

Original article:

Study of clinical presentation in cases of high grade glioma –glioblastoma multiforme and its variants

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Abstract:

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.

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 : 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 lobe 5%, 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%.

Conclusion: 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.

Keywords: CNS tumor , high grade glioma

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. 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. ¹Based 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. ²It 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.³Without 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 recurs 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.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:

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 16-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. 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.

Table-1 : TUMOR INCIDENCE(LOCATION) IN PRESENT SERIES OF 50 PATIENTS OF INTRACRANIAL HIGH GRADE GLIOMAS

Serial no.	Location		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

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%.

In comparison, in Roth et al series the incidence of High grade gliomas(GBM) was in frontal lobe 20%, temporal lobe 17%, parital 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.

Table-2 : SIDE DISTRIBUTION TUMOR IN 50 PATIENTS OF HIGH GRADE GLIOMAS(GLIOBLASTOMA MULTIFORME)

SIDE OF HEMISPHERE	NO. OF PATIENT	PERCENTAGE	BOHMAN ET AL SERIES(%)
RIGHT	19	43	46
LEFT	25	57	54

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. 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

Table-3 : 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
	GTC	12	24
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

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 wth 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%).

Table-4 : 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
		PAPILL-OEDEMA	31	62	66.3
	III			13.3	
	IV				
	V				
	VII				
	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	

Discussion:

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 % ⁵ 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 rest were remain stable. 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.^{6,7}

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.

Conclusion:

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.

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