e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(6); 1522-1530

Original Research Article

An Unusual Presentation of Ewing's Sarcoma of Soft Tissues of the Face

G. Harikrishna[1], D. Dakshina Murthy[2], Fathima[3], Gudiseva Ramya[4], D. Sivasankaraiah[5], Dummu Bhima Rao[6], P.V.S. Madhuri Devi[7], Akula Srinivasa Raghu Babu [8], Paluri Vinay[9], S. Hemalatha[10], K. Deepak[11], S. Veerabaghu[12], Dr. Sunidhi Sharma[13]

[1]Professor and HOD of ENT, Department of ENT, Andhra Medical College, Visakhapatnam, AP
[2]Associate Professor of ENT, Department of ENT, Andhra Medical College, Visakhapatnam, AP
[3, 5, 6] Assistant Professor of ENT, Department of ENT, Andhra Medical College, Visakhapatnam, AP
[7] Senior Resident in ENT, Department of ENT, Andhra Medical College, Visakhapatnam, AP
[4, 8, 9, 10, 11, 12, 13] Post Graduate Student in ENT, Department of ENT, Andhra Medical College, Visakhapatnam, AP

Received: 25-03-2024 / Revised: 23-04-2024 / Accepted: 26-05-2024
Corresponding Author: Dr. Gudiseva Ramya
Conflict of interest: Nil

Abstract:

Background: Ewing sarcoma occurs in bone and soft tissues with aggressive nature. It is an example of translocation positive sarcomas. Though genetically it is a simple disease, but with a specific neomorphic-potential therapeutic target. Its carcinogenic role was undoubtedly explained many decades ago. It has the property to micro metastasize and very poor prognosis. The present standard treatment consisted of giving multiple cycles of systemic therapy in addition to local treatment. But both of these modalities cause extreme morbidity and psychological trauma to the patients.

Aim of the Study: To present an uncommon condition of Primary Ewings Sarcoma in a pediatric patient's facial soft tissues by confirming it by clinical, radiological and histopathological report.

Materials: A 14 year old female patients presented with a single 4 x 4 cm swelling on right cheek area, no scars, sinuses, or dilated veins, skin above swelling is normal. On palpation a firm, non-tender swelling was felt with no local rise of temperature. Swelling was seen extending 1cm below the right medial canthus to adjacent to ala of right nostril to angle of mouth on right side. Examination of the nose ears and throat were normal. No palpable cervical lymphadenopathy.

Results: Ultrasound revealed a well-defined hypo echoic lesion with peripheral vascularity deep in subcutaneous planes in right cheek superficial to right maxillary bone. On Doppler study there was no intra lesional vascularity observed. On MRI- T2 hyper intense/ FLAIR hyper intense, T1 isointense contents was found in subcutaneous plane of right maxillary region with no bony involvement. Excision biopsy was done and sent for HPE.

Conclusions: Ewing sarcoma of soft tissue is an uncommon malignant disease belonging to the ESFT group. The Ewings sarcoma of soft tissues is the second most common bone malignancy in pediatric individuals. On HPE it is small, round, blue cells with large spherical nuclei and indistinct cytoplasmic borders. This Ewing soft tissue tumor is most aggressive and most recurrent tumor.

Keywords: Pediatric age, Ewings sarcoma, soft tissues, bone tumours and morbidity.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Ewing sarcoma was first described by Dr James Ewing in 1921 in which he described it as a diffuse hemangioendothelioma of bone where its etiology is unknown. (1) In the (ESFT) extra skeletal Ewing tumour accounts for 20% -30%. First case of Extra-skeletal Ewing (EES) was reported by Angervall and Enzinger in 1975. [1] EES accounts for 0.4 per million with bimodal presentation <5 yr and > 35 yrs without any sex or race predominance unlike Ewings of long bone. [2] EES is a rapidly growing mass which can develop within soft tissue of any anatomical region but most commonly upper thigh, buttocks, upper arm and shoulders, maxillofacial region. [2] This family of Ewing tumours characteristically derived from neural crest cells and mainly demonstrates 11 and 22(q24;q12) which leads to fusion of EWS and FLI-1 genes and thus production of oncogenic transcription factor resulting in cell proliferation. [3] Symptoms of EES depend on primary site where it occurs. ESS can be

