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CNS MESENCHYMAL TUMORS -A HISTOMORPHOLOGICAL INSIGHT

Pathology

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ABSTRACT

Background: Mesenchymal tumors originate from precursor mesodermal cells surrounding the brain parenchyma. These mesodermal cells differentiate into bone, cartilage and connective tissue(blood vessels, adipocyte, smooth muscle cells and fibroblasts), and give rise to the various CNS Mesenchymal tumors. Objective: The aim of the present study was to determine the spectrum, frequency and demographics of mesenchymal tumors at a tertiary care centre. Materials and Methods :A retrospective review of all the reported CNS mesenchymal tumors from the Department of Pathology in a period of 2.5 years from December 2017 to May 2020 was done.Results: On histopathological diagnosis , incidence of various tumors were meningioma 63.6%(359), solitary fibrous tumor/hemangiopericytoma 3.36%(n=19),Ewings/PNET 0.17%(n=1) , chondrosarcoma 0.17%(n=1), chondroma 0.17%(n=1),schwanoma 27.9%(n=158),neurofibroma 0.17%(n=1) ,Ewings sarcoma/PNET 0.17%(n=1),hemangioma 0.88%(n=5),and hemangioblastoma 18%(3.18%). Conclusions: Mesenchymal tumors occurred predominantly within 30-45 years of age with a .slight female preponderance (male to female ratio 0.68:1). Meningiomas and schwanomas were the most common mesenchymal tumor.

KEYWORDS

Mesenchymal tumor,CNS, meningioma

INTRODUCTION

CNS mesenchymal tumors are extremely rare, with the exception of meningioma and schwanoma.1 Mesenchymal tumours arise more commonly in the meninges than in the CNS parenchyma or choroid plexus. Clinically, they occur anywhere along neuroaxis . Histologically, they are homologous to neoplasms occurring in somatic soft tissues and bone. Similiarly, they have a wide spectrum of morphological features ranging from benign to malignant and are diverse in their behavior from being indolent to the rapidly fatal. This diversity makes it critical to accurately diagnose, stage, and treat tumors appropriately to improve prognosis and reduce morbidity. Moreover, little is printed or published on these tumors. The aim of the present study is to throw some light on this direction and determine the spectrum, frequency and demographics of cns mesenchymal tumors at a tertiary care hospital.

MATERIAL AND METHODS

An retrospective study was performed at the Department of Pathology , SMS Medical college, from December 2017 to May 2020. Purposive sampling of cases were done .The study subjects included all cases(564) of CNS mesenchymal tumours received in the department. Non neoplastic, inflammatory lesions , and other non mesenchymal tumors of the brain and spinal cord were excluded. We retrieved the slides of these cases and reviewed them. Immunohistochemistry in required cases were done for confirmation. Strict confidentiality of patient information was maintained. Those cases with incomplete data were excluded from the study. All the CNS tumours were divided into the following categories:, meningeal tumours, and non meningeal mesenchymal tumours. Non meningeal mesenchymal tumours were arranged into general categories of mesenchymal tumors based on the presumed cell of origin(illustrated in Table1). 2 Age and gender distribution, clinical presentation, site of tumour and histopathologic patterns with grade were noted and the data was analysed.

Table1.Categorisation of various CNS mesenchymal tumors based on the cell of origin

	Categories based on cell of origin	Tumors
Meningeal tumors	Meningeal tumors	meningiomas
Non meningeal tumors	Adipocytic Tumors	Lipoma, Angiolipoma, and Liposarcoma
	Bone Tumors	Osteoma, Osteoid Osteoma/ Osteoblastoma, and Osteosarcoma
	Cartilaginous Tumors	Chondroma and Chondrosarcoma
	Notochordal Tumors,	Benign Notochordal Cell Tumor and Chordoma
	Fibroblastic/Myofibroblastic Tumors	Solitary Fibrous Tumor , myofibroblastoma and Inflammatory Myofibroblastic Tumor
	Nerve sheath tumors	Schwanoma, Neurofibroma and Malignant intracerebral nerve sheath tumor(MINST)
	Smooth Muscle Tumors	Leiomyoma, Leiomyosarcoma, and EBV-Associated Smooth Muscle Tumor
	Skeletal Muscle Tumors	Rhabdomyosarcoma Subtypes: Embryonal, Alveolar, and Spindle Cell/Sclerosing Subtypes
	Vascular tumors	Hemangiomas, Hemangioendothelioma, and Angiosarcoma
	Primitive Small Round Cell Tumors	Ewing Sarcoma
	Sarcomas	Undifferentiated Sarcomas and Radiation-Associated Sarcoma

