

Primary Extraskkeletal Ewing Sarcoma of the Mediastinum: A Case Report

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How to cite this paper: Zhu, L.L. and Luo, L.P. (2026) Primary Extraskkeletal Ewing Sarcoma of the Mediastinum: A Case Report. *Journal of Biosciences and Medicines*, 14, 106-113.

<https://doi.org/10.4236/jbm.2026.147010>

Received: May 13, 2026

Accepted: July 4, 2026

Published: July 7, 2026

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Abstract

Ewing sarcoma is a small round cell malignancy originating from peripheral primitive neuroectoderm, predominantly affecting children and adolescents. Primary extraskkeletal Ewing sarcoma arising in the mediastinum is clinically rare but exhibits high malignant potential, with early hematogenous metastasis commonly occurring to the lungs, skeleton, and other organs; regional lymph node metastasis is also relatively frequent. With current combined-modality therapy including surgery and chemotherapy, the 5-year survival rate for patients with Ewing sarcoma has improved to approximately 70%; however, for those presenting with metastatic disease at initial diagnosis, the 5-year survival rate remains below 30%. This article reports a case of primary mediastinal Ewing sarcoma confirmed postoperatively by immunohistochemistry and genetic testing, aiming to enhance clinicians' understanding and diagnostic proficiency regarding this disease.

Keywords

Extraskkeletal Ewing Sarcoma, Mediastinum, CT, MRI, Immunohistochemistry, Genetic Testing

1. Introduction

Extraskkeletal Ewing sarcoma is a poorly differentiated small round cell malignant tumor originating in soft tissues [1] [2]. Its clinical incidence is relatively low, accounting for 1% of soft tissue malignancies. Due to the lack of specific clinical manifestations and diverse sites of origin, the clinical features, imaging findings, and prognosis of this tumor vary, leading to considerable diagnostic difficulty and a high misdiagnosis rate. However, the lesions often exhibit high malignancy and rapid growth, typically presenting as large masses at the time of diagnosis [3].

This article reports a case of Ewing's sarcoma primarily occurring in the mediastinum, aiming to further enhance the understanding of extraskeletal Ewing's sarcoma.

2. Case Report

2.1. Medical History

A 27-year-old male patient was admitted due to “right chest pain for 6 hours.” He experienced sudden-onset persistent severe pain in the right chest without any precipitating factor, radiating to the right shoulder and arm, accompanied by cold sweats and wheezing. He was unable to lie flat, with partial relief of pain when sitting. The pain subsided slightly after approximately half an hour but recurred several times subsequently. He then presented to our emergency department. Electrocardiography revealed no abnormalities, while chest CT showed a mediastinal mass. He was admitted to our department with a diagnosis of “mediastinal mass.” Since the onset of illness, the patient had poor appetite and normal bowel and bladder function, with no significant change in body weight. Past medical history: self-reported appendectomy more than 10 years ago, otherwise unremarkable.

