Clinico-pathological study of central nervous system tumors

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Abstract
Introduction: Central nervous system tumors show varied histomorphological spectrum although they are less frequent when compared to other sites. Central nervous system (CNS) tumors refer to neoplasms that originate in the brain and spinal cord of which over 90% are located in the brain. CNS malignancies account for approximately 1.7% of new cancers annually.

Aims and Objectives: 1: To study the demography and determine the relative frequency of the various histopathological types of CNS tumors; 2: To relate the occurrence of the various types of CNS tumors with age, sex, signs, symptoms, location and to study the various spectrum of histopathological features of CNS tumors and grade according to WHO classification (2007).

Results and Conclusion: The most frequent type of CNS tumor was meningioma followed by astrocytoma of which WHO grade IV tumor was frequent and schwannoma. The peak incidence was in 41-50 years age group. Overall Males are affected more than females, with male to female ratio of 1:2:1 except in meningioma where there is a female preponderance with male to female ratio of 1:2.1. The most frequent clinical feature was headache and seizures in supratentorial tumors. The most commonest site of occurrence was frontal lobe followed by multilobe involvement.

The most common neoplasms among adults are glioblastomas, meningiomas and metastasis to CNS neoplasms, whereas in the paediatric age group pilocytic astrocytomas, medulloblastomas and ependymoma, oligodendroglioma and various subtypes. It is important to identify oligodendroglial component in order to determine the most effective chemotherapy to treat gliomas.

Non glial tumors include embryonal tumors, choroid plexus tumors, pineal tumors, meningeval tumors, germ cell tumors, tumors of the sellar region and hematopoietic tumors.

The correct histological diagnosis of CNS tumors is essential to predict the prognosis. CNS tumors ranks ninth among the top ten malignancies in India.

The present study was conducted with a view to have insight into the pattern of CNS neoplasms in our institute due to rarity of study on the subject. In this study the incidence, age, sex and site of CNS tumors, including tumors of the cranial and peripheral nerves have been determined by analyzing 87 cases according to WHO classification and grading.

Aims and Objectives
1. To study the demography of central nervous system tumors and to determine the relative frequency of the various histopathological types of CNS tumors.

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2. To relate the occurrence of the various types of CNS tumors with age, sex, signs, symptoms and location.
3. To study the various spectrum of histopathological features of CNS tumors and grade according to WHO classification (2007).

**Materials and Methods**

The present cross-sectional study was conducted at the Department of Pathology, Kamineni Institute of Medical Sciences and General Hospital over a period of 4 years from July 2014 to July 2018 (retrospective period of 2 years and prospective period of 2 years). The study population included 87 cases (32 cases retrospective, 55 cases prospective) of CNS neoplasms reported during this period.

For retrospective cases, the histopathological reports maintained in the histopathology section of the department were reviewed and haematoxylin and eosin stained slides of every case were analysed and re-examined. For the prospective cases, 4-5 µm sections were prepared from the corresponding paraffin blocks. Standard procedure for H&E staining was performed using Harris haematoxylin and aqueous Eosin. Histopathological examination with WHO grading system was applied for each tumor.

The clinical information was obtained from case records of the patients retrieved from medical records section.

**Inclusion Criteria**

All primary and metastatic tumors presenting with neurological symptoms were included in the study.

**Exclusion Criteria**

Non neoplastic lesions presenting with neurological symptoms and tumors diagnosed on the basis of neuroimaging studies without histological confirmation were excluded.

![Fig. 1: Meningothelial meningioma showing whorls of tumour cell (H & E, A-X20, B-X40)](image1)

![Fig. 2: Fibrous meningioma with bundles of spindle shaped Cells (H&E, A-X10, B-X20)](image2)
Observations and Results

The patients age ranged from 3-72 years, with a peak age between 41 and 50 years and a mean age of 45 years. The age wise distribution of this tumors are 1-10 years (8.04%), 11-20 years (9.19%), 21-30 years (10.34%), 31-40 years (4.59%), 41-50 years (37.93%), 51-60 years (9.19%), 61-70 years (17.24%), 71-80 years (3.44%).

