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ORIGINAL ARTICLE

PATHOLOGICAL SPECTRUM OF CNS TUMOURS: FIVE YEAR STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT: **BACKGROUND**: Tumours form an integral part of disease process affecting the CNS and constitute a major part of all intracranial space occupying lesions. **AIM**: To study the histological findings of CNS tumors and to classify them according to WHO classification. **MATERIALS AND METHODS:** This is a five year study in which all the specimens of tumors of brain and spinal cord received in the department of Pathology were analyzed with reference to histological type and grade of tumors by examination of hematoxylin and eosin stained slides and from information in pathology reports. **RESULTS:** A total of 315 cases were analyzed in the present study. Brain tumors formed the major part with a percentage of 87.9%, and tumors of spinal cord constituted 12.1% of all CNS tumors. All the brain and spinal cord tumors showed male preponderance except meningiomas in which male to female ratio was 1:2.3. Mean age of presentation of CNS tumors was 45.5 years. Overall, astrocytomas were the most common CNS tumors followed by meningiomas. Among the astrocytic tumors, glioblastoma multiforme was commonest accounting for 69.5% of all astrocytic tumors. Transitional meningioma was the most commonly observed meningeal tumor in brain as well as spinal cord. Pilocytic astrocytoma and medulloblastoma were the commonest tumors seen in childhood.

KEYWORDS: CNS, Tumor, WHO classification, Astrocytoma, Meningioma, Medulloblastoma.

INTRODUCTION: Tumours form an integral part of disease process affecting the CNS. The spectrum of CNS tumors includes primary and secondary tumors (Metastatic). Symptomatology of tumors has a wide spectrum. The nature and severity of these symptoms depend on the location of the mass and its rate of growth. Establishment of a diagnosis is important to determine the prognosis and treatment. Tumors constitute a major part of all intracranial space occupying lesions. Although brain tumors amount to less than 2% of all malignant neoplasms and constitute a small fraction of overall human cancer burden, they form a significant proportion in children in whom CNS tumors rank second in incidence after leukemias.[1]

Patients of all races, sexes & ages develop primary brain tumors. Black population has a decreased incidence of glial tumours.[2] Most of the neoplasms of brain and spinal cord have predilection for males except meningiomas which show female preponderance. Diffusely infiltrating astrocytomas are the most frequently occurring intracranial neoplasms, accounting for >60% of all primary brain tumours.[3] Other commonly seen tumors in adults are glioblastomas, oligodendrogliomas, meningiomas, metastases, pituitary adenomas, neurilemmomas of the VIII nerve and hemangioblastomas.[4]

In children nearly two third appear infratentorially[4] and the most common tumors are astrocytomas of cerebellum and brain stem, PNET's, ependymomas and craniopharyngiomas. However pituitary adenomas & meningiomas rarely occur in children. Tumors of the spinal cord and

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its covering are quite rare in children and are relatively uncommon in adults. Common spinal tumors include neurilemmomas, meningiomas, ependymomas and sarcomas. CNS tumors are seen in all age groups though particular tumors may be prominent in specific age groups like medulloblastomas and pilocytic astrocytomas are mainly seen in children.

Glioblastoma multiforme usually affects the elderly age group. Brain tumors can also be divided on the basis of location into supratentorial and infratentorial tumors. Nearly two third of primary brain tumors of adults are supratentorial and of children are infratentorial in location. Astrocytomas, oligodendrogliomas and metastatic carcinoma account for most cerebral hemispheric tumors. Pilocytic astrocytomas and medulloblastomas exhibit a predilection for the cerebellum, whereas ependymomas frequent the fourth ventricles of children and spinal cord of adults. Myxopapillary ependymomas are nearly exclusively seen in conus medullaris and filum terminale region. Primary CNS lymphomas are seen most often within deep, periventricular white matter structures and basal ganglia.

