

## Intradural extramedullary Ewing tumor of the lumbar spine

Sofia Muzzafar, MD; Laurence D. Rhines, MD; Janet Bruner, MD; and Dawid Schellingerhout, MD

A 38-year-old man presented with a highly symptomatic lumbar intradural extramedullary tumor. MRI features strongly suggested a myxopapillary ependymoma, with a possible drop metastasis. No filum terminale or spinal cord attachment to the tumor was seen intraoperatively. Histopathology, surprisingly, indicated a malignant round-cell tumor, strongly CD 99-positive, and FISH indicated a rearranged ESWR1 locus. A diagnosis of Ewing tumor (ET) was made. Only eight cases in the lumbar region have been previously reported.

### Case report

A 38-year-old male presented with progressively worsening back pain, radiating down the bilateral lower extremities, over a period of one year. He developed difficulty in ambulating and sleeping, and numbness in the lateral aspects of both lower extremities, but no bowel, bladder, or sexual dysfunction. Physical examination revealed a distressed patient with an antalgic gait, mildly decreased strength in the right lower limb, and diminished sensation in the right anterolateral thigh.

MRI demonstrated a large intradural, extramedullary mass in the cauda equina extending from just below the conus medullaris at L1/L2 to the tip of the thecal sac behind S2. Superiorly, the mass was solid, extending from L1/L2 down to L3/L4, showing hypointensity on T1-weighted images (Fig. 1, yellow arrow), isointensity on T2WI (Fig. 2, yellow arrow), and modest enhancement (Fig. 3, yellow arrow). This solid component measured 6.5 cm in the vertical dimension and entirely filled the spinal canal. Below the

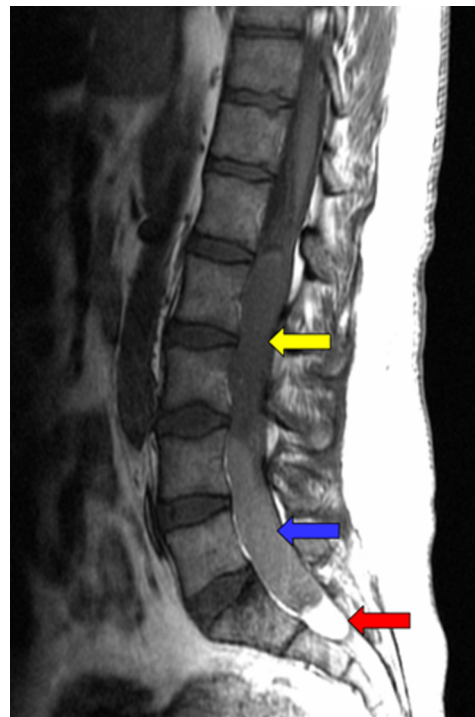


Figure 1. 38-year-old male with intradural extramedullary lumbar spinal Ewing tumor. Sagittal, noncontrast, T1-weighted image shows a large intradural tumor filling the spinal canal. It has a hypointense solid component (yellow arrow) and two cystic components. These are mildly and intensely hyperintense, the latter due to the proteinaceous nature of the cystic fluid (blue and red arrows, respectively).

**Citation:** Muzzafar S, Rhines LD, Bruner J, Schellingerhout D. Intradural extramedullary Ewing tumor of the lumbar spine. *Radiology Case Reports*. [Online] 2010;5:421.

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**Competing Interests:** The authors have declared that no competing interests exist.

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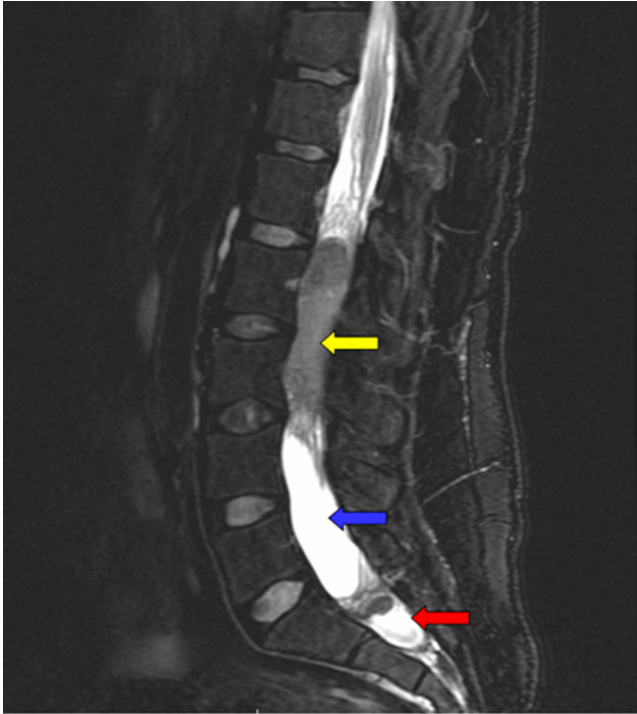