diagnosed with imaging however the imaging characteristics are non-specific for ESS. Ultrasonography, CT, MRI each imaging has its own specific indications. [4] Confirmative diagnosis of this ESS will be histopathological diagnosis of specimen either by CT guided needle biopsy or by specimen after surgical resection. [5] Initially EES was treated same as that of any other soft tissue tumor but later according to NCCN(National Comprehensive Cancer Network) the treatment modality has been changed to local treatment i. e, surgery and/or radiotherapy plus chemotherapy. Previous studies confirmed that wide surgical resection increases overall survival rate of patients. Ewings sarcoma is a rare, malignant tumor with micro metastases. [1, 2] Most of the patients are lost due to distant systemic metastases in micro form. More than 90% of the patients die from disseminated disease. [3] Ewings sarcoma is usually seen in the second decade of the life but patients in infant period and late life; in the eighth decade of life also it is reported. [4] Ewings sarcoma is reported in every body parts of human beings. [5]

A multimodality approach is recognized in the treatment of Ewings sarcoma following collaborative trials all over the world which has shown an improved survival rate among these patients. [6] Metasatic disease of Ewings sarcoma is noted in 20 to 25% of the patients. [7] Among the metastatic deposits 80 to 83% occurs in the lungs. [8] Ewings sarcoma recurs after treatment in 30 to 40 % of the patients with their primary increasing to 60 to 80%. [9, 10] Relapse of the disease was reported mostly from systemic sites (70 to 90%), [11] which are followed by combined relapse and lastly local relapse in 11 to 15%. [12] The local recurrence cases respond better than the systemic recurrence patients. [13] The unique feature of Ewings sarcoma is that it carries a balanced translocation. In nearly 85–95% of these patients, the rearrangement fuses the Ewing sarcoma breakpoint region 1 gene (EWSR1) on chromosome 22 to the friend of leukemia virus integration site 1 gene (FLI1) on chromosome 11 t(11;22), (q24;q12), [13] Thus the EWSR1-FLI1 fusion product functions as an oncoprotein that is both necessary and presumably sufficient for tumori-genesis. [14] Hence inactivation of EWSR1-FLI1 function is necessary for effective therapy but it is clinically not a must, as shown by effectiveness of non-targeted chemotherapy in a substantial proportion of patients with localized tumors. [16] Certain aspects of the disease are still not explained such as the cryptic cell of origin, phenomenon of oncogene addiction as well as oncogene plasticity, distinct molecular activities and clinical relevance of fusion proteins in EwS, CIC-rearranged sarcoma, sarcoma with BCOR genetic alterations, and round cell sarcoma with EWSR1-non-ETS fusions (all together formerly known as “Ewing-like sarcoma”. [17] Keeping these advancements in understanding the biological activity behind the pathogenesis of Ewings sarcoma the present uncommon case of Ewings sarcoma of soft tissues of the face of a child aged 14 years is being reported.

Materials:

A 14 year-old female child attended the department of ENT with presenting complaints of a swelling in the right cheek area for the past 3 months. The child was initially treated at Government ENT hospital in Vishakhapatnam. It was characterized by a rapidly progressive swelling in the absence of precipitating or associative influences. There were no complaints of nasal obstruction, bleeding, impaired eye sight, breathing or swallowing problems, loss of smell, loss of appetite or loss of weight. The swelling was characterized by rapidly progression with sometimes associated with pain. She was otherwise well without any other constitutional symptoms. No significant medical history and family history. No history of addiction to drugs or snuff. There was no history of consanguineous marriage among the child’s parents.

She was well oriented, afebrile, heart sounds were heard; CVS-S1,S2 +; Lungs presented with normal vesicular breath sounds; per abdomen was soft, no organomegaly was observed; no pedal edema or generalized lymphadenopathy were present. On inspection a single 4 x 4 cm swelling on right cheek area, no scars, sinuses, or dilated veins, skin above swelling is normal. On palpation a firm, non-tender swelling was felt with no local rise of temperature. Swelling was seen extending 1cm below the right medial canthus to adjacent to ala of right nostril to angle of mouth on right side. Nose examination: Showed on anterior rhinoscopy septum in the midline, floor of nasal cavity normal, and lateral wall normal. Oral cavity and oropharynx examination: Showed normal findings, no swelling or development in alveolar region. No palpable cervical lymphadenopathy. (Fig 1)

Figure 1: Swelling on the Face

Fig 1: Showing the Pre-Operative Photo of the Patient.

