A RARE PRESENTATION OF EWING SARCOMA AS A PRIMARY INTRADURAL EXTRAMEDULLARY MASS IN PAEDIATRIC PATIENTS

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Abstract

Ewing sarcoma (ES) is a highly malignant bone tumor that accounts for 25% of all bone tumors in childhood. Primary spinal ES is very uncommon. Primary intradural extramedullary Ewing sarcoma (IEES) is even rarer, and high clinical suspicion is vital to guide accurate management and tissue diagnosis. A 10-year-old boy presented with a 3-week history of non-specific back pain, which worsened and impaired his regular activities. Urgent magnetic resonance imaging (MRI) revealed a thoracic intradural extramedullary mass causing regional compression. Tumor debulking surgery was performed, and histopathological examination of the excised mass was consistent with ES. Early recognition and management of highly aggressive tumors are essential, more so in critical regions such as the spine. Our case emphasises the need to consider ES as a differential diagnosis for spinal tumors in intradural extramedullary locations in the pediatric age group, as the aim of treatment should be curative and not palliative due to high 5-year survivability.

Keywords: Ewing Sarcoma, Extra-skeletal Ewing Sarcoma, Intradural Extramedullary Ewing Sarcoma, Spinal Ewing Sarcoma, Magnetic Resonance Imaging.

Background

Ewing sarcoma (ES) is a highly malignant bone tumor and accounts for 25% of all bone tumors in childhood. Primary spinal ES is very rare and takes up only 3.5 to 14.9% of all primary bone sarcoma (1). The median age of presentation stands at 21 years old (ranges from 12 to 24 years of age) (2). Primary intradural extramedullary Ewing sarcoma (IEES) is even rarer, and diagnosis can only be made with high clinical suspicion, as the initial imaging and clinical presentations are similar to those of benign intradural spinal lesions. Here, we describe a rare case of IEES to highlight the need to include this entity in our differential diagnosis to improve awareness and aid clinicians in early intervention for better outcomes.

Case presentation

A 10-year-old boy presented to us with a 3-week history of non-specific back pain. He also developed lower limb weakness, which progressed to impair his regular activities, and he became unable to ambulate himself for three days, associated with difficulty in passing urine and passing motion for two days. He has no prior history of trauma, falls, or animal bites. His family reported no prior febrile events, flu, or contact with tuberculosis. There were no reported constitutional symptoms. Physical examination revealed loss of sensation from the level of T10 downwards, as well as hypotonia, hyporeflexia, and zero power for both lower limbs.

Urgent magnetic resonance imaging (MRI) was performed to rule out transverse myelitis due to the rapid progression of his symptoms. The MRI revealed a well-defined intradural extramedullary mass within the left spinal canal extending from T7/T8 to T10 levels. The mass was hyperintense on T2-weighted images and demonstrated homogenous enhancement post-gadolinium with no cystic component within. This mass also extended into the left

T8/T9 and T9/T10 neural foramina and caused T8 and T9 exiting nerve root obliteration. There was also T2W/STIR hyperintensity within the spinal cord lower from T7 to T11 level, suggestive of myelopathic changes. Retrospective scrutinisation of pre-MRI spine radiograph in frontal projection reveals subtle loss of left T9 vertebra pedicle, raising suspicion for intraspinal malignancy.

