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P53 NegativePEDIATRICGBM

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1. INTRODUCTION

Glioblastoma multiforme (GBM) is the most malignant histological form of astrocytoma, a malignant central nervous system (CNS) tumour of glial origin, and is graded as WHO grade IV. It is the most common and most malignant primary brain tumor in adults. In adults, high grade gliomas account for approximately half of all primary brain tumours of which approximately 75% are GBM, whereas, it is relatively rare in children and accounts for approximately 7-9% of CNS tumors [1-4].Pediatric CNS tumors in India accounts, on an average 14.8% of total intracranial tumors of which astrocytomas average 34.7% of which GBM constitutes 4.4%. [5]Mean age of Pediatric glioblastomas (pGBM) is reported to be in the range of 8.8-12.7 years [2,3,6,7,8] with a slight male preponderance. [6,8] Most of the pGBM are located in the cerebral hemispheres, often in the frontal lobe.[2,6,8]This case report documents a GBM that was located in the left cerebral hemisphere of a 13 year old child. Because this is a rare illness for a patient of this age, we also provide a brief literature review to supplement this case report.

2. CASE REPORT

A previously normal 13 year old boy with adequate neuropsychomotor development presented with loss of consciousness. He had a history of unilateral (left sided) headache of 2 months durationwhich gradually increased in intensity leading to loss of consciousness. CECT brain showed ring enhancing complex cystic region of 50x35x46 mm size with eccentric enhancing mural nodule and peri focal oedema in the left temporal region along with left frontal oedema with midline shift of 7mm from left to right. He underwent left temporal craniotomy and subtotal resection of lesion. The cystic fluid cytology showed high cellularity with large number of polyhedral to plasmacytoid cells and some round cell type arranged in sheets with moderate nuclear atypia. Histopathology report showed tumour fragments with high cellularity and marked nuclear atypia and prominent mitotic figures with areas of palisade necrosis and few spindle cell type cells arranged in fascicles along with vascular endothelial proliferation. The immunohistochemistry (see Table 1) was positive for the glial fibrillary acidic protein (GFAP), Ki-67 proliferation antigen and IDH1. These findings, along with the morphological features and the presence of necrosis, confirmed the diagnosis of GBM (see Figure 1,2,3,4,5,6,7).

Table 1: *IHC Markers*

IMMUNOHISTOCHEMISTRY REPORT:

Marker	Clone	Result
GFAP	GA5	Positive
P53	DO-7	Negative
Ki67	MIB-1	18-20%
IDH1	IDH-1/1152	Positive

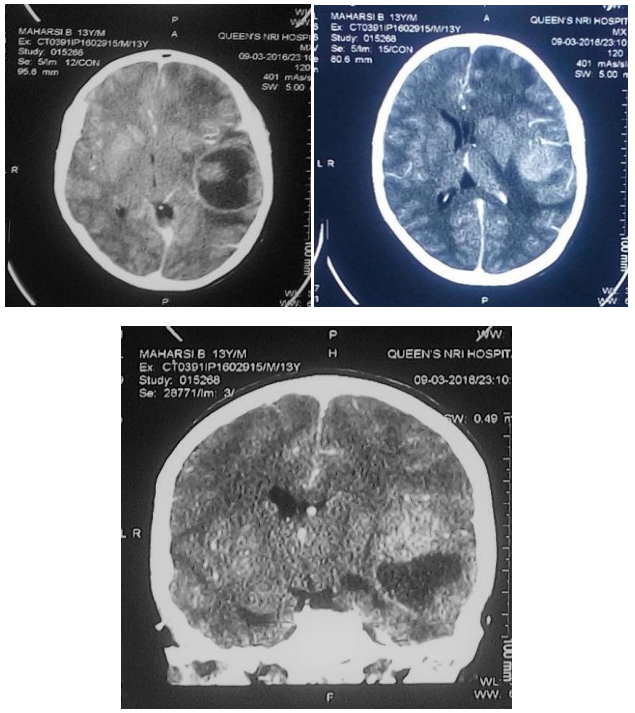
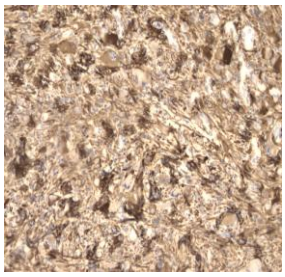
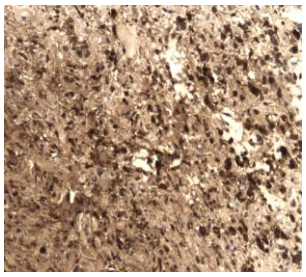