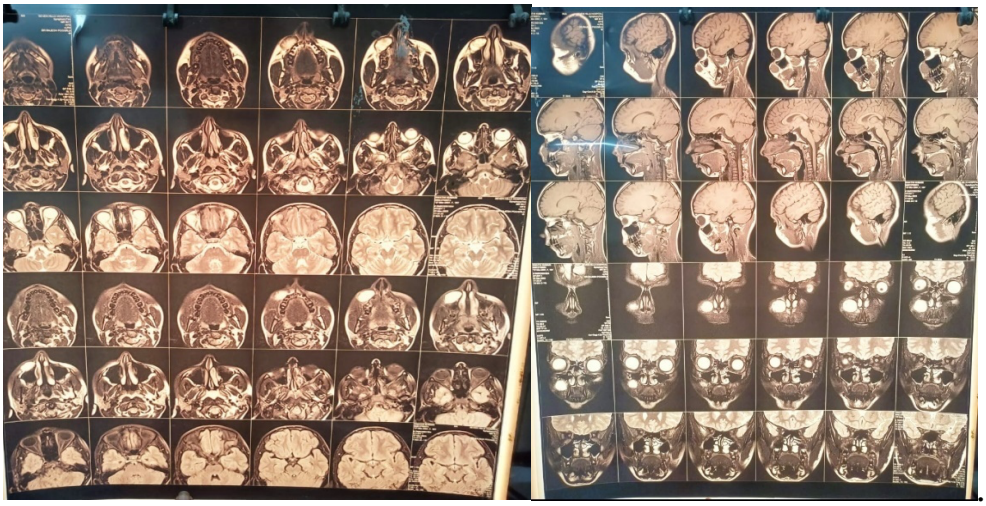


Figure 2: Showing the MRI Imaging of the Patient

Investigations:

Ultrasound revealed a well-defined hypo echoic lesion with peripheral vascularity deep in subcutaneous planes in right cheek superficial to right maxillary bone. On Doppler study there was no intra lesional vascularity observed. On MRI- T2 hyper intense/ FLAIR hyper intense, T1 isointense contents was found in subcutaneous plane of right maxillary region with no bony involvement.

Surgical Procedure: Surgery was performed under general anesthesia. Approach was both external and sublabial. Lesion was well circumscribed and confined to the soft tissues of buccal areas. Lesion was excised in total and sent for HPE.

Gross specimen was measuring 4x4 cm covered with Fibro fatty tissue. Microscopic examination revealed small round cells with tumor cells arranged in groups. The cells had round nucleus, inconspicuous nucleoli and scant cytoplasm.

Immuno-staining was performed, with tumor cell positive for CK, NKX2.2, and CD99. Later the patient was started on chemotherapy with alternating of vincristine-doxorubicin, cyclophosphamide and ifosfamide- etoposide cycles.

