Original Article

A Clinicopathological Study of Lesions of Spinal Cord and its Coverings: A Tertiary Care Hospital Experience

Nitin M.Gadgil, Chetan S. Chaudhari*, Sangeeta R.Margam, Mohd. Unzer Mohd. Umar Khan, and Prashant V Kumavat, Ganesh R Kshirsagar

Dept of Pathology, Lokmanya Tilak Municipal Medical College & General Hospital, Sion, Mumbai, India

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ABSTRACT

Background: The human central nervous system is highly evolved and an enormously complex system. Aim of our study was to analyse the clinical and radiological spectrum of spinal cord lesions with histopathological morphology, according to recent WHO classification of tumors of Central Nervous System and to highlight any changing trends in the spinal cord lesions if detected in context of Indian patient's profile.

Methods: Our study comprised of a total 85 surgical resection specimens of lesions of spinal cord and its covering studied over a consecutive period of 12 years in a tertiary care hospital. Primary vertebral tumors and paraspinal soft tissue lesions were excluded. Descriptive cross-sectional study of cases including detailed clinical data of age, sex, duration of disease, type of lesion, and radiological findings of the patients was obtained. All cases were analyzed by examining Hematoxylin and Eosin stained slides with use of special stains and immunohistochemistry, as needed.

Result: Male predominance was noted with ratio of 1.3:1 with maximum cases seen in 21-40 years. Pain was the most frequent symptom, followed by paraplegia and sensory dysfunction. Thoracic segment of the spinal cord was most commonly involved, followed by lumbar and cervical .The most common site was extradural , followed by intradural extramedullary and intradural intramedullary lesions. Out of total, we had 69.4% cases of tumors of spinal cord and its covering, 23.5% intraspinal tuberculosis and 7.1% cases of benign cystic lesions. Amongst the tumors,Commonest tumor was Nerve sheath tumors (42%) followed by meningioma (25%), astrocytoma (12.5%), metastasis (8%), ependymoma (7%). There were single rare cases of glioblastoma multiforme,paraganglioma, ganglioneuroma,PNET.

Conclusion: Tumors of spinal cord are considered to be rare .The management of spinal cord lesions requires proper diagnosis which depends on clinical manifestation, radiography and its correlation with histological type and grade.

***Corresponding author:**
Dr. Chetan Sudhakar Chaudhari, 11, Jagannath darshan, M. D. Keni Road, Near,RBI Quarters, Bhandup Village (E), Mumbai, India
Phone : +91 9819133606
Email: drchetanchaudhari26@yahoo.co.in

Introduction

Tumours of spinal cord are much less frequent that intracranial ones, showing approximately four intracranial tumours for a single spinal tumour with variation depending on histological types. The intracranial to spinal ratio of astrocytomas is 10:1, whereas for ependymoma it varies from 3:1 to 20:1 depending on specific histological variant. Spinal cord tumours occur predominantly in 21-40 age groups and are less common in childhood and old age. According to their location, spinal tumors are conveniently classified as extradural and intradural, although some can be both inside and outside the dura. Intradural tumors can be intramedullary (intramedullary spinal cord tumor) [IMSCT] or extramedullary (intradural extramedullary) [IDEM].Most of the intramedullary tumors are malignant and belong to the glioma group. [1] In the glioma group, ependymoma is the most frequent among adults constituting 60% of intramedullary tumors while astrocytoma is common in children. Among the extramedullary tumors, schwannoma and meningioma are frequently encountered. Non glial neoplasms like hemangioblastomas, metastasis, lymphoma, paraganglioma and primitive neuroectodermal tumors are much less common. Although tuberculosis remains a major health problem in developing countries, tuberculoma involving the central nervous system is still uncommon compared with the involvement of the other systems. Intramedullary tuberculomas are rare and constitute only 0.2 to 0.5% of all central nervous system (CNS) tuberculomas. Among patients with spinal tuberculosis, 55% present with vertebral body involvement, 39% with intraspinal granulomatous lesions without bone involvement, and only 7% with intramedullary lesions. [2, 3] The ultimate prognosis depends on the histopathological nature of the removed tissue hence pathologist has to play the most important and crucial role in diagnosing and assessing the nature of lesion.

