

Extraskelatal cervical Ewing sarcoma in a child mimicking tuberculous lymphadenitis: a diagnostic pitfall and review of the literature

Hiba DEHANE ^{1,*}, Rajae BORKI ^{1,2,3}, Amine ADRIUACH ¹, Abir OUTMANI ⁴, Hicham MIMOUNI ^{1,2} and Ilham RKAIN ^{1,2}

¹ Department of Otorhinolaryngology – Head and Neck Surgery, Mohammed VI University Hospital, Tangier, Morocco.

² Faculty of Medicine and Pharmacy, Abdelmalek Essaadi University, Tangier, Morocco.

³ Anatomy Laboratory, Abdelmalek Essaadi University, Tangier, Morocco.

⁴ Department of Radiation Oncology, Mohammed VI University Hospital, Tangier, Morocco.

World Journal of Advanced Research and Reviews, 2026, 30(02), 830-835

Publication history: Received on 28 March 2026; revised on 06 May 2026; accepted on 08 May 2026

Article DOI: <https://doi.org/10.30574/wjarr.2026.30.2.1251>

Abstract

Extraskelatal Ewing sarcoma (EES) is a rare and aggressive malignant tumor belonging to the Ewing sarcoma family of tumors, characterized by undifferentiated small round cells and recurrent chromosomal translocations involving the *EWSR1* gene. Cervical localization in children is exceptional and may mimic infectious or inflammatory conditions, particularly tuberculous lymphadenitis in endemic regions.

We report the case of an 11-year-old child presenting with a rapidly enlarging left laterocervical mass associated with constitutional symptoms. Initial imaging suggested a nodal conglomerate with deep cervical extension. A first biopsy revealed granulomatous inflammation with caseous necrosis, leading to a presumptive diagnosis of tuberculosis and initiation of antitubercular therapy. Clinical deterioration, tumor progression, and compressive symptoms prompted diagnostic reassessment. Repeat pathological evaluation with immunohistochemistry confirmed extraskelatal Ewing sarcoma. The patient was treated with alternating VDC/IE chemotherapy, resulting in an initial favorable clinical response.

This case highlights a major diagnostic pitfall and emphasizes the importance of reconsidering the diagnosis in cases of discordant clinical evolution. Early multidisciplinary management, repeat biopsy, and the use of immunohistochemical and molecular tools are essential to avoid diagnostic delay and improve outcomes.

Keywords: Extraskelatal Ewing sarcoma; Cervical mass; Tuberculous lymphadenitis; CD99; VDC/IE chemotherapy

1. Introduction

Extraskelatal Ewing sarcoma (EES) is a rare malignant neoplasm belonging to the Ewing sarcoma family of tumors, characterized by small round blue cells of neuroectodermal origin and defined by recurrent chromosomal translocations involving the *EWSR1* gene, most commonly *EWSR1-FLI1* [1], [2]. While classical Ewing sarcoma primarily arises from bone, extraskelatal forms account for approximately 10–25% of cases and originate in deep soft tissues [3]. Ewing sarcoma represents the second most common primary malignant bone tumor in children and adolescents, with a peak incidence between 10 and 20 years of age [4]. However, head and neck involvement is uncommon, representing less than 10% of cases, and cervical localization in pediatric patients is exceptionally rare [5], [6].

* Corresponding author: Hiba DEHANE

2. Case report

An 11-year-old child with no significant past medical history was admitted for the management of a large left laterocervical mass evolving over approximately two months in a context of general condition deterioration. Clinical examination revealed a large, firm, hard, painless left cervical swelling without overlying inflammatory signs (Figure 1).



Figure 1 Clinical image showing a large left cervical nodal mass

Initial cervicothoracic computed tomography showed a heterogeneous soft-tissue process, initially described as a nodal conglomerate, responsible for involvement of the nasopharynx, oropharynx, supraglottic region, and deep cervical spaces (Figure 2).

