VOLUME-8, ISSUE-9, SEPTEMBER-2019 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Neurosurgery

GLIOBLASTOMA MULTIFORME – OUTCOMES AND EXPERRIENCES AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Background - Glioblastoma Multiforme (GBM) is the most common primary brain tumour in adults. Although the survival rate for GBM has improved with recent advancements in treatment, the prognosis remains generally poor.

Method - We conducted a retrospective review of GBM patients seen in PGIMER & Dr. Ram Manohar Lohia Hospital, New Delhi from August 2015 to September 2017. Demographic data and clinicopathological data and treatment parameters were collected from the hospital medical records and correlated with patient survival.

Results – Data of 71 GBM patients including 3 pediatric patients was analysed. We observed an increase in incidence with increasing age with majority patients being in the age group of 50 – 60 years. Majority of our patients (28.2%) had a preoperative Karnofsky Performance Score (KPS) of 80 and 19.7% patients had a KPS of <50. All our patients were subjected to either near total or subtotal tumour resection depending on clinical features, radiological profile and intraoperative findings. After discharge, the treatment was continued with radiotherapy and adjuvant concurrent chemotherapy in all patients. The patient survival after discharge from hospital ranged from 2 months to 13 months with a median survival time of 6 months. 11 patients expired during their stay in the ICU. Using the Spearman's Rho test significant correlation between poor preoperative Karnofsky Performance Score (KPS) and poor survival was seen (correlation coefficient = 0.435, p= 0.01). Treatment with near total tumour resection, radiotherapy and adjuvant concurrent chemotherapy correlated with improved survival (p= 0.043) in comparison to patients subjected to subtotal tumour resection and chemoradiotherapy. The correlation between patient survival and patient age is very weak and insignificant (p = 0.12) in our patient group. The approximate total blood loss was tabulated and mean blood loss during surgery was found to be 1504.23 ml ± 554.059 ml. Type of resection showed no correlation with duration (in days) of postoperative ventilation (p = 0.284) and duration of ICU stay (p = 0.358).

Conclusion - GBM confers a poor prognosis especially at extremes of age. Extent of surgical resection, preoperative KPS show direct association with improved survival.

KEYWORDS :

INTRODUCTION

Glioblastoma multiforme is the most common and most malignant primary tumour of the brain and associated with one of the worst 5-year survival rates among all human cancers. Despite multimodal aggressive treatment, comprising surgical resection, local radiotherapy and systemic chemotherapy, the median survival time after diagnosis is still in the range of just 12 months (Smith and Jenkins, 2000), with population-based studies indicating even shorter median survival (Ohgaki *et al.*, 2004). Nevertheless, a small fraction of glioblastoma patients survive for more than 36 months. These patients are referred to as long-term survivors.

In addition, younger age and a good Karnofsky performance score (KPS) at the time of diagnosis are established clinical parameters associated with longer survival (Curran Jr *et al.*, 1993).

The investigation of glioblastoma long-term survivors could help to identify yet unknown clinical, environmental and/or molecular factors that are associated with favourable prognosis. Here, we report on a retrospective analysis of 77 glioblastoma patients including 3 pediatric patients recruited within our hospital.

MATERIALS AND METHODS

We conducted a retrospective review of GBM patients seen in PGIMER & Dr. Ram Manohar Lohia Hospital, New Delhi from August 2015 to September 2017. Demographic data and clinicopathological data and treatment parameters were collected from the hospital medical records and correlated with patient survival.

RESULTS

Data of 71 GBM patients including 3 pediatric patients was analysed. We observed an increase in incidence with increasing age with majority patients being in the age group of 50 – 60 years. Majority of our patients (28.2%) had a preoperative Karnofsky Performance Score (KPS) of 80 and 19.7% patients had a KPS of <50. All our patients were subjected to either near total or subtotal tumour resection depending on clinical features, radiological profile and intraoperative findings. After discharge, the treatment was continued with radiotherapy and adjuvant concurrent chemotherapy in all patients. The patient survival after discharge from hospital ranged from 2 months to 13 months with a median survival time of 6 months. 11 patients expired during their stay in the ICU. Using the Spearman's Rho test significant correlation between poor preoperative Karnofsky Performance Score (KPS) and poor survival was seen (correlation coefficient = 0.435, p= 0.01). Treatment with near total tumour resection, radiotherapy and adjuvant concurrent chemotherapy correlated with improved survival (p= 0.043) in comparison to patients subjected to subtotal tumour resection and chemoradiotherapy. The correlation between patient

survival and patient age is very weak and insignificant (p = 0.12) in our patient group. The approximate total blood loss was tabulated and mean blood loss during surgery was found to be 1504.23 ml ± 554.059 ml. Type of resection showed no correlation with duration (in days) of postoperative ventilation (p = 0.284) and duration of ICU stay (p = 0.358).