Likewise, craniopharyngiomas and pituitary adenoma is seen in the sellar and suprasellar region. The most accepted classification of CNS tumors is on the basis of histology and has been given by WHO in 1999.[5] Molecular genetics has helped to classify the nosologic place of some CNS neoplasms.[6]

The progression to glioblastoma is characterized by a clonal expansion of cells carrying a p53 mutation. Most frequent genetic alteration in oligodendroglial tumors is loss of heterozygosity on the long arm of chromosome 19(19q). Majority of meningiomas are characterized by allelic losses involving chromosome 22. Mutations in NF 2 gene are detected in up to 60% of sporadic meningiomas. Radiological examination is often essential for the evaluation of patients suspected of having meningeal, brain and spinal cord tumours.[7]

MATERIALS AND METHODS: This is a five year study in which all the specimens of tumors of brain and spinal cord received in the department of Pathology were analyzed with reference to histological type and grade of tumors. In each patient the clinical findings, type and size of specimen, tumor site and radiological findings, wherever possible, were obtained from the medical records. Pathological findings (histological type and grade) were obtained by examination of hematoxylin and eosin stained slides and from information in pathology reports. Histological types were classified according to WHO classification of tumors of the nervous system.

RESULTS: A total of 315 cases were analyzed in the present study. Brain tumors formed the major part with a percentage of 87.9%, and tumors of spinal cord constituted 12.1% of all CNS tumors (Table no. 1). The most common age group affected by the CNS tumors was between 41- 50 years (27.3%) (Table no. 2). Overall incidence of CNS tumors was high in males; the male to female ratio being 1.5:1(Table no. 3).The most common age group affected by brain tumors was 41 – 50 years accounting for 27.8% of all brain tumors.

The most common age group affected by the spinal cord tumors was between 41- 50 years accounting for 9 out of 38 cases (23.7%). Brain tumors showed male preponderance. Male to female ratio observed in brain tumors was 1.5:1 (Table no. 4). Male to female ratio observed in spinal cord tumors was 1.2:1 (Table no. 5). CNS tumors were most commonly seen in cerebral hemispheres accounting for 67.6% of total cases. CP angle was least commonly involved by tumors (3.5%). Overall

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most common tumor of CNS was astrocytoma (Figure 1 & 2) accounting for 105 cases (33.3%) followed by meningioma 89 cases (28.2%), pituitary adenoma 28 cases (8.9%) and Schwannoma constituting 19 cases (6%) (Table no. 6). Most common brain tumor was astrocytoma (37.9%) followed by meningioma (27.4%), pituitary adenoma (8.9%) and oligoastrocytoma (5.4%). Chordoma, hemangiopericytoma & choroid plexus papilloma were least commonly observed brain tumors in our study. Glioblastoma multiforme (Figure 3 & 4) was the most commonly observed astrocytoma in brain accounting for 69.5% of all astrocytic tumors (Table no. 7).

The most commonly observed meningeal tumor in CNS & brain was transitional meningioma (Figure 5) followed by meningothelial meningioma (Figure 6) (Table no. 8 & 9). Meningioma in brain was most commonly observed in the age group of 41-50 years accounting for 40 cases out of total 76 cases (52.6%) (Table no. 10). Female preponderance was observed in meningiomas in brain. Male to female ratio observed in meningioma was 1: 2.3(Table no. 11). Transitional meningioma was the most commonly observed meningeal tumor in brain accounting for 60.5% of all meningiomas.

Most common spinal cord tumor was meningioma (34.2%) followed by Schwannoma (31.6%). Female preponderance was observed in meningioma. Male to female ratio observed in spinal cord meningioma was 1: 2.25. Pilocytic astrocytomas (Figure 7) & medulloblastoma were the most commonly encountered CNS tumors in children accounting for 23.8% each. This was followed by Schwannomas (Figure 8) and ependymomas (Figure 9) constituting 14.3% each (Table no. 12).

DISCUSSION: This was a 5 year study conducted in a tertiary care hospital. All the specimens of CNS tumors submitted in the department of Pathology were analyzed with reference to light microscopy and were classified according to WHO classification of tumors.

Total number of cases analyzed-315: In the present study, brain tumors were more common (87.9%) in comparison to the tumors of spinal cord (12.1%). High incidence of brain tumors is in concordance with an epidemiological survey of primary tumors of brain and spinal cord done by Barker DJ et al[8] in 1976, Cole GC et al in 1982[9] and Wen ging H et al in 1983 [10]. The incidence of brain tumors in these studies was 95%, 90% and 89% respectively.

Most common age group affected by CNS tumors was between 41–50 years with mean age of presentation being 45.5±2.5 years. This is collaborated by studies done by Barker DJ, Weller RO et al in 1976[8] who reported the incidence of peak age for CNS tumors between 45–55 years. Mean age of presentation was 40.2 years and 44.8 years in studies conducted by Mehrazin et al[11] in 2005 and Yavari P et al[12] in 2006 respectively.

