



Original Research Article

Histopathological study of neuroepithelial tumors of central nervous system

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ABSTRACT

Introduction: Central nervous system tumours have diverse histomorphological appearances. Accurate characterization of space-occupying lesions by histology is important for appropriate treatment.

The present study is an attempt to evaluate the histomorphological patterns of the neuroepithelial tumors of central nervous system in order to provide accurate pre-therapeutic neuro-anatomic data and to facilitate better therapeutic results after surgery.

Aim of the study: To study the spectrum of neuroepithelial tumors presenting as space occupying lesions in the central nervous system.

Materials and Methods: This was a prospective study carried out in the department of Pathology at Medciti Institute of Medical Sciences over a two year period. Histopathological study of tissue specimens from neuroepithelial tumors from CNS was done. The tissue specimens were analysed for type of tumour, tumour grade and their distribution according to age, gender and topographic location.

Results: A total of 231 neoplastic space occupying lesions were studied of which neuro-epithelial tumours comprised 96 (41.5%) cases. The patient age for neuroepithelial tumors ranged from 2 years to 78 years and the male to female ratio was 1.2:1. Astrocytomas were the most frequent (75%), followed by oligodendrogliomas (8.3%), oligoastrocytomas and ependymal tumours. Astrocytoma, grade IV was most common and affected the fifth decade more commonly. Astrocytomas commonly affect the frontal, temporal and parietal regions.

Conclusion: Histopathological examination is mandatory for all space occupying lesions of CNS for correct categorization and grading of tumors. Astrocytomas are the most common of all neuroepithelial tumors. Grade IV astrocytomas most commonly affect men in fifth decade.

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1. Introduction

There are various types of space occupying lesions of the CNS that can be caused by infectious, neoplastic, inflammatory or vascular diseases. Identification of non-neoplastic causes from neoplastic lesions is important so as to prevent wrong diagnosis that can lead to unnecessary neurosurgery.¹

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The present study is an attempt to evaluate the morphologic and histological pattern of the space occupying lesions of central nervous system in order to provide accurate pre-therapeutic neuro-pathologic data and to facilitate better therapeutic results after surgery.

Central nervous system lesions have always been intriguing to histopathologists due to varied histomorphological appearances and sometimes requiring special diagnostic techniques such as Immunohistochemistry for confirmation.

(1) morphologic study of the lesions, (2) topographical analysis of the lesions, and (3) critical integration of these findings and their subsequent correlation with the clinical data are all involved, allowing an etiologic diagnosis to be determined in the majority of cases. The CNS lesions are complex and of diverse nature. An awareness and familiarity with the clinicopathological features will permit the general surgical pathologist to recognize and accurately diagnose these tumours.

The non-neoplastic lesions often present a considerable diagnostic challenge and can be source of much confusion and anxiety, so the role of a pathologist in evaluation of these lesions is important.²

2. Aims and Objectives

To know the relative frequencies of various neuroepithelial tumours of central nervous system and to compare the age, gender and topographic localization of these neoplasms.

3. Materials and Methods

This was a prospective study conducted in the section of Histopathology, Department of Pathology, Medciti Institute of Medical Sciences, Telangana, to determine the nature of neuroepithelial tumors occurring in the CNS. The study was done over a two year period from 1st August 2013 to 1st August, 2015. During this two year period, a total of 255 CNS SOLs were diagnosed of which 24 were non neoplastic lesions and were excluded from the study. All the surgical specimens received in the Department of Pathology were fixed in 10% neutral buffered formalin. Most of the biopsies were small biopsies which were completely processed, embedded and sectioned. Only few of them were relatively big and required sectioning from representative areas. Sections were processed as small bits of 2-3 mm in thickness in the automatic tissue processor and processed in the routine way. Sections of 5 μ thickness were cut and stained with Hematoxylin and Eosin, and in dilemma cases, slides were submitted for special stains such as Periodic acid Schiff stain (PAS), Reticulin stain etc. Immunohistochemistry, using monoclonal antibodies against GFAP-(Glial Fibrillary Acidic Protein), EMA (Epithelial Membrane Antigen), S-100, NSE (Neuron Specific Enolase), Synaptophysin, Vimentin, Ki 67, were performed to substantiate the diagnosis. Histological classifications and grading of these tumors was done as per WHO criteria. The frequency of the tumours over two year period and the distribution based on age, gender, and location were analysed.

