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TREATMENT OUTCOME AND RECURRENCE RATE IN PATIENTS WITH SUPRATENTORIAL HIGH GRADE GLIOMA

Anaesthesiology

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ABSTRACT

Introduction: Glioma is a term used to describe any tumor that arises from the supportive tissue of the brain. This tissue, called glia, helps to keep neurons in place. High grade glioma are WHO grade III and IV tumors. Aims and objective: To estimate the treatment outcome and recurrence rate in patients with supratentorial high grade glioma. **Materials and method:** This prospective study was carried out at on all the patient with the provisional radiological diagnosis of supratentorial glioma admitted in Department of Neurosurgery, J. A. Group of Hospitals, G. R. Medical College Gwalior, over a period of 24 month (from December 2017 to November 2019). **Results:** Most common KPS score at admission was 70 (17 of 50 patients) and at discharge was 80 (13 of 50 patients). Recurrence was found only in glioblastoma and grade III astrocytoma. 30% recurrence was found in grade III astrocytoma (6 in 20) and 35.7% in glioblastoma (10 in 28) within 6 month of surgery. **Conclusion:** Despite multimodality treatment (surgery and adjuvant therapy) prognosis is poor and recurrence is common.

KEYWORDS

Supratentorial tomor, high grade glioma, Recurrence rate in glioma

INTRODUCTION:

Glioma is a term used to describe any tumor that arises from the supportive tissue of the brain. This tissue, called glia, helps to keep neurons in place. Gliomas are graded from I to IV according to the World Health Organization (WHO) malignancy scale.

High grade glioma are WHO grade III and grade IV tumors. Grade III tumors include anaplastic astrocytoma, anaplastic oligoastrocytoma and anaplastic oligodendroglioma, which are characterized by a higher cellular density and the ample existence of atypia and mitotic cells. Grade IV tumors are most malignant and also most frequent gliomas and include gliosarcoma and glioblastoma.

Patients usually present with seizures, focal neurological deficit or headache. Few patients may present with rapid neurological decline, either due to brain hernation or tumor associated haemorrhage. Treatment options are surgery and adjuvant therapy include concomitant chemoradiotherapy and adjuvant chemotherapy (Temozolamide, Carmustin).

From 1975 to 1995, patients younger than 65 with primary malignant brain cancer made moderate improvements in survival, but older patients made no such advances(1).Glioblastoma remains the histological subtype with the poorest survival, with a mean survival of less than 1 yr and less than 3% of patients with glioblastoma multiforme surviving 5 yr after diagnosis (2). The mean survival for Anaplastic astrocytoma is slightly better, at 2 to 5 yr (74). Smith et al. demonstrated that loss of the pTENtumor suppressor gene is associated with poor survival (3). Additionally, epidermal growth factor receptor (EGFR and p53 expression have been studied in glioblastoma multiforme patients with the finding that EGFR overexpression (particularly when combined with normal p53 expression) may correlate with poorer survival in patients aged less than 55(4).

Age continues to be strong a prognostic indicator, although the age range associated with more-favorable outcome varies between studies(5). Recent publication reports that baseline mini-mental status score correlates more strongly with time to progression and survival than performance status. Tumor location, size, and extent of resection are variables that have also been studied in relation to predicting survival. Multivariate analyses have not shown tumor location or size to be significant prognostic factors(6).

MATERIALS AND METHOD:

This prospective study was carried out at Department of Neurosurgery, J. A. Group of Hospitals, G. R. Medical College Gwalior, over a period of 24 month (from December 2017 to November 2019). All patients with clinically and radiologically suspicious supratentorial glioma and all patients with biopsies of supratentorial tumor positive for high grade glioma were included in the study. Patients with infratentorial glioma, unfit for surgery, other pathology was proven in biopsy, blood coagulopathy and patient not willing for surgery were excluded from the study.

Study Procedure

Approval of the study was obtained from Ethical committee (medical). Preoperative operative assessment of consciousness level was done according to KPS Score, along with neurological assessment of all patient with the provisional radiological diagnosis of supratentorial glioma.

Patients taken for surgery with primary goal of obtaining a definitive tissue diagnosis and to achieve gross total resection while maintaining neurologic function. Operative technique included craniotomy with a free bone flap. The dura was closed primarily or pericranial duraplasty done as per need. Post-operative patient were also assessed for higher mental function, focal neurological deficit, pupillary reaction and KPS score. Post-operative CT/ MRI scan was performed. Final diagnosis (tissue diagnosis) was made by histopathological examination.

Assessment of patient according to KPS was done at the time of discharge and again at follow up in OPD.Patients were followed up after 15 days after discharge and then monthly up to 2 years.Patients were followed up for two years (maximum duration). Recurrence rate was noted by follow up by CT Scan and MRI.Recurrence was defined as new lesion at operative site or distant to it. Criteria for surgery in recurrent tumors was KPS score of 70 or more, mass effect and progressive focal neurological deficit

OBSERVATION AND RESULTS

Present study was conducted on 50 patients of supratentorial high grade glioma .