Materials and Methods

Our study comprised of a total 85 surgical resection specimens operated for lesions of spinal cord and its covering in all age groups including primary tumours, metastatic tumours invading or compressing the spinal cord and tuberculosis, studied over a consecutive period of 12 years in a one of the largest tertiary care hospital having 1700 beds. Primary bone tumors involving the vertebrae and paraspinal soft tissue were excluded. Tuberculosis remains a major health problem in developing countries, hence its lesions presenting as mass with clinicopathological profile was also included. Descriptive cross-sectional study of cases with detailed clinical data of age, sex, duration of disease, type of lesion, clinical and radiological findings of the patients was obtained. All cases were analyzed by examining Hematoxylin and Eosin stained slides with use of special stains and immunohistochemistry as required. Findings in the study were compared with previous ones in English literature with special emphasis on Asian studies to note any changing trends in patterns of presentation, location of different entities.

Result

Frequencies in results were calculated by Chi square test for categorical variables. Mann-Whitney U test was used for non parametric variables. The majority of cases were seen in the 21-30 years age group comprising 28.23% cases (24/85 cases) followed by 18.82% cases (16/85 cases) in the 31-40 years age group. In the 21-30 years age group, tuberculosis forms the largest group with 41.66% cases followed by schwannoma comprising 29.16% cases. In the 31-40 and 41-50 years age group, meningioma forms the largest group comprising

followed by schwannoma. In the 11-20 year age group, astrocytoma forms the major

group comprising 33.33% cases and 16.67% cases each of epidermal cyst, schwannoma and neurofibroma. In the 0-10 years age group, we have one case each of Astrocytoma, Ganglioneuroma, Neurofibroma, Schwannoma,PNET and Arachnoid cyst. In >60 years age group we have total 2 cases of which one belongs to Metastatic carcinoma (Table 1)

We had 59 cases of tumors of spinal cord and its covering. Out of which the commonest tumor was schwannoma comprising 32.2% cases (19/59 cases) followed by 25.42% cases (15/59 cases) of meningioma, third group was formed by astrocytoma with 13.55% cases (8/59 cases including glioblastoma) and fourth formed by Neurofibroma with 10.16% cases (6/59 cases) followed by metastatic carcinoma with 8.47% cases (5/59 cases) followed by ependymoma with 6.77% cases (4/59 cases). (Fig 1) it is evident that maximum number of cases was seen in the group of 31-40 year age group, followed by 21-30 year age. The youngest case was 0.5 years of age and the oldest patient was 66 years of age with mean age of presentation being 32.25 years. Overall there were 30 males and 29 females with Male to Female ratio 1.03:1 (p value 0.4)(Fig 2).

Tumors were distributed along various segments of spine with different frequencies but except meningioma, other lesions did not show segment specific propensity (p value 0.6) Tumors involved more commonly the thoracic level of the spine with 47.5% cases followed by cervical region comprising 24.5% cases. There were 22.9% cases of tumors involving the lumbar region and the last group

i.e. sacral region included 4.9% cases (Fig 3). Local pain (backache+neck pain) was the most common presentation comprising 57.64% cases (49/85 cases) followed by paraplegia/muscle weakness seen in 48.23% cases (41/85 cases); the third group is formed by referral pain (Pain in the limbs, radiating pain) seen in 22.35% cases (19/85 cases) followed by sensory dysfunction (paresthesia, sensory loss, impaired sensation) with 21.17% cases (18/85 cases). The other symptoms included swelling of the back,incontinence of urine, vomiting and headache. (Table 2). Duration of symptoms were ranging from 0.5month to 120 months with average duration of 14 months.

Most number of lesions were extradural comprising 43.52% cases (37/85 cases) followed by intradural extramedullary lesions constituting 41.17% cases (35/85 cases) and last group was formed by intradural intramedullary lesions with 15.29% cases (13/85 cases).Among tumors of spinal cord and its covering, most common group was intradural extramedullary with 50.84% cases (30/59 cases) followed by extradural group with 28.81% cases (17/59 cases) and last group is of intradural intramedullary with 20.33% cases (12/59 cases). Benign cystic lesions were commonly seen in extradural site with 83% cases (5/6 cases). Meningioma most commonly involves the thoracic spine constituting 80% of all cases of Meningioma (12/15 cases) and Schwannoma involves the lumbar spine frequently with 42.1% cases (8/19 cases). Astrocytoma was more commonly seen in the cervical spine with 71.4% cases (5/7 cases) and equal number of schwannoma cases were also seen in the cervical spine. Tuberculosis was more commonly seen in thoracic spine 45% (9/20 cases) followed by lumbar with 35% (7/20 cases). Benign cystic lesions were seen in thoracic 3/6 cases (50% cases) and lumbar region 2/6 cases (33.33% cases) frequently. (Table 3)