A higher incidence of CNS tumors was seen in the males. Male to female ratio in the present study was 1.5: 1. This is in concordance with a statistical analysis of CNS tumors done by Weller RO et al in 1976,[8] Shi–ju Z et al in 1982[10] and Mehrazin M et al in 2006[11] who reported male preponderance in the CNS tumours, with male to female ratio being 1.53: 1, 1.8:1 and 2:1 respectively.

In our study, all the brain tumours showed male preponderance except meningiomas which showed female preponderance. Male to female ratio observed in meningiomas was 1: 2.3 in brain tumours. This correlated with studies done by Barker J et al in 1976,[8] Cole JC et al in 1989.[9]

Christensen J et al in 1995[13] and Mehrazin M et al in 2006 [11] who reported male to female ratio as 1:2, 1:1.76, 1:1.8 and 1:2 respectively.

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Zuccaro G and Sosa F et al in 2007[14] found cerebral hemispheres as the most common site of involvement by brain tumours (62%) and cerebellopontine angle as the least common site (5%). Our study is in concordance with the above findings. In the present study, 76.9% of brain tumours were seen in cerebral hemispheres and only 4% were found in cerebellopontine angle.

Astrocytic tumours were the commonest tumours in CNS in the present study accounting for 33.3% of total cases. This is collaborated by a statistical analysis of CNS tumours conducted by Qing – Shenq T et al in 1982[10] in which astrocytic tumours constituted 42% of all cases of CNS tumours. Astrocytic tumours were second most commonly observed tumours following meningioma in the studies conducted by Yavari P et al in 2006[12] and Bouffe E et al in 2007 [15] accounting for 23.4% and 30.5% of all cases respectively.

Barker DJ et al in 1976,[8] Fleury A et al in 1997 [16] and Mc Carthy BJ et al in 1999 [17] observed glioblastoma multiforme as the commonest astrocytic tumor constituting 52%, 59.5% and 56% respectively. In our study also glioblastoma multiforme is the commonest astrocytic tumor. It constituted 69.5% of all astrocytic tumours.

Meningiomas and Schwannomas were the most commonly observed spinal cord tumours in the present study accounting for 34.2% and 31.6% cases respectively. This is in concordance with a statistical analysis of CNS tumours done by Qing – shenq et al in 1982 [10] and Yavari P et al in 2006 [12]who reported nerve sheath tumours and meningiomas as the commonest tumours of spinal cord accounting for 29.5% and 25.8% of all cases respectively.

In the present study, grade I meningiomas formed the bulk of meningeal tumours followed by grade II & III. Incidence of grade I, II and III meningiomas in our study was 94.4%, 4.5% & 1.1% respectively. Our findings matched with the study done by Rockhill J et al in 2007 [18] who reported the incidence of grade I, grade II and grade III meningiomas as 90%, 6% and 2% respectively.

Kepes JJ et al in 1982,[19] Fukuyama et al in 2006 [20] and Mehrazin M et al in 2006 [11]reported transitional meningioma as the commonest type of meningioma accounting for 55%, 60% and 51% of all meningeal tumours in brain. In the present study also this is the commonest histological type constituting 60.5% of all meningiomas in brain.

Boccardo F and Mina G et al in 1984[21] and Okinogami et al in 2006 [20] have reported CNS involvement by metastatic deposits in 11% and 7% cases respectively. However in the present study metastatic deposits were observed in 3.2% of all CNS tumours.

West RR and Wilkin PR et al in 1989[9] observed maximum cases of pilocytic astrocytoma (31.5%) in childhood in an epidemiological survey of primary tumours of brain and spinal cord in South East Wales. In the present study, pilocytic astrocytoma and medulloblastoma were the most frequent childhood tumours constituting 23.8% each.

CONCLUSION: This was a 5 year study conducted in a tertiary care hospital. A total of 315 specimens of CNS tumours submitted in the department of Pathology were analyzed with reference to light microscopy and were classified according to WHO classification of tumours. The following features were highlighted in this study: - Brain tumours were much common than tumours of spinal cord. These were 8 times the spinal cord tumours. All the brain and spinal cord tumours showed male preponderance except meningiomas in which male to female ratio was 1:2.3. Mean age of presentation of CNS tumours was 45.5 years. Overall, astrocytomas were the most common CNS tumours followed by meningiomas. Among the astrocytic tumours, glioblastoma multiforme was

commonest accounting for 69.5% of all astrocytic tumours. Transitional meningioma was the most commonly observed meningeal tumor in brain as well as spinal cord. Pilocytic astrocytoma and medulloblastoma were the commonest tumours seen in childhood.

