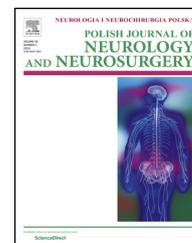


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## Case report

# Intradural extramedullary Ewing's sarcoma: A case report and review of the literature



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## ABSTRACT

**Introduction:** Extra-skeletal Ewing's sarcomas are very rare lesions to the spine surgeon, with the intradural, extramedullary lesions being even rarer. Herein we present a patient with an intradural, extramedullary form of Ewing's sarcoma and review the relevant literature. The medical records, operative reports, radiographical studies and histological examinations of a single patient are retrospectively reviewed.

**Case report:** A 31-year old male presented with back-pain, right-leg progressive paraparesis, and inability to walk. Both motor and sensory disturbances were revealed on the right leg at the clinical examination. Lumbar MRI showed two lesions. The first one was an intradural, extramedullary lesion at the L2-L3 level, while the second was smaller, located at the bottom of the dural sac. The patient underwent gross total resection of the L2-L3 lesion after a bilateral laminectomy. Histological examination was compatible with Ewing's sarcoma, and was verified by molecular analysis. No other extra-skeletal or skeletal lesion was found. A chemotherapy scheme was tailored to the patients' histological diagnosis. The patient presented with local recurrence and bone metastasis 2 years after his initial diagnosis. A second operation was performed and the follow up of the patient showed no disease progression 18 months after revision surgery.

**Conclusion:** The spine surgeon should be aware of the existence of such rare entities, in order to timely fulfill the staging process and institute the proper therapy. The management of patients with extra-skeletal Ewing's sarcomas involves professionals as members of a multidisciplinary team, all of which should co-operate for the patient's optimal outcome.

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Abbreviations: IEES, intradural extramedullary Ewing's sarcoma; MRI, magnetic resonance imaging; RT-PCR, reverse transcriptase polymerase chain reaction; GFAP, glial fibrillary acidic protein; EMA, epithelial membrane antigen; EWS/FLI1, oncogenic transcription factor; RT, radiotherapy.

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## 1. Introduction

Ewing's sarcomas are highly undifferentiated, primitive, malignant, small round-cell neoplasms, arising usually in children and young adults [1]. They are rare tumors that account for 10% of all primary malignant bone tumors in children and 3% of all childhood malignancies [2]. Moreover, they are very aggressive lesions; approximately 25% of patients have metastatic disease at the time of diagnosis [1]. Hereby we report an extremely rare case of an adult male with primary intradural extramedullary Ewing's sarcoma (IEES) of the spine and a skip lesion at the cul de sac of the dural sac, and review the pertinent literature.