4. Results and Observations

A total of two hundred and fifty five (255) biopsies of space occupying lesions of Central Nervous System performed in the Neurosurgery Department were studied. Of these

255 cases, 231 cases were neoplastic lesions and of these 231 tumors, 96 (41.5%) were neuroepithelial tumors. The patient age for neuroepithelial tumors ranged from 2 years to 78 years and the male to female ratio was (53/43) ie 1.2:1.

Table 1: Age and gender distribution of neuroepithelial tumors

Age in years	Males	Females	Total	Percent (%)
1- 10	6	1	7	7.2%
11-20	5	4	9	9.3%
21-30	4	9	13	13.5%
31-40	14	3	17	17.7%
41-50	5	12	17	17.7%
51-60	9	5	14	14.5%
61-70	7	6	13	13.5%
71-80	2	4	6	6.2%
Total	52	44	96	100%

In the present study, the fourth and fifth decades were the most commonly affected age groups.

Table 2: Histological types of Neuroepithelial tumours with gender distribution

Type of tumor	Males	Females	Total	Percent (%)
Astrocytic tumours	41	31	72	75%
Oligodendrogliomas	4	4	8	8.3%
Oligoastrocytomas	1	2	3	3.1%
Ependymal tumours	3	4	7	7.2%
Choroid plexus carcinoma	-	1	1	1.0%
Neuronal & mixed neuronal-glioma tumours	2	1	3	3.1%
Embryonal tumours	1	1	2	2.0%
Total	52	44	96	100%

In the present study under WHO classification, in the category of neuroepithelial tumors, astrocytomas were the most frequent, followed by oligodendrogliomas, oligoastrocytomas and ependymal tumours.

Among the neuronal and mixed neuronal-glioma tumors, there was one case each of Dysembryoplastic neuroepithelial tumor (DNET), central neurocytoma and ganglioglioma.

In the embryonal tumors, there were two cases of Medulloblastoma occurring in an 18 year male and 14 year female patient.

Grade IV astrocytomas were most common tumours (47.2 %) followed by Grade II and Grade III. In the present study, the commonly affected age group among astrocytomas was the fifth decade and males were commonly affected than females.

4.1. Topographic localization of astrocytomas

The frontal, temporal and parietal regions had 28 (38.8%), 13 (18%), 13 (10.8%) cases respectively. The

Table 3: Distribution of astrocytomas based on age, gender and histologic grade

Age in years	Grade I (M/F=3/4)	Grade II (M/F=11/8)	Grade III (M/F=8/4)	Grade IV (M/F=19/15)	Total (M/F=41/31)	Percent (%)
1- 10	2	3	-	-	5	6.9%
11-20	1	-	1	1	3	4.1%
21-30	-	4	4	1	9	12.5%
31-40	1	1	3	7	12	16.6%
41-50	2	4	2	7	15	20.8%
51-60	1	4	1	6	12	16.6%
61-70	-	3	1	6	10	13.8%
71-80	-	-	-	6	6	8.3%
Total	7 (9.7%)	19 (26.3%)	12(16.6%)	34 (47.2%)	72 (100%)	100%

M/F: Males/Females

frontotemporal and temporoparietal regions and thalamus had 6 (8.3%) cases each. The occipital region had 2 (2.7%) and parasagittal region had 1 (3.8%) cases.

Figure 1 Glioblastoma multiforme showing increased cellularity and cellular anaplasia H&E(40X).