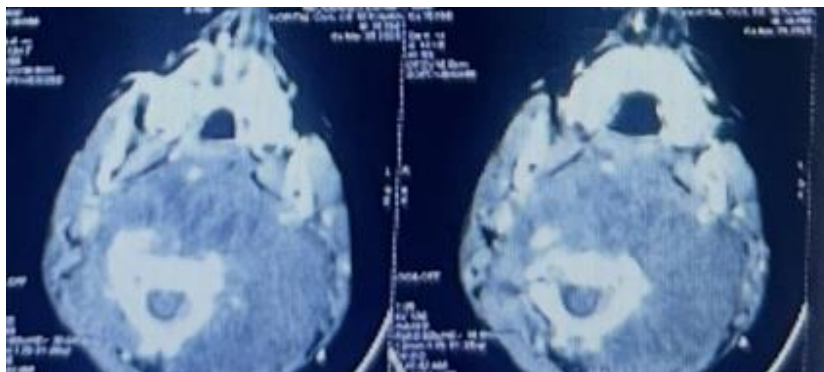


Figure 2 Axial cervical computed tomography (CT) scan showing an infiltrative soft-tissue process involving the cervical soft tissues, with mass effect on adjacent structures

A first biopsy revealed epithelioid and giant-cell granulomatous inflammation with areas of caseous necrosis, leading to the diagnosis of tuberculous lymphadenitis and initiation of antitubercular therapy. However, the clinical course was marked by progressive increase in tumor size, significant locoregional extension, and compressive cervical symptoms. The patient developed acute respiratory distress complicated by hypoxic cardiorespiratory arrest, successfully reversed after resuscitation.

This unfavorable evolution prompted complete diagnostic reassessment. Follow-up imaging demonstrated further tumor progression, with increased mass effect on cervical vascular structures, retropharyngeal and prevertebral extension, and significant compression of the upper aerodigestive tract (Figure 3).

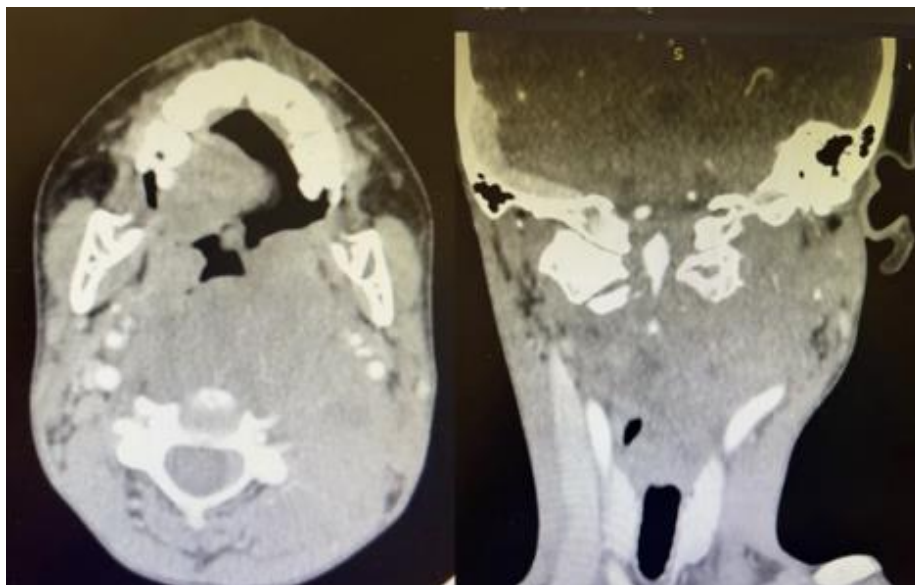


Figure 3 CT images demonstrating tumor progression and worsening mass effect

Given the discordance between the initial diagnosis and the clinical course, repeated biopsies were performed, and pathological reassessment supplemented by immunohistochemistry ultimately established the diagnosis of cervical extraskeletal Ewing sarcoma. Histological examination showed a diffuse proliferation of monomorphic small round cells with hyperchromatic nuclei and scant cytoplasm, associated with extensive necrosis. Immunohistochemistry demonstrated diffuse membranous CD99 expression and nuclear FLI1 positivity, supporting the diagnosis (Figure 4).

