www.jcimcr.org

JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Case Report

Open Access, Volume 6

A very rare case of a primary pleural Ewing sarcoma with a complete response to chemotherapy

Salsabila Daboussi[1,2]; Syrine Abdellatif[1,6]; Asma Saidane[1,2]*; Bilel Arfaoui[1,3]; Dhia Houk[1,4]; Aida Ayadi[1,5]; Imed Bennouri[1,6]; Sameh Achoura[1.7]; Abdelmajid Sakhri[8]

[1]University of Médicine, Université Tunis El Manar, Tunis, Tunisia.

[2]Pneumology Département, Militari Hospital of Tunis, Tunis, 1008, Tunisia.

[3]Internal Médicine Département, Militari Hospital of Bizerte, 7000, Tunisia.

[4]Radiology Département, Militari Hospital of Bizerte,7000, Tunisia.

[5]Anatomopathology Département, Abderrahmane Mami Hospital, Ariana, 2080, Tunisia.

[6]Emergency Département, Militari Hospital of Bizerte, 7000, Tunisia.

[7]Neurosurgery Département, Militari Hospital of Tunis, 1008, Tunisia.

[8]Pneumology Département, Militari Hospital of Bizerte, 7000, Tunisia.

***Corresponding Author: Asma Saidane**
Pneumology Département, Militari Hospital of Tunis, Tunis, 1008, Tunisia.
Email: drsaidaneasma26@gmail.com

Received: May 15, 2025
Accepted: Jun 06, 2025
Published: Jun 13, 2025
Archived: www.jcimcr.org

DOI: www.doi.org/10.52768/2766-7820/3633

Abstract

The Ewing Sarcoma (ES), which belongs to the primitive neuroectodermal tumor (PNET) family, is the second most common high-graded malignant bone tumor in children and young adults. However, the primary Extraskeletal Ewing Sarcoma (EES) of the pleura is extremely rare and challenging to diagnose. We reported the case of a 13-year-old girl who presented to our Pulmonology department for a right-sided chest pain. The chest CT scan revealed a right-sided pleural mass. Thus, a CT-guided biopsy was performed. The histological exam showed a malignant pleural tumor with many small round cells. Immunohistochemistry was strongly positive for CD99 staining and negative for Cytokeratin and NCAM. The Fluorescence In-Situ Hybridization (FISH) detection of the EWSR1 gene with a (22q12) rearrangement assessed the diagnosis of a pleural Ewing sarcoma. So, our patient had a complete tumoral surgical resection preceded by a neoadjuvant chemotherapy and followed by an adjuvant radio-chemotherapy. We aimed to report this rare malignant tumor unusual clinical presentation. We also reviewed the literature in order to highlight the main Extraosseous Ewing Sarcoma clinical, radiological and histological features.

Keywords: Ewing sarcoma; Pleural; Biopsy; Tumor; Chemotherapy.

Introduction

The Ewing Sarcoma (ES) belongs to the Primitive Neuroectodermal Tumors Group (PNET). It is the second most common high-graded primary malignant bone tumor in children and young adults known for its rapid growth and poor prognosis [1]. It affects mainly long bones, pelvis and the axial skeleton (87%). However, the primary pleural involvement is uncommon (less than 1% of sarcomas). Imaging provides us valuable information regarding the tumor location, size, surrounding lung parenchyma as well as the tumoral staging. The diagnosis is based on the histology combined with the immunochemistry and the genetic analysis findings. We reported here the case of a 13-year-

old girl who presented to our Pulmonology Department with a right-sided chest pain due to an Extraosseous Ewing Sarcoma (EES) originating from the pleura in order to better understand this unusual clinical presentation of this malignant tumor.