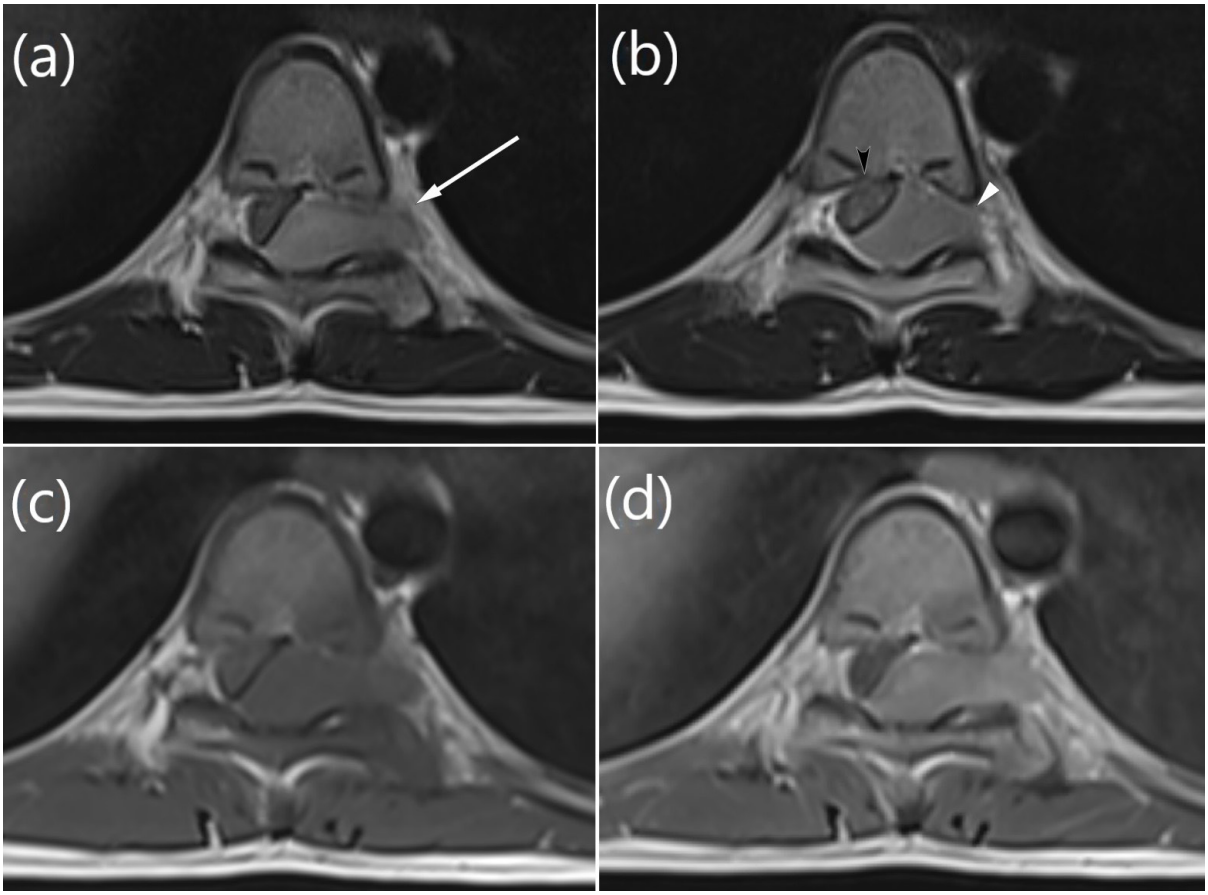

Figure 1: MRI image of the spine in axial view, **(a)** T1-weighted image showing well-demarcated intradural extramedullary mass displacing the spinal cord to the right, and **(b)** homogenous enhancement post-contrast. Further imaging also shows **(c)** obliteration of left T9 neural foramina and **(d)** obliteration of left T8 neural foramina.