Table 1: Table Shows Age Wise Distribution

S . No.	AGE GROUP (in years)	NUMBER OF PATIENTS	PERCENTAGE (%)
1	< 20	1	2
2	21-30	5	10
3	31-40	13	26
4	41- 50	15	30
5	51-60	10	20
6	>60	6	12
7	TOTAL	50	100

Most of the patients were in the age group between 31 to 50 years (56%). Only one patient was less than 20 years of age. Mean age at admission was 46 years.

Table 2: Table Shows Interval Between Symptoms And Admission

S. No.	INTERVAL BETWEEN SYMPTOMS AND ADMISSION	NUMBER OF PATIENTS	PERCENTAGE (%)
1	Less than 1 month	18	36
2	1 month to 6 month	25	50
3	More than 6 month	7	14
4	TOTAL	50	100

Most of the patients presented within 6 months of onset of symptoms (86%), 36% patients presented within 1 month only.

Table3: Table Shows Tumor Size On Contrast Ct Scan

S. No.	TUMOR SIZE (cm)	TOTAL PATIENTS	PERCENTAGE (%)
1	Less than4cm	18	36
2	4cm or larger	32	64
3	TOTAL	50	100

Tumor size was measured as maximum dimension of tumor in any axis on contrast CT scan. 64 % patients had tumor size of equal to or greater than 4 cm while 36% had tumor size less than 4 cm.

Table 4: Table Shows Extent Of Resection

S. No.	EXTENT OF RESECTION	NUMBER OF PATIENTS	PERCENTAGE (%)
1	GROSS TOTAL EXCISION	11	22
2	NEAR TOTAL EXCISION	27	54
3	PARTIAL EXCISION	12	24
4	TOTAL PATIENTS	50	100

Near total excision was done in 54% patients while Gross total excision was done in 22% patients and 24% patients had partial excision.

Table 5: Table Shows Histopathology Of Tumors

S. No.	HISTOPATHOLOGY	NUMBER OF PATIENTS	PERCENTAGE
1	GRADE- III ASTROCYTOMA	20	40
2	GLIOBLASTOMA	28	56
3	GLIOSARCOMA	1	2
4	ANAPLASTIC OLIGODENDROGLIOMA	1	2
5	TOTAL	50	100

Pathological diagnosis was made based on the 2007 WHO classification. Glioblastoma was the most common (56%) histopathology. 40 % patients had grade III astrocytoma while 2% patients had gliosarcoma and anaplastic oligodendroglioma each

Table 6: Table Shows Adjuvant Therapy

S.No.	MANAGEMENT	NUMBER OF PATIENTS	PERCENTAGE
1	NO ADJUVANT THERAPY	12	24
2	ADJUVANT RADIOTHERAPY	32	64
3	ADJUVANT CHEMORADIOTHERAPY	6	12
4	TOTAL	50	100

64% patients had adjuvant radiotherapy and 12 % patients had adjuvant chemo-radiotherapy. Of 12 patients who had no adjuvant therapy, 7 patients expired before adjuvant therapy and 5 patient refuse to take adjuvant treatment.

Table 7: Table Shows Kps At Admission, Discharge And At 6 Month Of Surgery

S. No.	KPS SCORE	AT ADMISSION	AT ISCHARGE	AT 6 MONTH
1	100	0	0	0
2	90	1	4	1
3	80	11	13	9
4	70	17	11	10
5	60	12	10	6
6	50	5	4	6
7	40	3	1	5
8	30	1	0	1
9	20	0	0	0
10	10	0	0	0
11	0	0	7	10

At admission, maximum (17) patients had KPS score of 70. At discharge, maximum (13) patients had KPS score of 80. At 6 month of surgery, maximum (10) patients of KPS score of 70. Total 7 patients died before discharge and total 10 patients died at 6 month. 2 patients lost follow up at 6 month.

Table 8: Table Shows Recurrence Percentage And Management In Recurrent Cases

S. No.	HISTOPATHOLOGY	TOTAL CASES	RECURRED	OPERATED	CONSERVATIVE
1	GRADE III ASTROCYTOMA	20	6	5	1
2	GLIOBLASTOMA	28	10	7	3
3	TOTAL CASES	48	16	12	4

Recurrence was found only in glioblastoma and grade III astrocytoma. 30% recurrence was found in grade III astrocytoma (6 in 20) and 35.7% in glioblastoma (10 in 28) within 6 month of surgery. Among total 16 recurrent cases, 12 were reoperated while 4 were managed conservatively because of poor KPS score and diffuse hemispheric involvement.In present study, 2 patients with grade III astrocytoma progressed to glioblastoma within 6 month of first surgery .