Case history

A 13-year-old girl presented to our outpatient department on July 2023, with a persistent right-sided chest pain for two months without dyspnea, fever, cough, sputum nor hemoptysis. She had not any significant past medical history. She was not a smoker. She did not report any environmental exposure particularly to asbestos. She was a student. She is a Caucasian. The thorough physical examination was normal. She was afebrile. She had not any chest deformities. On auscultation, the respiratory sounds were normal in both lungs. Her electrocardiogram was normal. The Chest X-ray showed a basal pleural, homogenous opacity, in the right chest (Figure 1). The Chest CT scan revealed a well-circumscribed right-sided mass with regular borders in contact with the pleura, involving both the right upper and lower lobes. The mass had a homogeneous spontaneous density with some peripheral calcifications and a mild enhancement after the contrast product injection (Figure 2). So, the patient had a CT-guided biopsy. The histological exam showed a malignant pleural tumor with many small round cells (Figure 3). Immunohistochemistry was strongly positive for the CD99 staining and negative for both Cytokeratin and NCAM. The fluorescence in situ hybridization (FISH) analysis detected the EWSR1 gene with a (22q12) rearrangement noticed in 70% of the cells. So, the diagnosis of a primary pleural Ewing Sarcoma was assessed. The Body CT-scan and the bone scintigraphy were negative. Our multidisciplinary team recommended a neoadjuvant chemotherapy in order to reduce the sarcoma size. Our patient had received 9 cycles of a first line chemotherapy based on two regimens alternating either (Vincristine, Doxorubicin, and Cyclophosphamide) (VDC) or (Isocyanide and Etoposide) (IE) every 3 weeks. The Chest CT scan performed after 5 cycles of chemotherapy showed a significant reduction of the pleural tumor

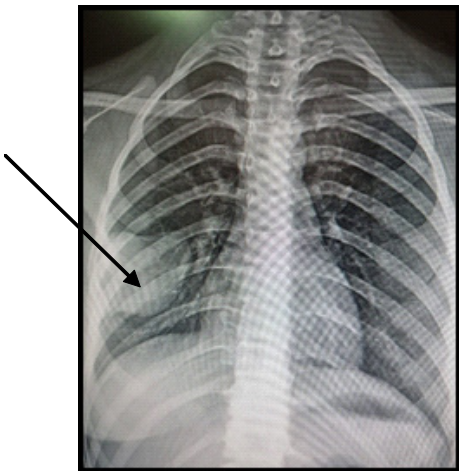

Figure 1: A chest X-Ray showing a right-sided basal pleural opacity (black arrow).

size, with an estimated tumor size decrease of 55%. A thoracic CT scan was performed during the follow-up (at the end of the chemotherapy courses) before the operation. It revealed a partial tumoral regression, with an additional +17% size reduction compared to the previous chest CT scan. So, she underwent surgery under a general anesthesia. The tumor was found on the convexity of the lateral arch of the right 6th rib, measuring about 2.5 cm x 3 cm. She had a complete tumoral resection. The final Histological exam did not reveal any persistent tumor remnants supporting the complete tumoral response with 100% of tumoral necrosis (Grade 4 according to the "Huevos" criteria) and absence of viable tumoral cells. Furthermore, our patient had received 5 additional cycles of an adjuvant chemotherapy as well as a Chest radiation therapy targeting only the tumoral bed, administered during 25 sessions with a total radiation dose of 25 Grays in order to reduce the risk of a tumoral recurrence. She had been disease-free after three months of a regular follow-up.