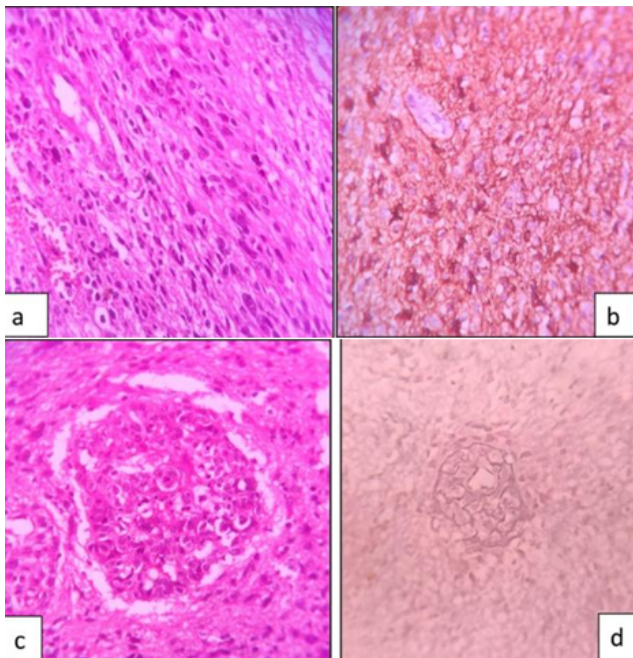


Fig. 1: Glioblastoma multiforme; **a).** H&E (40X) showing increased cellularity and cellular anaplasia, **b).** H&E (40X) showing strong GFAP expression in tumour cells, **c).** H&E (40X) showing glomeruloid proliferation of vasculature, **d).** Reticuline stain (40X) showing glomeruloid proliferation of microvasculature.

5. Discussion

5.1. Incidence of neoplastic lesions in CNS

In the present study, we found 90.5% of all SOLs to be of neoplastic origin. Butt et al³ studied 100

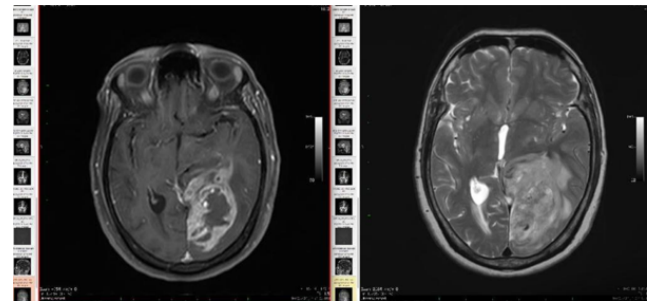


Fig. 2: Large well defined thick irregular, peripherally enhancing intra axial space occupying lesion noted in left parietooccipital lobe in subcortical and deep white matter showing heterogeneously hyperintense on T2 and showing restricted diffusion

cases of intracranial space occupying lesions in Lahore, and observed the incidence of neoplastic lesions to be 89%. Rathod et al⁴ studied clinicoradiological and clinicopathological correlation of intracranial SOLs. They found incidence of neoplasms were around 63% which is slightly lower than the present study. Present study did not include the traumatic group and hence found higher neoplastic lesions as compared with their study. Mahmoud et al⁵ studied 100 consecutive patients of which neoplastic lesions comprised 78%, Jamjoom et al⁶ studied intracranial space-occupying lesions in Saudi Arabia. They reported 87% lesions as neoplastic masses which is in concordance with the present study.

Soomro et al⁷ analysed a total of 200 cases of intracranial space-occupying lesions presenting at Neuro Clinic and Care retrospectively and found 82.5% as neoplastic lesions. Overall, the CNS tumours account for 2 to 5% of all tumours in the humans in India.⁸

5.2. Gender distribution

(Table 1) In the present study, the male to female ratio was 1.2:1 with almost equal predilection for both genders. Butt et al³ found a male to female ratio of 1.17:1 while Rathod et al⁴ observed it at 1.3:1. Mahmoud et al⁵ found it to be 1.7:1,

Jamjoom et al⁶ found a ratio of 1.45:1 and Soomro et al⁷ found a ratio of 1:0.8. The above studies included all SOLs of CNS ie neoplastic and non-neoplastic as well. In our study, the sub category of neuroepithelial tumors showed slight male preponderance. Qureshi et al⁹ studied 386 space occupying lesions in Karachi. Similar to the present series they reported a higher frequency of neuro-epithelial tumours in males with a male to female ratio of 2:1.

5.3. Age distribution

(Table 1) In the present study the median age at presentation was 45 years (range 2-78 years) which is in concordance with, Hashmi et al¹⁰ Das et al¹¹ and Sangeetha et al.

The median age at presentation was 51 years (range 0.58-87 years) according to Das et al,¹¹ with no significant gender propensity. CNS tumours were also found to be more common in the 4th to 7th decade. Higher grade astrocytic tumours, among the other tumour forms, were found in older patients, comparable to the current study.