RESULTS

A total of 564 cases of CNS mesenchymal tumors were identified .We classified them into meningeal tumors and non meningeal tumors, which were further subclassified as their homologue in the soft tissues.Finally,we reported a spectrum of 10 different types of histopathological CNS mesenchymal tumors(Table 1) on the basis of their histology.The incidence of various tumors were meningioma 63.6%(359), solitary fibrous tumor/hemangiopericytoma 3.36%(n=19), Ewings/PNET 0.17%(n=1) chondrosarcoma 0.17%(n=1), chondroma 0.17%(n=1),schwanoma 27.9%(n=158), neurofibroma 0.17%(n=1),hemangioma 0.88%(n=5),and hemangioblastoma 18%(3.18%).(Fig1)

Meningiomas constituted the largest group(63.6%).Most of these were supratentorial, while 16 cases of spinal meningiomas were also seen. Among the meningiomas, most common type of grade 1 meningiomas (meningothelial, followed by transitional, fibrous , psammomatous, microcystic and angiomatous.) 24 cases of grade 2 meningiomas were reported (mostly atypical meningiomas). Amongst the grade 3

meningiomas, 4 cases of papillary meningiomas and 2 cases of anaplastic meningiomas were seen. Majority cases were females of the age group 30-45 years. The female to male ratio is 1.76:1.

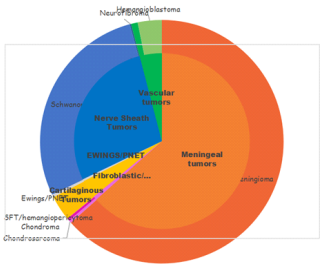
As per the new WHO classification mesenchymal fibroblastic tumors are classified into 'Solitary fibrous tumor/ hemangiopericytoma' category. We at our centre reported 19 cases under this category. Most of which were grade2 (8 cases). Only a single case of Grade3 HPC was reported. Grading was done on the basis of cellularity and nuclear grade. Most common age group was 30-45years and showed slight male predominance.

Two tumors with cartilaginous differentiation and supportive radiological evidence of dura based location were classified chondroma and chondrosarcoma on the basis of their specific histological features each.Schwanomas constituted the second largest group (27.9%).These were most common in the cerebellopontine angle (CP angle), with a few (n=5) cases of spinal schwanomas were also seen.Histologically, they(brain) were mostly grade1 schwanomas, 4 cases of cellular schwanoma and 1 case of ancient schwanoma was also seen. Spinal schwanomas were all grade1 schwanomas. 18 cases of hemangioblastoma were reported. Out of which 14 were located in the posterior fossa (cerebellum).Most of these were grade1.Majority cases were males of the age group 15-30 years.

Table2.Age wise distribution of various CNS mesenchymal tumors.

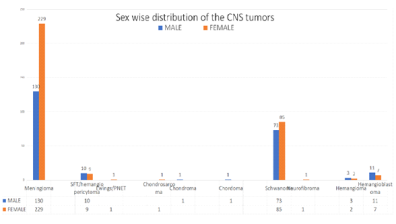
Tumors	TOTAL	0-15	15-30	30-45	45-60	>60
Meningioma	359	12(3.36 %)	70(19.6 %)	139(38.7 %)	80(22.4 %)	58(16. 24%)
SFT/hemangio pericytoma	19		5(26.3%)	6(31.57%)	5(26.3%)	3(15.7 %)
Ewings/PNET	1			1		
Chondrosarco ma	1		1			
Chondroma	1			1		
Chordoma	1				1	
Schwanoma	158		62(39.2 %)	80(50.6%)	16(10.1 %)	
Neurofibroma	1		1			
Hemangioma	5	3(60%)	2(40 %)			
Hemangioblast oma	18		7(38.8%)	10(55.5%)	1(5.5%)	
	564	15(2.6 %)	148(26. 2%)	237(42%)	103(18.2 6%)	61(10. 8%)

Fig1.Pie chart representing frequency of various CNS tumors



The overall male to female ratio was 0.62:1 asderived from fig 2.

Fig2. Bar chart representing sex wise distribution of the various CNS mesenchymal tumors

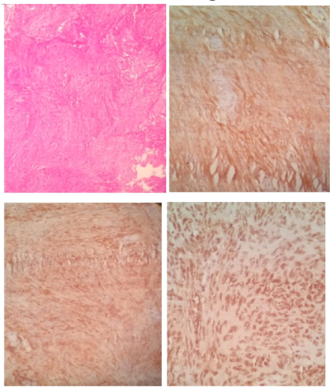


Discussion

Mesenchymal tumours of the CNS have similiar terminology as well as histological features corresponding to their soft tissue counterparts. They may arise within(primary) or as a result of secondary impact on the nervous system. Primary tumours are very rare. They can occur in any age and are common in supratentorial than in infratentorial or spinal locations.