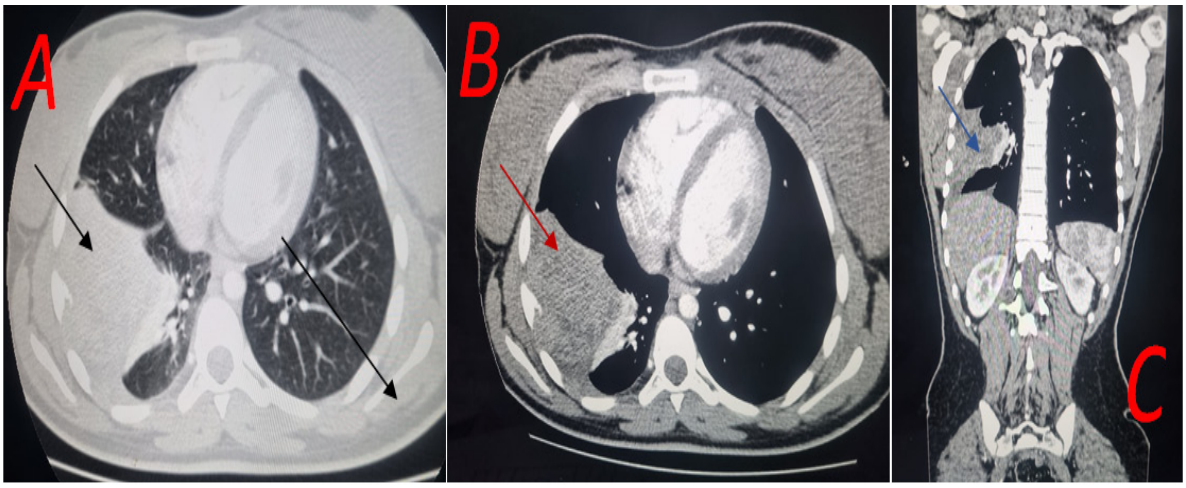

Figure 2: **(A)** Parenchymal CT section showed a right-sided pleural mass (black arrow).
(B) Mediastinal CT section revealed the pleural mass in the right chest (red arrow) without any associated pleural effusion nor mediastinal adenopathy.
(C) Coronal chest CT scan revealed the right-sided pleural mass (blue arrow) with a heterogeneous enhancement after the contrast product injection.

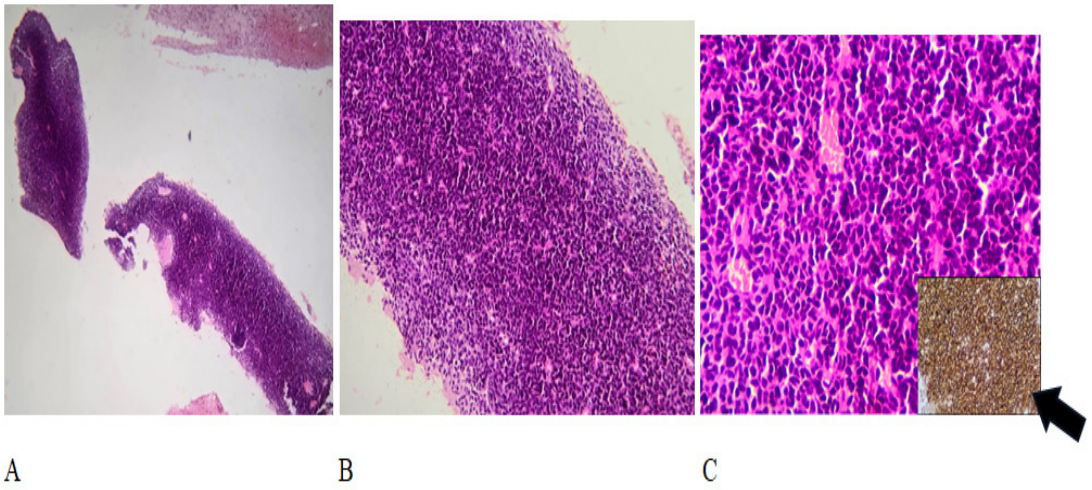

Figure 3: Histological exam findings:
(A) The histological exam revealed a dense, undifferentiated tumoral proliferation.
(B) The anatomopathological exam showed small, round tumoral cells associated with a richly vascularized stroma.
(C) The pleural biopsy examination found round tumoral cells, large monomorphic nuclei with scanty cytoplasm and many mitotic figures with an intense CD99 positive staining on immunohistochemistry (black arrow).

Table 1: Cases of Extra skeletal Ewing's sarcoma of the pleura.

Study, Year	Age (years)	Gender	Primary site	Pleural effusion	Clinical manifestations	Therapy
Juan.L ,2023	22	Male	Right pleura		Asymptomatic	Chemotherapy and surgical excision
Wu.Y, 2023	11	Male	Left pleura	+	Left Shoulder Pain	Chemotherapy and surgical excision
Zou.X, 2021	14	Male	Right pleura		Fever, dyspnea	Radiotherapy and chemotherapy
Bhaskaran.A, 2021	34	Female	Left pleura	+	Fever, Productive cough, right-sided chest pain and back pain	Surgical excision Chest Radiotherapy, Chemotherapy
Mathew.D, 2019	7	Male	Left pleura	+	Dyspnea	Chemotherapy
Tsunezuka.Y, 2012	27	Female	Left pleura		Asymptomatic	Thoracoscopic Surgical resection
Karatziou.C, 2011	21	Female	Left pleura	+	Fever, productive cough	Chemotherapy
Ozge.C ,2004	18	Female	Right pleura		Pain in the back, cough, dyspnea	Not mentioned