There were 48 (55.17%) males and 39 (44.82%) females with M:F ratio of 1.2:1. Majority of the cases were intracranial 82 cases (94.25%) whereas the remaining 5 cases (10.97%) were spinal. Of the intracranial cases, 73 cases (89.02%) were supratentorial and 9 cases (10.97%) were infratentorial. Of the supratentorial tumours there were 34 (39.08%) frontal lobe, 21 cases (27.13%) frontoparietal and multilobe involvement, 12 cases (13.79%) parietal lobe, 05 cases (5.74%) temporal lobe, 3 cases (3.44%) occipital lobe. Among the Infratentorial tumors 9 cases (10.17%), 5 cases (55.55%) were in cerebellum. The signs and symptoms of patients with intracranial tumours were headache and vomiting, supratentorial region tumours caused seizures and focal neurological deficits, while infratentorial tumours caused vertigo and confusion. Backache and weakness was a common symptoms in patients with spinal tumours.

Out of 32 cases of meningiomas, 27 cases (84.37%) were intracranial, 5 cases (15.62%) were spinal, 31 cases (96.87%) were benign (WHO I) including 16 cases (51.61%) meningotheliomatous meningioma, 5 cases (16.12%) fibroblastic meningioma, 3 cases (9.67%) psammomatous meningioma, 3 cases (9.67%) transitional meningioma, 1 case (3.22%) chordoid meningioma, 1 case (3.22%) clear cell meningioma and 1 case (3.22%) angiomatous meningioma. Of the remaining 1 case (3.22%) was atypical (WHO grade II) meningioma. The mean age of the meningiomas were 44.5 years, with M:F ratio of 1:2:1.

Among astrocytomas, there were 5 cases (26.31%) WHO I (pilocytic astrocytoma), 4 cases (21.05%) Grade II (diffuse astrocytoma), 3 cases (15.78%) WHO grade III (anaplastic astrocytoma) and 7 cases (36.84%) WHO grade IV (glioblastoma) excluding 2 cases of gliosarcoma.

The mean age for astrocytoma was 52.5 years with M:F ratio 1.7:1, the patient mean age was 19.5 years for grade I (pilocytic astrocytoma), 22.5 years for grade II (diffuse astrocytoma), 54.9 years for grade III (anaplastic astrocytoma) and 62.1 years for grade IV (glioblastoma).
Table 1: Distribution of CNS tumors with subtypes

| Tumors                          | No. of cases | Percentage |
|---------------------------------|--------------|------------|
| Astrocytoma                     | 19           | 21.83%     |
| Oligodendroglioma               | 07           | 8.04%      |
| Oligoastrocytoma                | 06           | 6.89%      |
| Medulloblastoma                 | 06           | 6.89%      |
| Schwannoma                      | 11           | 12.64%     |
| Meningioma                      | 32           | 36.78%     |
| Gliosarcoma                     | 02           | 2.29%      |
| Gangliocytic paraganglioma      | 01           | 1.14%      |
| Astroblastoma                   | 01           | 1.14%      |
| Haemangioblastoma               | 01           | 1.14%      |
| Metastatic deposits             | 01           | 1.14%      |
| Total                           | 87           | 100%       |

Table 2: Distribution of astrocytoma according to WHO grading

| Grade | No of cases | % of total cases |
|-------|-------------|------------------|
| I     | 5           | 26.31%           |
| II    | 4           | 21.05%           |
| III   | 3           | 15.78%           |
| IV    | 7           | 36.84%           |
| Total | 19          | 100%             |

Table 3: Frequency of age distribution of CNS tumors

| Age group in years | Males | Females | Total | % of total |
|--------------------|-------|---------|-------|------------|
| 1-10               | 4     | 3       | 7     | 8.04%      |
| 11-20              | 6     | 2       | 8     | 9.19%      |
| 21-30              | 5     | 4       | 9     | 10.34%     |
| 31-40              | 1     | 3       | 4     | 4.59%      |
| 41-50              | 12    | 21      | 33    | 37.93%     |
| 51-60              | 6     | 2       | 8     | 9.19%      |
| 61-70              | 12    | 3       | 15    | 17.24%     |
| 71-80              | 2     | 1       | 3     | 3.44%      |
| Total              | 48    | 39      | 87    | 100%       |

Table 4: Site wise Distribution of CNS tumors

| Site                            | No. of cases | Percentage |
|---------------------------------|--------------|------------|
| Frontal lobe                    | 34           | 39.08%     |
| Parietal lobe                   | 12           | 13.79%     |
| Temporal lobe                   | 05           | 05.74%     |
| Occipital lobe                  | 03           | 03.44%     |
| Multilobe Involvement           | 21           | 27.13%     |
| Cerebellum                      | 4            | 4.59%      |
| Sellar/suprasellar              | 3            | 3.44%      |
| Cerebellopontine Angle          | 5            | 5.74%      |
| Total                           | 87           | 100%       |
and visual disturbances. Sphincter disturbances were less common.