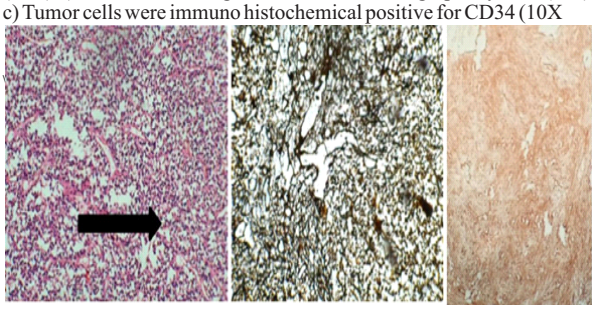
Meningiomas is the most common mesenchymal tumor accounting for 63.6%(359) in the present study.Meningioma was the second most common CNS tumor in studies by Chen et al (36%)and Abu et al . 4,5They were common in the third and fourth decade. A female preponderance (63.7%) was noted .The results were similar to studies done by Shah and Thomas6,7 .The most common clinical feature was headache and vomiting. In our study, meningothelial meningioma was 70% followed by transitional meningioma 20% , which is comparable with the study by Abu et al(61.1% and 15.5%).

Fig3 a)H&E section show fibroblastic meningioma(10X) b) Tumor cells were immunohistochemical positive for Vimentin(10X) d) Tumor cells were immunohistochemical positive for EMA (10X) e) Tumor cells were immunohistochemical positive for S 100 (40 X)



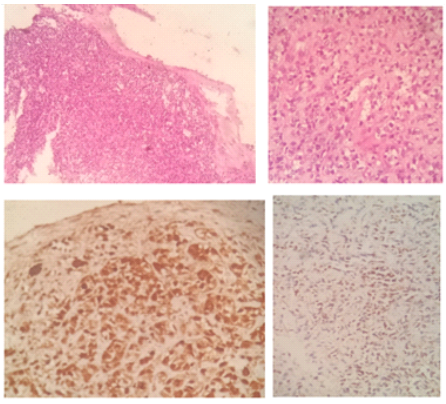
The World Health Organization (WHO)3 in 2016 combined these terms to SFT/HPCs due to frequent morphologic overlap.The incidence of SFT/HPCs was 3.36% of all the primary CNS mesenchymal tumors, and the ratio of HPCs to meningiomas was 1:21. Of 19 cases, 17 (89.5%) cases were HPCs and 2 (10.5%) case was of SFT. The mean age at the time of diagnosis was 30-45 years . Male-to-female ratio was 1.1:1. All our findings were comparable to Shukla et al.8

Fig4a)H&E section shows staghorn vessels in hemangio pericytoma (20X) b)RS stain show staghorn vessels in hemangiopericytoma (40x) c) Tumor cells were immuno histochemical positive for CD34 (10X



The incidence of spinal chondrosarcomas is estimated to be from 2% to 12% in various series.9,10 The thoracic spine is the most frequent localization, followed by the cervical and lumbar region .9,11 Conventional chondrosarcoma, which constitutes approximately 85% of all chondrosarcomas.12 We were presented with a spinal mass at L1-L2 in a 57 year old female.On microscopic examination it was a conventional chondrosarcoma grade1.Hence, our findings are in concordance with those of Pavlos.9

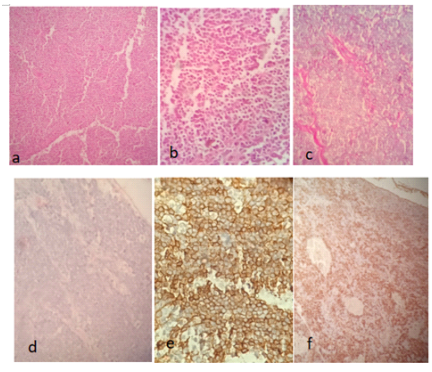
Fig 5a)H&E section shows cellular tumor composed of round or elongated tumor cells with hyperchromatic nuclei (Mesenchymal chondrosarcoma) (10x).b) High power view showing enlarged chondrocytes with multinucleated lacunae (40x) c) Tumor cells were immunohistochemical positive for S100 (40x) d)Tumor cells were immunohistochemical positive for Vimentin (10x)



We report a case of dural chondroma in a 32 year old male.Russell and Rubinstein reported that the aberrant growth of cartilage rests could cause chondroma in parts of the intracranial cavity apart from the base of the skull.12,13 About 70% of reported cases of chondroma originate from the dura mater, while the remaining cases are located inside the brain parenchyma or the choroid plexus.14 Eefting et al 15showed that a combination of five parameters (high cellularity, presence of host bone entrapment, open chromatin, mucoid matrix quality, and age above 45 years) allowed optimal differentiation between enchondromas and central grade 1 chondrosarcomas.15,16 Single case of chordoma of clivus in a 52year old male child was reported using Eefting's criteria. Intracranial chordomas are benign, slow-growing, cartilaginous tumors, which comprise only about 0.2% of all intracranial tumors.16 Intracranial chondromas are usually seen in females in the 2nd to 5th decades of life.16 Clinically, they usually do not have mild symptoms or are asymptomatic as they are slow growing. Imaging studies provide effective diagnosis but biopsy is diagnostic. The treatment of choice is total resection of the tumor.

