Survival patterns and clinicopathologic spectrum of Glioblastoma Multiforme (GBM)- experience at a tertiary cancer centre in South India

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Objective: Glioblastoma Multiforme (GBM) is the most common CNS malignancy worldwide. There is few data regarding this entity in South Indian population. Our objective is to evaluate the demographic, clinicopathologic, treatment and survival characteristics of this entity.

Materials and Method: A retrospective single centre study of 5 years (2013-2017) duration. Data of patients with tissue diagnosis of GBM, treated at Malabar Cancer Centre was studied.

Results: A total of 30 cases of GBM are studied. Male predominance noted with mean age of presentation 54.5 years. 93% cases are primary GBM. The tumours are predominantly left sided (57%) with frontal lobe being the most commonly affected site. The most common histological type is GBM-NOS. Surgery is the primary treatment modality undergone by 97% of cases followed by adjuvant concurrent chemo radiation (83%). In a median follow up period of 26 months, 5 are alive without disease, 7 are alive with disease, and 4 lost to follow up. The median Overall Survival (OS) is 17 months and the median Disease Free Survival is 12 months. All patients who survived beyond the median OS, where termed as Long Survivors (LS) and their characteristics were analysed.

Conclusion: Multi-centric studies on demographic and survival features of GBM are of great importance in establishing Indian geographic epidemiology. Specific features of GBM with better survival warranties further studies aimed at molecular characterisation and targeted treatment protocols.

Key words: Glioblastoma Multiforme (GBM), brain tumours, South India

INTRODUCTION

Glioblastoma Multiforme (GBM) is the commonest malignant neoplasm of brain and CNS. It accounts for 45.2% of malignant primary brain and CNS tumours, 16% of all primary brain and CNS tumours and 54% of all gliomas [1]. It is grouped into WHO Grade IV, being the most aggressive diffuse glioma of astrocytic lineage [2].

GBMs comprise of primary and secondary subtypes which evolve through different genetic pathways, affect patients at different ages and have differences in outcomes though histomorphologically no differences are seen between the two groups. The standard management has been maximum surgical resection followed by adjuvant radiotherapy with concurrent chemotherapy (CTRT) followed by adjuvant chemotherapy [3].

The overall prognosis for GB has changed little since the 1980s and it still remains an incurable disease [4]. The present study background is that there are very few studies regarding this entity in South Indian population. Hence we aimed to evaluate demographic, clinic-pathologic, treatment and survival characteristics of GBM treated at a tertiary cancer centre in rural area of North Kerala.

MATERIALS AND METHODS

It was a retrospective single centre study of five years duration. Data of patients registered from January 2013 to December 2017 with a histopathological diagnosis of GBM were retrieved from Institutional Cancer Registry and archives of Department of Oncopathology. The study was approved by the Institutional Review board before the start of the study.

The demographic features such as age, habits, occupational history, history of exposure to radiation and the treatment received were retrieved form patient records. H and E slides of these patients were retrieved from archives of Oncopathology department and specific histological characters noted.

The median Overall Survival (OS) and Disease Free Survival (DFS) was estimated by Kaplan Meier plot and the cohort was stratified as long and short term survivors and analysed further. Mann Whitney U test was used to study the differences...
in characteristics between long and short survivors. All the
data collected was double entered into MS Excel software
and validated. Duplicate version of the database was used for
statistical analysis using IBM SPSS Statistics (Version 20.0.
Armonk, NY: IBM Corp). Descriptive statistics of frequencies
and percentages were used for data analysis.

RESULTS
A total of 101 cases of CNS tumours were registered at MCC,
during the study period, of which 30 cases were GBM. Median
age at presentation was 54.5 years. Male: female ratio was 3:2.
None of the patients had past history of radiation. Affected
males were predominantly manual labourers and females were
predominantly housewives. Of the 18 people who had habits, 9
were smokers, 5 were pan chewers and 4 were occasional alcohol
users.