Studies by Sangeetha et al., indicated that in 39.08% of cases the tumors were in the frontal lobe, meningiomas showed female preponderance.

In contrasting, Aryal G et al. (2011) the ratio of male to female for all CNS tumors in their study was 0.9:1, where female preponderance is observed.

Sex Distribution According to the Histological Subtype:
In the present study all the histological tumors showed male preponderance. Except in meningiomas where there is a female preponderance with M:F Ratio 1.2:1.

Present study is correlating with the study observed by Masoodi T et al., Torres et al., Andrews et al., Jalali et al., and Jamal et al. In the study tumors like meningioma, oligodendroglioma, mixed gliomas, gliosarcoma were seen in the frontal lobe.

Clinical Manifestation of CNS Tumours
Masoodi T et al., has found headache was the commonest symptom followed by seizures, visual disturbances weakness limbs, sphincter disturbances, and personality changes.

In this study, commonest feature associated with CNS tumors were head ache, followed by seizures, weakness and vomiting.

The commonest tumor among the intra cranial tumors is headache, among spinal tumors is backache.

Histological typing of CNS Tumours:
The present study correlates with the studies by Sangeetha N et al., Das et al., Suh et al. and Lee et al. These studies observed meningioma made up the largest subgroup among all the CNS tumors.

Meningioma was the most common tumor among the clinically diagnosed tumors followed by neuroepithelial tumors, schwannoma and pituitary tumour among atomic bomb survivors in Hiroshima and Nagasaki, Japan.

Table 5: Clinical presentation of different types CNS tumors

| Histology                      | Headache | Vomiting | Weakness | Seizure | Visual Disturbance | Cranial Nerve Palsy | Back ache |
|--------------------------------|----------|----------|----------|---------|-------------------|---------------------|-----------|
| Astrocytoma                    | 19       | 7        | 8        | 11      | 3                 | 9                   | 1         |
| Oligodendroglioma              | 2        | 2        | 2        | 2       | -                 | -                   | -         |
| Oligoastrocytoma               | 1        | -        | 1        | -       | -                 | -                   | -         |
| Medulloblastoma                | 2        | 1        | 1        | -       | 2                 | 2                   | -         |
| Meningioma                     | 12       | 2        | 7        | 4       | 4                 | 4                   | 3         |
| Schwannoma                     | 3        | 1        | 7        | 2       | -                 | 4                   | 1         |

Table 6: Frequency of sex distribution of CNS tumors

| Histological subtype              | Male to female ratio |
|-----------------------------------|----------------------|
| Neuroepithelial Tumors            | 1.7:1                |
| Astrocytoma                       | 1.2:1                |
| Oligodendroglioma                 | 1:1.2                |
| Mixed neuronoglial tumors         | 1:2.1                |
| Meningioma                        | 1.3:1                |
| Schwannoma                        | 2:1                  |
| Total                             | 1.2:1                |

Discussion
The present study emphasizes the relative frequency of occurrence of CNS tumors and also to relate the various types of CNS tumors with age, sex, signs, symptoms, location and neurological findings.

Age Distribution of CNS Tumours
So it was concluded that peak incidence was in 41-50 years of age group and majority of cases 29.88% were seen between 41-50 years.

The present study is correlating with the study done by Sangeetha N et al. (2014) which showed the most common age group to be 41-50 years (23.89%).

It is contrasting with the study observed by Masoodi T et al., Intisar H et al.,(2008) found the most common age group to be 31-50 years and 50-59 years respectively.

Sex Distribution of CNS Tumours
In the present study, male to female ratio is 1.2:1.

The ratio of male to female in the overall evaluation of CNS tumors is 1.2:1 in the present study. CNS tumors showed male preponderance.

According to study conducted by Sangeetha N et al. (2014) the M:F ratio is 1.4:1, Massodi T et al. (2012) found the M:F ratio of the CNS tumors to be 1.12:1, Intisar P et al.,(2008) found M:F ratio is 1.5:1.