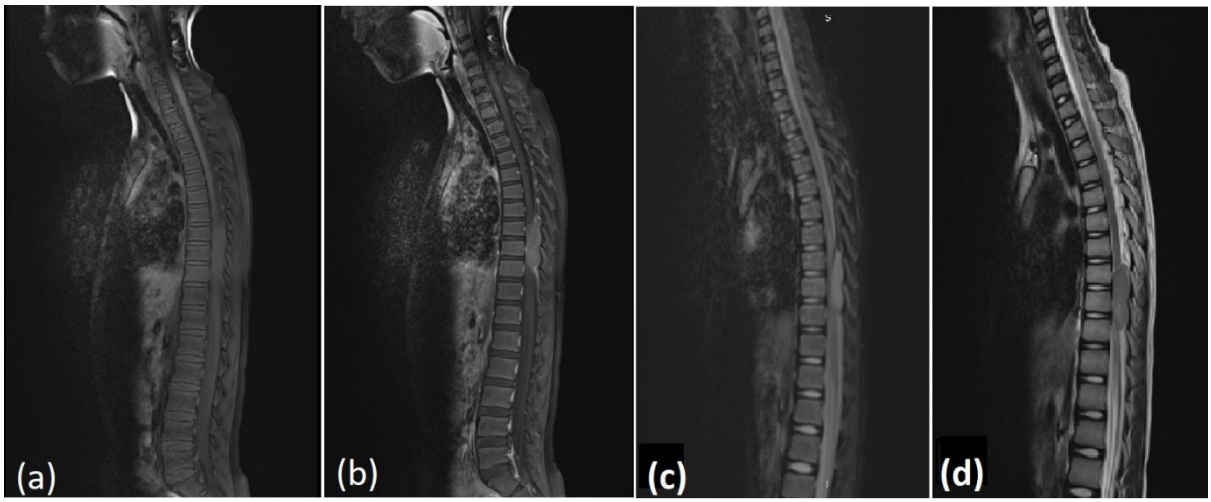

Figure 2: MRI image of the spine in sagittal view, **(a)** T1-weighted fat saturation images; **(b)** post-contrast T1-weighted fat saturation images showing well-defined mass extending from T7/8 to T10 level, with high signal intensity within the spinal cord for both STIR **(c)** and T2-weighted images **(d).**

