

Spectrum of Primary Brain Tumors in a Tertiary Hospital in India: A Retrospective Study

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Abstract- Introduction: Primary brain tumors are uncommon tumors demonstrating characteristics histopathological features. Variation of demographic profiles of these intracranial malignant tumors in different regions worldwide was there and understanding of these helps in prompt diagnosis and establish appropriate treatment strategy. Different nations have established their brain tumor registry. The current study also focusses on demographic profiles, treatment schedules and survival rates of patients with a brain tumor who attended in a tertiary care hospital in a northern state of India.

Material and Methods: Records of primary brain tumor patients over a period of 5-years were reviewed retrospectively. These records were analyzed for incidence, demographic pattern, different treatment modalities and their response evaluation.

Results: A total 168-patients of primary brain tumors were identified. The median age at presentation was 47-years and males slightly outnumbered females. Among all the tumors, frontal lobe involvement was most predominant and most common presentation was headache. Astrocytoma constituted the predominant histopathological types and glioblastoma forms the largest subtypes of astrocytic tumors. Majority of patients underwent surgery followed by adjuvant radiation therapy with concurrent oral temozolomide. Overall average survival was 23-months, with 17 patients had follow-up of more than 4-years. Clinically, the response at last follow-up was CR in 29% and PR in 41%.

Conclusion: Despite the fact that primary brain tumors are rare in our country, noticeable state-wise variation in incidence, demographic profile and mortality has been noted. The histopathological pattern of primary brain tumors in our institution established astrocytic tumors as the major health burden and gross total resection followed by radiotherapy with or without concurrent temozolomide is standard of care. The present study had several limitations, including its retrospective design, which may introduce selection bias. Finally, it is recommended to develop nationwide proper atlas of the cancer patients so that exact geographical plotting of the patients can be done to establish the accuracy of the scattered data.

Index Terms- Adjuvant radiation therapy, astrocytoma, demographic profile, histopathological, primary brain tumors, retrospective study, temozolomide

I. INTRODUCTION

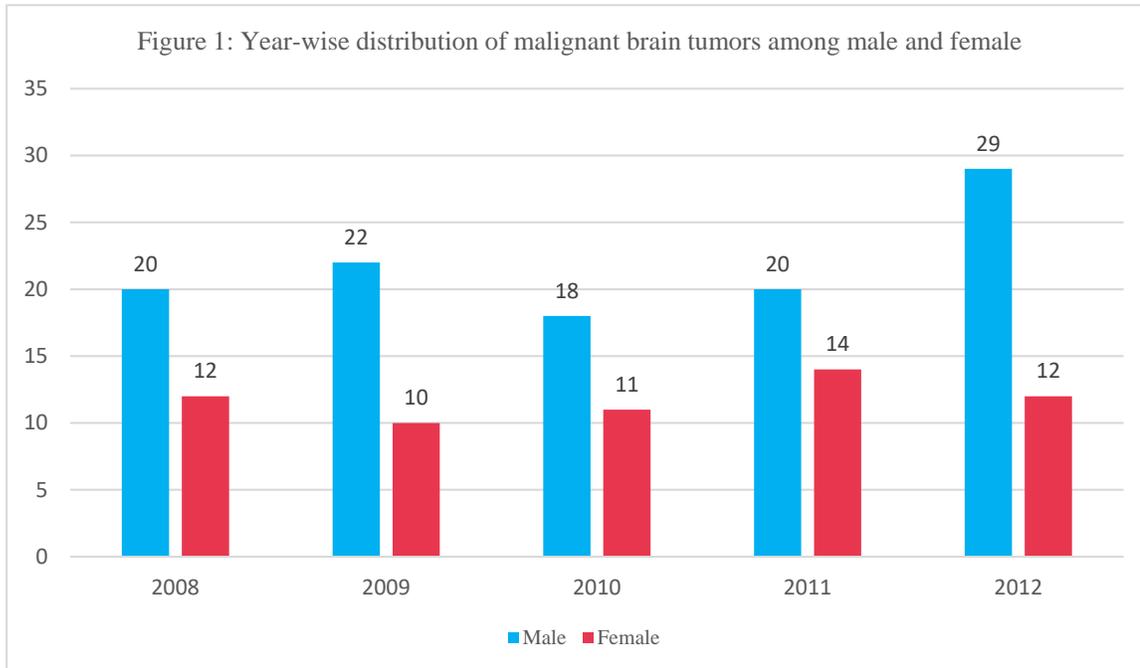
Primary brain tumors are out of the common entity having a rising trends in recent decades. These intracranial tumors demonstrate characteristics histo-pathological features related with stereotypical age and sex distribution. Understanding of this distinctive features of primary brain tumors helps in prompt clinical diagnosis and to select suitable treatment schedules on individual basis. These appropriate treatments, based on histological subtypes, grade of tumor and patient performance status, further improves longevity of patients. A number of previous studies, in different regions worldwide, have investigated the demographic profile, different treatment schedules and survival rates of patients with a brain tumor and have established brain tumor registries. The present retrospective study seeks to focus on current description of patterns and trends of primary brain tumor patients attended in a tertiary care hospital in a northern state of India.