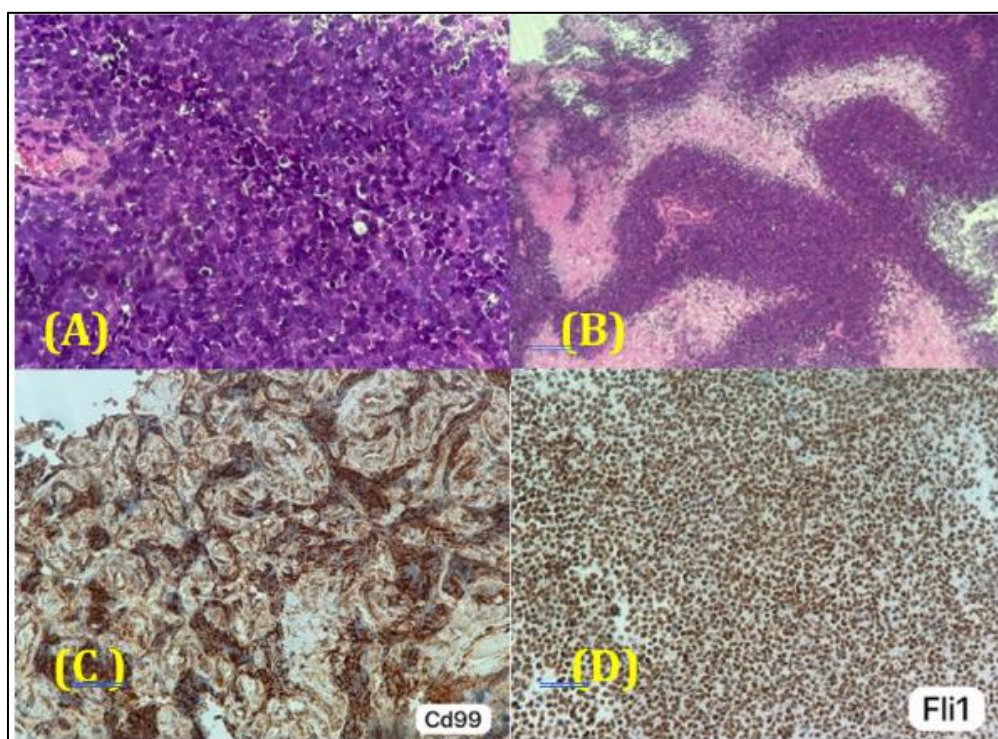


Figure 4 Histological images showing a diffuse tumor proliferation composed of monomorphic small round cells (A), with hyperchromatic nuclei and scant cytoplasm, associated with large areas of necrosis (B). Immunohistochemical analysis demonstrates strong diffuse membranous CD99 expression (C) and nuclear FLI1 expression (D), supporting the diagnosis of Ewing sarcoma

The patient was treated with a multimodal approach combining chemotherapy and radiotherapy. Chemotherapy was administered according to a VDC/IE-based regimen (vincristine, doxorubicin, and cyclophosphamide alternating with

ifosfamide and etoposide), in line with standard treatment protocols for Ewing sarcoma. Radiotherapy was delivered with a decompressive intent to the cervical region, with a total dose of 44.6 Gy in two phases: an initial dose of 32 Gy in 16 fractions of 2 Gy, followed by an adaptive boost of 12.6 Gy in 7 fractions of 1.8 Gy, over a total treatment duration of 34 days. The treatment was well tolerated overall, with only grade 1 radiomucositis and a noticeable reduction in the cervical mass. The patient is currently continuing chemotherapy under oncological follow-up.

3. Discussion

Extraskeletal Ewing sarcoma is an uncommon but aggressive malignancy that shares the same biological and molecular background as conventional osseous Ewing sarcoma. Both entities are currently classified within undifferentiated small round cell sarcomas and are most often driven by *EWSR1-FLI1* fusion, which acts as an aberrant transcription factor and plays a central role in tumor initiation and progression [1], [2]. Despite this well-defined molecular profile, EES remains diagnostically challenging because it may arise in unusual anatomical locations and present with nonspecific clinical findings [3], [4].