2.2. Image Performance

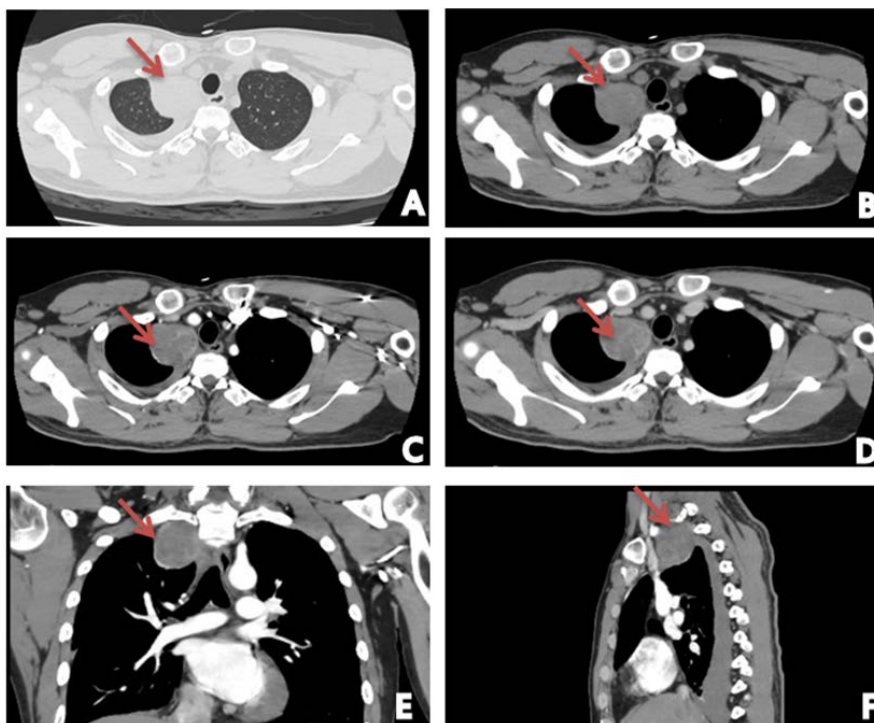


Figure 1. Unenhanced axial CT: lung window (A) and soft-tissue window (B) demonstrate a solid mass (4.5 cm × 4.6 cm × 5.2 cm) in the right superior mediastinum. Contrast-enhanced CT: axial images in the arterial phase (C) and venous phase (D), along with coronal (E) and sagittal (F) reformatted images, demonstrate heterogeneous enhancement of the solid mass.

Our CT showed that a round-like soft tissue density mass was observed in the right superior mediastinum, with smooth margins and relatively clear borders from adjacent tissues, measuring approximately 4.5 cm × 4.6 cm × 5.2 cm. Internal density was heterogeneous with CT values ranging from 35 to 62 HU. The apical segment of the right upper lobe was compressed. Contrast-enhanced imaging showed heterogeneous enhancement. Mild widening of the right neural foramen adjacent to the T2 vertebral body was noted, and fluid density was observed in the right pleural cavity. The aforementioned imaging findings are demonstrated in **Figure 1**.

Our MRI showed that a round-shaped abnormal signal mass was identified at the level of T2-T3 vertebrae in the right superior mediastinum, with smooth margins and relatively clear borders, measuring approximately 4.5 cm × 4.7 cm × 5.2 cm at the largest cross-section. The lesion showed mixed iso-hypointensity on T1WI and mixed hyperintensity on T2WI. Post-contrast imaging revealed marked enhancement of the solid components, with non-enhancing cystic areas within. The apical segment of the right upper lobe was compressed, and mild widening of the right neural foramen adjacent to the T2 vertebral body was observed. The aforementioned imaging findings are demonstrated in **Figure 2**.

