



## Primary Intradural Extramedullary Extra-Osseous Ewing's Sarcoma of Cervical Spine(C5-C7) -A CaseReport and Review of Literature

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### ABSTRACT

Ewing's sarcoma is a rare aggressive tumor common in bone or skeletal component. Primary Intradural Extra-medullary Extra-Osseous Ewing sarcoma of cervical spine is extremely rare malignant neoplasm and only few cases have been reported in the literature. There is a paucity of data regarding the clinical features, natural course, pre-operative diagnosis, treatment modalities and post-operative management. Herein, we report a case of a 22-year-old man who presented with inability to walk and numbness in both lower limbs. MRI findings suggested a possibility of nerve sheath tumor but was diagnosed as Intradural Extra-skeletal Ewing sarcoma on histopathological analysis. The literature with regard to primary spinal intradural extra-skeletal Ewing sarcoma was reviewed.

**Keywords:** *Intradural, Extra-skeletal Ewing's Sarcoma, Spine, Nerve Sheath Tumor*

### Introduction

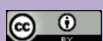
Spinal cord tumors are extremely rare and account for approximately 5-15% of the nervous system tumors <sup>(1,2)</sup>. These tumors are classified based on their anatomic location in relation to the dura mater and spinal cord as epidural, intradural extramedullary and intradural intramedullary. Intradural extramedullary (IDEM) spinal cord tumors account for about 60% of the intraspinal tumors <sup>(3)</sup> and in order of prevalence include schwannomas (30%; incidence rate, 0.3-0.4 cases annually per 100,000 people) <sup>(4,5)</sup>, meningiomas (25%; incidence rate, 0.32 cases annually per 100,000 people) <sup>(5,6)</sup>, neurofibromas, teratomas, lipomas, and metastatic tumors. Ewing's sarcoma is a rare aggressive tumor first discovered by James Ewing in 1921 and the name Ewing sarcoma was coined by Oberling in 1928. It is more common in bone or skeletal component compared to soft tissue or extraosseous location. Extra-osseous Ewing's sarcoma (ES) in intradural extramedullary location are uncommon and are confined to case reports only, thirty cases reported worldwide and only three in India.

### Case History

A 22-year-old gentleman reported to the neuro surgery department with complaints of inability to walk, numbness in both lower limbs, urgency of urine and stool, progressive weakness in the upper limbs and inability to stand and walk after getting up in the morning. Initial evaluation by Neurosurgeon revealed Grade 2 power in hand grip, absent triceps reflex in left upper limb, absent knee Jerk in right lower limb, and plantar and abdominal reflexes were not

elicitable. Right lower limb revealed Grade 4 motor power and Left Lower limb reveal Grade 2 power. There was no bony abnormality, deformity or tenderness in the cervical spine. Complete blood counts, Liver and Renal Function tests were normal. Mantoux test was Negative. Magnetic Resonance imaging reveal Intradural extramedullary mass lesion involving C5-C7 vertebrae with thickening of nerve roots and normal intervertebral foramina. There was no evidence of osteolytic or osteo sclerotic changes seen in the vertebral bodies and possibility of Nerve Sheath tumor was considered and cervical laminectomy was done.

Intra operative exploration revealed a large vascular friable mass pushing the cord dorsally and to the right. Tumor was encasing multiple nerve roots and as there was no plane of cleavage tumor was removed piecemeal and lesion encasing the nerve roots was retained. Histopathological examination revealed a malignant round cell tumor with scant vacuolated cytoplasm and peritheliomatous arrangement of tumor cells. Immunohistochemistry done revealed strong membranous CD-99 positivity and diffuse cytoplasmic positivity for vimentin. Histopathological and Immunohistochemical findings were consistent with Ewing's sarcoma and diagnosis was confirmed by fluorescence in-situ hybridization using a break-apart Ewing's sarcoma Region (EWSRI) probe. Post-surgery patient experienced dramatic relief with improved power in both lower limbs. Patient has subsequently undergone adjuvant treatment with systemic chemotherapy and post-operative radiation in view of residual tumor around the