Most common presenting symptom was headache. All cases were
intracranial, with 57% cases (n=17) involving right side of brain,
40% (n=12) left side and 3% (n=1) involving the centre. GBM
predominated in frontal lobe (28%) followed by temporal and
parietal lobes (14% each) (Figure 1). 93% cases were primary
GBM and 7% cases were secondary to diffuse astrocytomas.

The average size of lesions we encountered was 5cm × 4cm.
GBM-NOS (Figure 2) is the commonest histological type in our
study (93%). There were 2 cases of GBM-small cell type (Figure
3). 97% (n=29) cases had undergone definite surgery. 83% 
(n=25) had taken adjuvant CTRT and adjuvant chemotherapy
with Lenozolomide.

During the follow up period, 14 patients expired; 7 alive with
disease; 5 alive without disease and 4 were lost to follow-up. The
median Overall Survival (OS) was 17 months and the median
Disease Free Survival (DFS) was 12 months (Figure 4 and 5).
The two year OS was 40.7% and two year DFS is 44%.

All patients with OS, more than the observed median OS of 17
months were grouped as Long Term Survivors and those with
median OS less than 17 months were grouped as Short Term
Survivors. Their characteristic features were described in Table 1.
DISCUSSION

Cushing introduced the term Glioblastoma Multiforme (GBM) way back in nineteenth century [5]. Since then it has been one of the dreaded glial neoplasm, mainly owing to the fact that it remains an incurable disease with a median survival of 15 months [6, 7]. According to 2013 CBTRUS report, GBM has the highest average annual age-adjusted Incidence Rate (IR)- 3.19/100,000 population which is the highest among malignant brain tumours [1].

GBM accounted for 30% of brain tumours treated at our institution. This was relatively on a higher side when compared to similar studies in South India- where Jaiswal, et al, observed GBM constituted 15.5% of total primary brain tumours [8]. Median age of presentation of GBM in our study was comparable to that of other similar studies from India [4, 8].

Though CNS tumours are found to have a female predilection, astrocytic tumours are found more in males [8-10]. According to Ghosh et al, GBM showed a male predilection (2.5:1) [11]. Our study too showed a male predilection in accordance with the published literature [12]. Since Ionizing radiation is one of the few known risk factors to show a definite increase of glioma development, an attempt was made to obtain a history of radiation among our GBM patients, but none of our patients had such a history [11].

Primary GBM is defined as those that arise denovo, while secondary GBMs are those that arise in a pre-existing astrocytoma. Literature review has shown that secondary GBM constitute only 5% of total GBM cases [19, 20]. Similar finding were seen in the present study.

Ghosh et al, observed most lesions of GBM were of size more than 4cm [12]. The present study also observed similar findings, with 93% cases with maximum dimension more than 4cm.

As per the new NCCN guidelines, treatment of newly diagnosed GBM requires a multidisciplinary approach. Current standard therapy includes maximal safe surgical resection, followed by concurrent chemo-radiation and then adjuvant chemotherapy with Temodar® (Temozolomide(TMZ)), an oral alkylating chemotherapy agent [21]. Our institution follows the same guidelines, with 64% of our patients completing the treatment as per guidelines.

We took the freedom of defining those who survived more than the mean survival period as long term survivors and scrutinised their specific characteristic features. Young age is seen to offer better survival in our study, a finding consistent with previous studies [22]. Incidence of GBM in tempo-parietal region is seen to have good survival, in our study population.

Those who received adequate tumour debulking followed by CTRT and adjuvant chemotherapy had long survival compared with those who did not receive all three treatment modalities.

CONCLUSION

GBM is a highly aggressive CNS tumour, the prognosis of which is grim even with the use of multimodality treatment. Long term survivors in GBM were predominantly young with tempo-parietal lobe predominance. Specific features of GBM with better survival warrants further studies aimed at molecular characterisation and targeted treatment protocols. Racial differences in clinical and molecular patterns of tumours mandates further evaluation and modification of specific management protocols based on Indian population.

CONFLICT OF INTEREST

We have no conflict of interest to declare.
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