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Site	Total No. of Cases	Percentage of Cases
Brain	277	87.9%
Spinal Cord	38	12.1%
Total	**315**	**100%**

Table No. 1

Age Group (years)	Total No. of Cases	Percentage of cases
1-10	09	2.8%
11-20	12	3.8%
21-30	33	10.5%
31-40	60	19%
41-50	86	27.3%
51-60	59	18.7%
61-70	42	13.3%
71-80	14	4.4%
TOTAL	**315**	**100%**

TABLE No. 2: AGE WISE DISTRIBUTION OF THE CNS TUMOURS

Gender	Total no. of cases	Percentage of cases
Male	187	59.4%
Female	128	40.6%
TOTAL	**315**	**100%**

TABLE No. 3: DIVISION OF CNS TUMORS ON THE BASIS OF GENDER

Gender	Total No. of cases	Percentage of cases
Male	166	60%
Female	111	40%
TOTAL	**277**	**100%**

TABLE No. 4: DIVISION OF BRAIN TUMORS ON THE BASIS OF GENDER

Gender	Total No. of cases	Percentage of cases
Male	21	55.3%
Female	17	44.7%
TOTAL	**38**	**100%**

TABLE No. 5: DIVISION OF SPINAL CORD TUMORS ON THE BASIS OF GENDER

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Histological diagnosis	No. of cases	Percentage of cases
Astrocytoma	105	33.3%
Meningioma	89	28.2%
Pituitary adenoma	28	8.9%
Schwannomas	19	6%
Oligoastrocytoma	15	4.8%
Metastatic deposits	10	3.2%
Oligodendroglioma	08	2.5%
Medulloblastoma	07	2.2%
Hemangioblastoma	06	1.9%
Lymphoma	05	1.6%
Plasmacytoma	05	1.6%
Ependymoma	04	1.3%
Craniopharyngioma	04	1.3%
Chordoma	03	0.9%
Neurofibroma	02	0.6%
Ganglioglioma	02	0.6%
Choroid plexus papilloma	01	0.3%
Hemangiopericytoma	01	0.3%
Cavernous hemangioma	01	0.3%
TOTAL	**315**	**100%**

TABLE No. 6: DIVISION OF CNS TUMORS ACCORDING TO HISTOLOGICAL DIAGNOSIS

Histological subtype	No. of cases	Percentage of cases
Glioblastoma multiforme(GBM)	73	69.5%
Anaplastic astrocytoma	10	9.5%
Diffuse astrocytoma	09	8.6%
Pilocytic astrocytoma	06	5.7%
Gemistocytic astrocytoma	04	3.8%
Fibrillary astrocytoma	01	0.9%
Subependymal giant cell astrocytoma	01	0.9%
Gliosarcoma	01	0.9%
TOTAL	**105**	**100%**

TABLE No. 7: DISTRIBUTION OF VARIOUS HISTOLOGICAL SUBTYPES OF ASTROCYTOMA IN BRAIN

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Histological subtype	No. of cases	Percentage of cases
Transitional meningioma	52	58.4%
Meningothelial meningioma	11	12.4%
Psammomatous meningioma	09	10.1%
Angiomatous meningioma	06	6.7%
Atypical meningioma	04	4.5%
Fibroblastic meningioma	03	3.4%
Anaplastic meningioma	01	1.1%
Microcystic meningioma	01	1.1%
Secretory meningioma	01	1.1%
Metaplastic meningioma	01	1.1%
TOTAL	**89**	**100%**

TABLE No. 8: DISTRIBUTION OF VARIOUS HISTOLOGICAL SUBTYPES OF MENINGIOMA IN CNS

Histological subtype	No. of cases	Percentage of cases
Transitional meningioma	46	60.5%
Meningothelial meningioma	10	13.2%
Angiomatous meningioma	06	7.9%
Atypical meningioma	04	5.3%
Psammomatous meningioma	03	3.9%
Fibroblastic meningioma	03	3.9%
Anaplastic meningioma	01	1.3%
Microcystic meningioma	01	1.3%
Secretory meningioma	01	1.3%
Metaplastic meningioma	01	1.3%
TOTAL	**76**	**100%**