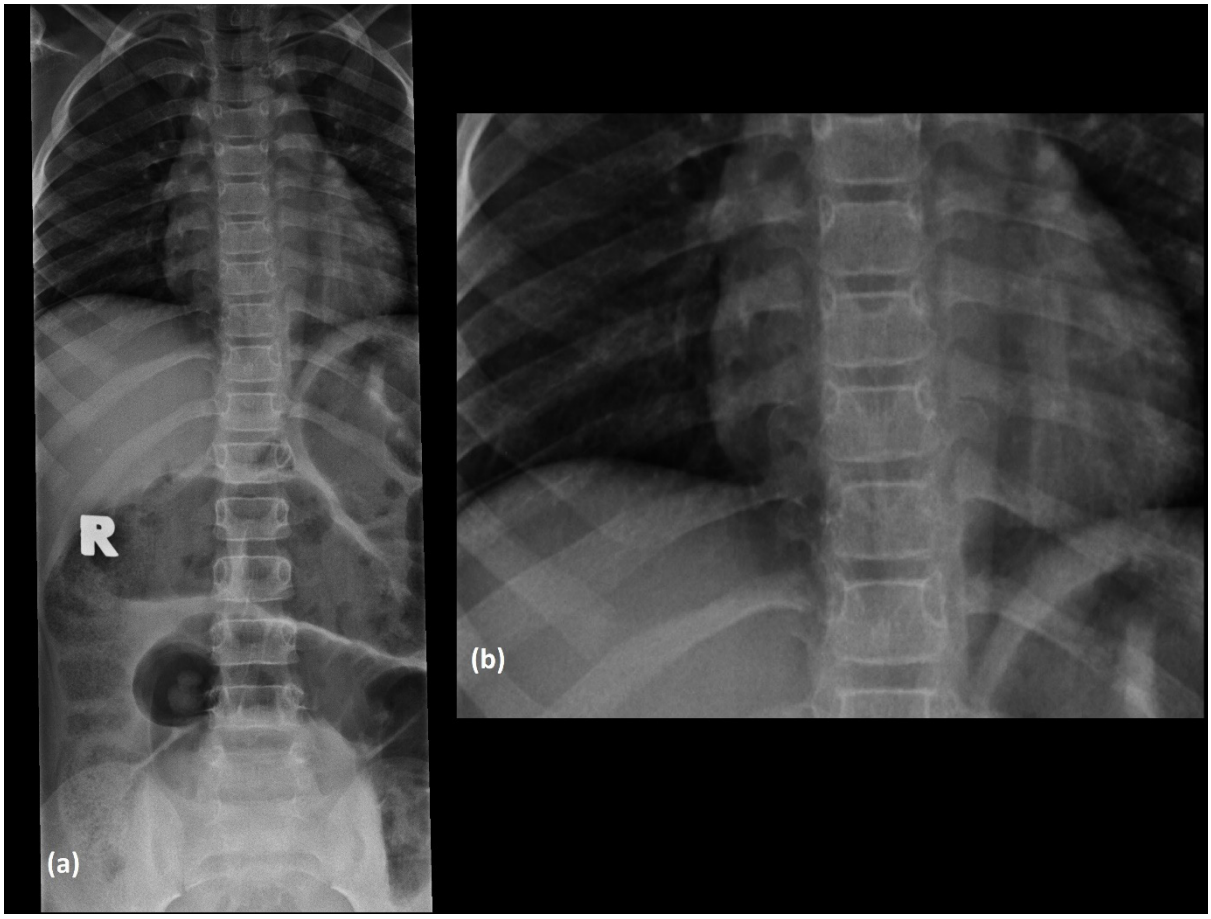

Figure 3: Radiograph of the thoracolumbar spine in frontal projection **(a)** shows loss of left T9 vertebra pedicle (enlarged in **(b)**), giving rise to the "winking owl sign." The differential diagnosis for this includes intraspinal malignancies, spinal metastases, infection or tuberculosis, or primary bone lesions.

We provided a differential diagnosis of peripheral nerve sheath tumor or meningioma. Tumor debulking surgery was performed. The histopathological examination of the excised mass revealed features that were in keeping with Ewing sarcoma. The additional immunohistochemical stain was positive for NKX2.2. A follow-up bone scan with Tc-99^{m} demonstrated no definite metastasis. The pediatric oncology team initiated chemotherapy. The child subsequently showed good responses with records showing progressive motor improvement, from the power of 3/5 at L1 to L3 myotomes, 4/5 at L4, L5 myotomes in June 2022 to the power of 5/5 at L1 to L3 dermatomes; 4/5 at L4/L5 myotomes in March 2023. As of the latest record in March 2023, the child was able to sit up without aid, ambulating well while passing urine and motion normally. Regrettably, the child was then lost to follow-up.

Discussion

Back pain with the presence of rapidly occurring and worsening neurological deficit usually raises suspicion of a sinister aetiology. In the absence of fever or any traumatic event, a tumor of spinal origin tops the list of working diagnoses. In the event that imaging reveals a mass within the spinal cord, it is essential to identify the site of origin to aid clinicians in formulating a plan of management. Conventionally, neoplasms of the spinal cord are classified based on their location, either intramedullary, intradural extramedullary, or at the cauda equina/filum terminale region (3). As for mass arising at the intradural extramedullary site, the list of differential diagnoses includes nerve sheath tumors (neurofibromas or schwannomas), meningiomas, metastatic diseases, myxopapillary ependymomas or paragangliomas (4). The latter two tend to occur more commonly at the filum terminale region (5). Attempts to characterise the lesions via imaging prove to be challenging, with the majority of growth well-demarcated, showing iso to low signal intensity on T1-weighted imaging, high signal on T2-weighted imaging, and with heterogenous contrast enhancement (4, 5). Hyperostosis may be a feature of meningioma but is not as common as its intracranial counterpart (4). As such, a final diagnosis is usually made only after resection and confirmation with immunohistochemical staining, such as in our case.

Our case highlights the need to consider IEES as part of the differential diagnosis of intradural extramedullary lesions in a young patient. ES, other than being known as a highly malignant bone tumor with multiple extra-skeletal sites, is