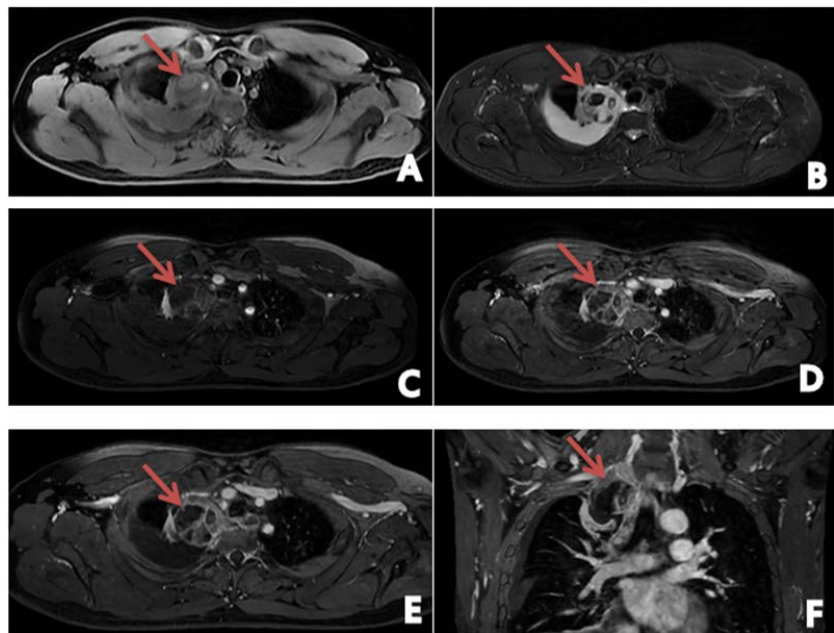


Figure 2. Unenhanced axial T1WI (A) and T2WI (B) show a mixed cystic and solid mass (4.5 cm × 4.7 cm × 5.2 cm) in the right superior mediastinum. Contrast-enhanced MRI: axial images in the arterial phase (C), venous phase (D), delayed phase (E), and coronal reformatted image (F) demonstrate marked enhancement of the solid components.

The basis for diagnosing this case as primary mediastinal extraskeletal Ewing's sarcoma is as follows: (1) Imaging studies showed that the main tumor mass was located in the right upper mediastinum, closely related to the sternum, pericardium, and great vessels, with no evidence of continuous connection to the perios-

teum or bone cortex. (2) Although whole-body bone scintigraphy or PET-CT was not performed, clinical and imaging examinations (including chest CT, abdominal ultrasound, and cranial imaging) revealed no evidence of a primary bone lesion or distant metastasis. (3) Despite the presence of slight right intervertebral foramen enlargement and hemothorax, neither intraoperative nor postoperative pathological findings demonstrated involvement of the spinal canal or vertebral bone. The hemothorax was considered to have resulted from spontaneous tumor rupture. Therefore, a primary bone-origin Ewing's sarcoma and distant metastasis were excluded, confirming a primary mediastinal origin.

2.3. Intraoperative

This patient was admitted emergently due to sudden onset of severe chest pain. Imaging revealed a mediastinal mass with hemothorax, and clinical suspicion was high for tumor rupture with bleeding. Considering the patient's acute symptoms, relatively stable hemodynamics despite the risk of rebleeding, and the close relationship between the tumor and the intervertebral foramen, which might affect the feasibility of complete resection, a multidisciplinary team decision was made to proceed directly with emergency surgical exploration rather than neoadjuvant chemotherapy. Therefore, after full disclosure to the patient and their family, surgical resection was performed directly.

The patient underwent video-assisted thoracoscopic surgery via right thoracic and right cervical incisions for combined cervicothoracic junction mediastinal tumor resection, hemothorax evacuation, and pleural adhesiolysis. After anesthesia, a 1.0 cm incision was made at the 5th intercostal space on the right midaxillary line for thoracoscope insertion. A 3.0 cm incision was made at the 3rd intercostal space on the right anterior axillary line for instruments, and an additional 0.5 cm incision at the 7th intercostal space on the right posterior axillary line served as an accessory port. Exploration revealed hemothorax in the right pleural cavity; approximately 700 mL of blood was evacuated. After pleural adhesiolysis, a tumor measuring about $5 \times 5 \times 5$ cm was identified in the right anterior superior mediastinum near the thoracic apex, with a firm texture. Tumor rupture was noted on its surface, with partial adhesion to the thoracic apex. The tumor was carefully dissected using electrocautery and ultrasonic shears, and mobilized up to the thoracic apex. Considering tumor connection to the thoracic apex and neck, a 4 cm oblique incision was made along the anterior border of the right sternocleidomastoid muscle. The tumor was dissected along the anterior margin of the sternocleidomastoid muscle and the right side of the trachea, then pushed from the neck into the thoracic cavity and completely resected. Frozen section was sent for intraoperative consultation, which indicated a mediastinal tumor with high likelihood of malignancy. After thorough hemostasis and no evidence of significant bleeding, the procedure was concluded. No active bleeding was noted upon re-inspection. The thoracic cavity was irrigated, the lung was fully expanded without air leak, a chest tube was placed, and the incisions were closed.

The patient was transferred to another hospital (a cancer specialty hospital) for further treatment after surgery; therefore, specific details regarding the adjuvant chemotherapy regimen and long-term follow-up data were not available at our center. At the time of last contact, the patient had been transferred to continue treatment.

