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Pathology

CURRENT TREND OF GLIOBLASTOMA- A 5 YEAR STUDY

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ABSTRACT The diagnostic aspect of brain tumours is evolving with emphasis on the molecular genetics. Hence there is a need to study the clinicopathological aspects of brain tumours and this article is put forth to have an overview of the burden of Glioblastoma in a tertiary care centre in TamilNadu. Methods: This is a retrospective study involving all the cases of Glioblastoma diagnosed over a period of 5 years at Institute of Neuro-Pathology in a tertiary care centre in TamilNadu. A total of 723 cases of Gliomas were reported over 5 years, from this the Glioblastoma were subcategorised and studied. The age group of the patients with brain tumours ranged from 3 years to 79 years. Result: It was inferred from our study that of the 723 cases reported as Gliomas, the total number of patients with Glioblastoma was 219, which accounts for 30.3%. The prevalence of Glioblastoma is 30.3% distributed among the age group of 14yrs-73yrs. The peak incidence of Glioblastoma was seen in patients above 50 years of age. Conclusion: This study conducted in Tamilnadu has shown that Glioblastoma is the most common primary brain tumours as observed from our study and various other studies. It was found from our study that Glioblastoma, the most aggressive brain tumours needs to be diagnosed for prompt treatment of the patients.

KEYWORDS : Glioblastoma, Brain Tumours, Clinicopathological Study, Tamilnadu,india.

INTRODUCTION

Glioblastoma is the most common malignant brain tumour of adults, accounting for ~15% of all intracranial neoplasms and ~45-50% of all primary malignant tumours of the brain (1,2). Glioblastoma is the second most common intracranial neoplasm in patients older than 55 years (2). In the Western countries, the annual incidence of Glioblasstoma is about 3-4/100 000 people (2), however, the incidence in eastern Asia, was found to be 0.59/100 000 population(3). Glioblastoma can occur at any age, but usually older adults(peaks at 55-85 years). Glioblastomas occurs rarely before 40 years of age.

The median age is 64.0 years, and the annual incidence rate in the 0-19 years age group, adjusted to the United States Standard Population, is 0.14 new cases per 100 000 population.(4)

The etiology of glioblastomas is unknown, while it has been postulated that Glioblastoma may be inherited as part of syndromes like Li-Fraumani, Turcot syndrome (3). One of the proven risk factor is increased risk after ionizing radiation by use of mobile phones to the head and neck while a decreased risk among individuals with a atopia (3).

MATERIALS AND METHODS

This is a retrospective study involving all the cases of Glioblastoma diagnosed over a period of 5 years at Institute of Neuro-Pathology in a tertiary care centre in TamilNadu. A total of 723 cases of Gliomas were reported over 5 years, from this the Glioblastoma were subcategorised and studied to look for the clinicopathological features of Glioblastoma in this part of India. All cases of stereotactic biopsy material was received in formalin. The biopsy was taken after a preliminary squash cytology report. In all cases, we received multiple grey white to grey brown friable soft tissue fragments measuring in toto 1cc to 4cc. the specimen was processed routinely and stained with haematoxylin and eosin.

RESULT

We have reported a total of 219 cases as Glioblastoma. This was found to be 30.3 % of all the cases of brain tumours reported in our hospital. The age group affected by Glioblastoma is shown in table I

TABLE-1: Age-wise distribution of Glioblastoma

AGE-GROUP	NO OF CASE	PERCENTAGE
0-10 YEARS	2	1%
11-20 YEARS	9	4%
21-30 YEARS	17	8%
31-40 YEARS	24	11%
41-50 YEARS	49	22%
51-60YEARS	83	38%
>60YEARS	35	16%

we reported 11 cases of Glioblastoma in patients < 20years of age which accounted for 5% of cases.

The youngest of all Glioblastoma was 7 year old male child. While the oldest was 73year old female.

Glioblastoma was found to be commonest among 50 to 60year old. Of the 219 patients, 143 were male and 76 were female as shown in TABLE-2. It was two times more common in male than in female.

TABLE-2 Sex predilection in Glioma

	CASES	PERCENTAGE
MALE	143	65.2%
FEMALE	76	34.8%

It was found in our study that Glioblastoma showed following distribution in brain.

TABLE-3: Distribution of Glioblastoma in brain

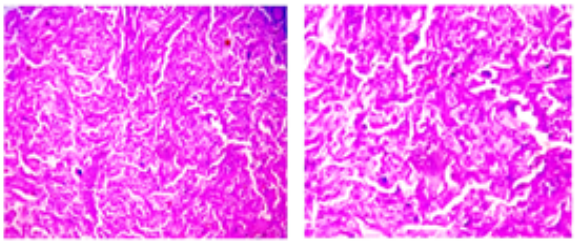
AREA INVOLVED IN BRAIN	NUMBER OF CASES	PERCENTAGE
FRONTAL LOBE	42	19.2%
PARIETAL LOBE	33	15.1%
OCCIPITAL LOBE	10	4.5%
TEMPORAL LOBE	17	7.7%
BI-LOBE INVOLVEMENT	76	34.7%
TRI-LOBE INVOLVEMENT	8	3.7%
INTRAVENTRICULAR	6	2.7%
OTHERS	27	12.4%

Of the 4 lobes of the Cerebrum, frontal lobe was most commonly involved by Glioblastoma. Occipital lobe involvement by glioma was rare but it was found that occipital lobe showed increased inclidence of Glioblastoma if tumour occurred. Bi- lobe involvement and tri lobe involvement was more common with glioblastoma. Cerebellar involvement in Glioblastoma was rare, we have reported 3 cases involving cerebellum. Only one case of spinal cord involvement was seen, it was a intradural and intramedullary lesion of D12-L1 vertebra. The other sites which were reported as Glioblastoma were one case in Thalamus, and Insula.