II. MATERIALS AND METHODS

The study is retrospective. Records of primary brain tumor patients who presented in Department of Radiation Oncology, PGIMS, Rohtak, Haryana, a tertiary care hospital and regional cancer centre over a period of 5-years from January 2010 to December 2015 were reviewed. A total of 168-cases of primary malignant brain tumor were registered during this period. These cases were analyzed for incidence, patterns, different treatment modalities and their outcome.

III. RESULTS

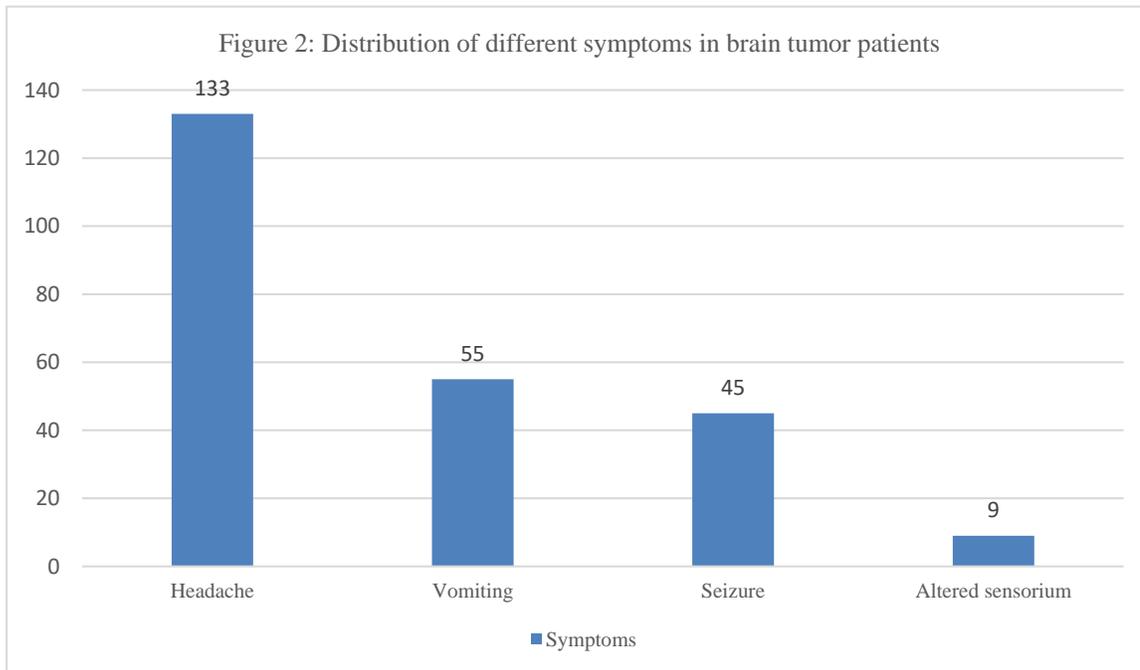
During this study total 168-patients of primary brain tumors were identified, which were malignant and constituted approximately 1.4% of total cancer patients in above institution. All the metastatic brain tumors with primary elsewhere in body were excluded from the study. The median age at presentation was 47-years (range 13 – 70), fourth decade of life being the commonest presentation. Overall males (n = 109; 64.9%) slightly outnumbered females (n = 59; 35.1%), ratio being 1.8:1. The year-wise distribution of brain tumor among both sexes is shown in figure 1.



