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Original Research Article.

A Clinical Analysis of High Grade Glioma at a Tertiary Care Centre: An Observational Research

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ABSTRACT

Background: Glioblastoma (GBM) is the most common and aggressive malignant brain tumor in adults. Current treatment options at diagnosis are multimodal and include surgical resection, radiation, and chemotherapy. High grade glioma is the most frequent primary brain tumor in adults, and accounts for most of the primary brain tumor cases diagnosed each year. Significant advances in the understanding of the molecular pathology of GBM and associated cell signaling pathways have opened opportunities for new therapies for recurrent and newly diagnosed disease. Innovative treatments, such as tumor-treating fields (TTFields) and immunotherapy, give hope for enhanced survival.

Aims: Prospectively study the surgical outcome in cases of high grade glioma (glioblastoma multiforme & its variants)

Methods and Materials: 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. Age, gender, clinical features, radiological features, extent of resection, adjuvant therapy and clinical outcome were considered for the analysis. Tumor removal was considered complete / near total if the surgeon was convinced that there had been complete removal and if postoperative contrast-enhanced MR imaging showed no evidence of residual tumor. Removal was considered subtotal when only a small portion of residual tumor remained because of firm attachment to vascular or neural structures or when postoperative imaging revealed a small contrast- enhancing or calcified area.

Results: The maximum incidence (70%) of High Grade Gliomas (GBM) is in 4th to 6th decade, with fairely uncommon in children. Male are more affected than female with ratio of 1.7:1. Usually the time period of starting of symptoms is 5 months or more than that, with headache (74%) being most common complaint, followed by convulsions and limb weakness. Papilloedema was the most common sign (62%) followed by limb weakness (40%). Postoperatively 85% patients with papilloedema recovered in average 1.5 months. Those having neurological deficit may have involvement of cranial nerve, with maximum 66% optic nerve involvement, mostly because of raised I.C.T or occasionally tumor compression over the nerve. This usually presented as papilloedema in fundus examination. CT scan as wells as MRI are the two most important tool of diagnosis; M.R.I has the added advantage of better soft tissue details, which help in planning operative strategy. 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. 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.

Keywords: Glioblastoma Multiforme; Survival Rate; Surgical Management; Adjuvant Therapy.

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INTRODUCTION

CNS tumor is the primary concern of neurosurgeons as well as neurosurgical patients, accounting for approximately 20% of all childhood malignancies and 10% of cases in young adults. Brain tumors are the second most common malignancies and the most common solid tumor seen during childhood.[1] High grade glioma is the most frequent primary brain tumor in adults, and accounts for most of the primary brain tumor cases diagnosed each year. Recently according to Revised WHO classification of CNS Tumours 2016 along with correlation to Modified Ringertz Grading, High Grade Gliomas are now classified as WHO Grade IV Tumours. Based on standard histopathological grading & as per Revised WHO classification of

CNS Tumours 2016, more than 40% of the CNS tumors are WHO grade IV - i.e. High grade glioma (glioblastoma multiforme & its variants) that accounts for 50% of all malignant gliomas. High grade glioma (glioblastoma multiforme) is one of the most devastating human cancers because of its rapid growing nature, infiltrating growth, resistance to radiotherapy and chemotherapy, and rapid progression from diagnosis to death. It is considered as systemic disease of brain rather than local hence difficult to eradicate. It is a rapidly fatal tumor, and most patients succumb to this disease within 12–18 months from the time of diagnosis in natural progression of disease. Without therapy patients dies within 4 months, while median survival of those receiving optimal, aggressive treatments such as surgery, radiation, and chemotherapy, is 15 months. Despite aggressive management, High grade gliomas invariably recur and prognosis remains dismal, with a median survival of only 3–5 months at recurrence. In fact this primary brain tumor is virtually incurable despite advances in neurosurgical techniques and adjuvant therapies. These statistics clearly show that glioblastoma is among the most aggressive neoplasms.[2-11]

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.[12,13]

High grade gliomas however, consist mainly of undifferentiated anaplastic cells of astrocytic origin, which exhibit marked nuclear pleomorphism, necrosis, and vascular endothelial proliferation.[14,15] 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. 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. 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.[16] 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.

This manuscript highlights the clinical and radiological features of High grade glioma (glioblastoma multiforme & its variants) at presentation and analyzes the pros and cons of the available therapeutic options with respect to clinical status, survival and tumour recurrence.