Figure 2. 38-year-old male with intradural extramedullary lumbar spinal Ewing tumor. Sagittal, noncontrast, T2-weighted image shows the solid (yellow arrow) and the cystic components (blue and red arrows) clearly.

solid component, two cystic components measured 6.5 cm and 1.7 cm vertically; they were mildly and very hyperintense, respectively, on T1-weighted images (Fig. 1, blue and red arrows respectively), and both very hyperintense on T2 (Fig. 2, blue and red arrows). These cystic components did not show significant enhancement, although enhancing septations (Fig. 3, green arrow) and mural nodules were present (Fig. 4, red arrow). The high T1-weighted signal in the cystic component suggested high protein content and/or hemorrhage.

Imaging of the rest of the rest of the neuraxis was negative. We made a radiological diagnosis of a probable myxopapillary ependymoma of the cauda equina or filum terminale, with several infratumoral cysts or possibly associated drop metastases.

Intraoperative exploration showed a large, dark purple-gray, tumor mass filling the thecal sac centrally from L1 to the top of L4. It was covered by a thick layer of nerve roots on its dorsal aspect, which were dissected away. No filum terminale or dural attachment was seen. At its inferior pole, the tumor abutted a loculated, xanthochromic CSF collection, consistent with prior episodes of bleeding. The high T1-weighted signal in the inferior cystic component probably represented old blood products. The tumor had to be removed piecemeal because of its large size and soft, fragile texture. We took care to preserve the sensory rootlets, and only two rootlets required sacrifice. The capsule was frail

and the color was a deep dark purple. This was atypical for a myxopapillary ependymoma.

Histopathology demonstrated a malignant small round-cell tumor arranged in patternless sheets (Fig. 5), strong

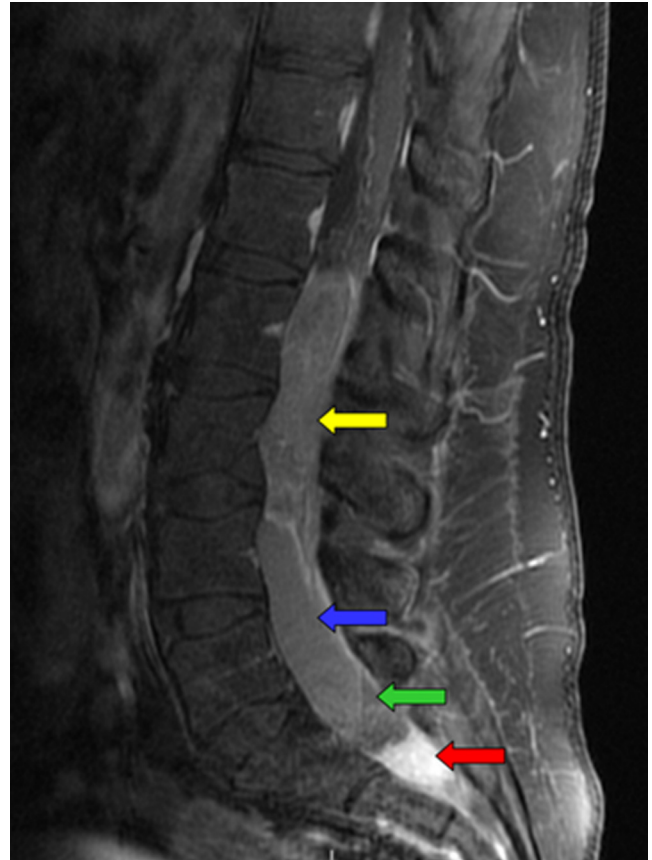


Figure 3. 38-year-old male with intradural extramedullary lumbar spinal Ewing tumor. Sagittal, contrast-enhanced, T1-weighted image with fat saturation (0.1mmol / kg of Magnevist) shows modest enhancement of the solid component (yellow arrow). The cystic component (green arrow) shows enhancing septa. The blue and red arrows indicate the cystic component; the T1 hyperintensity of the inferior component is possibly due to old blood products.

immunopositivity for CD99 with a membranous pattern (Fig. 6), and scattered cytoplasmic immunoreactivity for S-100 protein though negative for keratin--suggesting a Ewing sarcoma. Fluorescence in-situ hybridization using a break-apart Ewing's Sarcoma Region 1 (EWSR1) probe set showed a split signal in about 50% of the interphases, indicating a translocation involving the Ewing sarcoma (EWS) locus (Fig. 7, arrows).