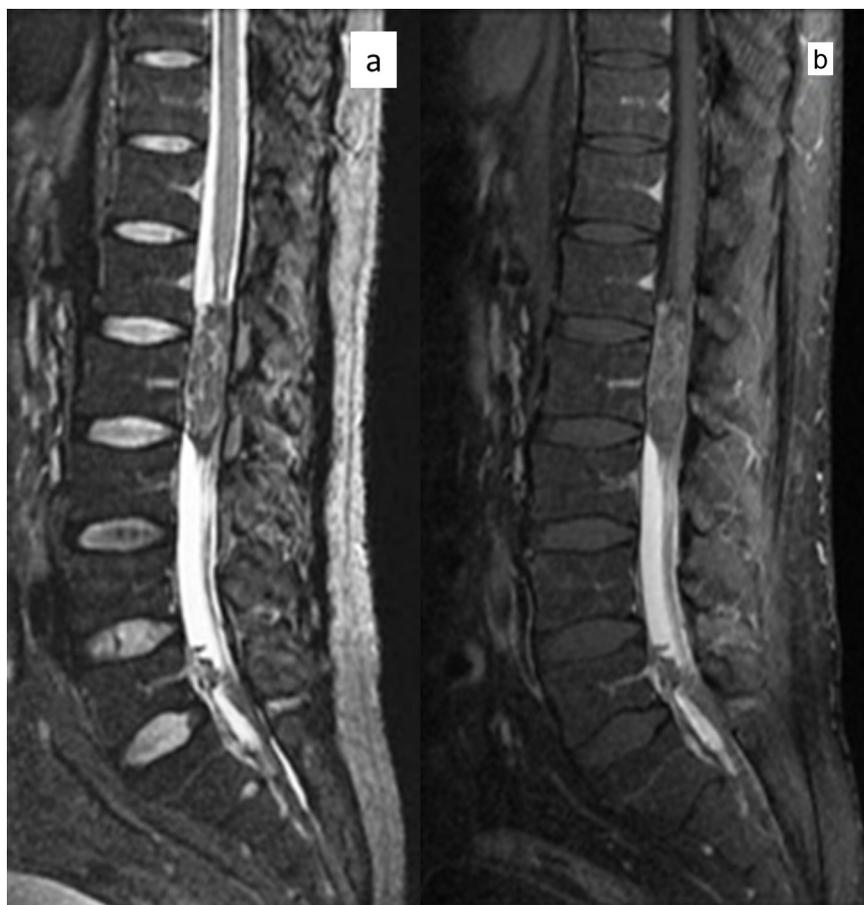
## 2. Case report

A 31-year old male with unremarkable medical history, presented with back-pain, right leg progressive paresis (3/5 in all key muscle groups), causalgia and decreased sensation of the same limb, consistent with cauda equina syndrome. His lumbar spine magnetic resonance imaging (MRI) showed an intradural, extramedullary space occupying lesion behind the

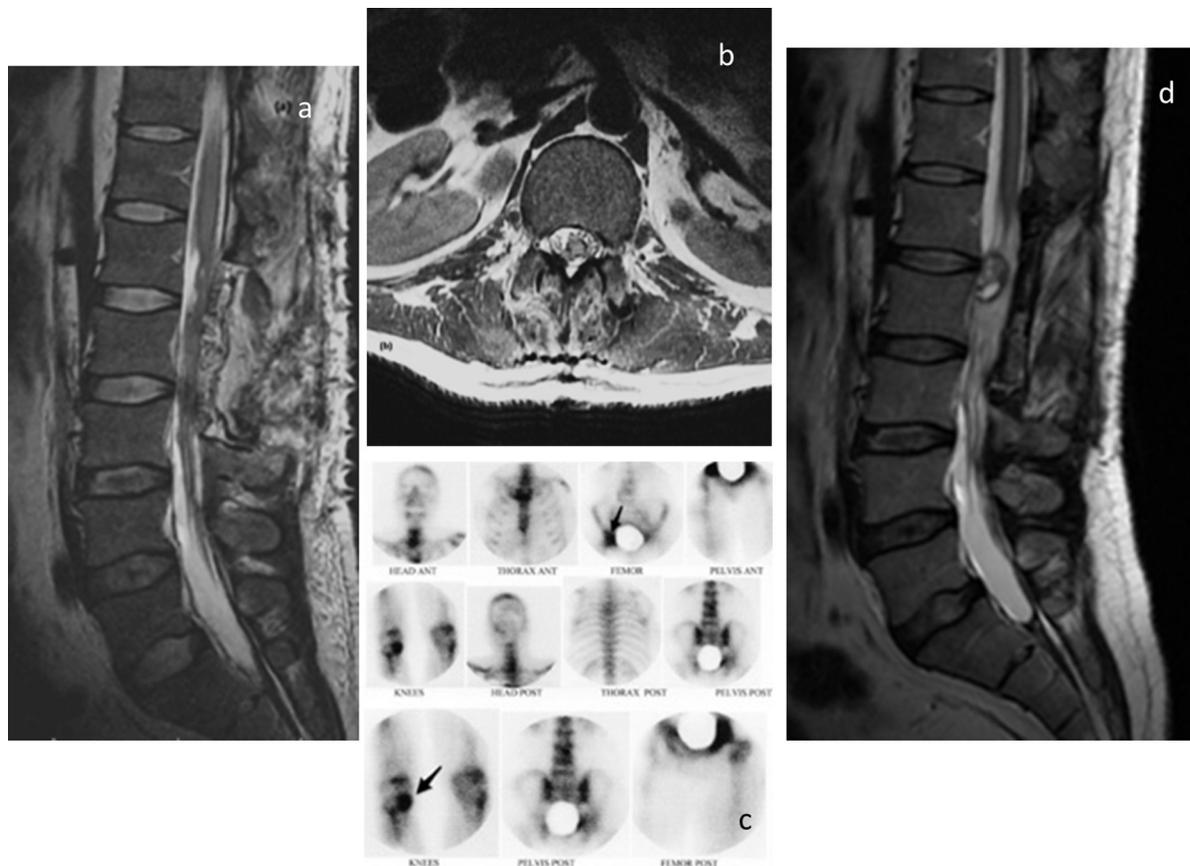
L2-L3 vertebral bodies, 5.2 mm × 1.3 mm in size, occluding the spinal canal and displacing the cauda equina to the left side and posteriorly. A second smaller lesion was found behind the L5 vertebral body with similar imaging characteristics. Both lesions enhanced inhomogeneously after contrast administration (Fig. 1a and b). The differential diagnosis included neoplasms such as the ependymoma, meningioma, neuroinoma and spinal metastasis. Imaging of the neuraxis and thoraco-abdominal staging showed no evidence of other pathologic lesions.