Jalali et al.,¹² who studied the frequency of CNS tumours in India across all age groups, found 580 cases of primary CNS neoplasms and 78 cases of metastatic CNS tumours. Primary brain tumours most typically manifest in middle-aged men, according to their findings. Astrocytomas were the most prevalent of all CNS tumours in their analysis, accounting for 30% of all primary CNS tumours, with high-grade gliomas outnumbering low-grade gliomas, which matches the findings of this study. (Table 3)

In Hashmi et al¹⁰ study mean age was 38.26 ± 17.24 (1-75 years) with most common presentation in middle age group between 18 and 50 years (64.3%). Only 12% of patients presented before 18 years of age, similar to our findings where 11% of patients presented before 20 years of age.

5.4. Topographic location

In the present study, frontal lobe was the most common site of involvement for astrocytomas followed by other sites as seen in the study by Sangeetha et al. Also in our study, intracranial location of neoplasms was seen in all the cases. Patty et al¹³ encountered 91.3% and 8.7% intracranial and spinal lesions respectively. Masoodi et al⁸ observed frontal lobe as the commonest intracranial site (20.7%).

Neuroepithelial tumors were common CNS neoplasms across all the studies as mentioned in the above table. (Table 4)

Masoodi et al⁸ observed an incidence of 53.7% for neuroepithelial tumors and astrocytomas were the commonest (77.1%).

The largest study, Chen et al,¹⁴ covered 34140 cases from 1950 to 2009, with parts from 1990 to 2009 reviewed according to WHO 2007 categorization and cases from 1950 to 1989 classified according to previous pathological

diagnosis. Neuroepithelial tumors were concordant in both studies while tumours of the sellar region and germ cell tumours were encountered more frequently in the Chen et al¹⁴ study.

Retrospective analysis of 180 patients by Sangeetha et al during 2009 to 2013 had shown 41.69% of neuroepithelial tumours which compares well with our observation of 41.5% for neuroepithelial tumors.

Jamjoom et al⁶ identified 87 percent neoplasms in a retrospective examination of 212 patients diagnosed and treated at King Khalid University Hospital in Riyadh over a 5-year period, which was the first attempt to give preliminary data on intracranial space-occupying lesions in Saudi Arabia. Neuroepithelial tumours were 39.7% which is in close concordance with present study. (Table 4)

Aryal et al¹⁷ studied 8 metastatic tumours, in which the most common histological type was adenocarcinoma (7 cases, 87.5%). Lee et al¹⁸ in their study from Korea observed both germ cell tumors and embryonal or primitive tumors / medulloblastomas to be more common in children less than 19 years of age. In our study also there were two cases of medulloblastoma that occurred in an 18 year and 14 year old patient.

CNS tumours are currently classified by histology and location within the CNS. In the present study neuro-epithelial tumours are the commonest SOLs of CNS. Neuro-epithelial tumours are further categorized as astrocytomas, oligodendrogliomas, ependymomas, oligoastrocytomas, choroid plexus tumours and tumours of mixed neuronal-glia tumours and embryonal tumours, based on the cell of origin. They are the most prevalent CNS lesions in the world, accounting for over 70% of all cases. In highly developed, industrialised countries, there is a stated trend for a higher prevalence of neuro-epithelial tumours, and some findings suggest that Caucasians are more susceptible than African or Asian populations.¹⁹

In the present study, astrocytomas were the commonest tumours (72 cases) constituting 75% of all neuroepithelial neoplasms. Our observations compare well with other authors. (Table 5)

Butt et al³ study also had similar results with neuro-epithelial tumours being 41%. Among total 39 neuro-epithelial tumours in their study, astrocytomas comprised the largest group, low grade astrocytomas being more common relative to glioblastoma WHO grade IV type. In contrast, the present study though had largest number of astrocytomas and glioblastoma multiforme (WHO Grade IV) were maximum (47.2%). Histological grading is a method of predicting neoplasm biological behaviour. The elements that determine grading have an impact on the therapy that is chosen. The incidence of oligodendroglioma and oligoastrocytoma was 4.8 percent and 2.4 percent, respectively, which was slightly lower than the current study.

