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Unique Presentation of Glioblastoma with Acute Onset Symptomatology and Disease Recurrence

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ABSTRACT

Background: The most common and dangerous type of primary brain tumor is glioblastoma. Focused neurological abnormalities are common in the brief clinical histories that patients typically bring to the clinic.

Objective: Aim was to determine the clinical presentation of glioblastoma and it's postoperatively outcomes.

Methods: This prospective/observational study was conducted at Hayatabad Medical Complex, Peshawar from December 2022 to March 2024. Total 35 patients of both gender were presented after providing informed written consent. The CNS tumor registry was used to gather demographic information as well as data on adverse occurrences. Means and standard deviations were the results of the data analysis. SPSS 23.0 was used to analyze all data.

Results: The included cases had mean age 65.9 years. 22 (62.9%) cases were males and 13 (37.1%) were females. Post-operatively psychiatric/neurological adverse events were observed early as compared to cardiovascular/respiratory and general adverse events. Frequency of seizure was 25 (71.4%) among all cases.

Conclusion: The adverse events that patients with glioblastoma experience are categorized as follows: psychiatric/neurological, cardiovascular/respiratory, and general. At least one seizure will be experienced by the majority of patients.

Keywords: *glioblastoma, adverse events, seizure*

1. INTRODUCTION

Brain tumors can be classified as either primary (having their origin in the brain) or secondary (having spread to the brain) [1]. Grades for brain tumors are based on a four-point system (1-4). A wide range of behaviors are included in grades 1-4, from mildest to most severe. The four most common primary brain tumors are gliomas, meningiomas, pituitary adenomas, and tumors of the nerve sheath. Glioma subtypes are defined by the cell types that give rise to the tumor. On this page, glioblastoma and astrocytoma will be the main points.

A subtype of glioma, astrocytoma originates in the brain's glial cells. Isocitrate dehydrogenase (IDH) mutations in these tumor cells also permit further categorization. Improvements in prognosis are associated with the mutation. Grade 4 astrocytomas lacking an IDH mutation are referred to as glioblastomas following glioblastoma multiforme. Compared to astrocytomas IDH mutants, these tumors have a substantially worse prognosis and are far more aggressive [3]. The way glioblastoma shows itself is very dependent on the tumor's size and location [4]. Some of the symptoms include headaches, changes in personality, nausea, mood swings, and signs that are similar to those of a stroke. It is common for these symptoms to appear slowly, in line with the tumor's development. The lack of significant preceeding symptoms before to the primary presentation is what distinguishes this glioblastoma presentation from others and emphasizes the tumor's rapid growth rate.

One important aspect in the molecular classification of glioblastomas is whether or not they have mutations in isocitrate dehydrogenase (IDH). The bulk of glioblastomas are IDH-wildtype, which indicates that they are more aggressive and do worse than glioblastomas that have the IDH mutation. The latter are better at what they do and are more prevalent among younger people [5].
Another crucial molecular feature is the methylation state of the O6-methylguanine-DNA methyltransferase (MGMT) promoter. The effects of alkylating chemotherapeutic medicines, such temozolomide, are reduced by the DNA repair enzyme MGMT. By methylating the MGMT promoter, the repair activity of this gene is inhibited and the tumor's sensitivity to chemotherapy is enhanced. When compared to patients without MGMT promoter methylation, those with it have better treatment efficacy and overall survival [6].