AIMS AND OBJECTIVES

Aims

Prospectively study the surgical outcome in cases of high grade glioma (glioblastoma multiforme & its variants)

Objectives

To assess

- Various clinical presentation in cases of high grade glioma (glioblastoma multiforme & its variants)
- Various surgical approaches pertaining to the management of these tumours
- Morbidity and Mortality with respect to surgical management
- Radiological correlation with clinical outcome
- Complete / Near Total Excision
- Subtotal Excision
- Recurrence free survival after initial treatment with surgery and/or adjuvant therapy
- Asymptomatic Recurrence
- Symptomatic Recurrence
- No Recurrence

MATERIALS AND METHODS

The present study was conducted in the Department of Neurosurgery, Tertiary care hospital - Ahmedabad, Gujarat.

Study Design: The study design was prospective analysis.

Study Period: 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.

Place: This study was conducted in the department of neurosurgery at tertiary care hospital - Ahmedabad, Gujarat.

Source of Data: 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. Outpatient and inpatient data along with radiological and histopathological data was reviewed from the hospital information system of NHL municipal medical college & V S Hospital - Ahmedabad, Gujarat.

Sample Size: This study consists of 50 cases of intracranial high grade glioma (glioblastoma multiforme & its variants)

Ethical Clearance: Ethical clearance was obtained for the study from institutional ethical clearance committee.

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.

Method

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.

Tumor removal was considered complete / near total if the surgeon was convinced that there had been complete removal and if postoperative contrast-enhanced MR imaging showed no evidence of residual tumor. Removal was considered subtotal when only a small portion of residual tumor remained because of firm attachment to vascular or neural structures or when postoperative imaging revealed a small contrast- enhancing or calcified area.

All patients who were alive and contactable, were assessed clinically and radiologically with MRI at regular interval. The group of patients where serial imaging was available, the progress of the disease could be monitored with follow up MRI. The patients who died, were assessed to know the time and cause of death. Survival curve for the group of patients was plotted. The assessment was made at the OPD with regards to:

- Present neurological status
- Radiological features

Statistical Analysis

The data obtained was coded and entered into microsoft excel spreadsheet. Categorical data were expressed as rates, ratios and percentages and the comparison was done using chi-square test. Continuous data was expressed as mean ± standard deviation (SD). This was done with respect to extent of tumor resection based on post-operative radiological imaging. Extent of tumor resection was correlated with clinical status and tumor recurrence. Probability of recurrence free survival rate was computed applying Kaplan-Meier Analysis.

Table 1: Age Incidence

S.N.	Age Group (Yr)	Total No.Patient	%
1.	1-10	0	0
2.	11-20	6	12
3.	21-30	4	8
4.	31-40	13	26
5.	41-50	12	24
6.	51-60	10	20
7	61-70	4	8
8.	≥ 71	1	2

Table 2: Tumor Incidence (Location) In Present Series of 50 Patients of Intracranial High Grade Gliomas

Sr. No.	Location	Side	Total no.	Percentage (%)	Roth et al series (%)
1	Frontal	Rt	8	16	11.5
		Lt	10	20	8.1
2	Temporal	Rt	3	6	7.7
		Lt	4	8	9.1
3	Parital	Rt	2	4	7.5
		Lt	1	1	7.1
4	Occipital	Rt	0	0	1.4
		Lt	1	2	1.4
Single Lobe total			29	58	53.7
5	Frontoparietal	Rt	1	2	3.2
		Lt	2	4	3.0
6	Frontotemporal	Rt	1	2	1.2
		Lt	3	6	1.6
7	Temporoparietal	Rt	2	4	2.2
		Lt	1	2	3.6
8	Paritooccipital	Rt	2	4	2.6
		Lt	2	4	2.8
9	Frontotemporoparietal	Rt	0	0	1.0
		Lt	1	2	8.1
10	Temporoparietooccipital	Rt	0	0	0.6
		Lt	0	0	1.0
11	Frontoparietooccipital	Rt	0	0	2.6
		Lt	0	0	0.6
Multiple lobe total			15	30	39.8
12	Deep structures (Thalamus,brain stem)		4	8	4.8
13	Cerebellar		2	4	0.4

Table 3: Side Distribution Tumor In 50 Patients Of High Grade

Side 0f Hemisphere	No. Of Patient	Percentage	Bohman et al Series(%)
Right	19	43	46
Left	25	57	54

Table 4: Sex Incidence In Present Series Of 50 Patients Of GBM.