Discussion

Primary tumors of the spinal cord are ten to fifteen times less common than primary intracranial tumors. Spinal tumors are classified based on their anatomical location as extradural, intradural extramedullary and intradural intramedullary. Primary spinal tumors are typically intradural in location whereas extradural tumors are typically due to metastatic disease. [4] Spinal tumors are rare and potentially devastating lesions that threaten the patient's mobility or even life. The incidence of various tumors in our study is closely comparable to the study conducted by Lalitha and Dastur et al [5] (Table 4) (metastatic group excluded). In our study, thoracic spine was the most common location for spinal cord tumors which was comparable to other national and international studies [5, 6, 7, 8, 9,10].There was almost an equal distribution of cases in cervical and lumbar spine which was similar to study conducted by Moein P et al[10]. Spinal cord tumors may cause pain, sensory changes, and motor problems. Nerve pain in the leg may indicate a problem in the spine at the nerve's origin. Given the relative infrequency of spinal tumors, however, these types of symptoms more commonly result from degenerative disc disease, or other, more common problems especially at cervical and lumbar spine levels. Although degenerative disc disease is not so common at thoracic level, but it is the most common location for spinal cord tumors and so the role of pathologist in determining the etiology of symptoms by examining tissue along with radiological correlation is immense, for offering proper mode of management.

In our study we reported a total of 25 cases of nerve sheath tumors with 19 cases of schwannoma and 6 cases of neurofibromas, of these 68% were intradural extramedullary and 32% were extradural comparable to Govada N et al [11] . Spinal schwannoma accounts for about 25% of intradural spinal cord tumors in adults. We reported 19 cases with M: F ratio slightly lower than the other studies. Most common location was lumbar (42.1% cases) and Pain was the most common complaint, as similarly observed by Jagadesh BK et al [12] followed by muscle weakness. Histologically, it is composed of two components, Antoni A and Antoni B areas, Antoni A is cellular and consists of spindle shaped Schwann cells which show nuclear palisading. Antoni B is less cellular with Schwann cells suspended in a loose myxoid matrix. One of the cases showed cystic degeneration. On MRI all the cases had well circumscribed masses with 4 cases isointense and 15 cases hypointense on T1W images and all were hyperintense on T2W images with variable contrast enhancement. Neurofibromas are much less common than schwannoma within the spine. Out of 25 cases of nerve sheath tumors we had 6 cases of neurofibromas. In our study they were most commonly seen in the 3rd to 4th decade. They were commonly seen in the cervical spine with 50% cases in concordance with Hirano K et al [13] (43.5% cases) followed by sacral and lumbar spine. In our study we had no cases associated with neurofibromatosis. Microscopically it showed a tumor composed of elongated spindle cells with poorly defined pale cytoplasm and buckled nuclei admixed with small nerve fibers. All the cases had well circumscribed lesion that were hypo to isointense on T1 weighted and hyperintense on T2 weighted images usually with uniform contrast enhancement.

Spinal meningioma constitute 25% of all spinal cord tumors, it is the second most common intradural extramedullary tumor after the nerve sheath tumors comparable to our study. We had 15 cases of meningioma predominantly seen in the 4th and 5th decade with mean age 42.8.There is a female preponderance with M: F ratio being 1:2. This female preponderance was seen in most of the studies. Thoracic (80% cases) was the commonest site as is found in many national and international studies followed by lumbar and cervical spine. [12, 13] Compared with reports from other parts of the world, there are evident differences in the frequencies of nerve sheath cell tumors (NSCTs: schwannoma and neurofibromas) and meningioma. In Asian countries, including our study the frequency of NSCTs is higher than that of meningioma while in non Asian countries the incidence of meningioma is almost equal to or higher than that of NSCTs. Histologically meningioma exhibit wide range of appearances reflecting the mesenchymal and epithelial histogenetic potential of arachnoid cells. We had 8 cases of meningothelial meningioma, 6 were psammomatous meningioma and one was papillary variant. Meningothelial meningioma shows large lobules of cells with poorly defined cell borders and formation of characteristic whorls. The cells have nuclei with finely distributed chromatin and inconspicuous nucleoli. Psammomatous meningioma shows tumour cells arranged in whorls with hyalinised and calcified centers called psammoma bodies (Fig 3). All the cases had a circumscribed mass primarily hypo to iso intense on T1 weighted and hyper to isointense on T2 weighted images with uniformly contrast enhancing tumors. A solitary intradural extramedullary (IDEM) thoracic spine mass in a middle aged female should suggest the diagnosis.