L1-L3 laminectomy was undertaken and a fleshy mass was revealed after opening the dura that intermingled with the lumbar nerve roots. Gross total resection of the tumor was achieved and the specimen was sent for histopathological examination. No attempt was made to remove the second lesion, since there were no neurologic deficits and the surgical decision was to wait for the histology of the resected mass.

Hematoxylin – Eosin stains highlighted neoplastic cells with small, round or ovoid intensely stained nuclei and little cytoplasm with clear demarcation. Immunohistochemistry showed intense and diffuse positivity for CD-99, while did not stain for GFAP, EMA, cytokeratin 8 and 18, AE1/AE3, S-100 and neurofilaments. Reverse transcriptase polymerase chain reaction (RT-PCR) revealed the presence of the EWS/FLI1 fusion



**Fig. 1 – (a) Sagittal short tau inversion recovery MR image shows an intramedullary mass in the conus medullaris, extending from L1-L2 disc, along the L2 vertebral body up to L2-L3 disc. The mass has a heterogeneous low signal and there is a second, skip lesion at the level of L5 vertebral body. (b) Sagittal T1 MR image after intravenous administration of gadolinium shows patchy, moderate enhancement from the mass. Note that the CSF between the main and satellite lesion has abnormal high signal in T1 sequence that enhances, indicative of high protein content or blood.**



**Fig. 2 – (a and b) Postoperative MR images verify the gross total removal of the L2-L3 lesion. (c) 99Tc bone-scan 2 years after the initial diagnosis. The increased technetium uptake (arrows) indicates new metastatic lesions. (d) A 2-year follow-up MRI study shows local recurrence of the sarcoma at the L2-L3 level.**

transcript, specific for the Ewing's family sarcomas/PNET. The immediate postoperative contrast-enhanced MRI showed no remaining mass behind the L2-L3 level (Fig. 2a and b). There was impressive relief of the symptomatology after surgery. Subsequently, the patient was referred to the tumor board meeting of our University Hospital for further management, but was not fully compliant with the treatment protocol proposed including radiotherapy and chemotherapy. His treatment was complemented only with chemotherapy (Vincristine, Doxorubicin, Cyclophosphamide-Mesna, Dactinomycin, Ifosfamide-Mesna and Etoposide), which resulted in complete remission of the residual tumor at the L5 level. Imaging follow-up 3 months after surgery showed no evidence of recurrence at any lumbar level, including L5.