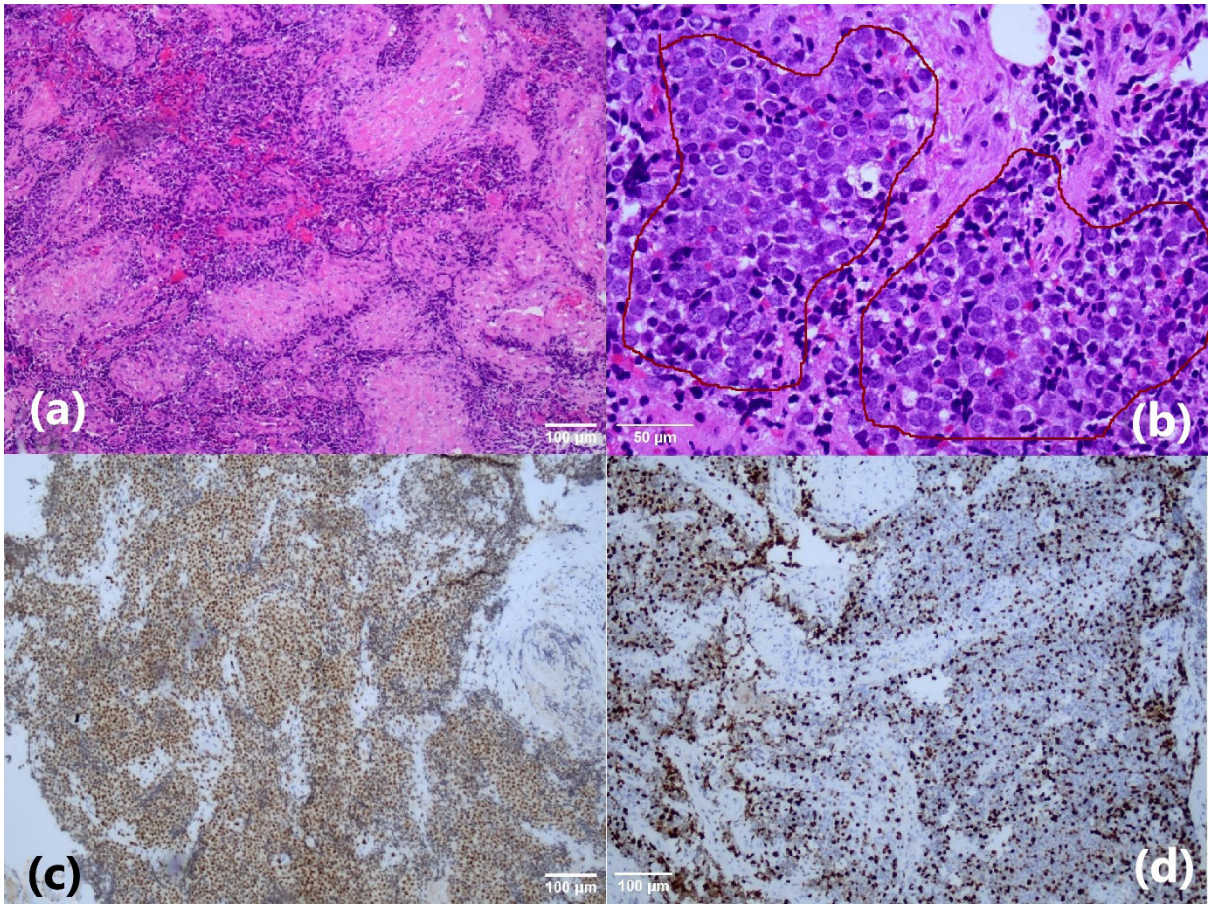

Figure 4: Histopathological examination of the mass: **(a)** Fragments of fibro adipose tissue infiltrated by malignant cells arranged in diffuse patternless sheets, divided by incomplete fibrous bands with a ramifying capillary network; **(b)** The malignant cells (marked in red) are small and round, with round nuclei, finely stippled chromatin, inconspicuous nucleoli and indistinct cytoplasmic membranes; **(c)** The malignant cells are positive for NKX2.2; **(d)** The Ki-67 proliferative index is 70-80%.

also notorious for its high recurrence rate (6-8). Mindful of its possibility, surgeons can plan for better local resection to prevent recurrence once the margins are demarcated clearly on pre-operative MRI (1). The 5-year survivability of EES was reported to be between 38% and 67% but drops to between 0 and 37.5% if the spinal column is involved (8-10). Zöllner et al. (6) recommends Positron Emission Tomography/Computed Tomography (PET/CT) for detection of metastasis. Once diagnosis and staging are confirmed, treatment is usually multimodality and includes excision of mass to achieve local control followed by chemotherapy (2, 11).

Surgical resection with a wide margin yields better survivability, with progressive improvement in neurology, as was reported in our case, which is also mirrored in the cases reported by Electricwala et al. (2) and Joshua et al. (12). Although the cases involving young patients, as reported by Joshua et al. (12), showed overall good outcomes among patients receiving gross total resection of tumor versus that of subtotal resection, Kim et al. (8) caution against the high rate of recurrences in patients with subtotal resection, which in turn increases the mortality rate. Radiation therapy, although sensitive, remains in decline due to complications in immature skeletal patients, and its role is limited to localised, non-resectable cases (13). As for follow-up, a contrasted MRI study along with diffusion-weighted imaging will give additional information to assess response to treatment and to detect recurrences, if any (13, 14).