Head and neck Ewing sarcoma is rare, and cervical extraskeletal localization in children is exceptional. Recent reviews of head and neck Ewing sarcoma emphasize that these tumors frequently present as enlarging masses with variable pain, inflammatory signs, or compressive symptoms, depending on tumor site and local extension [5], [6].

In the cervical region, deep space involvement may lead to compression of the upper aerodigestive tract, vascular displacement, dysphagia, dyspnea, or acute airway compromise. In our case, the rapid increase in tumor volume and the occurrence of respiratory distress complicated by hypoxic cardiorespiratory arrest illustrate the potentially life-threatening behavior of cervical EES when diagnosis is delayed.

Pathologically, Ewing sarcoma belongs to the spectrum of malignant small round cell tumors. It is typically composed of sheets of relatively uniform small round cells with hyperchromatic nuclei, scant cytoplasm, high mitotic activity, and variable necrosis [1], [2]. Immunohistochemistry is crucial but must be interpreted carefully. Strong diffuse membranous CD99 expression is highly sensitive but not specific, as it may also be observed in other small round cell neoplasms. Nuclear FLI1 expression supports the diagnosis, while NKX2.2 has emerged as a useful adjunctive marker with improved specificity when combined with CD99 and morphology [7]. In the current case, the presence of monomorphic small round cells associated with diffuse CD99 and nuclear FLI1 expression strongly supported the diagnosis of Ewing sarcoma.

Molecular confirmation remains a major diagnostic step, especially in unusual sites or diagnostically difficult cases. The detection of *EWSR1* rearrangement by fluorescence in situ hybridization, reverse-transcription polymerase chain reaction, or next-generation sequencing is considered the gold standard for confirming Ewing sarcoma and distinguishing it from Ewing-like sarcomas [1], [2], [8], [9]. This distinction is increasingly important because the latest classifications recognize several genetically defined round cell sarcoma subtypes, including CIC-rearranged sarcoma, sarcoma with BCOR genetic alterations, and round cell sarcomas with *EWSR1* non-ETS fusions, which may show overlapping morphology but different clinical behavior [2], [8], [9].

The differential diagnosis of cervical EES in children is broad and includes lymphoma, rhabdomyosarcoma, neuroblastoma, poorly differentiated carcinoma, desmoplastic small round cell tumor, and other undifferentiated round cell sarcomas [2], [10]. This diagnostic spectrum reinforces the need for adequate biopsy material, expert pathological review, and a broad immunohistochemical panel [2], [4], [9]. In cases showing discordance between the initial pathological diagnosis and clinical course, early re-biopsy should be considered rather than prolonging ineffective medical treatment.

Management of Ewing sarcoma relies on an integrated therapeutic strategy combining systemic chemotherapy with local control through surgery and/or radiotherapy. Contemporary guidelines and consensus recommendations emphasize that all patients should receive multi-agent chemotherapy because Ewing sarcoma is considered a systemic disease from presentation, even when clinically localized [11], [12]. VDC/IE-based regimens, alternating vincristine, doxorubicin, and cyclophosphamide with ifosfamide and etoposide, are widely used as standard systemic therapy and have improved outcomes compared with older approaches [11], [12]. In cervical EES, local control must be individualized according to resectability, response to induction chemotherapy, expected functional morbidity, and proximity to major neurovascular and aerodigestive structures. Radiotherapy may be preferred or added when complete surgical excision would be mutilating or unsafe [11], [12].

Prognosis depends mainly on metastatic status, tumor volume, anatomical site, completeness of local control, and histological response to chemotherapy [11], [12]. Localized disease has substantially better outcomes than metastatic

or recurrent disease, but head and neck tumors may still pose specific challenges because of delayed diagnosis, complex anatomy, and difficulty achieving complete resection [5], [11]. Our case highlights that early diagnostic reassessment is essential when a presumed infectious cervical mass progresses despite appropriate treatment. In such situations, multidisciplinary collaboration between otolaryngologists, radiologists, pathologists, pediatric oncologists, and radiation oncologists is critical to reduce diagnostic delay and prevent severe compressive complications.

