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Original article:

Study of surgical approaches pertaining to the management of high grade glioma –glioblastoma multiforme and variants

[1]Dr Bhagirath P More , [2]Dr T V Soni ,[3] Dr Mayuri Salunke

[1]Assistant Professor, Department of Neurosurgery, Dr D Y Patil Medical College Hospital and Research Centre, Pune

[2]Professor, Department of Neurosurgery, Smt NHL MMC & HOSPITAL, Ahmedabad

[3]Consultant Neuro-Anesthetic and Intensivist , Pune

Corresponding author *

Abstract:

Introduction: High grade gliomas display extensive morphological and molecular heterogenicity, and thus may reflect their origin from different population of astrocytes, and possibly from oligodendrocytic and ependymal cell lineages.

Material and methods: The present study was conducted in the department of neurosurgery, NHL municipal medical college & V S Hospital - Ahmedabad, Gujarat. In present study all patients who underwent craniotomy and excision / decompression of high grade glioma (glioblastoma multiforme & its variants) during the period of october 2014 to January 2017 were included for the prospective analysis.

Results: By frontal approach, 18% patients by parieto-occipital & 12% patients by temporo- parietal craniectomy/craniotomy approach. 8% patients were operated by fronto- parietal & another 8% patients by parietal , 4% by temporal approach.SuboccipitalCraniectomy was done in 2 patients.

Conclusion: Median survival in our study was 12.7 months (51weeks) with maximum survival of those patient who were younger (<35 Yr), good preop condition with KPS score (>80) , having near total resection and postoperatively took both radiotherapy and chemotherapy . Adjuvant chemotherapy following radiotherapy provided survival advantage 3.36 months in our study .

Keywords : CNS tumor , SuboccipitalCraniectom

Introduction:

High grade gliomas display extensive morphological and molecular heterogenicity, and thus may reflect their origin from different population of astrocytes, and possibly from oligodendrocytic and ependymal cell lineages. [1]High grade gliomas however, consist mainly of undifferentiated anaplastic cells of astrocytic origin, which exhibit marked nuclear pleomorphism, necrosis, and vascular endothelial proliferation. These tumor cells are arranged radially with respect to the necrotic region, and occur most frequently in the cerebrum of adults. Giant cell glioblastoma is a histological form with large often multinucleated unusual tumor cells.[2] The highly invasive nature of High grade gliomas makes surgical resection rarely curative. In addition, these invading cell types are more resistant to radiation and chemotherapy. Glioblastoma cells invade initially as single cells, and travel along white matter tracts and blood vessel walls, and through the subpial glial space. Some of these cells travel long distances and do not generally invade through blood vessel walls and/or bone.[3] Glioblastomas rarely metastasize outside the brain. This invasive behavior differs from that shown by other cancer cells that metastasize to the brain. Moreover, the latter invading cells are more

delineated from the surrounding brain tissue, subsequently invade short distances as groups of cells, and invade through blood vessel walls and/or bone.

Glioblastoma can be classified into primary type and secondary type. Although these two types develop through mutations of different genetic pathways both behave in a clinically indistinguishable manner and the survival rates are also similar. Primary glioblastoma shows amplification of the epidermal growth factor receptor (EGFR), accompanied by deletions in the INK4a gene with loss of p14 and p16. These tumors also show marked amplification of the loss of heterozygosity (LOH) on chromosome 10 (10q), PTEN mutation, deletion of CDKN2A and MDM2 genes. Primary glioblastomas, in addition, are thought to show over expression of the G protein coupled receptor 26 (GPR26) . This biomarker could be a suppressor of primary glioblastoma development. On the other hand, secondary glioblastoma frequently acquires mutations within the tumor suppressor protein p53 (p53). Such mutations allow the accumulation of additional aberrations, resulting in the progression of malignancy from low-grade astrocytoma to high-grade glioblastoma, but rarely in the development of primary glioblastomas. Secondary glioblastomas also show over expression of PDGF and PDGF receptors.[4]

Material and methods:

The present study was conducted in the department of neurosurgery, NHL municipal medical college & V S Hospital - Ahmedabad, Gujarat. In present study all patients who underwent craniotomy and excision / decompression of high grade glioma (glioblastoma multiforme & its variants) during the period of october 2014 to January 2017 were included for the prospective analysis.

Patients selected for study were those who underwent craniotomy and excision / decompression of high grade glioma (glioblastoma multiforme& its variants) during the period of October 2014 to January 2017 were included for the prospective analysis. Out patient and in patient data along with radiological and histopathological data was reviewed from the hospital information system of NHL municipal medical college & V S Hospital - Ahmedabad, Gujarat. This study consists of 50 cases of intracranial high grade glioma (glioblastoma multiforme & its variants).