The patient experienced dramatic relief of pain postoperatively, but persisted in having right-lower-extremity dysfunction with paresthesias and gait abnormality. By one month after surgery, these deficits were steadily improving. His postoperative course was complicated by left-lower-

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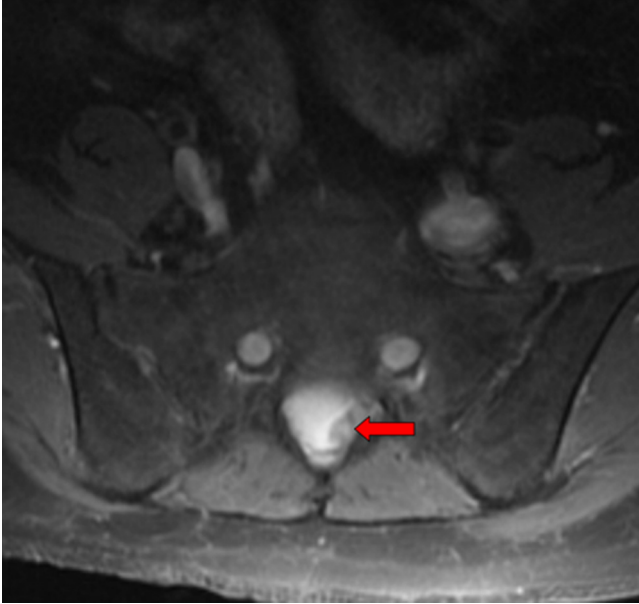


Figure 4. 38-year-old male with intradural extramedullary lumbar spinal Ewing tumor. Axial, noncontrast, T2-weighted image with fat saturation shows the mural nodule (red arrow) in the cystic collection. This was thought to be a drop metastasis initially, but blood products were seen intraoperatively.

extremity deep venous thrombosis, which required treatment with low-molecular-weight heparin. The patient has subsequently undergone adjuvant treatment with systemic chemotherapy.

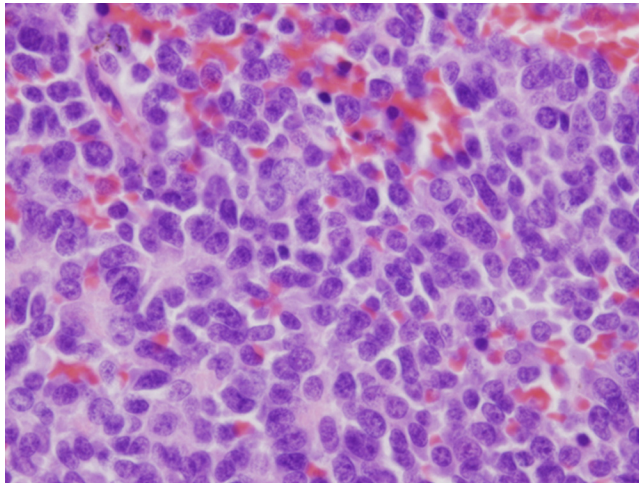


Figure 5. 38-year-old male with intradural extramedullary lumbar spinal Ewing tumor. Tumor consisted of undifferentiated small round cells arranged in patternless sheets. Haematoxylin and eosin. X400.

## Discussion

Extraskelatal ET was first described in 1969 (1) when five soft-tissue, paravertebral, round-cell tumors in children were described. After six years, it was described as a separate entity (2). Extraskelatal ET occurs equally in both sexes