DISCUSSION

In general, glioblastomas are more frequent in males, with a male/female ratio between 1.3 and 1.45, corresponding to a proportion of female patients of 43 and 41%, respectively (Barnholtz-Sloan *et al.*, 2003; Ohgaki and Kleihues 2005). In line with these data, the male to female ratio in our series of 71 unselected glioblastoma patients was 1.43. The long-term survivors showed a trend to a higher proportion (50%, 95% CI 38–62%) of female patients, although the proportion reported in the literature is still within the limits of the confidence interval. Nevertheless, it seems that glioblastoma long-term survival is favoured by the combination of two basic clinical parameters—young age and female gender. Unfortunately, the median follow up time in the control group did not allow validation of these findings. Several environmental and socioeconomic risk factors have been associated with the development of malignant glial tumours (Lee *et al.*, 1997; Inskip *et al.*, 2001; Huncharek *et al.*, 2003; Schlehofer *et al.*, 2005). One might assume that the absence of such factors could be associated with a better prognosis in those tumours. However, in the present study we failed to identify any of those factors to be obviously under- or overrepresented in long-term survivors. Also such data are difficult to obtain in a retrospective setting. All patients of our series were initially treated by (gross total or near total) tumour resection. Recent data have confirmed that the extent of resection is associated with improved progression-free survival (Stummer *et al.*, 2006). The fact that majority glioblastoma long-term survivors had undergone gross total resection as initial treatment confirms that tumour resection enhances the chances for a favourable outcome.

All patients had adjuvant radiotherapy. Standard treatment for glioblastoma includes postoperative radiotherapy; hence radiotherapy is unlikely to be a positive selection factor. Chemotherapy for malignant gliomas has experienced a renaissance since the publication of the EORTC 26981/22981-NCIC CE3 phase III randomized trial, which demonstrated that concomitant and adjuvant temozolomide chemotherapy has a positive effect on survival of patients with glioblastoma (Stupp *et al.*, 2005). However, the study design does not allow to define chemotherapy as a prognostic factor. Here, the same limitations apply as for the number of surgical interventions. Patients who have a less malignant course of disease also have more options to undergo multiple surgical and chemotherapeutic interventions.

There are very few case series of glioblastoma long-term survivors reported to date. We provide a clinical characte rization of 71 primary glioblastoma patients.

The median age of glioblastoma patients is >60 years according to population-based studies (www.cbtrus.org) (Ohgaki and Kleihues, 2005; Chakrabarti *et al.*, 2005). In contrast with these data, the median age of our glioblastoma patients was 48 years. The median age of the long-term survivors in our study was also considerably lower, i.e. 42 years ($P < 0.001$). This is in accordance with numerous clinical studies indicating that young age at the time of diagnosis is an important parameter associated with longer survival (Burger and Green 1987; Curran Jr *et al.*, 1993; Devaux *et al.*, 1993; Chang *et al.*, 2005). Taking data from all 281 published glioblastoma long-term survivors (Table 4), their median age is 36.9 years, which supports that age is of predictive value in glioblastoma. On the other hand, four of our long term survivor patients were 65 years or older, indicating that older age does not exclude long-term survival of glioblastoma. Interestingly, the median age in our study is much below that of all published cases. This might in part be explained by the fact that older studies are possibly contaminated with low-grade tumours in older adults that were mistaken for glioblastoma, in particular pleomorphic xanthoastrocytomas. A contam ination of glioblastoma patients' cohorts by high grade tumours of the oligodendroglial lineage may also occur. However, in our series, only two cases showed a minor oligodendroglial component in an otherwise typical glioblastoma.

We assume that further molecular analyses employing large-scale microarray-based genomic and expression profiling approaches will identify molecular features that are specific to glioblastomas of long-term survivors. For this purpose, the German Glioma Network is prospectively collecting fresh tissue from all glioblastoma patients operated at its participating centres and shall thus be able to perform comparative profiling experiments on a reasonable number of long-term survivors from this large population within the next few years.

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