Gross specimens showed Multiple grey brown friable soft tissue fragments which altogether measured 1cc to 4cc which were all embedded. Microscopy usually composed of poorly differentiated, pleomorphic tumour cells with atypical nucleus and brisk mitosis. Prominent microvascular proliferation with or without necrosis is the diagnostic feature.(4)

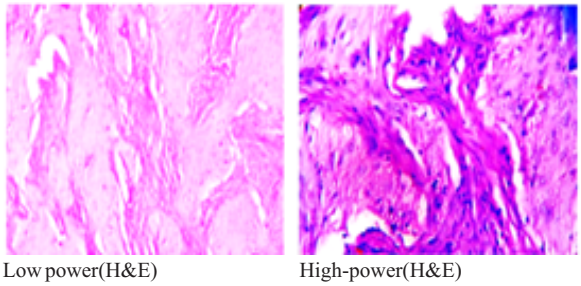
Figure-1: Glioblastoma,Giant cell variant shows bizzare giant cells admixed with fusiform syncytial cells , reticulin network and extensive areas of necrosis vascular proliferation.(4)

Figure 2- sows low power and high power view of Gliosarcoma. Microscopy shows, gliomatous component intermingled with the sarcomatous tumour cells.



Low-power(H&E) high power-(H&E)

FIGURE-1: Giant Cell Variant of Glioblastoma



Low power(H&E) High-power(H&E)

FIGURE-2: Gliosarcoma

DISCUSSION

Of the brain tumours reported in our institute over a period of 5 years, we have found that Glioblastoma constitutes about 30.2% of all Gliomas reported. There was a clustering of cases with Glioblastoma in the age group of 50 to 60 years as observed from our studies. It was more common in males (143 patients), with a male female ratio of 1.9:1. This is in concordance with the study conducted in USA, which has shown that the male to female ratio of glioblastoma is 1.60:1 (2). Glioblastoma is centred in the subcortical white matter infiltrating into grey matter of the cerebral hemispheres. Dowling et al in USA, has shown that the predilection of Glioblastoma is temporal lobe, parietal lobe, the frontal lobe, and the occipital lobe in descending order of frequency (2). It was noted from our study that the most common site of Glioblastoma is Frontal lobe which is in concurrence with other studies like that of Perry et al that IDH-mutant secondary glioblastomas have a unusual predilection for the frontal lobe (5). Glioblastoma occurs rarely in sites like cerebellum, spinal cord. In our study, we reported only one case of spinal Glioblastoma involving the D12-L1 vertebra in a 56year old male. And cerebellar Glioblastoma has been reported in 3 cases over a period of 5 years. Glioblastomas is a rapidly growing tumour, the symptoms of which depends on tumour site, primarily presenting with nausea, vomiting, pulsating headache, hemiparesis, aphasia, raised intracranial pressure, intractable seizure and behavioural changes (6).

According to the current WHO guidelines, the term Glioblastoma multiforme is obsolete, instead Glioblastoma has been subtyped into three categories depending upon IDH genomic status as 1) IDH-wildtype Glioblastoma, 2) IDH-mutant Glioblastoma and 3) Glioblastoma-nos.(4) IDH-wildtype Glioblastoma is the terminology used to describe the primary Glioblastoma with no precursor lesions and they arise de-novo and they lack IDH gene mutation. This term applies to lesions which are high-grade glioma with usually astrocytic differentiation; exhibiting cellular pleomorphism (in most cases), nuclear atypia, diffuse growth pattern, mitotic activity, along with microvascular proliferation and necrosis.(4) It is the most common type of Glioblastoma as well as the most malignant astrocytic glioma, constituting about 90% of all the cases of glioblastomas. It has a predeliction for affecting adults, with a mean age at diagnosis of 62 years. The male:female ratio of about of Glioblastoma,IDH-wildtype is 1.35:1. (4)

IDH-mutant,Glioblastoma, also known as “secondary glioblastoma, IDH-mutant”. It accounts for 10% of Glioblastoma. It is similar to IDH-wildtype, Glioblastoma except that they have lesser extent of necrosis. They develop from diffuse astrocytoma (WHO grade II) or anaplastic astrocytoma (WHO grade III) along with mutation in either the IDH1 or IDH2 gene. The mean patient age at diagnosis is 45 years), has a predilection for frontal lobe, and has a significantly better prognosis (7,8).

This terminology is given to lesions in which IDH mutation status is not assessed. This terminology is used for lesions excluding giant cell glioblastoma, epithelioid glioblastoma and gliosarcoma.(4)

Glioblastoma in paediatric age-group has been termed recently as Paediatric high-grade diffuse astrocytic tumours(WHO grade lll/IV). It is a single category encompassing both paediatric glioblastoma and paediatric anaplastic astrocytoma and is considered together as same entity for therapeutic purposes.

Glioblastoma is a fatal disease, with < 5% of patients surviving >5 years (9). MGMT promoter methylation is a good predictive marker for testing the efficiency and response to alkylating as well as methylating chemotherapeutic agents.(4)

CONCLUSIONS

There is a dire need to subtype Glioblastoma for assessing prognosis, to anticipate disease progression and for better treatment of the patients. The pathology of Glioblastoma is rapidly evolving with the advent of molecular genetics for a patient tailored treatment protocol. And this study will help to understand the emerging trend and clinicopathological aspects of Glioblastoma in this subset of population in India.

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