Conclusion

Early recognition and management of highly aggressive tumors are essential in critical regions such as the spine. Our case emphasises the need to consider ES as a differential diagnosis for spinal tumors in intradural extramedullary locations in the pediatric age group, as the aim of treatment should be curative and not palliative due to high 5-year survivability. Imaging studies such as CT or MRI not only play an important role in early recognition to allow for laboratory confirmation and prompt treatment but also further follow-up, as ES is notorious for high rates of local recurrences.

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Ethical Clearance

Verbal informed consent was obtained from the patient's next of kin for inclusion in this report. According to the Medical Research and Ethics Committee and Institute for Clinical Research Malaysia, research and ethics committee approval for case reports is not a requirement.

Competing interest

The authors declare that they have no competing interests.

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References

1. Dini LI, Mendonça R, Gallo P. Primary Ewings sarcoma of the spine: case report. Arq Neuropsiquiatr. 2006; 64(3A):654-659.
2. Electricwala AJ, Electricwala JT. Primary Ewing's Sarcoma of the Spine in a Two-Year-Old Boy. Case Rep Orthop. 2016; 2016:8027137.
3. Castillo M. Neuroradiology Companion: Methods, Guidelines, and Imaging Fundamentals. Fourth Edition. LWW. 2011.
4. Soderlund KA, Smith AB, Rushing EJ, Smirniotopolous JG. Radiologic-pathologic correlation of pediatric and adolescent spinal neoplasms: Part 2, Intradural extramedullary spinal neoplasms. AJR Am J Roentgenol. 2012; 198(1):44-51.
5. Koeller KK, Shih RY. Intradural Extramedullary Spinal Neoplasms: Radiologic-Pathologic Correlation. Radiographics. 2019; 39(2):468-490.
6. Zöllner SK, Amatruda JF, Bauer S, et al. Ewing Sarcoma-Diagnosis, Treatment, Clinical Challenges and Future Perspectives. J Clin Med. 2021; 10(8):1685.
7. Galyfos G, Karantzikos GA, Kavouras N, Sianou A, Palogos K, Filis K. Extraosseous Ewing Sarcoma: Diagnosis, Prognosis and Optimal Management. Indian J Surg. 2016; 78(1):49-53.
8. Kim SW, Shin H. Primary Intradural Extraosseous Ewing's Sarcoma. J Korean Neurosurg Soc. 2009; 45(3):179-181.
9. Applebaum MA, Worch J, Matthay KK, et al. Clinical features and outcomes in patients with extraskeletal Ewing sarcoma. Cancer. 2011; 117(13):3027-3032.
10. Harimaya K, Oda Y, Matsuda S, Tanaka K, Chuman H, Iwamoto Y. Primitive neuroectodermal tumor and extraskeletal Ewing sarcoma arising primarily around the spinal column: report of four cases and a review of the literature. Spine (Phila Pa 1976). 2003; 28(19):E408-E412.
11. Kunwald M, Straszek CL, Bjarkam CR, Ettrup MS, Skajaa T, Thomsen JL, Thusgaard M, Steiness MZ. Intradural Extramedullary Ewing Sarcoma in an Adolescent Female. Adolesc Health Med Ther. 2022; 13:39-43.
12. Joshua T. Scantland, Mercia J. Gondim, Andrew S. Koivuniemi, Daniel H. Fulkerson, Chie-Schin Shih. Primary Spinal Intradural Extraosseous Ewing Sarcoma in a Pediatric Patient: Case Report and Review of the Literature. Pediatr Neurosurg. 2018; 53(4):222–228.
13. Wright A, Desai M, Bolan CW, et al. Extraskeletal Ewing Sarcoma from Head to Toe: Multimodality Imaging Review. Radiographics. 2022; 42(4):1145-1160.
14. Degnan AJ, Chung CY, Shah AJ. Quantitative diffusion-weighted magnetic resonance imaging assessment of chemotherapy treatment response of pediatric osteosarcoma and Ewing sarcoma malignant bone tumors. Clin Imaging. 2018; 47:9-13.