Inclusion criteria

All patients who underwent craniotomy and excision / decompression of high grade glioma (glioblastoma multiforme& its variants) during the period of october 2014 to January 2017 were included for the prospective analysis.

Exclusion criteria

All patients whose follow up was not available were excluded. Extracranial (Spinal)
glioblastoma multiforme

All patients who underwent craniotomy and excision / decompression of high grade glioma (glioblastoma multiforme & its variants) during the period of october 2014 to January 2017 were included for the prospective analysis. Age, gender, clinical features, radiological features, extent of resection, adjuvant therapy and clinical outcome were considered for the analysis.

This study consists of 50 patients of intracranial high grade glioma(GBM) operated at our department in NHL municipal medical college & V S Hospital - Ahmedabad, Gujarat. during 2.5 year period from october 2014 to january 2017. The results observed in the study are discussed below.

Results:

Table 1) POSITION OF THE PATIENT DURING SURGERY

POSITION OF PATIENT	NO. OF PATIENTS	PERCENTAGE
SUPINE WITH HEAD TILT	48	96%
PRONE	2	4%

Out of the total 50 patients, 48 patients were operated in supine position, 2 Patients with cerebellar GBM was operated in prone position. Choice of position was dependent on location of tumor as well as surgeon's comfort.

Table 2 : SURGICAL APPROACHES IN PATIENTS

APPROACH	NO. OF PATIENTS	PERCENTAGE
RT/LT FRONTAL	9	18
RT/LT TEMPOROPARIETAL	6	12
RT/LT FRONTOPARIETAL	4	8
RT/LT FRONTO-PARIETOTEMPORAL	13	26
RT/LT PARIETAL	4	8
RT/LT TEMPORAL	2	4
RT/LT PARIETO-OCCIPITAL	9	18
RT/LT FRONTO TEMPORAL	1	2
RT / LT SUBOCCIPITAL	2	4

In majority of the patients in our study with intracranial GBM, fronto-parieto- temporal (RT/LT) craniectomy/craniotomy (26%) was done. 18% patients were operated

By frontal approach, 18% patients by parieto-occipital & 12% patients by temporo- parietal craniectomy/craniotomy approach. 8% patients were operated by fronto- parietal & another 8% patients by parietal , 4% by temporal approach.SuboccipitalCraniectomy was done in 2 patients.

Table 3 : DURA REPAIR IN HIGH GRADE GLIOMA (GBM) SURGERY

PROCEDURES		PATIENTS	%	SURVIVAL(MONTHS)			
				≤ 18		≥18	
				PT.	%	PT.	%
DURA KEPT OPEN		7	14%	6	85%	1	15%
CLOSED	PRIMARY	6	12%	31	62%	12	38%
	PERICRANIAL	37	74%				

In our institute dura was closed in 86% of the patients either primarily (12%) or pericranial/G patch duraplasty (74%). Dura was kept open in 14% of the patients with majority of them in poor preop KPS, massive peritumoral edema, intraoperative swollen brain and where duroplasty was not possible. Postop. Survival (9.5 vs 13.1 months) as well as long term survivors (15% vs 38%) were significantly high in dural closure group. These was attributable to better preoperative and postoperative variables (selection bias).

Table 4 : EXTENT OF SURGICAL REMOVAL OF HIGH GRADE GLIOMA(GBM)

S.N.	EXTENT OF* SURGERY	NO. OF PATIENTS	PERCENTAGE	LACROIX ET AL SERIES	MEDIAN SURVIVAL (MONTHS)
1	NEAR TOTAL	38	76%	47%	13.4
2	SUB TOTAL	12	24%	53%	12.1