General condition of patients was evaluated using karnofsky performance status (KPS) scale and all patients were divided in three groups according to KPS; good to fair, average and poor respectively. At the time of initial presentation, 102 out of total 168-patients (61%) had karnofsky performance status >70, i.e. fair to good general condition and 22 patients (13%) had very poor general condition [KPS <30].

All the primary spinal tumors, having secondary spread in brain, were excluded from the study. Among all the intracranial tumors, frontal lobe involvement (47%) was most predominant followed by parietal lobe (31%); temporal lobe tumor (19%) was also there with negligible primary site being occipital lobe and insula.

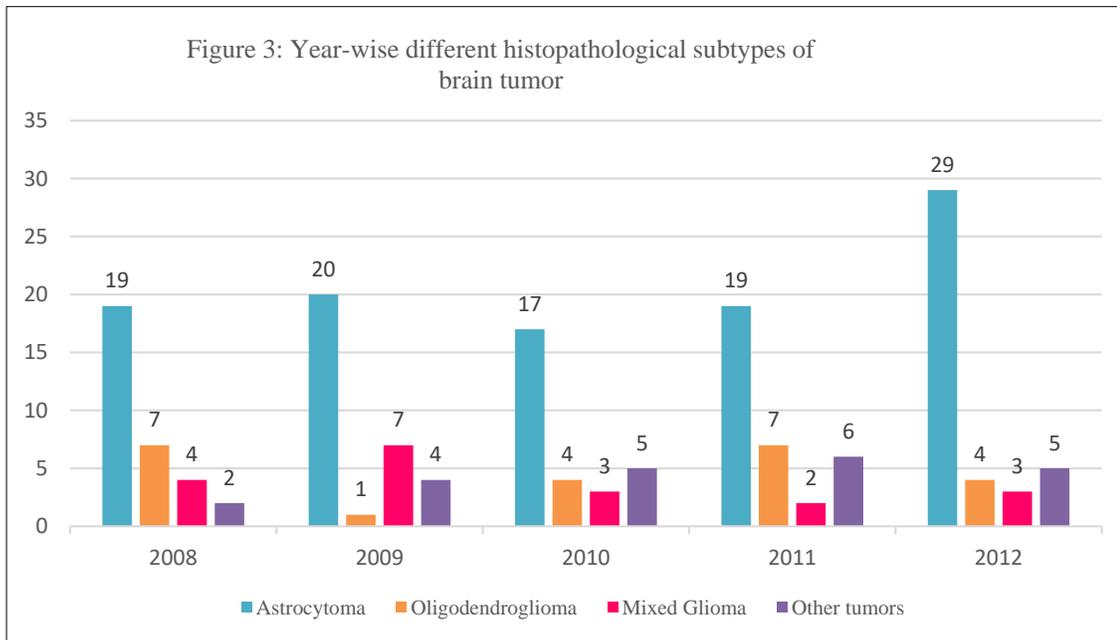
Mean duration of symptoms was 4-months. The most common presentation was headache (79%), followed by vomiting (33%), seizure (27%) and altered sensorium (5%). Distribution of different symptoms among patients was shown in figure 2.