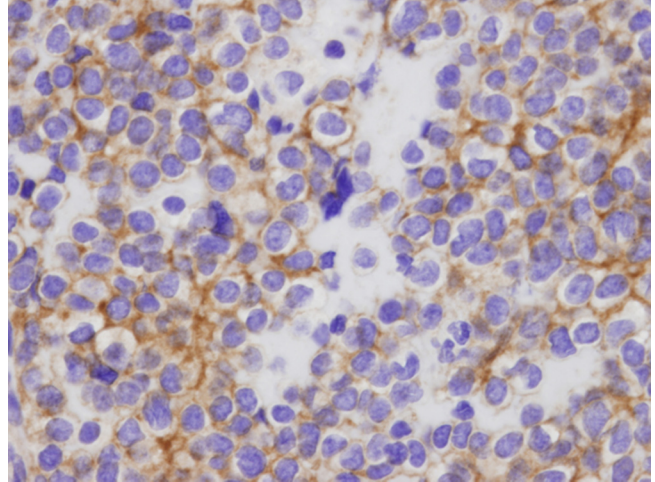


Figure 6. 38-year-old male with intradural extramedullary lumbar spinal Ewing tumor. Immunohistochemistry with CD99 antibody showed diffuse reactivity with a membranous pattern (brown stain), characteristic of Ewing sarcoma. CD99 immunoperoxidase. X400.

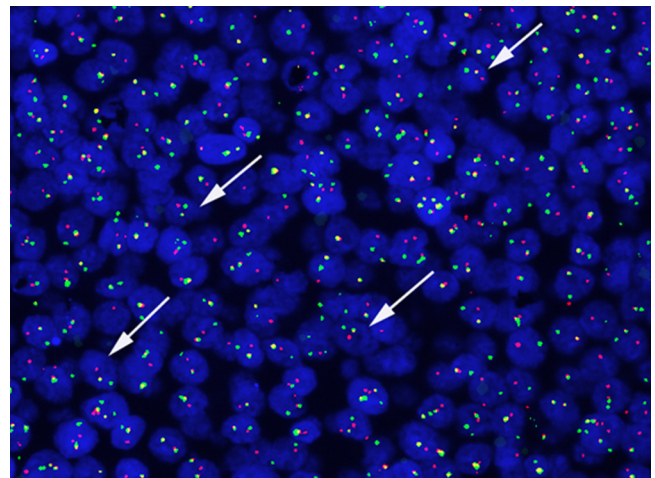


Figure 7. 38-year-old male with intradural extramedullary lumbar spinal ET. Fluorescence in-situ hybridization (FISH) with an EWSR1 breakapart probe set showed numerous nuclei with separate red and green signals (white arrows), indicating rearrangement of the EWS locus, characteristic of Ewing sarcoma. FISH with Vysis EWSR1 probe set. X1000.

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and commonly affects the lower extremities, paravertebral and intercostal regions, head, neck, pelvis, and peritoneum (3-5).

Spinal cord tumors are rare and account for only approximately 5% to 15% of nervous-system neoplasms (6). Intradural, extramedullary spinal-cord tumors constitute approximately two-thirds of these tumors. Schwannomas, meningiomas, and (less frequently) myxopapillary ependymomas are most commonly encountered (7). Intradural, extramedullary ET is extremely rare (8), and only eight cases in the lumbar region have been reported so far. These prior cases are summarized below in the table at the end of this paper. Note that for the purposes of our literature review, we limit ourselves strictly to cases that meet all the following criteria: a) ET (strict histological definition, as opposed to primitive neuroectodermal tumor (PNET)); b) primary tumors only; and c) intradural, extramedullary location.

Three of these cases showed multiple lesions (8, 9) with involvement of the thoracic spine; five others (10-14) showed a single, predominantly solid lesion involving the cauda equina; All of them showed modest postcontrast enhancement on postcontrast MRI scans. One case (12) showed clublike enlargement of the right S1 nerve root, and widening of the lateral recess and the neural foramen. An extradural component was also seen intraoperatively.

Our case is the only one with no involvement of the cauda equina or the filum terminale. The imaging features were unique in that two cystic collections were seen below the solid component of the tumor, and the former were hyperintense on T1- and T2-weighted images. These could be due to cystic expansion and hemorrhage in the tumor.

Our first consideration was myxopapillary ependymoma, a slow-growing tumor arising from the ependymal glia of filum terminale and the most common spinal tumor in this region. Its main imaging features are an enhancing cauda equina mass with hemorrhage. It is usually isointense on T1-weighted images; hyperintensity due to intracellular and perivascular accumulation of mucin may also be seen. It is almost always hyperintense on T2-weighted images. A hypointense hemosiderin rim, the "cap sign," indicating superficial siderosis, is also seen. 70% of intradural spine tumors with hemorrhage are ependymomas. They are intensely enhancing on postcontrast T1-weighted images. Cystic change with a mixture of differing elements such as protein, old hemorrhage, and necrotic tumor tissue is also seen (15-16). Many of these features were seen in our case, but histology and operative findings were discordant and pointed to ET.