The extraosseous intracranial Ewing sarcoma-peripheral primitive neuroectodermal tumor (EWS-pPNET) is a very rare, small, round cell tumor described as a mesenchymal, nonmeningothelial tumors in the World Health Organization classification . 3,17 Present study included a case of Ewings sarcoma of the parietal lobe of a 33year old male was seen.On IHC, it expressed CD 99 , Vimentin and negative for GFAP.PAS was positive in the cytoplasm and d PAS sensitive. These tumors are aggressive, multicompartmental, vascular, and growing rapidly, so missing or overlooking the primary symptoms of dural stretching/bony involvement leads to delay in management and poor outcome.[17]

.Fig6 a)H&E stained section shows sheets of small, round, uniform cells with scant clear cytoplasm, divided into irregular lobules by fibrous strands (10x) b)High power view show monomorphic cells with scant clear cytoplasm (40x) c) Tumor cells shows cytoplasmic PAS positivity (10x) d) Tumor cells were dPAS sensitive (10x) e)IHC stained section shows tumor cells expressing strong membranous positivity for CD99 (10x) f)Tumor cells were immunohistochemical positive for Vimentin (10x)



The vast majority of schwannomas occur outside the CNS.3 Spinal schwannomas account for about 25% of primary intradural spinal cord tumors in adults.18 Intracranial schwanomas are relatively common neoplasms, accounting for 8% of all primary intracranial neoplasms .19In the cerebello-pontine angle, they are the most common lesions: 59% of all space-occupying lesions and constitute 80 -90% of all tumours .19 Schwannomas are the most common primary tumor in the spinal cord and constitutes 30 % of cases. They occur in all ages, but are most common in the 30-50 years and show no gender predisposition.19 In the present study,schwanomas constituted the second largest group (27.9%).These were most common in the cerebellopontine angle (CP angle), with a few (n=5) cases of spinal schwanomas were also seen.Our study is in concordance with Jean 18 and Lunardi [19]

Neurofibromas present typically as a cutaneous nodule, less in a peripheral nerve, and occasionally in spinal roots. 20 Multiple neurofibromas are typically associated with neurofibromatosis (NF) 1.20 Only a few cases are reported in literature. A single case of spinal neurofibroma was reported in a 35 year old male, located in cervical spine.IHC stains- neurofilament and S100 were done for confirmation. Cavernoma was the most common AV Malformation encountered by Karri et al 21 while intracranial capillary hemangioma (ICH) is a rare entity, with approximately 24 reported cases in the literature.22 5 cases of hemangiomas were reported , out of which 2 were capillary hemangiomas and 3 cavernous type were seen.

Hemangioblastomas are benign neoplasms that originate in the central nervous system . 23They represent 1.5–2.5% of all intracranial neoplasms and 7–12% of posterior fossa tumours. 28 They are usually infratentorial, mostly over the cerebellum (76%) around the fourth ventricle and few in the cerebral hemispheres (9%), spinal cord (7%) and brainstem (5%) .23 18 cases of hemangioblastoma were reported. Out of which 14 were located in the posterior fossa (cerebellum).Most of these were grade1.Majority cases were males of the age group 15-30 years.Our findings are in concordance with Hussein .23

Conclusion

Mesenchymal tumors represent a heterogeneous group of neoplasms exhibiting a wide spectrum of histomorphologies, some with overlapping features, and numerous molecular alterations contributing to their diversity. Multimodal therapies including surgery, chemotherapy and radiotherapy have improved clinical outcomes of patients , thereby plateauing the prognosis over the recent years.Biopsy plays an important role in the classification and diagnosis of these tumors.The above study describes the various mesenchymal CNS tumors that were commonly encountered in a tertiary centre and also highlights few of the rare tumors.We conclude that mesenchymal CNS tumors can affect a wide range of age groups ,menigiomas are most common mesenchymal tumors and show female preponderance. Non-meningeal mesenchymal tumors, are relatively rare but early detection and diagnosis is essential for treatment of these malignant tumors.

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