Among all the patients included in study, 58% were locally advanced, having WHO (World Health Organization) grade III & IV tumors. On histopathological evaluation, astrocytoma (61.9%) constituted the largest group followed by oligodendroglioma (13.7%) and mixed gliomas (11.3%). Ependymal tumor, medulloblastoma and meningioma were the other histopathological variants occurred less frequently and there were 4-rare tumors found occurred as sole entity. These were 1-case each of primary CNS lymphoma, schwannoma, pineoblastoma and paraganglioma. Glioblastoma forms the largest subtypes of astrocytic tumors (57.7%) followed by diffuse astrocytoma (32.7%). Incidence of different histopathological variants along with their gender distribution are illustrated in table 1 and figure 3.

Table 1: Histopathological types of various primary brain tumors and their gender-wise distribution

Histopathological types	Male	Female	Total (%)
Diffuse Astrocytoma	73	31	104 (61.9)
Oligodendroglioma	14	9	23 (13.7)
Mixed glioma	10	9	19 (11.3)
Ependymal tumor	3	5	8 (4.8)
Medulloblastoma	4	2	6 (3.5)
Meningioma	2	2	4 (2.4)
Rare tumors	3	1	4(2.4)



Regarding treatment received by patients, majority (97%) of patients underwent surgery, craniotomy followed by total or subtotal resection of primary tumor was most commonly performed surgical intervention, others being decompression surgery. Among all, 148-patients (88%) received radiation therapy. Concurrent chemotherapy with radiation was given as per indication; in all patients of WHO grade III and IV patients receiving radical radiation and patients of WHO grade II with high risk features. Most common chemotherapeutic drug used was oral temozolomide, whereas intravenous nivolumab was used experimentally in 6 patients with no survival benefit. Radical and palliative radiotherapy was given in 84% & 4% patients respectively. Radical dose used predominantly was either 60 or 54 grey (depending upon WHO grade) in 30 Fractions over 6 weeks. Palliative schedule was given either 20 grey in 5 fractions over 5 days, 30 grey in 10 fractions over 2-weeks or 8 grey single session mainly in very poor general condition. After initial assessment at our department, 12-patients (7% of total) lost to follow-up. Overall average survival was 23-months, with 17 patients had follow-up of more than 4-years. Clinically, the response at last follow-up was as follows: complete response (CR) in 29%, partial response (PR) in 41% and death in 23%. Only one patient had recurrent tumor at the same site after 9-months of completion of treatment.

IV. DISCUSSION

There were approximately 3 lacs new brain and CNS (central nervous system) tumor cases in 2020 (1.6% of the total cancer incidence) with 2.5 lacs deaths (2.5% of total number of cancer deaths). [1] These tumors are not so common having ranked 20 in the list of cancer incidence in 2020 around the globe. [1] However, with the dawn of 20th century, there is a continuous surging in the incidence of malignant brain tumors, highly attributed to improved diagnostic techniques. In India, the estimated number of new malignant brain tumor cases were 31460 (2.4% of total cancer incidence) in 2020, with an increasing trend among young and middle-aged individuals. [2,3]

Although incidence increasing with ages, brain tumors typically have a bimodal distribution with the first peak seen in children and the second large peak seen in elderly after 5th decades of life. [4] However, there are certain differences in brain tumors of adult to that of children in both clinical features and histopathological appearance. Pediatric brain tumors mostly occur in posterior fossa, have a more indolent course, more sensitive to irradiation and chemotherapy; whereas majority of adult brain tumors are supratentorial, occur in anterior fossa, have more aggressive course and more chance to recur. [5] Male predominance of primary brain tumors, especially in gliomas, is acknowledged, except a little female predominance in meningioma. [6-8] Among all primary brain tumors, frontal lobe involvement is prevailing followed by temporo-parietal lobe involvement. [9] Observation of our study in this regard is similar. Astrocytoma is the most common histological variant of primary brain tumors in most of the studies done in India, glioblastoma being the most common subtype. [10,11] Incidence of different histopathological variant in pediatric age group is well matched with a prior study done in the same institution. [12]