DISCUSSION:

Gliomas are the most common type of primary brain tumor. Nearly two-thirds of gliomas are highly malignant lesions that account for a disproportionate share of brain tumor-related morbidity and mortality. Surgery and radiation have been the mainstays of therapy for most glioma patients, but temozolomide chemotherapy `has recently been proven to prolong overall survival in patients with glioblastoma. Despite recent advances, two-year survival for glioblastoma with optimal therapy is less than 30%.[7]

Age wise distribution

In present study, maximum (30 %) patients were between 41 to 50 yrs of age. Youngest patient was of 19 yrs of age. Mean age at admission was 46 years. 50% patients were between 41 to 60 years and 76% patients were between 31 to 60 years, which matches with M Ghosh et al study. M Ghosh et al[8] had maximum (26%) patients of age group 51 to 60 yrs.Song T TCheo et al[9] had maximum (38.3%) of case of age group more than 60 yrs of age.

Interval between onset of symptoms and admission

In present study, 36% patients presented within 1 month of symptoms , 50% patients presented between 1 month to 6 month of symptoms and 14% patients presented 6 month after onset of symptoms. In C. Abrudan et al[10] study the interval between the debut of symptoms and admission in the hospital was one month for 39% of cases. An evolution of symptoms longer than 6 months has been met for 12% cases. In M . Ghosh et al[8] study, 68 % patients had clinical history of less than 3 month, 16 % patients had clinical history of 3 to 6 month and 16% patients had clinical history of more than 6 month in primary glioblastoma.

Size of tumor

In present study , 36% tumors were less than 4 cm and 64 % were 4 cm or larger which matches with study of M Ghosh et al[8]. M Ghosh et al [8] had 34.4% tumors of size < 4cm and 65.5% of size > 4cm. N Jiancun Wang et al [11]had 37.63% tumors <5 cm and 62.37% tumors > 5 cm.

KPS at admission:

Recent studies also show that preoperative KPS is a good prognosis indicator for glioma patients. For example, the median survival time of patients with KPS of >70 is longer than that of patients with KPS of < 70 (21.5 months vs 11.5 months), indicating that a higher KPS predicts better prognosis[11].In present study, maximum (34%) patients had KPS

70 at admission and 58% patients were of KPS 60 -70 at admission.M Ghosh et al[120-8] had 75.4% patients of KPS 80-100 at admission. Jiancun Wang et al[11] had 78.5% patients of KPS score70 or greater and 21.5% patients with KPS score less than 70.In present study, KPS at admission was relatively poor probably due to late presentation. The late presentation was attributable to the ignorance by patients, treatment in remote area and late referral to higher centre.

Extent of resection

The gold standard for high-grade gliomas includes combination of surgery, radiotherapy, and chemotherapy. High grade gliomas are widely infiltrative , fact them makes quite impossible to completely resect[10]. In present study, 22% cases had gross total resection, 54% had near total resection, 24% had subtotal excision. C. Abrudan et al[10] had gross total removal in 10% of anaplastic astrocytoma and 5% in GBM. Chaichana et al[12] had 38% gross total removal of tumor and 62% near total removal of tumor. Ivan Ciric et al[13] had 64% gross total removal of tumor and 24% subtotal removal of tumor.

Histopathology

Among adults, more than half of gliomas are high-grade (malignant gliomas). They include glioblastomas (glioblastoma multiforme GBM; WHO grade IV), anaplastic astrocytomas (AA; WHO grade III), anaplastic oligodendrogliomas (AO), and anaplastic oligoastrocytomas (AOA)[14]. Suvi Larjavaara et al[15] study had 47 % grade IV and 23% grade II +III astrocytoma. C. Abrudan et al[10] had 64% with glioblastoma, 28% patients with anaplastic astrocytoma and 5% anaplastic oligodendroglioma. In present study , 40% case were grade III astrocytoma, 56% were grade IV gliomas, 2% were anaplastic oligodendroglioma and 2% were gliosarcoma among high grade glioma. In present study, Glioblastoma was most common histopathology which matches with finding in study of C. Abrudan et al[10] and most of the other study.

Recurrence

Nearly all patients with Glioblastoma suffer from tumor recurrence despite initial aggressive treatment [16]. Studies have shown the mean time to Glioblastoma recurrence is approximately 32–36 weeks after initial multimodal treatment, and this is most frequently a result of continuous neoplastic growth within 2–3 cm from the original neoplasm [17]. In our study 30%(6 out of 20) of grade III glioma and 35% (10 out of 28) of grade IV glioma had recurrence within 6 month of surgery. Xiaofeng Zhou et al[18] had central recurrence rate of 56% within a year for high grade glioma. In Kazuyuki Uehara et al[19] study the median follow-up periods were 13 months for all patients and 19 months for those remaining alive. Of 26 anaplastic astrocytoma, 16 recurred (61.5%) while of 105 glioblastoma, 58 recurred (55%).

CONCLUSION:

Despite multimodality treatment (surgery and adjuvant therapy) prognosis is poor and recurrence is common. 35.7% patients of glioblastoma and 35% patients of grade III astrocytoma had recurrence within 6 month of surgery.

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