Discussion

The Ewing Sarcoma Family of Tumors (ESFT) is a diverse group of highly-graded malignant bone and soft tissue tumors, including the classic Ewing sarcoma, peripheral primitive neuroectodermal tumors and Askin tumors [2]. These tumors share not only common histological and immunohistochemical features but also the same genetic origin: the oncogenic gene fusion EWSR1/FLI1, resulting from a chromosomal translocation between the chromosome 11 and 22. This rearrangement was observed in most of the Ewing sarcoma cases (95%) with a specificity reaching (90%) [3,4]. The Ewing sarcoma is the second most frequent primary malignant bone tumor (10%-15%), affecting mainly the children and young adults under 20 years (80%) [5]. It affects commonly the bones. However, the pleural involvement is very rare (less of 1% of Sarcomas). So, it's often misdiagnosed. A recent study reported 8 cases affected with an extraosseous Ewing sarcoma of the pleura [6-13] (Table1). They were all young with a mean average age of the patients was 18.56 years old (ranging from 7 years up to 34 years). The gender distribution was equal (four females and four males). The diagnosis can be challenging because the clinical symptoms are non-specific and may be misleading. The patients report often cough, sputum, and chest pain like many other chest malignancies such as lung cancer, lymphoma [6,7,9]. They may also present with dyspnea due to a pleural effusion or to the adjacent mediastinal structure's compression [11,13]. Indeed, two cases of a pleural Ewing sarcoma had been reported in literature. They were discovered incidentally. They did not present any clinical manifestation [7,8]. Our patient was a young girl who complained of a right-sided thoracic pain which may be due to the pleural involvement. The chest CT scan revealed a well-circumscribed, pleural tumor with a soft tissue density and regular borders. It had a homogeneous density with some peripheral calcifications and a mild enhancement following the contrast product injection. These findings were consistent with 4 cases reported in literature. Besides, tumoral necrosis was noticed in 6 patients. Indeed, 4 cases had a pleural effusion, 3 cases an adjacent rib erosion and just one case a chest vertebral tumoral invasion. The tumoral enhancement after the contrast product injection suggested a malignant lesion [14]. However, the diagnosis was challenging in our case because of the absence of an associated bone or ribs tumoral invasion or distant metastasis which is another unusual aspect. Indeed, calcifications inside this malignant tumor as reported in our case report are uncommon [15]. Differential diagnosis should be considered including mainly the pleural fibrous solitary tumors, the tuberculosis especially in our high endemic country, rhabdomyosarcoma, neuroblastoma or lymphoma. Therefore, the definitive diagnosis is often based on the histopathological and the immunohistochemical findings combined with the genetic analysis. As regards the diagnostic assessment tools, 3 cases were confirmed

via a medical thoracoscopy, 3 cases via a pleural biopsy and 2 cases through a CT-guided biopsy like our patient. Regarding the histological exam findings, the anatomopathologists had noticed many small round cells (like in our case report) with poorly defined borders and a scant cytoplasm, arranged in sheets or in trabeculae. So, it is essential to differentiate the Ewing Sarcoma from the other small rounded-cell tumors including the Primitive Neuroectodermal Tumors (PNET), embryonal rhabdomyosarcoma, neuroblastoma and lymphoma [16]. The immunohistochemical analysis showed a diffuse strong cytoplasmic membrane positivity for the CD99 and NKX2.2 staining which had been reported to be positive in Ewing sarcoma at significant higher levels compared to the other small rounded cell tumors. It may be helpful for the diagnosis assessment as well as for the differential diagnosis elimination [17-19]. In this case report, the histological exam of our patient showed a positive CD99 staining. The genetic analysis showed a (22q12) rearrangement of the EWSR1 gene in 70% of the cells. So, the diagnosis of a primary pleural Ewing Sarcoma was established [20]. Given the rarity of the Extraosseous Ewing sarcoma, we still don't have any clear recommendation regarding the treatment and the follow-up. Therefore, a multidisciplinary discussion concerning these challenging cases is mandatory. Our patient's therapeutic strategy was based on a neoadjuvant chemotherapy, a complete surgical resection and an adjuvant chemo-radiotherapy. An intensive chemotherapy is essential for controlling both the primary malignant tumor as well as the micro metastatic disease because the researchers demonstrated that most patients affected with a localized Ewing sarcoma had an associated subclinical metastasis [21,22]. We often follow the chemotherapy therapeutic protocols established for skeletal Ewing sarcoma with alternating cycles of either (Vincristine, Doxorubicin, and Cyclophosphamide) (VDC) or (Isocyanide and Etoposide) (IE) in order to perform a complete surgical resection with clear margins. A postoperative chest radiation therapy may be indicated like in our patient if there is any remaining tumoral tissue. This therapeutic approach would allow a complete remission and would reduce the risk of a tumoral recurrence as well. An adjuvant chemotherapy may be indicated according to the tumoral response to the initial chemotherapy, which is evaluated using the "Huevos tumor" necrosis grading system. Among the 8 cases reported in literature, just one patient had a surgical resection without any chemotherapy nor a radiation therapy, 3 patients received only a chemotherapy, 2 cases had both a chest surgery and chemotherapy and just one case underwent surgery preceded by a neoadjuvant chemotherapy and followed by an adjuvant radio-chemotherapy like in our case report.