TABLE No. 9: DISTRIBUTION OF VARIOUS HISTOLOGICAL SUBTYPES OF MENINGIOMA IN BRAIN

Age Group (years)	Total No. of Cases	Percentage of cases
21-30	03	3.9%
31-40	13	17.1%
41-50	40	52.6%
51-60	16	21%
61-70	04	5.3%
TOTAL	**76**	**100%**

TABLE No. 10: AGE WISE DISTRIBUTION OF THE MENINGIOMA IN BRAIN

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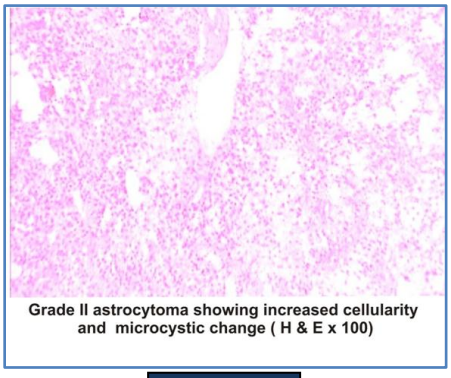
Gender	Total No. of cases	Percentage of cases
Male	23	30.3%
Female	53	69.7%
TOTAL	**76**	**100%**

TABLE No. 11: DIVISION OF MENINGIOMA IN BRAIN ON BASIS OF GENDER

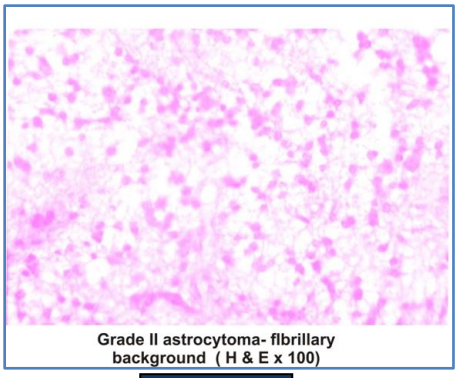
Tumor	No. of cases	Percentage of cases
Pilocytic astrocytoma	05	23.8%
Medulloblastoma	05	23.8%
Schwannomas	03	14.3%
Ependymoma	03	14.3%
Craniopharyngioma	02	9.5%
SEGA	01	4.8%
Anaplastic oligoastrocytoma	01	4.8%
Meningioma	01	4.8%
TOTAL	**21**	**100%**

TABLE NO. 12: COMMONLY SEEN CNS TUMORS IN CHILDREN & ADOLESCENTS (1-20 YEARS)



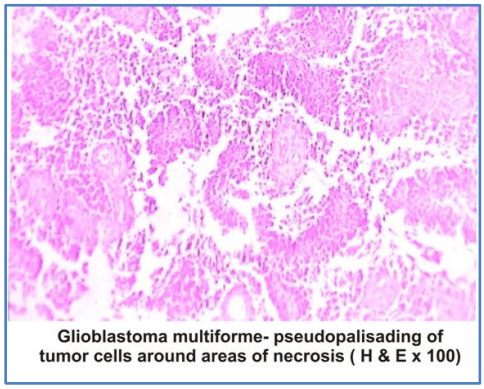
Grade II astrocytoma showing increased cellularity and microcystic change (H & E x 100)

Figure 1



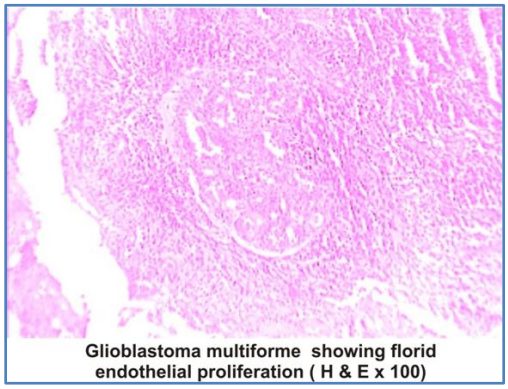
Grade II astrocytoma- fibrillary background (H & E x 100)

Figure 2



Glioblastoma multiforme- pseudopalisading of tumor cells around areas of necrosis (H & E x 100)

Figure 3



Glioblastoma multiforme showing florid endothelial proliferation (H & E x 100)