S.N.	Total No. Patient	Percentage	Roth et al series
Male	32	64	71
Female	18	36	29

Table 5: Incidences of Different Symptoms in 50 Patients of High Grade Glioma (GBM)

Symptom		No. of Patients	Percentage (%)	Roth et al Series (%)
Headache		37	74	74
Giddiness		8	16	10.6
Vomiting		23	46	27.4
Convulsion	Focal	5	10	13.5
	GTC	12	24	12.5
Altered sensorium		14	28	7.8
Unconsciousness		4	8	10.4
Diplopia		3	6	8.8
Decreased vision		4	8	27.4
Facial pain		0	0	4.2
Facial asymmetry		0	0	1
Hearing loss		0	0	0.2
Tinnitus		0	0	0.2
Difficulty in swallowing		0	0	0.8
Difficulty in speech		7	14	28.8
Change of voice		5	10	0.4
Limb weakness		20	40	42.1
Difficulty in walking		17	34	11.3
Bowel bladder incontinence		6	12	_
Scalp Swelling		3	6	_
Behavioural Changes		7	14	11.5
Sensory Symptom		3	6	10.2

Table 6: Incidences of Signs

Signs			No. Of Patients	Percentage	Roth Et Al Series. (%)
Cranial Nerve Palsy	**I**		0	0	
	Optic	**V.A**	3	6	8.8
		PapillOedema	31	62	66.3
	III				
	IV				
	V				
	VII				13.3
	VIII				
	IX,X		3	6	
	XI,XII				
	VI		3	6	9.4
Motor System (Plegia / Paresis)			20	40	66.6
Cerebellar Signs			2	4	0
Nystagmus			4	8	0.8
Gait Abnormality			17	34	11.3
Non Ambultory			19	38	
Sensory Signs			2	4	11.3

Table 7: Incidence Of Prior History Of Glioma

S.N.	History Of Glioma	No. Of Patient	Percentage
1	Present	4	8%
2	Absent	46	92%

Table 8: Site of Tumor

Site	No. of patient N=50	Percentage (%)	Roth et al series. (%)
Supratentorial	48	96	99.6
Infratentorial	2	4	0.4

Table 9: MRI Findings In 50 Patients of High Grade Glioma (GBM)

S.N.	Feature	Total No. Patient	Percentage	Lacroix et al Series (%)
1	Mass Effect	45	90	89
2	Edema	42	84	81
3	Enhancement	43	86	88
4	Necrosis	43	86	88

Table 10: Position Of The Patient During Surgery

Position Of Patient	No. Of Patients	Percentage
Supine With Head Tilt	48	96%
Prone	2	4%

Table 10: 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

Table 11: 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%				
	Pericranial	37	74%	31	62%	12	38%

Table 12: 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

Table 13: Incidence Of Complications Of High Grade Glioma (GBM) Surgery

Complications	No. Of Patients (Present Series)	Percentage
Meningitis	2	4
CSF Leak	3	6
Haematoma + IVH	4	8
Wound Infection	3	6
Limb Weakness	7	14
Pseudomeningocele	3	6
Unconciousness	2	4

Table 14: Overall Outcome Of Surgery Of High Grade Glioma (GBM)

Outcome	Present Series		Hollerhage et al 1991	Salcman et al
	No. of patients	%	%	%
Neurologically Intact	40	80%	76.9%	89.3%
Neurologically Disabled	7	14%	19.7%	8%
Vegetative	1	2%		
Expired	2	4%	3.4%	2.7%

Table 15: Karnofsky Perfoermance Status Scale Definitions Rating (%) Criteria

Able to Carry on normal activity, and to work, no special care needed	**100**	Normal no complaints, no evidence of disease
	90	Able to carry on normal activity, minor signs or symptoms of disease
	80	Normal activity with effort, some signs or symptoms of disease.
Unable to work, able to live at home and care for most personal needs, varying amount of assistance needed	**70**	Cares for self, unable to carry on normal activity or to do active work
	60	Requires occasional assistance, but is able to care for most of his personal need
	50	And considerable assistance and frequent medical care.
Unable to care for self , requires equivalent of institutional or hospital care, disease may be progressing rapidly	**40**	Disabled , requires special care and assistance
	30	Severely disabled , hospital admission is indicated although death not eminent
	20	Very sick ,hospital admission necessary, active supportive treatment necessary
	10	Moribund, fatal processes progressing rapidly
	0	Dead