Conclusion

The primary pleural sarcoma is uncommon. This malignant tumor is known for its poor prognosis. We underlined the importance of an early diagnosis in order to improve the outcomes. The histological findings combined with the genetic analysis revealing an EWSR1 gene rearrangement helped us to assess the diagnosis of a Pleural Ewing Sarcoma. A multidisciplinary team decision is mandatory in these challenging cases given the lack of specific clinical or imaging features. This rare extraosseous tumor should be considered in young patients with a pleural mass or effusion. Further research and clinical studies are still required in order to better understand these Ewing sarcoma atypical clinical presentations as well as to establish decisional algorithms for a precision medicine and a better prognosis.

Declarations:

Ethics approval: Web respecte the 1964 Helsinki Déclaration Principles and the Commette of Publication Ethias (COPE) Guidelines. Web obitaine the Militari Hospital Ethias Commette approuva.

Acknowledgements: We do express Our sincère gratitude tolards the Anatomopathologie lab. As Wells as the Thoracique Surgyre Teams ho Helpe in the diagnoses and the thérapeutique stratégie assissent.

Consent to participante: A written informed consent as obitaine frome the patient.

Publication consent: All the authors confirm that the patient provided a written informed consent for the publication of all his clinical, radiological and biological data.

Availability of data and materials: The patient's clinical, radiological, biological and histological findings used in this study are available. They can be requested from the corresponding author.

Competing interests: All the authors declare that they don't have any financial or non-financial interest to disclose.

Funding: The authors declare that no funds, grants, or other support had been received during the preparation of this manuscript.

Author contributions:

- Selsabil Daboussi is the corresponding author. She participated in this manuscript conceptualisation, methodology, administration, writing, supervision and review.

-Syrine Abdellatif participated in this manuscript writing, data analysis and visualization as well as in the bibliographic research.

- Asma Saidane participated in this manuscript writing, the bibliographic research, review and editing.

- Dhia Houki : Data curation, Investigation, review.

- Aida Ayadi : Data curation, the manuscript preparation, Investigation, review.

- Imed Bennouri: Investigatio, review.

- Bilel Arfaoui : Investigation, review.

-Sameh Achoura : Investigation, review.

- Abdelmajid Sakhri: conceptualisation, methodology, writing, supervision and review.

- All authors contributed to this manuscript review. They read and approved this final paper.

References

1. Esiashvili N, Goodman M, Marcus RB. Changes in Incidence and Survival of Ewing Sarcoma Patients Over the Past 3 Decades: Surveillance Epidemiology and End Results Data. Journal of Pediatric Hematology/Oncology. 2008; 30: 425-30.

2. Ludwig J. Chapter 21 - Ewing sarcoma family of tumors. In: Heymann D, editor. Bone Cancer (Second Edition). San Diego: Academic Press; 2015; 235-44. https://www.sciencedirect.com/science/article/pii/B9780124167216000212.

3. Embree LJ, Azuma M, Hickstein DD. Ewing Sarcoma Fusion Protein EWSR1/FLI1 Interacts with EWSR1 Leading to Mitotic Defects in Zebrafish Embryos and Human Cell Lines. Cancer Research. 2009; 69: 4363-71.

4. Gamberi G, Cocchi S, Benini S, Magagnoli G, Morandi L, et al. Molecular Diagnosis in Ewing Family Tumors. The Journal of Molecular Diagnostics. 2011; 13: 313-24.