In our study we observed a total of 8 cases of astrocytoma with male predominance having M: F ratio of 3:1 higher than the other studies. They were most commonly seen in 2nd and 3rd decade with mean age of 19.5 years. In our study the most common location was cervical followed by thoracic and majority of the cases (63%) belonging to lower grade (grade I or II) and 37% were high grade which was comparable to study by Lee SM et al[14], Moein P et al[10]. We had a single case of glioblastoma multiforme in a 12 year old male child. Primary GBM of the spinal cord is a rare condition. The relatively low proportion of absolute number of neuroglial cells as compared to brain in the spinal cord probably accounts for the rarity of these neoplasms in the spinal cord. [15] Glioblastoma represents approximately 3% of all intramedullary spinal cord tumors. The spinal variety is mostly seen during the second and third decades and shows a predilection for the cervical and thoracic region. In the literature there are few case reports of primary glioblastoma of spinal cord. [15,16] Pilocytic astrocytoma on H &E showed classic biphasic pattern with compacted piloid cells and loosely textured multipolar cells with Rosenthal fibers (tapered corkscrew shaped, intense eosinophilic hyaline masses) and eosinophilic granular bodies(Fig 3). Anaplastic astrocytoma showed increased cellularity, nuclear pleomorphism and prominent mitotic activity. Micro vascular proliferation and necrosis were absent.

We observed 4 cases of ependymoma with M: F ratio of 3:1 with mean age of 34.7 years comparable to Moein P et al. We had 3 cases of cellular ependymoma and a single case of myxopapillary ependymoma variant.MRI showed Intense homogenous contrast enhancement in 3/4 cases and 1 case showed multiple minimal enhancing lesions. Here we find well defined lesions which are an important finding as for such tumors complete resection is possible. The histology of the ependymoma WHO grade II showed moderately cellular glioma with monomorphic nuclear morphology, characterized by round to oval nuclei. Mitoses were absent. Characteristic perivascular pseudo rosettes and ependymal rosettes were seen. In our study we had 5 cases of metastasis compressing the spinal cord with mean age of 55.4 years. Spinal epidural metastases are found in 5–10% of all patients with cancer and are much more frequent than spinal leptomeningeal or intramedullary metastases. The Prostate, breast and lung cancer are the most common origin of spinal epidural metastasis followed by non-Hodgkin lymphoma, multiple myeloma and renal cancer. [17] In our study we had 2 cases with lung cancer as the primary lesion, 2 cases with primary breast carcinoma and one with unknown primary cancer.

Miller and Torack described the first case of Paraganglioma and since then only isolated cases have been reported in the literature. [18, 19] This uncommon entity comprises only 3.4 to 3.8% of all tumors affecting cauda equina region. We report a case of 35 year old female who presented with lower backache and pain in the lower limbs since 4 years. . MRI showed presence of intradural extramedullary space occupying lesion extending from L3-S1 which was well defined. The tumor appeared as iso to hypointense with respect to the spinal cord on the T1-weighted sequences and hyperintense on T2 weighted image, contrast MRI showed uniform enhancement of the tumor. Histopathology shows nests of tumor cells separated by a fine vascular network representing a Zellballen pattern. (Fig 4) Immunohistochemistry showed positivity for synaptophysin and chromogranin. We had a very rare case of multifocal PNET tumour, IDEM by location, nowadays generally known as Ewing's sarcoma family

tumors (ESFTs), in a 30 year old male. Multifocal ES is extremely rare, with an incidence ranging from 1.1% to 4.3%.chromosomal translocations t(11;22)(q24;q12) gene characterises these spinal ESFTs with positive CD 99 expression.A rare case of Ganglioneuroma was seen in our study of 9 year old female child, presented with backache since 2 months. MRI shows presence of an extradural space occupying lesion which is hypointense on T1 and hyperintense on T2 extending from D7-D10. . H&E stained section showed large ganglion cells scattered in a stroma composed of spindle shaped cells.(Fig 5)

Tuberculosis still remains major public health problem in India, hence to study its disease pattern involving spinal region is essential. Tuberculomas of central nervous system are more common than of spinal column. The approximate proportion between intraspinal and intracranial tuberculomas is 1:20 .We had 20 cases of tuberculosis of spinal cord, 14 males and 6 females, with 50% cases occurring in the range of 21-30 years with mean age 31.4 years and M: F ratio 2.3:1. Most common location was in the thoracic spine with 45% cases.18 cases were extradural in location and 2 cases with intramedullary location. Intramedullary tuberculomas are rare with subacute presentation of progressive spinal cord compression symptoms and constitute only 0.2 to 0.5% of all central nervous system tuberculomas. Given the rarity of spinal intramedullary tuberculoma, there is no standardized treatment protocol for this condition. Our results matched with Jain AK et al [19] who reported 17 cases with same clinical and pathological features. Spinal tuberculoma may occur at any level although it shows a predilection for the thoracic region as seen in our study.