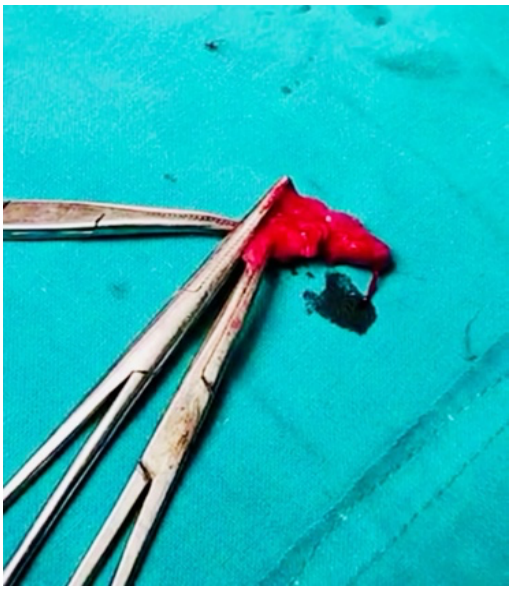


Fig 3: Showing the intra-operative picture

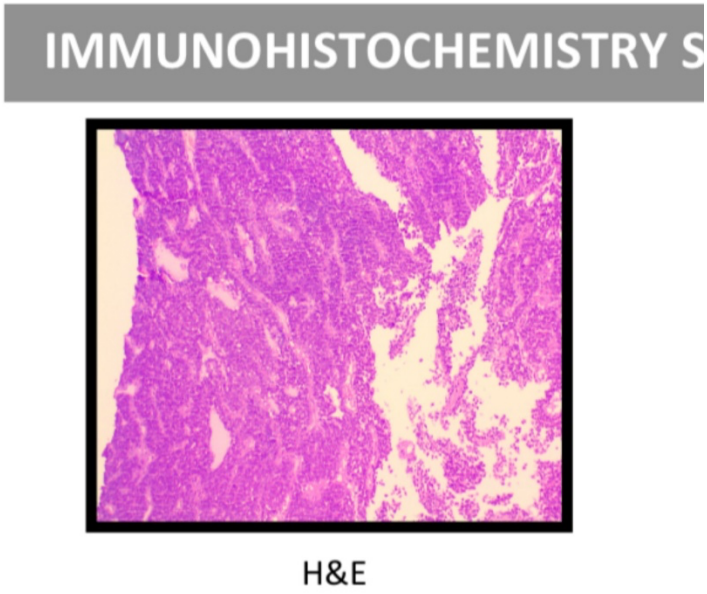
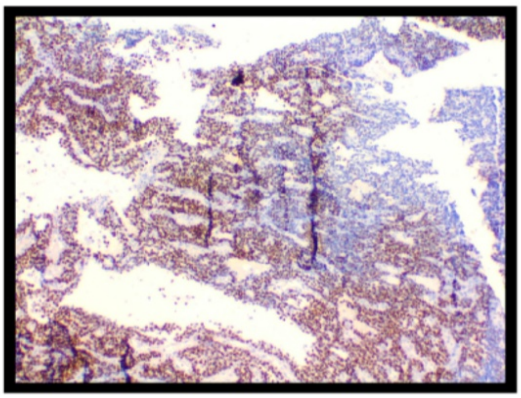
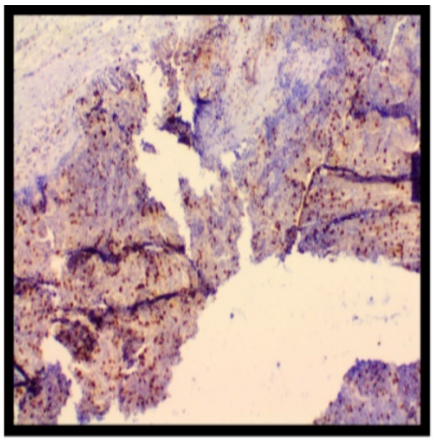


Figure 4:



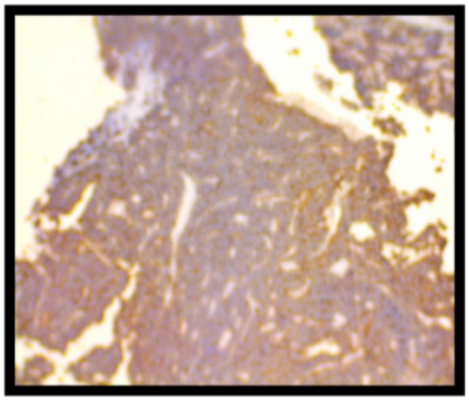
NKX2.2 (NX2/294)

Figure 5:



Ki67 (BH360)

Figure 6:



CD99 (EP8)

Figure 7:

Fig: 4, 5 6 and 7Showing the Immuno-histochemistry microscopy pictures.

Fig 8: Showing the Post-Operative Picture

Discussion:

Extra skeletal Ewing sarcoma (EES) is an uncommon tumor affecting soft tissues and especially the facial soft tissues.02 to03% of Ewings Sarcoma cases occur in the maxillofacial region especially involving the maxilla, mandible, and zygoma. [18] In the present case, it presented as a swelling within soft tissue. The differential diagnosis for such a painless, rapidly enlarging, non odontogenic mass usually thought of mucocele, and salivary gland tumor. ESFT group typically represents as a single entity with common antigenic profiles, cytogenic aberrations and proto-oncogene expression. [19] Symptoms of EES depend on primary as well as metastatic site which accounts for 25% of all cases. [20] Diagnosis of EES by means of radiological modality is non-specific. However they can play a role in staging, treatment monitoring and surveillance of EES. [21] With Ultrasonography lesions appear as heterogenous masses of low echogenicity. On Doppler the tumor vascularity and intra-tumor blood flow signals could be assessed. On CT scan it appears as sharply demarcated mass with similar intensity as that of surrounding muscles with calcification. [22]