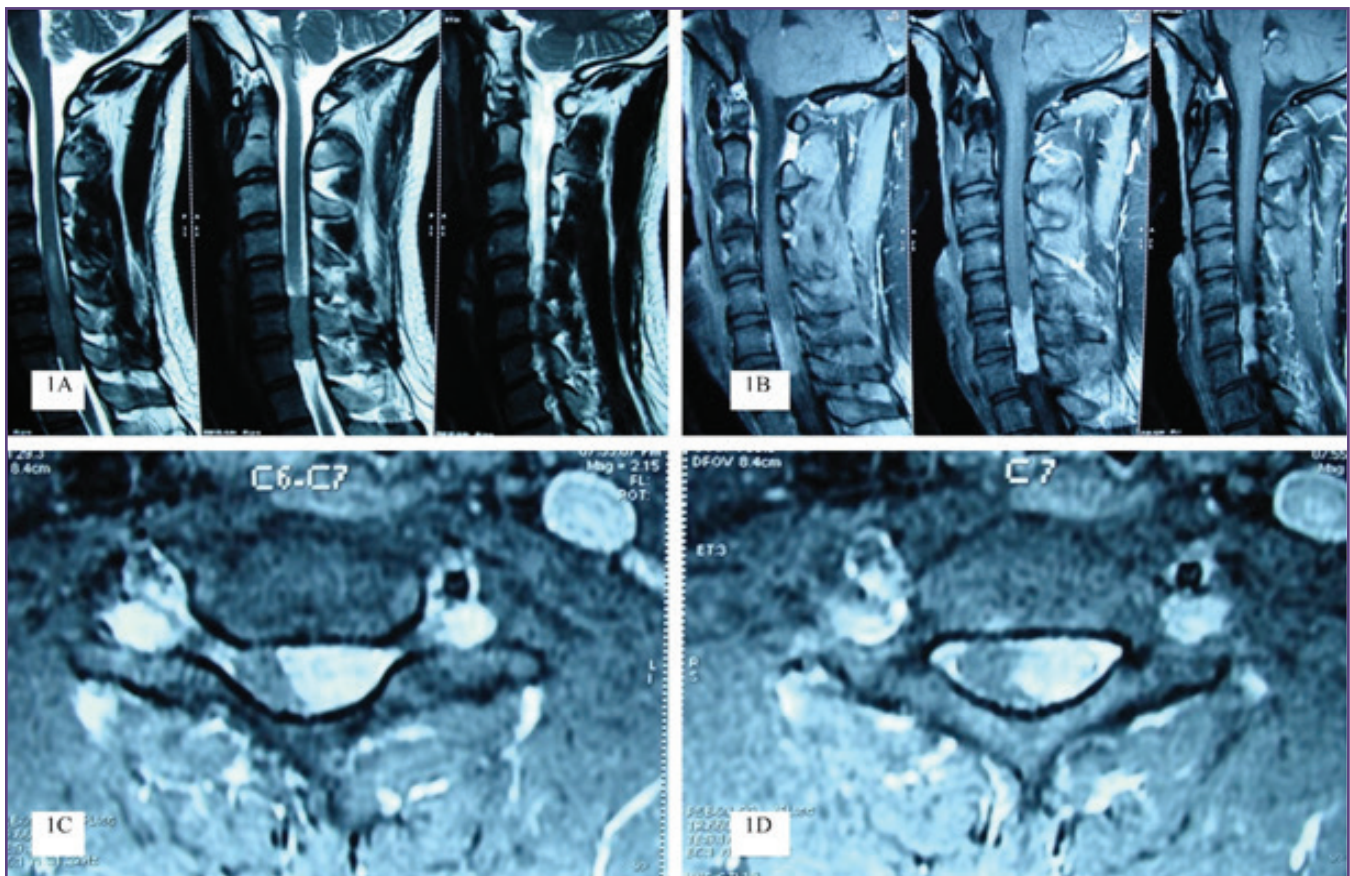
nerve roots. Follow-up metastatic workup which included Chest X-ray, Ultrasound Abdomen, Bone scan, and Bone marrow biopsy were normal.