The spectrum of neurological symptoms normally experienced by glioblastoma patients is dependent on the tumor's location, size, and development pace inside the brain. One typical symptom is persistent headaches, which are characterized by a pattern of gradually increasing discomfort due to high intracranial pressure [7]. The frequency and intensity of seizures experienced by patients are influenced by the tumor's location. Cognitive and behavioral disorders, such as memory loss, personality changes, and disorientation, are common in patients with brain tumors because the tumors impact multiple regions of the brain that are involved in higher-order thinking [8]. When glioblastomas attack the motor, sensory, or speech areas, respectively, they cause localized neurological deficits including a loss of feeling or strength in a specific area, changes to vision, or difficulties with language or speaking (aphasia). Because the tumor and cerebral edema continue to grow, symptoms typically worsen as the disease progresses. To reduce intracranial pressure, immediate medical attention is usually required. Because adults' neurological symptoms are typically not specific enough to support a prompt diagnosis, it is critical that they be very careful and get neuroimaging help right enough if their symptoms develop or worsen [9,10].

2. MATERIALS AND METHODS

In this prospective/observational study 35 patients were included. All participants must be adults (18+) and have either been treated with or be eligible to receive BCNU biodegradable wafers for CNS cancer. They must also have signed an informed consent form and not have any medical history that could increase their risk of adverse events.

In the data set, we found information about the following: age, sex, date of diagnosis, date of surgery, survival, tumor size, tumor location, tumor histology, biomarkers IDH1, IDH2, MGMT, KPS scores every three months, treatment regimens, and adverse events that were documented with the date they happened. We included an adverse event in the study if multiple patients reported it. Afterwards, we assigned a mild to severe rating to each adverse effect. The characteristics of minor adverse effects were tolerance and the absence of interference with everyday activities. An adverse event was considered substantial if it produced pain significant enough to interfere with daily activities. Severe adverse events were defined as those that substantially impaired daily functioning.

The utilization of means and standard deviations provides granularity to the demographic and clinical characteristics of the patients. The data includes the number of months that elapsed between the date of initial surgery and the occurrence of the first adverse event of that type, as well as monthly ranges, medians, and standard deviations for those events. All computations were performed using Excel, version 16.68. Both the data screening and the statistical testing assumptions were met by the data.

3. RESULTS

The included cases had mean age 65.9±7.57 years. 22 (62.9%) cases were males and 13 (37.1%) were females. Mean tumor size was 4.19±5.33. Right side was the most common affected side. Mean time of follow up was 13.9±6.22 months.(table 1)

Table-1: Patients with detailed information

Variables	No./%age
Mean age (years)	65.9±7.57
Mean tumor size (cm)	4.19±5.33
Mean time of follow up (months)	13.9±6.22

Gender	
Male	22 (62.9%)
Female	13 (37.1%)
Affected Side	
Right	23 (65.7%)
Left	12 (34.3%)

Post-operatively psychiatric/neurological adverse events were observed early as compared to cardiovascular/respiratory and general adverse events.(table 2)

Table-2: Time of post-operatively adverse events

Adverse events	**Time (Months)**
psychiatric/neurological	2.9±4.35
cardiovascular/respiratory	3.45±5.57
general	3.79±9.64

Frequency of psychiatric/neurological adverse events was 19 (54.3%), cardiovascular/respiratory adverse events were found in 12 (34.3%) and 4 (11.4%) were general adverse events.(Table 3)

Table-3: Frequency of AE types

Variables	**No./%age (35)**
psychiatric/neurological	19 (54.3%)
cardiovascular/respiratory	12 (34.3%)
general	4 (11.4%)

Frequency of seizure was 25 (71.4%) among all cases. Survival rate of patients was 14 (40%) within 36-months,(table 4)

Table-4: Association of seizure

Variables	**No./%age**
Seizure	
Yes	25 (71.4%)
No	10 (28.6%)
Survival Rate	
Yes	14 (40%)
No	16 (60%)

4. DISCUSSION

In our cohort, the median age at diagnosis was 65.9 years, which is in line with the median age of 65 years seen in the CBTRUS report of CNS cancers detected in the US from 2015 to 2019.[11] Additionally, there were 12 male patients and 7 female patients in our sample, which is consistent with the CBTRUS analysis that found a higher prevalence of gliomas in males from 2015 to 2019.[11] With a median time to survival assessed by Kaplan-Meier at 19 months, 42.1% of our patients survived across the 36 months of the experiment. The median overall survival time after surgery is fourteen to twenty-two months, which is in line with other studies.stated in references [12-14]As a result, our cohort might be considered representative of glioblastoma patients generally.
We found that patients reported adverse events in a specific order, with psychiatric/neurological, cardiovascular/respiratory, and general adverse events coming first. Serious adverse events occurred at a higher rate in the cardiovascular and respiratory group. Rather than occurring at the end of a patient's illness, this kind of painful incident occurred frequently during the duration of the disease.