The patient returned with right lower limb symptoms 2 years after the operation. MRI of the right hip and knee showed osseous lesions with imaging features indicative of metastatic deposits. A bone scintigram confirmed increased radioisotope uptake at the right hip and knee region due to distant metastases (Fig. 2c). MRI of the lumbar spine showed local recurrence of the intraspinal tumor at the L2-L3 level without evidence of any other skip lesion (Fig. 2d). The patient underwent revision surgery with subtotal removal of the recurrent tumor due to firm fibrous attachments of the lesion with the adjacent dural walls. After the second operation the patient was referred to oncologists for further treatment. The

patient again received only chemotherapy and refused RT; the patient reported no symptoms suggestive of disease progression 18 months after his second operation.

### 3. Discussion

A total of 27 cases with IEES have been described in the literature (Table 1). This neoplasm is more common in males [3-14] during the 4th decade of life [1,11,15,16] and usually affects the thoracic and lumbar regions [3-7,9-13,15-20]; however, there are a few reports involving cervical spine [14,21-23]. The symptomatology is similar with any other space-occupying lesion of the spinal cord [3-18,20,22]. The MRI usually reveals one or more inhomogeneous lesion, with solid (isointense on T1, hyperintense on T2 and irregularly enhancing after gadolinium administration) and cystic components (hyperintense on T1, with numerous septations and mural nodules) [3,11,15,18]. Systematic screening and screening of the neuraxis for synchronous lesions is justified [3,5,8,9,13,17,22].

The simultaneous existence of two intradural tumors in our patient at the L2-L3 level and the L5 level may be considered as a very unusual presentation pattern. Based on the histological confirmation of the surgically removed lesion, it may be suggested that the excised lesion was the primary tumor and

**Table 1 – Review of reported cases with intradural, extramedullary Ewing's sarcomas.**

Author (year)	Sex/age	Region	Secondary Ewing lesions	Treatment	Follow-up	Outcome	Comments
Bouffet (1997) [3]	M/9.5	T11-T12	L3-L5	Surgery, XRT, Chemo	4 m	Death	–
	M/16	L2-L3	T4-T6, lungs, brain	Surgery XRT, Chemo	5 m	Death	Extra-CNS metastasis
Weil (2001) [13]	M/21	T10-T11	No	STR, XRT, chemo	30 m	Disease free	Concomitant parietal lobe leiomyoma
Rock (2002) [15]	F/61	L4-L5	No	GTR, XRT, Chemo, spinal radiosurgery	5 y	Stable	Recurrence at 4 years, L3 burst fracture
Uesaka (2003) [22]	F/11	C7-T1	No	STR	NA	NA	–
Woestenborghs (2005) [14]	M/11	C4-T2	No	STR, Chemo	NA	NA	–
Mobley (2006) [10]	M/32	L2-L4	No	GTR, XRT, Chemo	12 m	Death	Recurrence at 8 m
Hareesh (2008) [5]	M/26	T11-S2	T6-T7	GTR, XRT, Chemo	6 m	Clinically stable	–
Jia (2009) [6]	M/28	T12-L3	No	GTR	9 m	Recurrence	Misdiagnosed as meningitis, Concomitant hydrocephalus
Klimo (2009) [7]	M/10	L4	No	GTR, XRT, Chemo	12 m	Disease free	–
Kim (2009) [23]	F/32	C3-C5	No	STR, XRT, Chemo	12 m	Disease free	–
Muzzafar (2010) [11]	M/38	L2-S2	No	GTR, XRT, Chemo	2 m	Stable	Two nerve rootlets were sacrificed, DVT
Vincentelli (2010) [16]	F/40	T11-L4	No	STR, XRT, Chemo	6 m	Disease free	Hemorrhagic lesion
Mateen (2011) [9]	M/60	L2-L3	Whole CNS	STR, XRT, Chemo	48 m	Death	Affected the whole CNS
	M/50	T10-L1	No	GTR, XRT, Chemo	26 m	Disease free	–
Karikari (2011) [18]	F/56	L1	No	GTR, XRT, Chemo	NA	Disease free	–
Ellis (2011) [4]	M/35	T12-L2	No	STR	2 m	NA	–
Bazzocchi (2013) [17]	F/44	L4-L5	Thoracic and lumbar levels	GTR, XRT, Chemo	31 m	Recurrence	Breast cancer
Khalabatari (2013) [19]	F/28	L5-S1	No	GTR, XRT, Chemo	6 y	Disease free	Acute hemorrhage and cauda equina syndrome
	M/55	L4-S2	No	GTR, XRT, Chemo	13 m	Disease free	Intratumoral bleeding
Pancucci (2013) [12]	F/25	L2-L3	No	GTR	14 m	Recurrence	History of degenerative leukoencephalopathy
	F/44	L1-S3	No	GTR, XRT, Chemo	6 m	Neurological improvement	Multiple masses
Mardekian (2014) [8]	M/26	T12/L1	No	GTR	NA	NA	–
	M/70	T12-L1	No	STR	NA	NA	History of multiple tumors
Zhao (2014) [24]	M/14	L2-S1	No	GTR, XRT, Chemo	12 m	Clinically stable	Mimicking a giant nerve sheath tumor
Gong (2015) [21]	F/39	C4-C6	No	GTR, XRT, Chemo	3 y	Recurrence and metastasis in cauda equina	–
Present case	M/31	L2-L3	L5-S1	GTR of the L2-L3 lesion, Chemo	3.5 y	Recurrence and metastasis	IEES with skip lesion