Most patients with ET of spine present with back pain. Other symptoms are radicular pain (100%), paresis of one or more limbs (83%), sensory disturbances, and bladder and bowel dysfunction (17). At the cauda equina level, EWS produced less dramatic neurological findings (18).

The Ewing sarcoma family of tumors (ESFT) is a group of morphologically heterogeneous tumors that exhibit non-random chromosomal translocations involving the EWS on chromosome 22p12 and fusion with one of several mem-

bers of the E-twenty-six (ETS) transcription factors. The most frequent translocation is t(11:22) (q24;q12), seen in 90% of ESFT cases. It leads to the formation of EWS/FLI-1 fusion protein, which modulates the expression of target genes and contributes to ESFT pathogenesis (19). Primitive neuroectodermal tumors (PNET) and ET are closely related malignant, small, round-cell tumors of soft tissues and bones. Both strongly exhibit a membranous pattern of immunopositivity for CD99, the product of the MIC2 gene. PNET and ET are neurally differentiated, as evidenced histologically by the expression of at least two neural markers and the presence of Homer-Wright rosettes in PNET. Thus ET is a less differentiated tumor with more primitive histology than PNET (13, 20, 21). PNET of the lumbar spine is also a rare tumor; only six cases have been reported so far (22).

Surgery is necessary to decompress the spinal cord and nerve roots, to resect the tumor, and to establish the diagnosis. The combination of surgical resection, chemotherapy, and radiotherapy offers the best chance to retard the spread of disease and provide disease-free survival. The overall 5-year survival rate for patients with ET was 61%, and the disease-free survival rate was 54%. The majority of intradural, extramedullary ETs reported to date have gone on to develop metastases (22-24). This compares to a survival rate of 94% for myxopapillary ependymomas after surgical resection and 11.5 years of followup (25).

In conclusion, although ETs are very rare, they should be considered in the differential diagnosis of spinal tumors, as the imaging features can be similar to myxopapillary ependymoma. Only molecular and immunohistochemical analysis after resection of the tumor can distinguish these two entities. This is important, as Ewing tumor has a much worse prognosis than myxopapillary ependymoma.

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Table: Summary of lumbar intradural extramedullary Ewing tumor cases					
Year	Age/sex	Number/location of lesions	Metastases	MRI features	Outcome
1997 Bouffet et al (8)	9.5 yrs, M	Multiple lesions T11-T12 + L3-L5	None	Not available	4-month survival
1997 Bouffet et al (8)	16 yrs. M	Multiple lesions T4-T6 + L2-L3	lung, brain, and CSF	Not available	5-month survival
1997 Hisaoka et al (9)	14 yrs. M	Single lesion, lumbar spinal canal; involvement of single nerve root	None	Solid mass with niform postcontrast enhancement	Well 3 months postsurgery
2000 Isotalo (10) et al	52 yrs. M	Single L2/3-L5; 10-cm-long intrathecal tumor; encased spinal nerve roots	None	Solid; postcontrast enhancement	Well 1 year postsurgery
199 Dorfmuller et al (11)	32 yrs M	Single lesion arising from S1; extradural component seen intraoperatively	None	Clublike homogeneous enlargement of right S1 nerve root; widening of the lateral recess and neural foramen	Local recurrence at 4 months with CNS metastases; DOD at 29 months
2006 Mobley et al (12)	32 yrs M	Single lesion L2-4, cauda equina original adherent to and encased by nerve roots	None	Showed postcontrast enhancement	Local recurrence at 8 months, DOD at 12 months
2008 Haresh et al (7)	26 yrs M	Multiple lesions T11-S2; compression of conus; cauda equina involvement; final diagnosis was extradural Ewing tumor	Skip metastases at T6-T7 2 months after surgery and radiotherapy	Minimally enhancing, multiple intradural lesions	Stable 6 months posttherapy
2010 Vincentelli et al (14)	40 yrs F	Single intradural lesion involving cauda equina T11-L4 level	None	Large hemorrhagic mass; no contrast features described	Stable with normal neurological exam 6 months after radiotherapy and chemotherapy

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Table: Summary of lumbar intradural extramedullary Ewing tumor cases					
Year	Age/sex	Number/location of lesions	Metastases	MRI features	Outcome
2008 present case	38 yrs M	Single lesion L1/L2-S2	None	T1W1: minimally hypointense, T2W1: isointense; modest enhancement post-contrast; two fluid collections seen in the sacral canal, slightly hyperintense on T1W1, very hyperintense on T2W1	Stable 2 months postsurgery