Figure 1: *CT scan images (axial and coronal) showing the lesion*

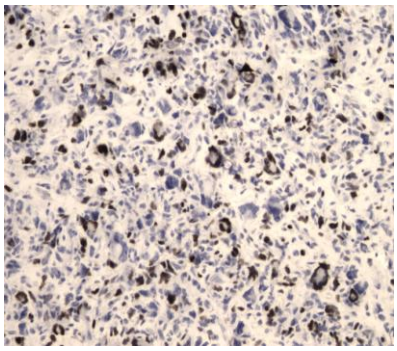
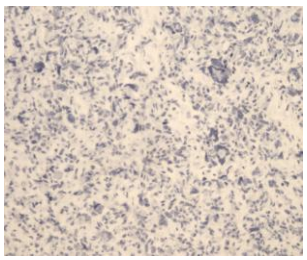
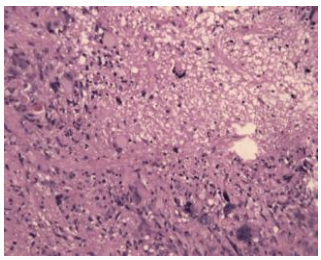


Figure 2: *GFAP Positive* **Figure 3:** *IDH1 Positive*

Figure 4: *MIB1 Positive*

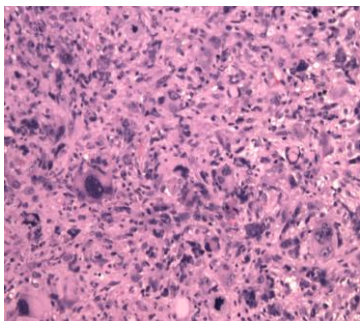


Figure 5: *P53 Negative* **Figure 6:** *Necrosis* **Figure 7:** *Mitosis*

He received radiotherapy to the brain with concurrent temozolamide followed by 6 cycles of adjuvant temozolamide and is on followup.

3. DISCUSSION

GBMis characterized by cellular pleomorphism, numerous mitotic figures, nuclear atypia, proliferation of the vascular endothelium and areas of necrosis with pseudopalisading of the neoplastic cells. The clinical picture at onset is variable, depending on the location of the tumor. The most frequent signs and symptoms are: seizures, motor deficits, signs and symptoms of intracranial hypertension (headache, vomiting, papillary edema) [9,10].

pGBM being mostly of de novooccurrence, exhibit high incidence of p53 mutations and low incidence of epidermal growth-factor receptor (EGFR) amplification,[11] the features of adult secondary GBM. In few studiesof pGBM, mutations of phosphatase and tensin homolog(PTEN), EGFR were found to be rare while p53 mutations were found to be more common when compared to adult GBM, [7,12]Most significant independent prognostic factor among all age groups as per SEER database analysis of paediatric glioma was shown to the grade of the tumour,except in children of1 year where the extent of resection was the most significant indicator of survival.The prognosis of pGBM is definitely poor when compared to other histological grades of astrocytomas but seems to be better than that of adult GBM as the mean survival time in children is much longer than in adults. Different clinical and histopathologic characteristics of pGBM compared to adults could be a reason for this. [1-4, 6]

The treatment of pediatric high grade glioma lackstherapy options, partly because these tumors are invasive and aggressive. However, pediatric high grade glioma cases arerelatively rare, making large randomized clinical trialsdifficult. Until recently, physicians have generally attempted totreat pediatric high grade glioma patients on the basis of data fromtrials in adults. A standard protocol for treatment is yet to be defined, and the difference of opinion exists. Various chemotherapy regimens have been tried in the adjuvant setting but none of them fared better and still the PCV protocol under the auspices of CCG 943 and CCG 945 continue to be the standard.