2.4. Pathology

Microscopy showed tumor proliferation with an irregular nodular pattern. Tumor cells exhibited scant vacuolated cytoplasm, and conspicuous mitotic figures and necrosis were present. Stromal fibrous tissue proliferation with mild lymphocytic infiltration was observed. The findings are shown in **Figure 3**.

Immunohistochemistry: P-CK(-), EMA(-), Vimentin(+), CD99(+), Syn (focal+), CgA(-), TdT(-), CD3(-), CD20(-), INSM1(-), SALL4(-), Ki-67 (approximately 40%+), WT-1(-), Desmin(-), FLI-1(+), ERG(+), CD19(-), PAX-5(-), NUT(-). Based on morphology and immunohistochemistry, the diagnosis was a small round cell undifferentiated tumor, suggestive of possible neuroblastoma or Ewing sarcoma. Genetic testing was recommended for definitive diagnosis to guide treatment and prognosis.

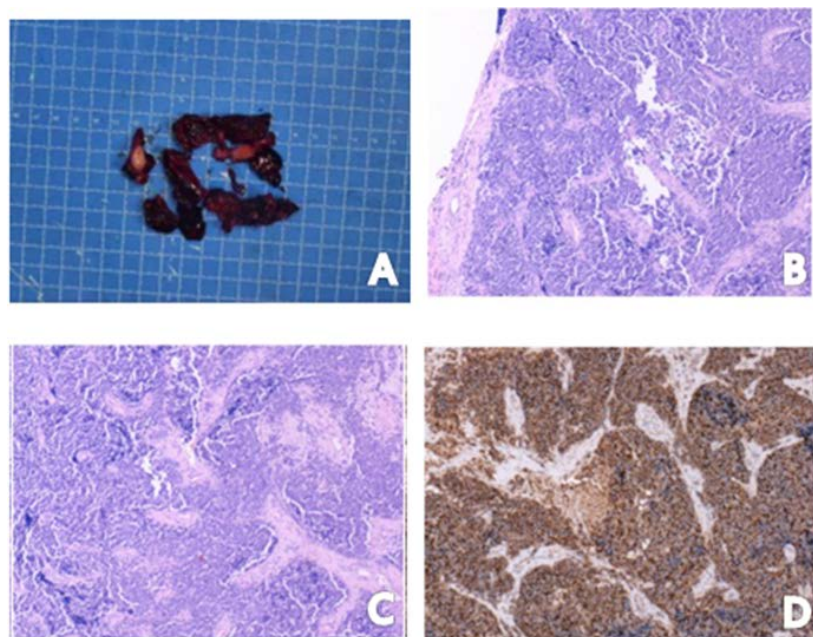


Figure 3. (A) Gross specimen of the mediastinal mass: a collection of gray-white and gray-red fragmented tissue, measuring $5 \times 5 \times 2.5$ cm, containing one gray-yellow to gray-white nodule with a diameter of 1.3 cm. (B)-(D) Microscopy shows irregular nodular tumor proliferation. Tumor cells exhibit scant vacuolated cytoplasm. Conspicuous mitotic figures and necrosis are present. Stromal fibrous tissue proliferation with mild lymphocytic infiltration is also noted.

2.5. Immunohistochemical Analysis

Using next-generation sequencing (NGS) technology based on the Illumina sequenc-

ing platform, testing was conducted on fixed tissue (unstained pathological sections) from the surgically resected specimen. The EWSR1-FLI1 fusion gene was detected in this sample. The EWSR1-FLI1 fusion is predominantly found in extraskelatal Ewing sarcoma/peripheral primitive neuroectodermal tumor (EWS/pPNET) and has also been reported in clear cell sarcomas of soft tissue (soft tissue melanoma), fibrosarcoma, and malignant peripheral nerve sheath tumors, among others.