Table 1: Incidence of lesions of spinal cord in various age groups

AGE GROUP →	1) 0-10 YEARS	2) 11-20 YEARS	3) 21-30 YEARS	4) 31-40 YEARS	5) 41- 50 YEARS	6) 51-60 YEARS	7) >60 YEARS	M	F	Total	Avge age in yrs	Avge duration of symptoms in months
LESIONS ↓												
TUBERCULOSIS	–	1	10	3	4	2	–	14	6	20	31.4	5.23
ARACHNOID CYST	1	–	1	–	–	1	–	1	2	3	41	5.33
GANGLIONEUROMA	1	–	–	–	–	–	–	–	1	1	9	3
EPIDERMAL CYST	–	2	1	–	–	–	–	3	–	3	17.33	23.27
ASTROCYTOMA	1	4	1	2	–	–	–	6	2	8	19.5	7.20
MENINGIOMA	–	1	1	5	5	2	1	5	10	15	42.8	8.16
NEUROFIBROMA	1	2	1	1	–	1	–	3	3	6	27.6	22.27
SCHWANNOMA	1	2	7	3	4	2	–	10	9	19	34	13.8
EPENDYMOMA	–	–	2	1	–	1	–	3	1	4	34.75	2.75
PARAGANGLIOMA	–	–	–	1	–	–	–	–	1	1	35	48.67
METASTATIC CARCINOMA	–	–	–	–	2	2	1	3	2	5	55.4	2.93
TOTAL	**5**	**12**	**24**	**16**	**15**	**11**	**2**	**48**	**37**	**85**	**31.61**	**12.96**

Table 2: Clinical Manifestations in lesions of spinal cord and its covering

CLINICAL FEATURES	NUMBER OF CASES	PERCENTAGE (n=85)
Swelling of back	4	4.7
Backache	48	56.47
Weakness of lower limbs	16	18.82
Paraplegia	25	29.41
Pain in limbs	18	21.17
Paresthesia	18	21.17
Radiating pain	1	1.17
Incontinence of urine	4	4.7
Headache	2	2.35
Painful neck rotation	1	1.17
Vomiting	1	1.17
Sinus Discharge	1	1.17
Previous surgery	1	1.17

Table 3: Site wise distribution of lesions of spinal cord and covering

Lesions	Extradural	Intradural Extra–medullary	Intradural intra–medullay	Cervical	Thoracic	lumbar	sacral	total
TUBERCULOSIS	15	4	1	2	9	7	2	20
EPIDERMAL CYST ARACHNOID CYST/	5	1	–	1	3	2	–	6
METASTASIC CARCINOMA	5	–	–	–	4	1	–	5
GANGLIO-NEUROMA	1	–	–	–	1	–	–	1
ASTROCYTOMA	–	–	8	5	2	1	–	8
MENINGIOMA	3	12	–	1	12	2	–	15
NEUROFIBROMA	2	4	–	3	–	1	2	6
SCHWANNOMA	6	13	–	5	5	8	1	19
EPENDYMOMA	–	–	4	–	3	1	–	4
PARAGANGLIOMA	–	1	–	–	–	1	–	1
Total	**37**	**35**	**13**	**17**	**39**	**24**	**5**	**85**

Table 4: Comparison of common entities of spinal cord tumors with various International & National studies.

References	NSCTs* (%)	Meningioma (%)	Neuroepithelial Tumors (%)	Vascular Tumors(%)	Metastasis (%)
Lalitha and Dastur [5]	39.92	25.5	20.9	5.8	–
Schellinger et al [6]	24.4	28.9	29.2	–	–
Kaye et al [7]	32.3	29.7	24.4	–	–
Cheang et al [8]	52.2	15.2	10.9	3.3	–
Herbert H Engelhard et al[9]	21.2	24.4	23.7	–	–
Moein P et al[10]	33.0	15.0	38.0	–	–
Present Study	42.36	25.42	23.52	–	8.47

(* Nerve Sheath Cell Tumor)