Table 4: Comparative analysis of incidence of neuroepithelial tumors with other studies

Study	Jamjoom et al ⁶	Butt et al ³	Chen et al ¹⁴	Sangeetha et al	Present study
Year of Study	1982-1987	1990-2000	1990-2009	2009-2013	2013-2015
Neuroepithelial tumours	39.7%	41%	38%	41.6%	41.55%

Table 5: Comparative analysis of neuroepithelial tumors with other studies

Study	Ahmed et al ¹⁵	Butt et al ³	Jamjoom et al ⁶	Hashmi et al ¹⁰	Mahmoud et al ⁵	Jalali et al ¹²	Present
Astrocytomas	71.4%	82.8	56.2	51.6	77.1	75.4	75
Oligodendrogliomas	15	4.8	1.4	23	5.2	0.06	8.3
Oligoastrocytomas	3.2	-	-	15.9	1.7	-	3.1
Ependymal tumors	9.3	4.8	6.8	7.9	8.7	13.6	7.3
Choroid plexus tumors		2.4	-	-	-	-	1
Neuronal and mixed neuronal-glia tumors		2.4	-	-	-	-	3.1
Embryonal tumors		2.4	9.6	-	7	-	2
Others-Not specified	1.1		24.6	-	-	-	-

Table 6: Comparative analysis of astrocytomas with other studies

Study	Patty et al ¹³	Sangeetha et al	Masoodi et al ⁸	Chawla et al ¹⁶	Present study
Year of study	2003-2004	2009-2013	2005-2010	Jan2012-Dec2012	2013-2015
WHO I	12.5	21.7	4.5	13.9	9.7
WHO II	8.9	32.6	27.2	44.1	26.3
WHO III	19.6	10.8	27.2	20.9	16.6
WHO IV	58.9	34.7	40.9	20.9	47.2

Qureshi et al⁹ found astrocytomas in 80%, oligodendrogliomas in 8.8% and oligoastrocytoma in 2% of neuroepithelial tumours. The present study showed concordant results (Astrocytomas-75%; oligodendrogliomas-8.3% and oligoastrocytomas-3.12%).

In India, Jalali et al¹² looked at the incidence of CNS tumours in people of various ages. 580 cases of primary CNS neoplasms and 78 cases of metastatic tumours were discovered. Primary brain tumours most typically manifest in middle-aged males, according to their findings, which are similar to the findings of this study. In their analysis, astrocytes were the most prevalent CNS tumours, accounting for 30% of all primary CNS tumours, with high-grade gliomas outnumbering low-grade gliomas, which was consistent with the current study. (Table 3)

Lodhi et al²⁰ in Karachi studied a total of 100 CNS tumours in all age groups. According to their study neuro-epithelial comprised 58% of all CNS tumours with astrocytomas accounting for the bulk of neuro-epithelial tumours (75%) and glioblastoma at the top of the list similar to the present study comprising 47.7%. Again in their series the frequency of oligodendroglioma (12.5%) and oligoastrocytoma (0.03%) was comparable to the present study.

Aryal et al¹⁷ studied 57 CNS tumours in Nepal. The most frequent type of CNS tumour was astrocytoma similar to the

present series.

Several important reviews of CNS tumours have been published, with information on the incidence and relative percentages of various neoplasms in the United States, Europe, and Asia. In Taiwan (32.9 percent),²¹ and Germany, astrocytoma was the most prevalent CNS tumour (41.7 percent).²² In contrast to our study, the most common primary CNS tumours in Korea as observed by Lee et al¹⁸ were meningiomas (31.2%). The same was observed by Ghanghoria et al²³ in their study in Madhya Pradesh, India. Walker et al²⁴ reported gliomas and neuromas to be more common in males similar to our study and meningiomas to be twice more common in females.

The difference in the relative frequency and the tumour distribution among populations in different countries may be due to genetic and environmental factors.

According to WHO classification, majority of lesions belonged to Grade I in comparison to grade III or IV. But in cases of astrocytoma, grade IV lesion was more common in comparison to Grade I lesion while in Ghanghoria et al²³ study grade III lesion was more common than grade IV.

The present study is in concordance with the above studies.^{8,13,16}

6. Conclusion

Histopathological examination is mandatory for all space occupying lesions of CNS for correct categorization and grading of tumors as the further management and prognosis depends on the exact nature of the tumor. Astrocytomas are the most common of all neuroepithelial tumors. Among astrocytomas, Grade IV are the most common and usually affect men in fifth decade.

7. Source of Funding

None.

8. Conflict of Interest

None.

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