3. Discussion

Extraskelatal Ewing sarcoma typically grows rapidly but insidiously, with no specific clinical manifestations [4]. When the tumor primarily arises in the mediastinum, patients often lack typical symptoms in the early stage, and the onset is usually characterized by non-specific presentations such as cough, sputum production, hemoptysis, or chest pain. In the event of distant metastasis, corresponding symptoms and signs may develop in the affected organs or tissues.

Radiologically, CT and MRI typically show a round or oval lesion with relatively well-defined borders and heterogeneous internal architecture, which may be complicated by hemorrhage, necrosis, or cystic change; calcification can be observed in some cases. Contrast-enhanced imaging demonstrates heterogeneous enhancement. On MRI, flow-void vascular signals may also be observed. The tumor shows signal intensity similar to muscle on T1-weighted images. In some early cases, abnormal signal intensity in adjacent bone without overt bone destruction may be seen, which could be a relatively characteristic feature of this tumor.

The diagnosis of this disease requires integration of histopathology, immunohistochemistry, and genetic testing results [5]. Microscopically, the tumor is composed of small round cells often arranged in a rosette-like pattern, with hyperchromatic nuclei and scant eosinophilic cytoplasm [6]. Immunohistochemically, diffuse expression of CD99 and FLI-1 is a relatively specific immunophenotypic marker for this disease [7]. For challenging cases, genetic testing is recommended. The characteristic genetic alteration is the fusion of the EWSR1 gene with a member of the ETS gene family (mainly FLI1, ERG, ETV1, etc.), resulting in EWSR1-ETS fusion genes [8], among which EWSR1-FLI1 is the most common and serves as an important molecular diagnostic basis for this disease [9]. Due to its insidious onset, aggressive behavior, and potential for early distant metastasis, the overall prognosis is poor. Therefore, the treatment strategy emphasizes active neoadjuvant chemotherapy before surgery and appropriate timing of surgical intervention. At initial diagnosis, neoadjuvant chemotherapy should be prioritized after comprehensive assessment, followed by radical surgical resection, and supplemented by chemotherapy or local radiotherapy as indicated [10].

Compared with previously reported cases, the distinctive features of this case are as follows: (1) Spontaneous tumor rupture presenting as acute hemothorax was the initial manifestation, which is relatively uncommon in clinical practice. (2) Although intervertebral foramen widening was present, no intraspinal canal invasion was observed, suggesting that the tumor may have grown along the nerve

root sheath without breaching the osseous boundary. A recent review indicated that for localized mediastinal Ewing's sarcoma, neoadjuvant chemotherapy followed by surgical resection can improve prognosis [11]. However, in this case, due to rupture and hemorrhage, emergency surgery was performed rather than elective surgery after neoadjuvant chemotherapy, providing a reference for treatment decisions in emergent situations.

4. Conclusions

Primary extraskeletal Ewing sarcoma arising in the mediastinum is clinically rare, highly aggressive, prone to early hematogenous metastasis, and associated with a poor prognosis. Its insidious onset, nonspecific symptoms and imaging findings contribute to frequent misdiagnosis. In this case, differential diagnosis was established through imaging, immunohistochemistry, and molecular testing [12] [13]. Imaging findings showed no classic dumbbell sign or visible connection to nerve roots, arguing against a neurogenic tumor; no symmetric lymphadenopathy with fusion excluded lymphoma; and no significant calcification or intraspinal canal invasion did not support neuroblastoma. Immunohistochemically, only sporadic Syn positivity did not support neuroblastoma; negative CD3, CD20, PAX-5, and TdT excluded lymphoma; negative NUT ruled out NUT midline carcinoma; and negative WT-1 did not support desmoplastic small round cell tumor. Ultimately, molecular testing revealed a positive EWSR1-FLI1 fusion, which, in combination with CD99 positivity, FLI-1 positivity, and ERG positivity, confirmed the diagnosis of Ewing's sarcoma [14] [15].

Multimodality treatment primarily consisting of neoadjuvant chemotherapy followed by radical surgery can improve outcomes in some patients, but the survival rate remains low for those with metastatic disease at initial diagnosis. Enhanced awareness of this entity, prompt molecular pathological confirmation, and standardized treatment are key to improving prognosis.