However calcification is reported in 10% of cases. On MRI EES shows low intensity signals on T1 imaging and high intensity signals on T2 imaging. This MRI is also helpful for restaging prior to local control when neo-adjuvant chemotherapy given. Gerth et al reported that PET/CT is 87% sensitive and 97% specific for detection of distant metastasis. [23] Overall diagnosis or confirmative diagnosis was done by USG guided biopsy or gross specimen for histopathological examination. [23] On HPE Ewings sarcoma appears as round, small, monomorphic blue cells which have spherical nuclei with indistinct cytoplasmic borders. [24] These cells have less extracellular matrix with low mitotic activity. Immuno-histochemistry studies using a spectrum of markers are more useful than a single marker as the specificity was improved. [25] The markers included CD99 antigen which is highly sensitive but not specific, S-100 protein and Synaptophysin (both are neural proteins), FLI1 which was recently discovered. [26] DNA binding transcription factor was found to be more specific than CD99. [27] Usually histopathology and immune-histochemistry were enough for the diagnosis but in certain cases additional genetic analysis was required. [28] It includes RT PCR or FISH in which two most common translocations were identified. As per National Comprehensive Cancer Network (NCCN) local treatment consisted of surgery and /or radiotherapy in addition to systemic chemotherapy.

The overall 5- year survival rate was found to have improved from 5-10% to more than 65 % following the administration of systemic chemotherapy; also helped in to decrease the recurrence rate. Presently the regimens in use are alternating of vincristine-doxorubicin, cyclophosphamide and ifosfamide-etoposide cycles for every 3 weeks. For localized lesion such as the present case both the surgery and radiotherapy are very useful. Even though the Ewings sarcoma is radiosensitive local excision of the lesion has been proved to be giving better

results. [29] At present definitive radiotherapy recommended for inoperable cases was of 54- 55 Gy. The Ewings sarcoma metastases usually to the lungs and the lungs are treated as similar to the primary tumor protocol. [30]

The 5 year survival rate for Ewings sarcoma was reported as 42% in localized but with metastatic disease it is 15%. In Ewings sarcoma affecting Maxillo-facial region the prognosis is better than other sites. [31] A structured proforma was designed to record the clinical details, which included age, gender, presenting symptoms, site of the tumor, radiological findings (chest X-ray, computerized tomogram (CT), positron emission tomogram (PET) scan), and diagnostic investigations (ultrasound or computed tomography (CT)-guided biopsy), pathological, immunohistochemical, and molecular characteristics [t(11:22) (q24:q12)] of the tumor, and other laboratory investigations and treatment modalities. The patients were categorized according to their age (>20, 20-40, and <40 years) and based on the primary site of the tumor. Histopathological and immunohistochemical slides belonging to all the study cases were retrieved and analyzed. IHC markers of other small round blue cell tumors like CD-45, Desmin, Myogenin, SAT-B2, etc. were done to differentiate ES from them. Molecular testing by NGS was performed for a few of the cases. The grading and staging of excision specimens were based on the FNCLCC (French Federation of Cancer Centers Sarcoma Group) grading system. Variables following normal distribution were expressed as mean (standard deviation), and variables that followed skewed distribution were expressed as median.

Conclusions:

Ewing sarcoma of soft tissue is an uncommon malignant disease belonging to the ESFT group. The Ewings sarcoma of soft tissues is the second most common bone malignancy in pediatric individuals. Histologically it is small, round, blue cells with large spherical nuclei and indistinct cytoplasmic borders. MRI and CT are useful in staging and for follow up and recurrence. Mainstay of treatment lies first in diagnosing and differentiating it from other soft tissue tumours. Because of rarity and involvement of soft tissues and lack of literature this EES poses a diagnostic and therapeutic challenge. In the above said case report female with swelling in cheek area has been diagnosed with EES based on its hisopathogical features of small round cells and immunohisto chemistry marker positive for CD99, CK, NKX2.2. Overall for proper diagnosis, successful management and surveillance of recurrence of EES a multidisciplinary team is required.

