact, have a constant correlation with the prognosis. In GBM vascular proliferation assumes two forms. Most common is a well-known variant that forms globular masses resembling the glomerular tufts of the kidney, this proliferation, now referred to as “microvascular proliferation”. The second form of vascular hyperplasia has a more legitimate claim to the term “endothelial proliferation” since it is intraluminal and consists largely of endothelial cells within small to medium-sized vessels. Endothelial proliferation is less common than glomeruloid microvascular proliferation and it appears to have a more constant correlation with high-grade glioma and a poor prognosis. [15]

CONCLUSION

GCG has a more benign entourage than common GBM. Neverthless the individual patient variables, biological features of tumour and complication, despite giant cell morphology, should be well taken into account since an omnious course is also a possibility.Adequate treatment with surgery, chemotherapy and radiotherapy is beneficial along with daily patient. monitoring

and sincere supportive care is required for better results otherwise patient. may die suddenly leading to poor prognosis in spite of favourable histopathology.

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