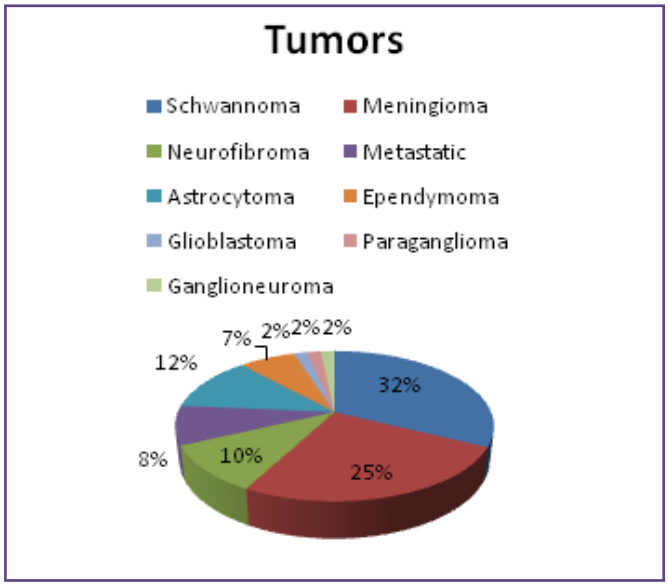

Fig. 1: Spinal cord tumors with their respective percentage

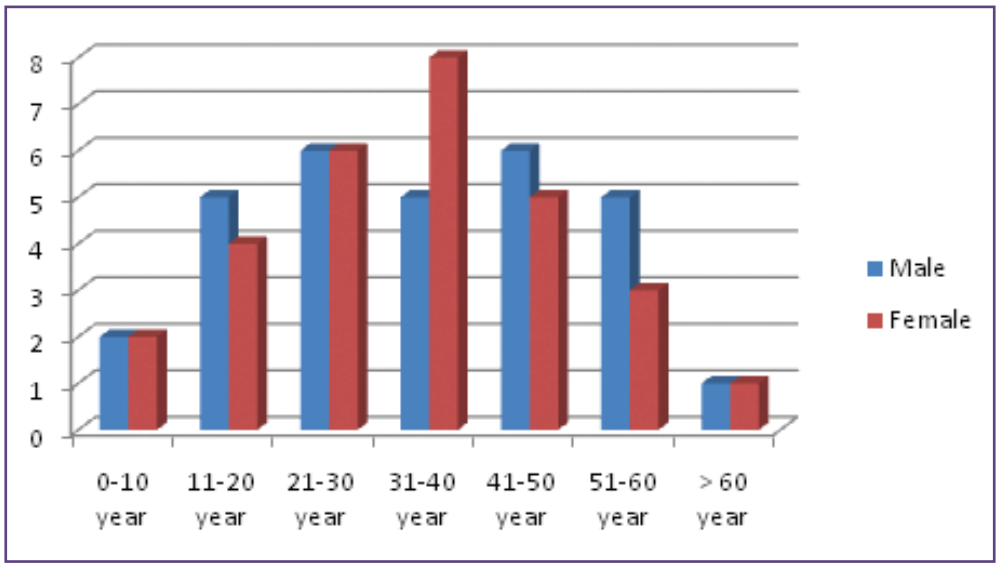

Fig. 2: The relative distribution of spinal cord tumors with respect to age & sex