References:

1. Wang C.C., Schulz M.D. Ewing's sarcoma; a study of fifty cases treated at the Massachusetts General Hospital, 1930-1952 inclusive. N. Engl. J. Med. 1953; 248:571–576. doi: 10.1056/NEJM195304022481401. [PubMed] [CrossRef] [Google Scholar]
2. Dahlin D.C., Coventry M.B., Scanlon P.W. Ewing's sarcoma. A critical analysis of 165 cases. J. Bone Joint. Surg. Am. 1961;43-A:185–192. doi: 10.2106/00004623-196143020-00004. [PubMed] [CrossRef] [Google Scholar]
3. Ewing J. The Classic: Diffuse endothelioma of bone. Proceedings of the New York Pathological Society. 1921; 12:17. Clin. Orthop. Relat. Res. 2006; 450:25–27. doi: 10.1097/01.blo.0000229311.36007.c7. [PubMed] [CrossRef] [Google Scholar]
4. Anderton J., Moroz V., Marec-Berard P., Gaspar N., Laurence V., Martin-Broto J., Sastre A., Gelderblom H., Owens C., Kaiser S., et al. International randomised controlled trial for the treatment of newly diagnosed EWING sarcoma family of tumours-EURO EWING 2012 Protocol. Trials. 2020; 21:96. doi: 10.1186/s13063-019-4026-8. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
5. Gaspar N., Hawkins D.S., Dirksen U., Lewis I.J., Ferrari S., Le Deley M.C., Kovar H., Grimer R., Whelan J., Claude L., et al. Ewing Sarcoma: Current Management and Future Approaches Through Collaboration. J. Clin. Oncol. 2015; 33:3036–3046. doi: 10.1200/JCO.2014.59.5256. [PubMed] [CrossRef] [Google Scholar]
6. Wheatley K.M.V., Marec-Berard P. First results of the EURO EWING 2012 trial comparing two chemotherapy regimens in newly diagnosed Ewing sarcoma; Proceedings of the Connective Tissue Oncology Society (CTOS)-Oral Presentation/Abstract; Tokyo, Japan. 13–16 November 2019. Annual Meeting 2019. [Google Scholar]
7. Whelan J., Le Deley M.C., Dirksen U., Le Teuff G., Brennan B., Gaspar N., Hawkins D.S., Amler S., Bauer S., Bielack S., et al. High-Dose Chemotherapy and Blood Autologous Stem-Cell Rescue Compared With Standard Chemotherapy in Localized High-Risk Ewing Sarcoma: Results of Euro-E.W.I.N.G.99 and Ewing-2008. J. Clin. Oncol. 2018; 36:JCO2018782516. doi: 10.1200/JCO.2018.78.2516. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
8. Haeusler J., Ranft A., Boelling T., Gosheger G., Braun-Munzinger G., Vieth V., Burdach S., van den Berg H., Juergens H., Dirksen U. The value of local treatment in patients with primary, disseminated, multifocal Ewing sar-