Seizures and headache are the two most common symptoms of brain tumors irrespective of primary or metastatic origin, others being focal neurologic deficits like weakness, visual difficulties, language & personality dysfunction, altered sensorium and many more. [13] Typically patients with low grade tumors presented with one or more seizure episodes due to long time disease course, whereas high grade glioma patients presented with headache as a result of rapid tumor progression leading to increased intracranial pressure. In our study, as high grade tumors predominated, patients complaining of headache were more common.

The standard of care for all the primary brain tumors is maximal safe resection followed by irradiation with or without chemotherapy. [14] However, in WHO grade I tumors with low risk of recurrence, adjuvant radiation can be avoided with careful observation and application of radiation in high risk patients and on recurrence. [15,16] Concurrent chemotherapy with radiation is indicated in high grade gliomas with high risk of recurrence. [17] Both PCV (combination chemotherapy consists of procarbazine, lomustine and vincristine) and temozolomide are explored as standard chemotherapy regimens with comparable outcome, still oral temozolomide is mostly preferred in both concurrent and adjuvant settings. [18-20] For high grade glioma, after postoperative adjuvant chemoradiotherapy, 6-12 cycles of adjuvant temozolomide is well established to control late recurrence. [21] The role of targeted therapy like cilengitide, bevacizumab, nimotuzumab, nivolumab in recurrent and refractory brain tumors is evaluated in different studies but remain inconclusive. [22-27] Radiation in brain tumor patients should be given with recent more precise techniques like intensity modulated radiotherapy (IMRT), image guided radiotherapy (IGRT), stereotactic radiotherapy (SRS) and stereotactic body radiation therapy (SBRT) to spare normal brain parenchyma as much as possible. However, in developing countries with limited infrastructures like ours, 2-dimensional radiation by cobalt-60 teletherapy machine and 3-dimensional conformal radiation is also welcomed than no adjuvant radiation. In recurrent tumors, recent studies with proton therapy has amazing results. [28,29] In some particular brain tumors like medulloblastoma, craniospinal irradiation is indicated to get a better tumor control, although chances of second malignancy in there in children. [30,31] The dose and fractionation of radiation used in our institution is similar to that of standard guidelines. [32,33] The survival outcome is also matched well with similar studies in other parts of world. [34] However, due to the limitation of retrospective analysis and poor compliance of patients, proper survival cannot be estimated accurately.

V. CONCLUSION

Primary brain tumors are not among frequent tumors occurring in our country. However, the burden of the disease within the community remains high due to poor survival outcome in high grade tumors. Despite the fact that primary brain tumors are rare in our country, noticeable state-wise variation in incidence, demographic profile and mortality has been noted. The histopathological pattern of primary brain tumors in our institution established astrocytic tumors as the major health burden and gross total resection followed by radiotherapy with or without concurrent temozolomide is standard of care. In Conclusion, it is recommended to develop nationwide proper atlas of the cancer patients so that exact geographical plotting of the patients can be done to establish the accuracy of the scattered data. These data base helps to evaluate different radiation therapy protocols alone or in combination with chemotherapy depending upon the general condition of the patients and grade & histology of tumor so as to prolong survival and improve the quality of life. As such careful monitoring of primary malignant brain tumors in other institutions of other region remain priorities to conclude proper nationwide demographic profile and survival outcome.

APPENDIX

Ethical Approval:

This is a retrospective study without disclosing any patient identity, thus ethical approval is not necessary according to The National Code on Clinical trials recent guidelines.

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Nil

Conflict of Interest:

None of the authors has any conflicts of interests or any financial disclosure.

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