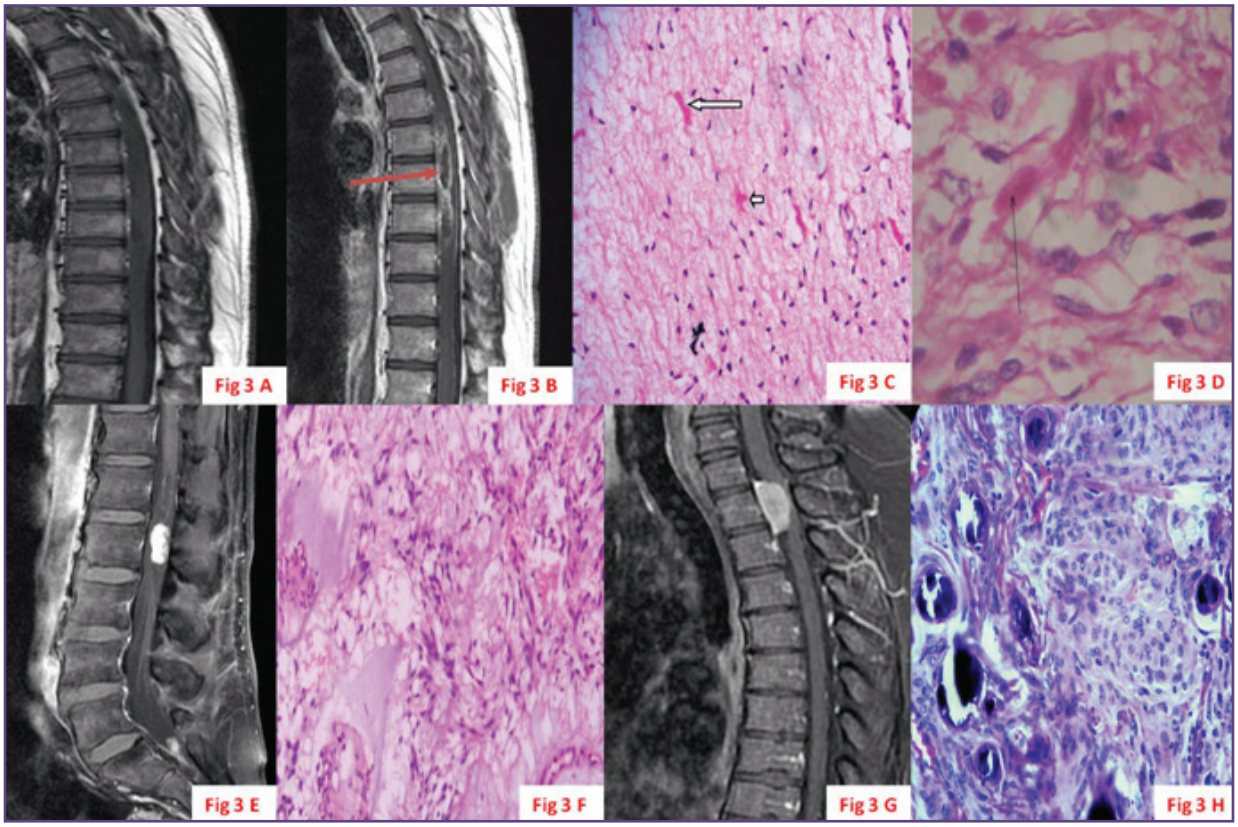

Fig 3: Astrocytoma:MRI-Hypointense lesion with cord expansion extending from T5 to T8 level on T1w image (3 A), Post contrast images demonstrate patchy irregular peripheral enhancement (3 B).Pilocytic astrocytoma (WHO grade I) showing bipolar piloid cells, Rosenthal fibres(arrow) and eosinophilic granular body(arrowhead)(H&E 100x) (3C), showing Rosenthal fibres(arrow) which are PAS positive(PAS Diastase 400x)(3D).Myxopapillary ependymoma (WHO grade I):MRI-well defined post contrast image shows homogenous enhancement of the lesion at the level of L2 (3 E), cuboidal to elongated tumor cells dispersed in a myxoid background (H&E 100x, 400x) (3 F).Meningioma:MRI- intense homogenous enhancement on contrast with a dural tail (3 G), Psammomatous meningioma(WHO grade I) with numerous calcified psammoma bodies and meningothelial cells(H&E 400x)(3 H)