### Discussion

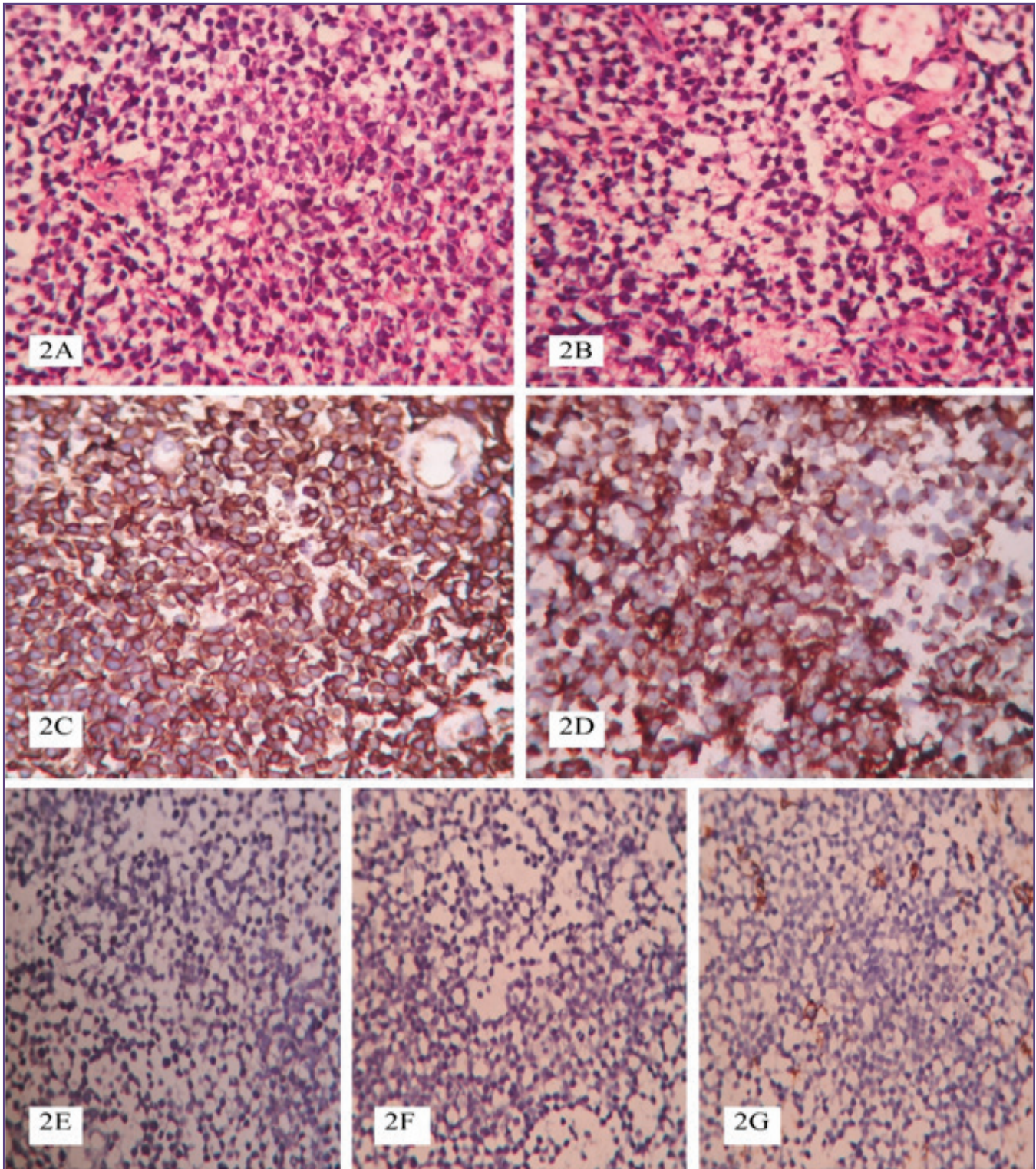
Spinal cord tumors are rare and account for approximately 5% to 15% of nervous-system neoplasms <sup>(2)</sup>. Intradural, extramedullary spinal-cord tumors constitute approximately two-thirds of these tumors. The most common primary intradural extramedullary neoplasms, include meningioma, Schwannoma, neurofibroma and less common entities include solitary fibrous tumor malignant peripheral nerve sheath tumor and leptomeningeal metastasis <sup>(7)</sup>. Intradural, extramedullary Ewing's sarcoma is extremely rare highly malignant tumor and primarily affects pre-adolescents and adolescents with a slight male predilection <sup>(8)</sup>. Total 30 cases of Spinal Extra-osseous Ewing's sarcoma including present case of Intradural extramedullary Ewing's sarcoma have been reported so far in literature worldwide. Out of 30 cases 19 cases were reported in men. Peak age group was

10-20 years. Twenty-two cases involved the lumbar spine and eight cases involved cervical spine. <sup>(9)</sup> In 2003 Uesaka et al. reported first case of intradural extramedullary Ewing's Sarcoma in C7-T1 location in an 11-year-old girl treated by subtotal resection. <sup>(10)</sup> Bouffet et al. in their series of 35 children with spinal metastases described two cases of intradural ES. <sup>(11)</sup> Two cases were reported in India prior to our case. First case was reported by Haresh et al which involved T11-S2 Vertebral levels with skip metastasis. <sup>(8)</sup> Another case of spinal extra skeletal Ewing's sarcoma was reported by Kutty RK et. al and involved cervical epidural space. <sup>(12)</sup> Our case is unique in this context as it involved C5-C7 Vertebrae in intradural extramedullary location.