Patients' experiences from diagnosis until death are underrepresented in glioblastoma literature, which mostly focuses on the benefits and drawbacks of different treatment outcomes. As a result, new studies on this subject are scarce. Surprisingly, there is a lack of studies that focus on the side effects experienced by GBM patients after their diagnosis and the typical window of time when they appear.

Researchers from Austria tracked 42 patients with glioblastoma for three months after their diagnosis and kept tabs on their neurocognitive function and quality of life for another sixteen months. The normal treatment was administered to all patients.[15] Median survival was 18.5 months, and progression-free survival (PFS) was 9.5 months, according to the results.This was found using the Kaplan-Meier technique [15]. Our cohort's median time to survival, as determined using the Kaplan-Meier method, was 19 months, which is similar to this. The authors found that patients' weariness became worse on average seven months after diagnosis, and that the quality of life score on the global health index remained stable throughout the first year of illness. But it went down after the sixth test.[15] Patients reported fatigue approximately 6.5 months after their diagnosis and tumor removal, according to our study. Results showed that patients' cognitive capacities remained constant up until tumor progression, although their quality of life had already diminished prior to tumor progression.In a separate study, the same authors looked at long-term glioblastoma survivors, who were characterized as having had the condition for over three years [16]. Cognitive performance, quality of life, anxiety, depression, mobility, and disability were among the variables evaluated. Tumor traits were also considered.Despite the fact that we had just one patient who nearly met the criterion for a long-term survivor (surviving 35 months), our goal was to investigate similar adverse outcomes. On one quality-of-life poll, people rated social functioning and cognition lower, while on another, issues with money, lack of energy, and uncertainty about the future were rated higher.As indicated earlier, two patients were additionally diagnosed with major depressive illness and anxiety [17].A well-documented adverse event, seizures affect up to 80% of GBM patients at some point along their illness progression.the earliest and the ninth We found that 91.4% of patients experienced seizures, which aligns with this. After the initial seizure, we began treating all of our patients with levetiracetam, a drug that has been studied extensively in glioblastoma patients.Two patients were transferred to lacosamide and one was given valproic acid in addition to levetiracetam due to behavioral problems [18].

When investigating adverse events that patients experience, it is crucial to take into account demographic characteristics linked to improved overall survival. Reason being, these traits might explain why our sample had a better median survival rate. Some have postulated that the total survival rate is affected by the tumor's location. Twelve of the nineteen tumor patients were located on the right side of the body, while seven were located on the left. Three people had tumors on the right side of their brains, specifically in the parietal lobe, four in the temporal lobe, and five in the frontal lobe. The left temporal lobe had five tumors, while the left frontal lobe had two. A study conducted in Italy found no significant effect of tumor site on overall survival. Conversely, individuals with tumors located in the occipital lobe had a higher probability of survival, according to researchers from the United States and China [19].Most cancers were found in the temporal, parietal, and occipital lobes, according to [19].In contrast, no occipital lobe cancers were found in our sample [20].

The strength of this study lies in its prospective design, which allows for the accurate depiction of patients' experiences following diagnosis and the availability of comprehensive medical records for all adverse events.[21]

5. CONCLUSION

The adverse events that patients with glioblastoma experience are categorized as follows: psychiatric/neurological, cardiovascular/respiratory, and general. At least one seizure will be experienced by the majority of patients.

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