Informed Consent Statement

The patient has signed an informed consent form, agreeing to the use of their clinical and pathological data for academic publication.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Song, Q., Liu, L.L., Zhang, Q.S., *et al.* (2022) Extra Skeletal Ewing Sarcoma: A Case Report. *Journal of Practical Hospital Clinical Medicine*, **19**, 211-212. (In Chinese)
- [2] Liu, H.A. and Wang, C.F. (2023) Advances in Molecular Pathology of Ewing Sarcoma. *Diagnosis Theory and Practice*, **22**, 587-592. (In Chinese)
- [3] Chen, K.F., Xie, B.S., Yang, Y., *et al.* (2021) Primary Intrathoracic Extra Skeletal Ewing Sarcoma: A Case Report. *Zhejiang Clinical Medicine*, **23**, 1222-1223. (In Chinese)

nese)

- [4] Lu, Y.L., Niu, H.Y., Hong, C., *et al.* (2025) Primary Intracranial EWSR1-FLI1 Fusion Ewing Sarcoma: A Case Report. *Journal of Diagnostic Pathology*, **32**, 463-464,468. (In Chinese)
- [5] Li, Z.W., Li, T.Y., Xie, F., *et al.* (2015) Imaging Diagnosis of Ewing Sarcoma. *Modern Oncology*, **23**, 3474-3477. (In Chinese)
- [6] Xiong, Z., Yang, G.H., Shi, H.G., *et al.* (2019) Primary Intrathoracic Extra Skeletal Ewing Sarcoma: Two Case Reports. *Chinese Journal of Lung Diseases (Electronic Edition)*, **12**, 121-123. (In Chinese)
- [7] Guan, Y.L., Wang, J., Gong, J.Y., *et al.* (2024) CT Imaging Findings of Renal Extra Skeletal Ewing Sarcoma: A Case Report. *Radiologic Practice*, **39**, 1423-1424. (In Chinese)
- [8] Chen, Y.H., Han, J.X., Zhang, Z.Y., *et al.* (2025) Rare Gastric Ewing Sarcoma: A Case Report and Literature Review. *Journal of Gastroenterology and Hepatology*, **34**, 777-780. (In Chinese)
- [9] Ye, Y., Wen, F. and Wu, Y. (2023) CT and MRI Findings and Pathological Analysis of Extraskeletal Ewing Sarcoma/Primitive Neuroectodermal Tumor. *Journal of Clinical Radiology*, **42**, 1519-1522. (In Chinese)
- [10] Guo, C.Y., Jie, Y.Z., Xu, N., *et al.* (2024) Extraskeletal Ewing Sarcoma: Report of Two Cases and Literature Review. *Journal of Bio-X Research*, **6**, E0876. (In Chinese)
- [11] Chen, L., Qin, Z.D., Zhang, C.F., *et al.* (2025) Pulmonary Ewing Sarcoma: A Case Report and Literature Review. *Medical Theory and Practice*, **38**, 3160-3162. (In Chinese)
- [12] Sun, Y., Lu, Y., He, M., *et al.* (2014) Clinicopathological Observation of Extra Skeletal Ewing Sarcoma. *Journal of Qiqihar Medical University*, **35**, 965-967. (In Chinese)
- [13] Yu, H., Qiu, X., Zhao, Y.T., *et al.* (2017) CT Findings of Renal Primitive Neuroectodermal Tumor/Ewing Sarcoma: A Case Report. *Diagnostic Imaging & Interventional Radiology*, **26**, 337-339. (In Chinese)
- [14] Yang, Y.Q., Liu, L.X., Ji, Y.H., *et al.* (2024) Primary Mediastinal Ewing Sarcoma: A Case Report. *Journal of Practical Radiology*, **40**, 1035-1036. (In Chinese)
- [15] Sun, Q.L., Zhao, X.Y., Tian, B.W., *et al.* (2024) Cutaneous Metastasis of Mediastinal Ewing Sarcoma. *Journal of Clinical Dermatology*, **53**, 358-360. (In Chinese)