The present study is correlating with Sangeetha N et al., Masoodi et al., Intisar P et al where the studies concluded with male preponderance.

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In the present study, most common tumour tumour was meningioma 32 cases (36.78%). Meningiomas exhibited a wide range of histological appearances like.

1. Meningothelioamatos meningioma (51.61%)
2. Fibroblastic meningioma (16.12%)
3. Psammomatous meningioma (9.67%)
4. Transitional meningioma (9.67%)
5. Clear cell meningioma (3.22%)
6. Chordoid meningioma (3.22%)
7. Angiomatous meningioma (3.22%)
8. Atypical meningioma (3.22%)

Of the above subtypes, meningothelial, fibrous are most common showing 15 and 12 cases respectively, followed by psammomatous meningioma, clear meningioma, chordoid meningioma, angiomatous meningioma and atypical meningioma.

In contrast to the present study, Massodi T et al.10, 2012 has observed astrocytoma was the commonest tumour constituting 41.5% of all neoplasms. Ahmad et al.,16 Gosh et al.,17 also reported astrocytoma as the commonest tumour in their respective studies.

In the present study astrocytoma was the second commonest tumour 19 cases (21.83%) which is correlating with Sangeetha N et al.8, 2014 which constitutes 46 cases (25.56%).

Among astrocytoma most tumour type was WHO grade IV (glioblastoma) constitutes 7 cases (33.33%) similar to that observed by Sangeetha N et al.,9 and in contrasting to the present study, Irfan A et al.,18 has observed low grade astrocytoma I and II was highest in number which comprised of only 16.9% of glioblastomas out of total 63.7% astrocytomas.

Meningioma was the second common tumour in the study conducted by Massodi T et al.,10 which showed 21 cases(19.8%) of all CNS neoplasms. Similar observations are made by Ahmad et al.,16

Summary
1. The present study was conducted over a period of 4 years which included 2 years of retrospective and 2 years of prospective study. During these 4 years, 87 cases of CNS tumors were noted.
2. The distribution of cases included 19(21.83%) cases of astrocytoma, 07(8.04%) cases of oligodendrogloma, 06(6.89%) cases of oligoastrocytoma, 06(6.89%) cases of medulloblastoma, 11 (12.64%) cases of schwannoma, 32 (36.78%) cases of meningioma, 02(2.29%) cases of gliosarcoma and 01(1.14%) case each of gangliocytic paranglioma, Astroblastoma, haemangioblastoma and metastatic deposits. (Table 1)
3. The most frequent type of CNS tumour observed was meningioma (32 cases, 36.78%) followed by astrocytoma (19 cases, 21.83%) among which, WHO grade IV (Glioblastoma) was high in frequency (7 cases, 36.84%). (Table 2)
4. Of the 87 cases, 7 cases (8.04%) were in the age range of 1-10 years, 8 cases (9.19%) were in the age range of 11-20 years, 9 cases (10.34%) were in the age range of 21-30 years, 4 cases (4.59%) were in the age range of 31-40 years, 33 cases (37.93%) were in the age range of 41-50 years, 8 cases (9.19%) were in the age range of 51-60 years, 15 cases (17.24%) were in the age range of 61-70 years age group and 3 cases (3.44%) were in the age group of 71-80 years. (Table 3)
5. Out of 87 cases, 48 were male (55.17%) and 39 were female (44.82%). These tumors showed preponderance in males with M:F ratio of 1.2:1. Except in meningioma where there was a female preponderance with M:F ratio of 1:2.1.(Table 6)
6. The most common presenting symptom was Headache (42%). (Table 5)
7. The most common site of occurrence of CNS tumor was frontal lobe (39.08%) followed by multilobe involvement (27.13%). (Table 4).

Conclusion
The most frequent type of CNS tumor was meningioma followed by astrocytoma of which WHO grade IV tumor was frequent and schwannoma. The peak incidence was in 41-50 years age group. Overall Males are affected more than females, with male to female ratio of 1.2:1 except in meningioma where there is a female preponderance with male to female ratio of 1:2.1. The most frequent clinical feature was headache and seizures in supratentorial tumors of intracranial region, backache, weakness and sensory disturbances in spinal cord tumors. The most commonest site of occurrence was frontal lobe followed by multilobe involvement.

Conflict of Interest: None

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