4. Conclusion

Extraskeletal Ewing sarcoma of the cervical region is a rare but aggressive pediatric malignancy that may mimic infectious diseases such as tuberculosis. Diagnostic delay remains a major challenge. Any atypical cervical mass with poor response to treatment should prompt early reconsideration, repeat biopsy, and comprehensive pathological analysis. Early multidisciplinary management is essential to improve outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

This study was conducted in accordance with the Declaration of Helsinki.

Statement of informed consent

Informed consent was obtained from the patient for publication of this case report and accompanying images.

References

- [1] A. Yoshida, « Ewing and Ewing-like sarcomas: A morphological guide through genetically-defined entities », *Pathology International*, vol. 73, n° 1, p. 12-26, janv. 2023, doi: 10.1111/pin.13293.
- [2] C. A. Dehner, A. J. Lazar, et J. S. A. Chrisinger, « Updates on WHO classification for small round cell tumors: Ewing sarcoma vs. everything else », *Human Pathology*, vol. 147, p. 101-113, mai 2024, doi: 10.1016/j.humpath.2024.01.007.
- [3] A. Alexander, K. Hunter, M. Rubin, et A. P. Bhat, « Extrasosseous Ewing's Sarcoma: Pictorial Review of Imaging Findings, Differential Diagnosis, and Pathologic Correlation », *Indian Journal of Radiology and Imaging*, p. s-0041-1729770, mai 2021, doi: 10.1055/s-0041-1729770.
- [4] S. Durer, D. P. Gasalberti, et H. Shaikh, « Ewing Sarcoma », in *StatPearls*, Treasure Island (FL): StatPearls Publishing, 2026. Consulté le: 2 mai 2026. [En ligne]. Disponible sur: <http://www.ncbi.nlm.nih.gov/books/NBK559183/>
- [5] M. H. Spiguel *et al.*, « Ewing's sarcoma of the head and neck: A systematic review », *Oral Diseases*, vol. 30, n° 4, p. 1784-1792, 2024, doi: 10.1111/odi.14644.
- [6] G. A. Almohaisen, S. F. Alhuwairini, M. A. Aljrayed, M. M. Alenezi, et F. Alsaab, « Extraskeletal Ewing's sarcoma of the head and neck region in pediatric patients: A case report and literature review », *International Journal of Surgery Case Reports*, vol. 106, p. 108142, mai 2023, doi: 10.1016/j.ijscr.2023.108142.
- [7] S. Pasricha *et al.*, « Correlation NKX2.2 IHC and EWSR1 break-apart FISH in the diagnosis of Ewing sarcoma: Can combined NKX2.2 and CD99 immunoeexpression obviate or minimize the need of FISH testing? First assessment study from Indian tertiary cancer care center », *Indian Journal of Pathology and Microbiology*, vol. 66, n° 1, p. 58-62, janv. 2023, doi: 10.4103/ijpm.ijpm_535_21.
- [8] M. Sbaraglia, E. Bellan, et A. P. Dei Tos, « The 2020 WHO Classification of Soft Tissue Tumours: news and perspectives », *Pathologica*, vol. 113, n° 2, p. 70-84, nov. 2020, doi: 10.32074/1591-951X-213.
- [9] « Ewing sarcoma and the new emerging Ewing-like sarcomas: (CIC and BCOR-rearranged-sarcomas). A systematic review », *Histology and Histopathology*, n° 11, p. 1169-1181, 2016, doi: 10.14670/HH-11-792.

- [10] S. L. Cohn, « Diagnosis and Classification of the Small Round-Cell Tumors of Childhood », *The American Journal of Pathology*, vol. 155, n° 1, p. 11-15, juill. 1999, doi: 10.1016/S0002-9440(10)65092-4.
- [11] A. Gupta *et al.*, « Consensus recommendations in the management of Ewing sarcoma from the National Ewing Sarcoma Tumor Board », *Cancer*, vol. 129, n° 21, p. 3363-3371, nov. 2023, doi: 10.1002/cncr.34942.
- [12] C. Mata Fernández *et al.*, « Clinical practice guidelines for the treatment of Ewing sarcoma (Spanish Sarcoma Research Group-GEIS) », *Clin Transl Oncol*, vol. 27, n° 3, p. 824-836, août 2024, doi: 10.1007/s12094-024-03602-5.