Table 16: Preoperative And Postoperative KPS Scale Of Patients

KPS Scale	Number Of Patients		Survival (Months) According To Preop KPS				Average Survival (Months)
	Preop	Postop	< 18		>18		
			PT	%	PT	%	
100	3	20		61%	7	39%	14.4
90	8	9	11				
80	7	4					
70	9	7	21	81%	5	19%	12.2
60	9	3					
50	8	5					
40	5	1	5	83%	1	17%	10.1
30	1	0					
20	0	0					
10	0	0					
00	0	1					
			74%		26%		

Table 17: Postoperative Survival Of High Grade Glioma (GBM) Patients

S.N.	Post Op Survival (Months)	No. Of Patient	Percentage (%)		Roth et al Series (%)	
			Without RT	With RT	Without RT	With RT
1	**0-3**	48	60	96	74.3	96.8
2	**4-6**	44	40	86	45.2	83.4
3	**7-12**	27	20	54	16.2	34.4
4	**13-18**	13	-	26	11.8	20.8
5	**19-24**	5	-	10	7.5	17.7
6	**25-36**	-	-	-	3.2	10.4
7	**37-48**	-	-	-	3.2	7.3
8	**49-60**	-	-	-	2.2	5.2

Table 18: Post-Operative Chemotherapy And Radiotherapy

Patients Category	Mode Of Therapy	No. Of Patients	%	Postop. Average Survival (Months)
CAT I	Only Radiotherapy	28	56%	12.54
CAT II	Only Chemotherapy (Post-Reoperation)	2	4%	4.45
CAT III	Recieved Both Chemo/Radiotherapy	17	34%	15.9
CAT IV	Not Recieved Chemo/Radiotherapy	3	6%	1

RESULTS AND DISCUSSION

This study consists of 50 patients of intracranial high grade glioma(GBM) operated at department of neurosurgery in a tertiary care hospital - Ahmedabad (Gujarat) during 2.5 year period from October 2014 to January 2017. The results observed in the study are discussed below.

Age Incidence of High Grade Glioma (GBM)

In our series, incidence of GBM was maximum in 30 to 60 year age group with 0% in 1st decade, 12% in 2nd decade,8% in 3rd decade, maximum 26% in 4th decade , 24% in 5th decade,20% in 6th decade,8% in 7th decade and 2% beyond that. The average age at admission was 46.4 years. The youngest patient was a l6-year-old male with a tumour of the left frontal region; the oldest was a 73-year-old man with a tumour of the left frontoparietal region. This age incidence is quite comparable with Davis et al series except for the first decade.[5,6] There appeared to be a much better prognosis, in operated cases, for the younger age groups; of the group under 35 years of age, than of those over 35 years. Survival of GBM patients in extremes of age was significantly less.

Tumor Incidence (Location) In Present Series

In present study of 50 cases of High grade gliomas(GBM) – tumor incidence in single lobe is 58% of which in frontal lobe 36% , Temporal lobe 14%, parietal lobe5%, occipital lobe 2% and in multiple lobe it is 30% with maximum share of frontotemporal and parietooccipital lobe 8% each. Incidence in deep structures eg. Thalamus, basal ganglion is 8% and in posterior fossa it is 4%.[17]

In comparison, in Roth et al series the incidence of High grade gliomas (GBM) was in frontal lobe 20%, temporal lobe 17%, parietal lobe 15%, in occipital lobe 3%, in deep structures 4.8% and in post fossa 0.4 % .These difference in incidence of location seems to be statistically insignificant, could be because of small sample size. Postoperative survival for patients with various supratentorial locations was also statistically insignificant.

Gliomas (Glioblastoma Multiforme)

In our series, High grade gliomas occurred on right side in 43% and on left side in 57% of patients, showing predilection for left side. In Bohman et al series incidence of High grade gliomas (glioblastoma multiforme) was 46% on Right side and 54% on left side which is comparable with our series.

Sex Incidence

In our series, sex incidence of GBM in male is 64% and 36% in female with male: female ratio 1.7:1 i.e. male preponderance.

Clinical Features

In our series of 50 cases of intracranial GBM , patients presented with headache (74%) as the most common complain followed by vomiting (46%), limb weakness (40%), convulsion (34%) difficulty in walking (34%), Altered sensorium (28%), giddiness (16%), behavioural changes (14%), incontinence (12%) change in voice(10%), decreased vision (8%), and with sensory complaint(6%) .

Difficulty in speech which is found in 7 patients (14%), is well correlated with tumour with left sided multilobar involvement with mainly involving left sided frontal and temporal lobes.