The Stupp et al., trial 2005 , prompted the development of a pediatric trial, the Children's Oncology Group (COG) ACNS-0126 study. ACNS-0126, a phase II trial, in which children with newly diagnosed high grade glioma received daily temozolomide during radiotherapy followed by maintenance temozolomide, did not find any survival benefit of temozolomide compared to historic controls.But still, the improved tolerability and ease of administration have lead many clinicians to continue to utilize this strategy when treating newly diagnosed patients with good results. In a retrospective study on treatment outcome of pGBM done at AIIMS, India, there seemed to be improved overall survival with Stupp et al., protocol.

Lot of research still needs to be done at the molecular level which may result in evolution of newer and better cytotoxic drugs, targeted therapies, immune therapies, antiangiogenic agents which may in future change the outlook of this dreadful disease in terms of overall survival and also a better quality of life.

REFERENCES

[1] Keith HM, Craig WM, Kernohan JW. Brain tumors in children. Pediatrics 1949; 3:839-844.

[2] Artico M, Cervoni L, Celli P, Salvati M, Palma L. Supratentorial glioblastoma in children: A series of 27 surgically treated cases. Childs Nerv Syst 1993; 9:7-9.

[3] Sánchez-Herrera F, Castro-Sierra E, Gordillo-Domínguez LF, et al. Glioblastoma multiforme in children: Experience at Hospital Infantil de Mexico Federico Gomez. Childs Nerv Syst 2009;25:551-557.

[4] Stark AM, Fritsch MJ, Claviez A, Dörner L, Mehdorn HM. Management of tectal glioma in childhood. Pediatr Neurol 2005; 33:33-38.

[5] Jain A, Sharma MC, Suri V, Kale SS, Mahapatra AK, Tatke M, et al. Spectrum of pediatric brain tumors in India: A multi-institutional study. Neurol India 2011;59:208-211.

[6] Dohrmann GJ, Farwell JR, Flannery JT. Glioblastoma multiforme in children. J Neurosurg 1976; 44:442-448.

[7] Suri V, Das P, Pathak P, Jain A, Sharma MC, Borkar SA, et al. Pediatric glioblastomas: A histopathological and molecular genetic study. Neuro Oncol 2009;11:274-280.

[8] Marchese MJ, Chang CH. Malignant astrocytic gliomas in children. Cancer 1990;65:2771-2778.

[9] Perry A (2005) Glial and glioneural tumors. In: Prayson RA, Goldblum JR (eds) Neuropathology 2005. Elsevier, Philadelphia, pp 421–488.

[10] Rorke LB (1999) Pathology of brain and spinal cord tumors. In: Choux M, Di Rocco C, Hockley A, Walker M (eds) Pediatric neurosurgery. Churchill, London, pp 396–426.

[11] Pollack IF, Hamilton RL, Sobol RW, Burnham J, Yates AJ,Holmes EJ, et al. O6-methylguanine-DNA methyltransferase expression strongly correlates with outcome in childhood malignant gliomas: Results from the CCG-945 Cohort. J Clin Oncol 2006; 24:3431-3437.

[12] 12. Ganigi PM, Santosh V, Anandh B, Chandramouli BA, Sastry Kolluri VR. Expression of p53, EGFR, pRb and bcl-2 proteins in pediatric glioblastoma multiforme: A study of 54 patients. Pediatr Neurosurg 2005;41:292-299.