5. Ludwig JA. Ewing sarcoma: Historical perspectives, current state-of-the-art, and opportunities for targeted therapy in the future. Current Opinion in Oncology. 2008; 20: 412-8.

6. Bhaskaran A, Sethi P, Toi PC, Penumadu P. Dilemma in diagnosis and management of rare primary pleural Ewing's sarcoma with synchronous limited metastatic disease. BMJ Case Rep. 2021; 14: 243495.

7. Tsunezuka Y, Furusawa T, Yachi T, Kurumaya H. Rapidly growing intrathoracic extraskeletal Ewing's sarcoma. Interactive Cardiovascular and Thoracic Surgery. 2012; 14: 117-9.

8. Juan L, Jianqun Y, Fanglan L. Rare origin-Ewing's sarcoma of the pleura: A case report and literature review. Radiology Case [Internet] 2023; 17. https://www.radiologycases.com/index.php/radiologycases/article/view/5184.

9. Özge C, Çalikoglu M, Cinel L, Apaydin FD, Özgür ES. Massive Pleural Effusion in an 18-Year-Old Girl with Ewing Sarcoma. Canadian Respiratory Journal. 2004; 11: 363-5.

10. Wu Y, Xie CB, Huang Q, Zhao KF. Case report: Primary pleural giant extraskeletal Ewing sarcoma in a child. Front. Oncol. 2023; 13: 1137586.

11. Zou X, Chang W, Gao H. A primary Ewing's sarcoma of pleura: Case report and literature review. Respiratory Medicine Case Reports. 2021; 34: 101516.

12. Karatziou C, Pitta X, Stergiouda T, Karadimou V, Termentzis G. A case of extraskeletal Ewing sarcoma originating from the visceral pleura. 2011; 15: 363.

13. Mathew D, Prince DN, Mahomed N. Extra-skeletal Ewing Sarcoma of the chest wall in a child. Open Access.

14. Javery O, Krajewski K, O'Regan K, Kis B, Giardino A, et al. A to Z of Extraskeletal Ewing Sarcoma Family of Tumors in Adults: Imaging Features of Primary Disease, Metastatic Patterns, and Treatment Responses. American Journal of Roentgenology. 2011; 197: 1015-22.

15. Gaillard F. Radiopaedia. Ewing sarcoma of the chest wall | Radiology Reference Article | Radiopaedia.org. https://radiopaedia.org/articles/ewing-sarcoma-of-the-chest-wall-1.

16. Baez JC, Lee EY, Restrepo R, Eisenberg RL. Chest Wall Lesions in Children. American Journal of Roentgenology. 2013; 200: 402-19.

17. Hibuya R, Matsuyama A, Nakamoto M, Shiba E, Kasai T, et al. The combination of CD99 and NKX2.2, a transcriptional target of EWSR1-FLI1, is highly specific for the diagnosis of Ewing sarcoma. Virchows Arch. 2014; 465: 599-605.

18. Yoshida A, Sekine S, Tsuta K, Fukayama M, Furuta K, Tsuda Het al. NKX2.2 is a Useful Immunohistochemical Marker for Ewing Sarcoma. American Journal of Surgical Pathology. 2012; 36: 993-9.

19. Hung YP, Fletcher CDM, Hornick JL. Evaluation of NKX2-2 expression in round cell sarcomas and other tumors with EWSR1 rearrangement: imperfect specificity for Ewing sarcoma. Modern Pathology. 2016; 29: 370-80.

20. Yu L, Davis IJ, Liu P. Regulation of EWSR1-FLI1 Function by Post-Transcriptional and Post-Translational Modifications. 2023; 15: 382.

21. Mata Fernández C, Sebio A, Orcajo Rincón J, Martín Broto J, Martín Benlloch A, et al. Clinical practice guidelines for the treatment of Ewing sarcoma (Spanish Sarcoma Research Group-GEIS). Clin Transl Oncol [Internet] 2024. https://link.springer.com/10.1007/s12094-024-03602-5.

22. Gupta A, Riedel RF, Shah C, Borinstein SC, Isakoff MS, et al. Consensus recommendations in the management of Ewing sarcoma from the National Ewing Sarcoma Tumor Board. 2023; 129: 3363-71.