When compared, in Roth et al series the most common symptom was Headache (74%) followed by limb weakness (42%) ,difficulty in speech (28%), decreased vision (27%) vomiting (27%), convulsion (26%), behavioural changes (11.5%) and sensory complaint (10.2%).[18]

In our study the most common signs were papilloedema (62%), motor signs like hemiplegia or hemiparesis (40%), gait abnormalities (34%) and followed by cranial nerve palsies, of which optic nerve , VI th nerve , IX th and X th cranial nerve (6% each) were most commonly involved.

In Roth et al series the most common sign was of hemiplegia or paresis (66.6%), papilloedema (66.3%), gait abnormality (11.3%), sensory system (11.3%) followed by cranial nerve palsies 13%, reduced vision or visual deficit at 8.8%.

Out of the 50 patients in our study 62% had papilloedema and 6% patients had optic atrophy. Post operatively 85% patients with papilloedema recovered gradually in average 1.5 months, while rests were remain stable.

In our study of 50 cases of GBM, 4 patients had previous history of glioma, suggestive of 8% incidence of Secondary GBM and 92% incidence of Primary or de- novo GBM. Two of them had astrocytoma grade -2 and progressed to GBM in 1.5 years and 2.8 years while other two had astrocytoma grade -3 who progressed to GBM in 8 months and 3 months.

One of them presented with recurrence of headache and survived 25 months postoperatively while other three presented with limb weakness, convulsion and altered sensorium respectively and died within 4 months after surgery .

Radiological Findings of Intracranial GBM

Supratentorial GBM (98%) are much more common than Infratentorial GBM (2%) while in ROTH ET AL SERIES this incidence was 0.4%. Prognosis of infratentorial GBM (median survival 4 months) was also very poor as compared to supratentorial GBM (median survival 12.5 months).

MRI give better anatomical and pathological details. Most GBM were heterogenous Gadolinium contrast enhancing with peripheral ring pattern contrast enhancement in most of cases. In our series, mass effect is found in 90% of cases, peritumoral edema was present in 84% cases, contrast enhancement found in 86%, and necrosis found in 86% cases. When compared with LACROIX ET AL SERIES incidence of various MRI findings were comparable with our series.

Position and Approach of Surgery in Various Tumors

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.

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.

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 were attributable to better preoperative and postoperative variables (selection bias).

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 total 13.4 months vs subtotal 12.1 months.

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).

Operative site haematoma developed in 4 patients ,out of them 2 presented with immediate postop unconsciousness ,they were reexplored urgently, one of them died on next postoperative day while other improved upto preop status. Rest 2 haematoma patients were managed conservatively and they survived 6.2 months and >10 months (still alive and in follow up) respectively. 3 patients developed wound infection and 2 patients developed meningitis, all were treated conservatively with sensitive antibiotics for at least 3 weeks and all of them recovered.

3 Patients developed pseudomeningocoele with CSF leak, one patient required. Thecoperitoneal shunt , while rest two were managed conservatively by resuturing and 3 days consecutive lumbar puncture.

In our series of 50 patients of high grade glioma (GBM), at the time of discharge 80% patient recovered or remain neurologicaly intact after surgery, 14% patients developed neurological deficit, 2% patients became vegetative and 4% patients got expired.

Out of 2 patients expired on first post-operative day, one patient of right frontal glioma, 73 year, left hemiparetic male with preop KPS 60 and history of smoking and HTN died on the very next day due to sudden cardiopulmonary arrest. Other patient 11 year male with right frontal glioma developed sudden unconsciousness immediate postoperatively, urgent postop CECT done which reveal large operative site haematoma with residual. Urgent re-exploration and evacuation of haematoma along with resection of residual tumor was done but patient didn't regain consciousness and expired due to brain herniation on next day.

In our series of 50 patients of high grade glioma (GBM), preoperatively 18 patients had KPS score >80, 26 patients had KPS score of 50-70, and 6 patients had KPS score <40.

Postoperatively 33 patients had KPS score >80, 15 patients had KPS score of 50-70, and 2 patient had KPS score <40.

Preop KPS score has significant prognostic value, as patients with KPS >80 had median survival 14.4 months and 39% long term survivor, KPS 50-70 had median survival 12.2 months and 19% long term survivor while pt with KPS <40 had median survival 10.1 months and 17% long term survivor irrespective of other prognostic factors. In our series of 50 patients of high grade glioma (GBM), postoperatively 96% patients survived for 3 months, 86% survived for 6 months, 54% patients survived for 12 months, 26% patients survived 18 months, and 10% patients survived for 24 months and beyond, follow up for these patients are still continued. Overall Median survival in our study was 12.7 months.