M, male; F, female; CNS, central nervous system; GTR, gross total resection; STR, subtotal resection; XRT, external beam irradiation; Chemo, chemotherapy; NA, not available; m, months; y, years; DVT, deep vein thrombosis.

the distal L5 mass represented a skip lesion that fully responded to chemotherapy. Skip intradural metastasis that present simultaneously with the primary intradural lesion is extremely uncommon for Ewing sarcomas with only two cases reported in the literature [3,21].

IEES lesions are soft, friable and fleshy, purple in color and highly vascular [7–9,12,22]. It invades both the spinal cord and nerve roots, without any clear dissection plane [7,9]. Histologically there are numerous small round blue cells arranged in patternless sheets [3,6,9,11,18]. They express high levels of the MIC-2 antigen when stained with the CD99 antibody [3,6,11,18]. RT-PCR analysis depicts a EWS-FLI-1 fusion transcript [22] and fluorescence in situ hybridization analysis highlights the chromosomal translocation t(11;22)(q24;q12) [3,11,18].

The treatment of IEES is multidisciplinary. Gross total resection is usually the goal of surgery [5–12,15–18,22]. However, that is not always possible. Most of the patients benefit from 5–6 cycles of chemotherapy [3,5–7,9,10,12–18,20,22,23] with vincristine, doxorubicin, cyclophosphamide and consolidation with etoposide and ifosfamide. Irradiation with 30–50 Gy at the tumor bed, delivered at approximately 25–28 fractions improves treatment outcome [3,5,7,9–13,15–18,22,23]. However, there is considerable disagreement regarding the management of secondary lesions.

The literature is characterized by huge variations in the duration of follow-up. Pain is relieved in most cases immediately after surgery and there is variable improvement in the neurological deficits [8,24]. IEES have a high tendency for local recurrences [6,10,12,15,17] and distal metastases [3,9,15]

irrespective of the addition of adjuvant treatment (chemotherapy and/or conformal radiation). Prognosis in terms of morbidity and mortality is dismal despite the fact that recent treatment advances have increased disease free survival and extended life expectancy [6,7,9,12,13,15,16,19,24]. The compliance of the patient is also important with respect to tumor response; however, in our case the patient was reluctant to proceed with RT with relative compromise of his survival.

Extraskelatal Ewing's sarcomas should be included in the list of differential diagnosis of intradural extramedullary spinal lesions. Immunohistochemistry and molecular analysis set the diagnosis. Such patients should undergo neuraxis screening and be controlled for intraspinal skip lesions, distant metastatic deposits and disease recurrence. Therefore, a multidisciplinary approach is necessary in order to optimize the treatment planning and final outcome of this subgroup of patients.

### Conflict of interest

None declared.

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### Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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