Patients present with signs and symptoms of spinal cord or nerve root compression which include weakness, localized back pain, radicular pain, sensory deficits, paresis of one or both legs, bladder and bowel dysfunction and gait ataxia <sup>(13,14)</sup>. Our case presented with complaints of inability to walk, numbness in both lower limbs, urgency of urine



**Fig 1: 1A: T2 Weighted Sagittal MRI. 1B: T1 Weighted Gadolinium contrast enhanced MRI. 1C: T2 Weighted Axial MRI at C6-C7. 1D: T2 Weighted Axial MRI at C7. Impression: Isointense -Hypo intense Homogenous enhancing solid Intra-dural extramedullary spinal mass lesion at level of C5-C7 causing compression of spinal cord with adjacent cord edema. Possibility of Malignant Nerve sheath Tumor is considered.**



**Fig. 2A:** Ewing's Sarcoma, H/E stained section showing discretely arranged Round cell tumor X 400. ;**2B:** Ewing's Sarcoma, H/E stained section showing peritheliomatous arrangement of Round cells X 400; **2C:** CD-99/MIC-2, Diffuse Membranous Positivity X 400. **2D:** Vimentin, Diffuse Cytoplasmic Positivity X 400; **2E:** LCA (Leukocyte common antigen), Negative X 400. **2F:** C-KIT/CD-117, Negative X 400. **2G:** MPO (Myeloperoxidase), Negative X 400.

and stool, progressive weakness in the upper limbs and inability to stand and walk after getting up in the morning.

Histopathological analysis is of paramount importance in establishing a diagnosis of Extra-skeletal Ewing's sarcoma and although MRI is non-specific for determining the histology of malignant tumors, it is useful for determining the extent of local involvement with the surrounding structures. With regard to our case after initial clinical evaluation Magnetic Resonance imaging revealed an Intradural extramedullary mass lesion involving C5-C7 vertebrae with thickening of nerve roots and normal intervertebral foramina. There was no evidence of osteolytic or osteo sclerotic changes seen in the vertebral bodies and possibility of Nerve Sheath tumor was considered and cervical laminectomy was done. Histopathological analysis revealed a malignant round cell tumor and possibilities considered were Lymphoma, Ewing's Sarcoma and Extramedullary myeloid tumor. Correlating with immunohistochemical profile of Diffuse membranous positivity with CD 99/MIC-2, diagnosis of Extra-skeletal Ewing's Sarcoma was made and was confirmed by fluorescence in-situ hybridization (FISH) with an EWSR1 break apart probe indicating t (11;22) and rearrangement of the EWS locus. Definitive diagnosis of extra skeletal Ewing sarcoma relies on histopathological assessment and in association with molecular or cytogenetic analysis of the translocation t (11;22) (q24; q12) has been recognized as the diagnostic gold standard<sup>(15)</sup>. Ewing's sarcoma is generally responsive to multimodal therapy comprised of Surgery, Post- Operative radiotherapy and Systemic Chemotherapy. Our case had dramatic clinical recovery with improved power in both lower limbs. Patient underwent adjuvant treatment with systemic chemotherapy and post-operative radiation and follow-up metastatic workup comprised of Chest X-ray, Ultrasound Abdomen, Bone scan, and Bone marrow biopsy were normal.

The 5-year survival rate reported in the literature for Extra-skeletal Ewing's sarcoma of the spinal canal was between 0% and 37.5% consequent to high rates of partial resection of the tumors which in turn resulted in local recurrence, higher mortality and poor prognosis.<sup>(16,17)</sup> Therefore in order to improve prognosis in these cases, it is imperative for the surgeon to remove as much of the tumor and take a call for prompt initiation of post-operative radiotherapy and systemic chemotherapy. In view of the late relapses reported in patients with extra-skeletal Ewing's sarcoma, a longer and closer follow-up and larger series of studies are both required to improve our understanding of the natural course of this disease.

## Conclusion

Extra-skeletal Ewing's sarcoma in intradural extramedullary location is very rare, however it should be considered in the differential diagnosis for initiation of prompt optimal multimodal therapy which includes surgery, local radiotherapy and chemotherapy as Ewing's Sarcoma carries worse prognosis compared to other known common clinical entities described in this region. Histopathological analysis in conjunction with radiological, molecular and immunohistochemical analysis after resection distinguishes the tumor from other common entities in this region.

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## Competing Interest

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