Figure 4

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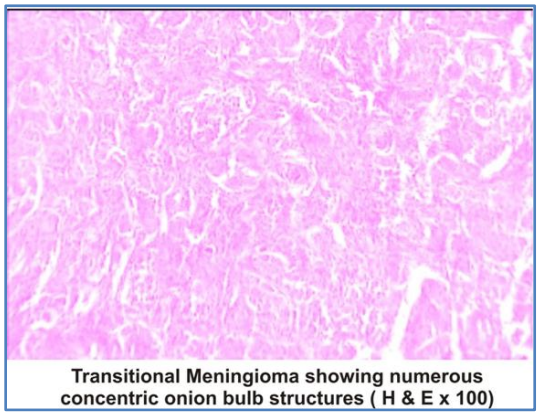
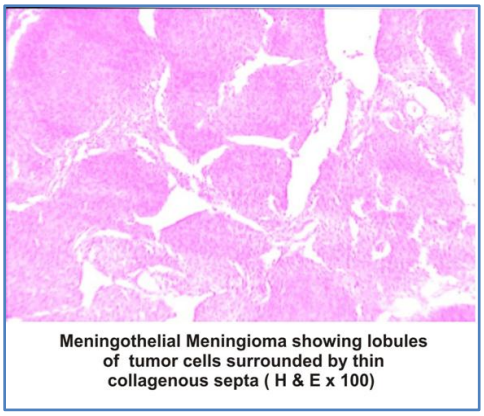


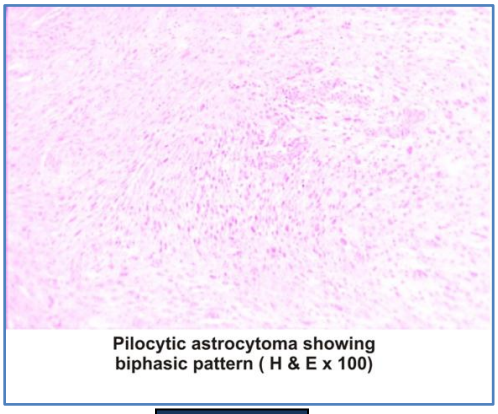
Transitional Meningioma showing numerous concentric onion bulb structures (H & E x 100)

Figure 5



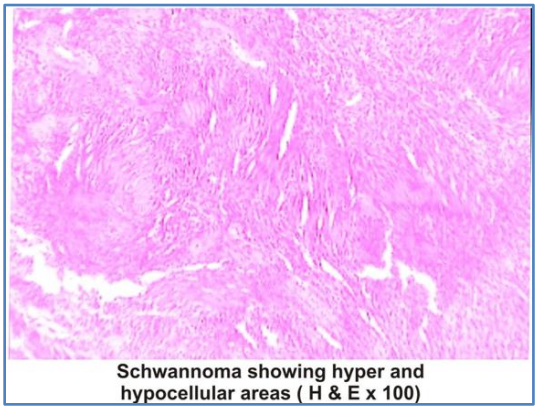
Meningothelial Meningioma showing lobules of tumor cells surrounded by thin collagenous septa (H & E x 100)

Figure 6



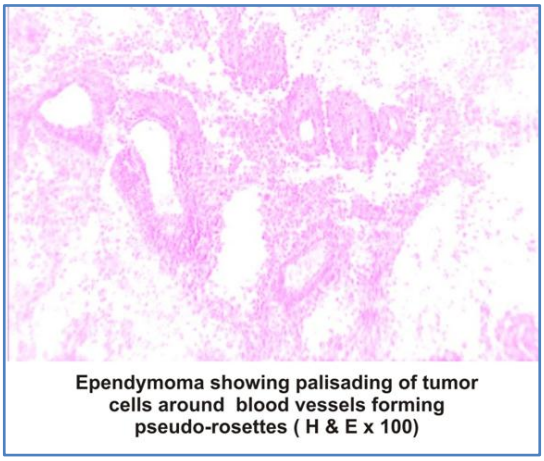
Pilocytic astrocytoma showing biphasic pattern (H & E x 100)

Figure 7



Schwannoma showing hyper and hypocellular areas (H & E x 100)

Figure 8



Ependymoma showing palisading of tumor cells around blood vessels forming pseudo-rosettes (H & E x 100)

Figure 9

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