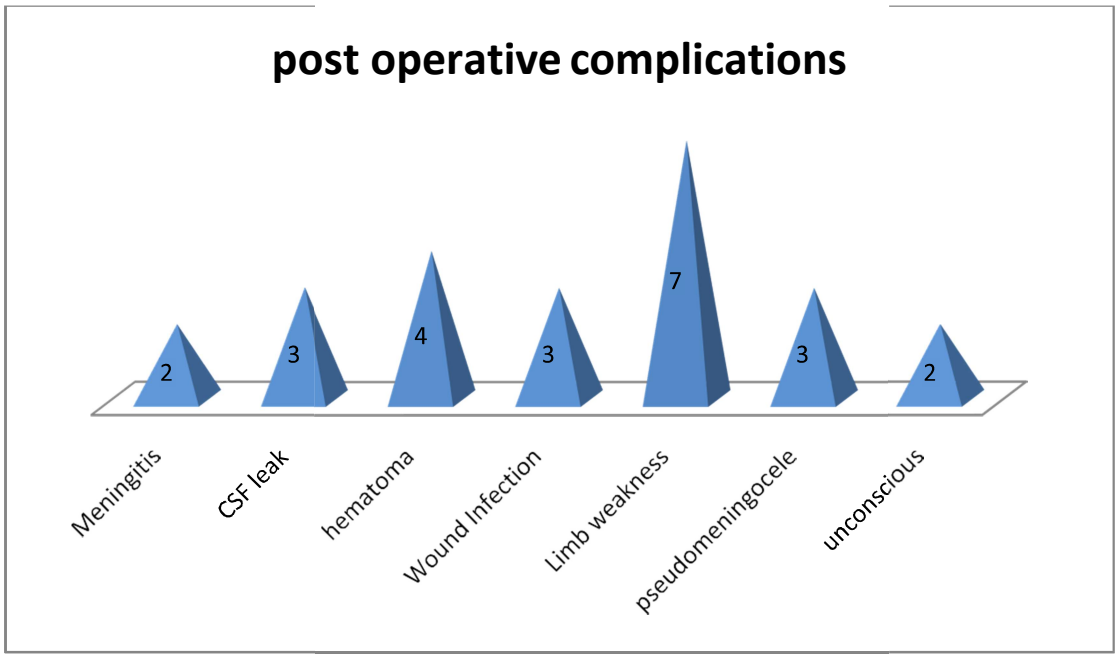
***NEAR TOTAL** - NO RESIDUAL ENHANCEMENT ON POST OPERATIVE CONTRAST IMAGING/NO RESIDUAL ON POST OPERATIVE FLAIR IMAGE **SUBTOTAL-** RESIDUAL ENHANCEMENT ON POST OPERATIVE CONTRAST IMAGING/ RESIDUAL ON POST OPERATIVE FLAIR IMAGE

In our series of 50 patient of GBM 76% underwent near total excision and 24% underwent subtotal excision which were defined on the basis of post operative contrast enhancement on CT Scan. In LACROIX ET AL SERIES 47% patient underwent near total excision and 53% underwent subtotal excision which were defined as more than 98% and less than 98% resection respectively. Difference in two series could be because of observer bias and differences in defining criterias.

Overall median survival in our series in two groups i.e. near t subtotal 12.1 months. tal 13.4 months vs

TABLE 5 : COMPLICATIONS IN HIGH GRADE GLIOMA SURGERIES

COMPLICATIONS	NO. OF PATIENT (PRESENT SERIES)	PERCENTAGE
MENINGITIS	2	4%
CSF LEAK	3	6%
HEMATOMA+IVH	4	8%
WOUND INFECTION	3	6%
LIMB WEAKNESS	7	14%
PSEUDOMENINGOCELE	3	6%
UNCONSCIOUSNESS	2	4%



DISCUSSION:

The commonest complication noted in present series was post operative limb weakness either hemiparesis or monoparesis, seen in 14 % patients. Followed by operative site haematoma in 8% ,wound infection in 6% , Pseudomeningocoele in 6%, meningitis in 4% ,unconsciousness in 4%.

Out of 7 patients who developed postoperative limb weakness, three were due to vessel infarction and four were due to damage of motor cortex while operating nearby cortical high grade glioma. Two of them developed dense hemiplegia which didn't improved, one survived 3.4 months and died due to chest infection while other survived 22 months and is in follow up at present. Rest 4 patients improved slightly (maximum upto grade 4^{-}) with vigorous physiotherapy in 6 months. Average survival of patients with limb weakness was (10.3 months) less than overall survival (12.7 months).

High grade gliomas(GBM) are most common(96%) in Supratentorial subcortical location. Diencephalic (8%) and Posterior fossa GBM are less common, 4% in our study . Among Supratentorial GBM, frontal lobe involvement is most common (36%), followed by temporal lobe(14%). Surrounding edema was present in majority (84%) of patient, posterior fossa tumor had no surrounding edema. Mass effect was present in 90% of patient of which majority (70%) have midline shift. Most of the patient had near total resection (76%) with median survival of 13.4 months as compared subtotal resection (24%) with median survival of 12.1 months .

Those tumors having deep grey matter involvement were difficult to remove completely. [5,6]We found Intraoperative Ultrasonography of great help in localization of tumor and evaluation of extent of resection. The neurological morbidity (20%) and mortality (4%) associated in our study mainly comprises of this group. Limb weakness (14%) was the most common postoperative complication having poor prognostic effect with median survival of 10.3 months. Most of the patient in our series ,took radiotherapy postoperatively (90%), while 34% patient took both radio and chemotherapy. Median survival in our study was 12.7 months (51weeks) with maximum survival of those patient who were younger (<35 Yr), good preop condition with KPS score (>80) , having near total resection and postoperatively took both radiotherapy and chemotherapy . Adjuvant chemotherapy following radiotherapy provided survival advantage 3.36 months in our study .

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