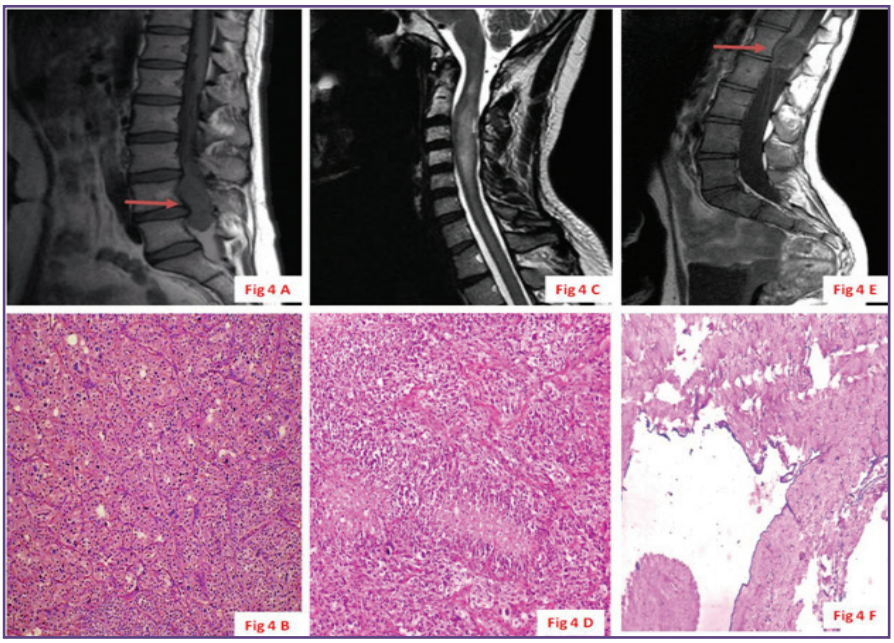

Fig 4: Paraganglioma (WHO grade I): MRI-: Well defined isointense lesion on T1w from L3 to S1 level and hyperintense on T2w (4 A), characteristic "zellballen" pattern of nests of tumor cells separated by fibrovascular stroma (H &E100 (4B). Glioblastoma Multiforme (WHO grade IV): MRI- hyperintense lesion is seen expanding the spinal cord from C2 to C5 on T2w images. The cord is swollen and edematous at this level (4C), foci of necrosis surrounded by radially oriented small fusiform and few undifferentiated glioma cells in a pseudopalisading pattern (H&E 100x) (4D).Arachnoid cyst :MRI- sagittal T1w hypointens showing a sharply defined tumor extending from T12-L1 compressing the spinal cord (4 E), arachnoid cyst showing a cyst wall demonstrating a thin arachnoid layer lined by discrete meningothelial cells (H&E 100x). (4 F).

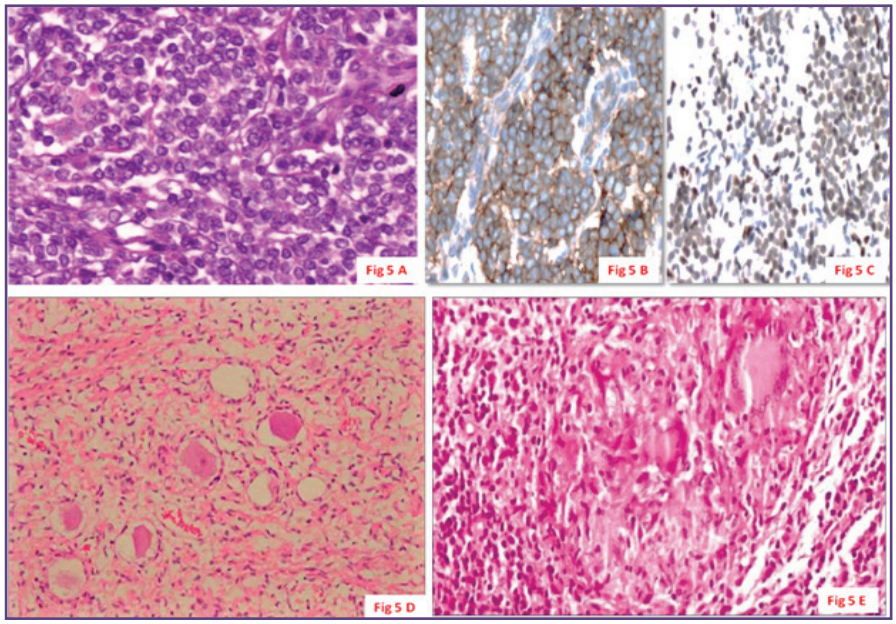

Fig 5: Ewings Sarcoma/p PNET (WHO grade IV): Highly cellular tumor, consisting mainly of small round to oval cells with hyperchromatic nuclei and remarkably scanty cytoplasm (H &E X 400x) (5A), Immunoreactive for MIC2- Strong Cytoplasmic Membranous Positivity (5B), FLI-1 Weak Positive (5C). Ganglioneuroma (WHO grade I): Large ganglion cells scattered in a stroma composed of spindle shaped cells(H &E X 100x) (5D), Characteristic tubercular lesion with Epitheloid cell granuloma with rim of lymphocytes and central caseous necrosis(5E).

Conclusion

The incidence of spinal meningioma is less in developing countries than western populations. Rare histological variants like primitive neuroectodermal tumors should also be considered for histological differential diagnosis of spinal tumors. Intramedullary tumors present at a younger age in developing countries and tuberculosis still should be considered as possible lesion presenting as compressive mass like lesions at this site in Indian population. The ultimate prognosis depends on the histopathological type and grade of the removed tumour, hence pathologist has to play the most important and crucial role in diagnosing and assessing the nature of lesion.

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Competing Interests

None declared

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