In Roth et al series postoperatively 96.8% patients survived for 3 months, 83.4% survived for 6 months, 34.4% survived for 12 months, 20.8% survived for 18 months, 17.7 % patients survived for 24 months , 10.4% patients survived 36 months, 7.3% patients survived 48 months and only 5.2% patient survived for 60 months. These datas are comparable with our findings. Post-operative Median survival for GBM patients in Lacroix et al series was 13 months.[19] In our series of 50 patients of High grade glioma (GBM), postoperatively 45 patients received radiotherapy (2 Gy daily, 5 days a week, for 30 days), 2 patients received only chaemotherapy (200mg/M2/daily for 5 days a month for 6 cycles) as they were secondary GBM and had already received radiotherapy previously, 17 patients received both radiotherapy and chaemotherapy (75mg/M2 daily till radiotherapy then 200mg/M2/daily for 5 days a month for 6 cycles),and3 patients didn't receive either radiotherapy or chaemotherapy as two of them expired on day 1 postoperatively and 3 have socioeconomic constraint. Postoperative radiotherapy and chaemotherapy have definitive prognostic value as patient who received only surgical treatment had median survival of only 1 month (it could be false representative, because of small number sample size and selection of patient with poor preop variables ie. Selection bias),

patients who received only chemotherapy (secondary GBM) had median survival of 4.45 months, patients who received both surgery and radiotherapy had median survival of 12.54 months, and patients who received both radiotherapy and chaemotherapy postoperatively had median survival of 15.9 months. Thus adjuvant chemotherapy provided survival advantage of 3.36 months.

SUMMARY

- The maximum incidence (70%) of High Grade Gliomas (GBM) is in 4th to 6th decade, with fairly uncommon in children. Male are more affected than female with ratio of 1.7:1.
- Usually the time period of starting of symptoms is 5 months or more than that, with headache (74%) being most common complaint, followed by convulsions and limb weakness. Only 5% of the patient presented with normal neurology.
- Papilloedema was the most common sign (62%) followed by limb weakness (40%). Postoperatively 85% patients with papilloedema recovered in average 1.5 months.
- Those having neurological deficit may have involvement of cranial nerve, with maximum 66% optic nerve involvement, mostly because of raised I.C.T or occasionally tumor compression over the nerve. This usually presented as papilloedema in fundus examination.
- CT scan as wells as MRI are the two most important tool of diagnosis; M.R.I has the added advantage of better soft tissue details, which help in planning operative strategy.
- Contrast enhancement on MRI was found in 86% patients, which was poor prognostic with median survival of 12.1 months as compared to 13.4 months for patients with non-contrast enhancing tumor.
- 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. 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 (<35Yr), 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

CONCLUSION

High grade Glioma is a cancer with a poor prognosis, and tumors generally recur after standard multimodal treatments. The management of patients with these tumours has historically been one of the most challenging and disheartening fields in medicine, where failure is the rule and longevity is the exception.

Several variables affect the prognosis of patients with High grade Glioma, including age, preoperative performance status according to the KPS, tumor location, and preoperative MR imaging characteristics of the tumor, as well as whether the patient undergoes reoperation for recurrent tumor and whether the patient receives radiation therapy and/ or chemotherapy.

We conclude that a gross-total resection should be performed whenever possible for these patients, although not at the expense of neurological function. Tumor removal that falls short of statistical cutoff point determined in various series, may still provide diagnostic and symptomatic benefits.

Patients with these devastating tumors have a median survival of approximately 13 months only. This poor survival rate places an emphasis on understanding the effects of surgery on QOL for patients harboring high grade glioma. A key component of QOL, regardless of disease, is functional independence.

The factors that were independently associated with prolonged functional independence were: a preoperative KPS score ≥ 80, age < 35 year, primary tumour, Gross total resection, radiotherapy and temozolomide chemotherapy.

The factors that were independently associated with decreased functional independence were: older age at the time of surgery, coexistent Cardiovascular disease and incurring a new postoperative motor deficit. A decline in functional status was independently associated with tumor recurrence.

Genomic profiling of high grade glioma tumors has identified potential new treatment options that target molecular receptors and signaling pathways.

Aggressive symptom management and honest discussion of patient goals and wishes offer patients hope for enhanced survival and improved quality of life.

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