coma (PDMES) Cancer. 2010;116:443–450. doi: 10.1002/cncr.24740. [PubMed] [CrossRef] [Google Scholar]
9. Ladenstein R., Potschger U., Le Deley M.C., Whelan J., Paulussen M., Oberlin O., van den Berg H., Dirksen U., Hjorth L., Michon J., et al. Primary disseminated multifocal Ewing sarcoma: Results of the Euro-EWING 99 trial. J. Clin. Oncol. 2010; 28:3284–3291. doi: 10.1200/JCO.2009.22.9864. [PubMed] [CrossRef] [Google Scholar]
10. Barker L.M., Pendergrass T.W., Sanders J.E., Hawkins D.S. Survival after recurrence of Ewing's sarcoma family of tumors. J. Clin. Oncol. 2005; 23:4354–4362. doi: 10.1200/JCO.2005.05.105. [PubMed] [CrossRef] [Google Scholar]
11. Rodriguez-Galindo C., Billups C.A., Kun L.E., Rao B.N., Pratt C.B., Merchant T.E., Santana V.M., Pappo A.S. Survival after recurrence of Ewing tumors: The St Jude Children's Research Hospital experience, 1979–1999. Cancer. 2002; 94:561–569. doi: 10.1002/ cncr.10192. [PubMed] [CrossRef] [Google Scholar]
12. Stahl M., Ranft A., Paulussen M., Bolling T., Vieth V., Bielack S., Gortitz I., Braun-Munzinger G., Hardes J., Jurgens H., et al. Risk of recurrence and survival after relapse in patients with Ewing sarcoma. Pediatr. Blood Cancer. 2011; 57:549–553. doi: 10.1002/pbc.23040. [PubMed] [CrossRef] [Google Scholar]
13. Delattre O., Zucman J., Plougastel B., Desmaze C., Melot T., Peter M., Kovar H., Joubert I., de Jong P., Rouleau G., et al. Gene fusion with an ETS DNA-binding domain caused by chromosome translocation in human tumours. Nature. 1992; 359:162–165. doi: 10.1038/359162a0. [PubMed] [CrossRef] [Google Scholar]
14. Kovar H., Aryee D.N., Jug G., Henockl C., Schemper M., Delattre O., Thomas G., Gadner H. EWS/FLI-1 antagonists induce growth inhibition of Ewing tumor cells in vitro. Cell Growth Differ. 1996; 7:429–437. [PubMed] [Google Scholar]
15. Lambert G., Bertrand J.R., Fattal E., Subra F., Pinto-Alphandary H., Malvy C., Auclair C., Couvreur P. EWS fli-1 antisense nanocapsules inhibits ewing sarcoma-related tumor in mice. Biochem. Biophys. Res. Commun. 2000; 279:401–406. doi: 10.1006/bbrc.2000.3963. [PubMed] [CrossRef] [Google Scholar]
16. Anderson W.J., Doyle L.A. Updates from the 2020 World Health Organization Classification of Soft Tissue and Bone Tumours. Histopathology. 2021 doi: 10.1111/ his.14265. [PubMed] [CrossRef] [Google Scholar]
17. Gerrand C., Bate J., Seddon B., Dirksen U., Randall R.L., van de Sande M., O'Donnell P., Tuckett J., Peake D., Jeys L., et al. Seeking international consensus on approaches to primary tumour treatment in Ewing sarcoma. Clin. Sarcoma Res. 2020; 10:21. doi: 10.1186/s13569-020-00144-6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
18. Ulaner G., Hwang S., Landa J., Lefkowitz R.A., Panicek D.M. Musculoskeletal tumours and tumour-like conditions: Common and avoidable pitfalls at imaging in patients with known or suspected cancer: Part B: Malignant mimics of benign tumours. Int. Orthop. 2013; 37:877–882. doi: 10.1007/s00264-013-1824-6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
19. Ulaner G., Hwang S., Lefkowitz R.A., Landa J., Panicek D.M. Musculoskeletal tumors and tumor-like conditions: Common and avoidable pitfalls at imaging in patients with known or suspected cancer: Part A: Benign conditions that may mimic malignancy. Int. Orthop. 2013; 37:871–876. doi: 10.1007/s00264-013-1823-7. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
20. Daniel A., Jr., Ullah E., Wahab S., Kumar V., Jr. Relevance of MRI in prediction of malignancy of musculoskeletal system--a prospective evaluation. BMC Musculoskelet. Disord. 2009; 10:125. doi: 10.1186/1471-2474-10-125. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
21. Lodwick G.S. Radiographic diagnosis and grading of bone tumors, with comments on computer evaluation. Proc. Natl. Cancer Conf. 1964; 5:369–380. [PubMed] [Google Scholar]
22. Caracciolo J.T., Temple H.T., Letson G.D., Kransdorf M.J. A Modified Lodwick-Madewell Grading System for the Evaluation of Lytic Bone Lesions. AJR Am. J. Roentgenol. 2016; 207:150–156. doi: 10.2214/AJR.15.14368. [PubMed] [CrossRef] [Google Scholar]
23. Rana R.S., Wu J.S., Eisenberg R.L. Periosteal reaction. AJR Am. J. Roentgenol. 2009; 193:W259–W272. doi: 10.2214/AJR.09.3300. [PubMed] [CrossRef] [Google Scholar]
24. Wenaden A.E., Szyszko T.A., Saifuddin A. Imaging of periosteal reactions associated with focal lesions of bone. Clin. Radiol. 2005; 60:439–456. doi: 10.1016/j.crad.2004.08.017. [PubMed] [CrossRef] [Google Scholar]
25. Erlemann R. [MRI morphology of bone tumors and tumor-like lesions] Radiologe. 2010; 50:61–80. doi: 10.1007/s00117-009-1845-8. [PubMed] [CrossRef] [Google Scholar]
26. Kasalak O., Overbosch J., Adams H.J., Dammann A., Dierckx R.A., Jutte P.C., Kwee T.C. Diagnostic value of MRI signs in differentiating Ewing sarcoma from osteomyelitis. Acta

Radiol. 2019; 60:204–212. doi: 10.1177/0284185118774953. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
27. Brady E.J., Hameed M., Tap W.D., Hwang S. Imaging features and clinical course of undifferentiated round cell sarcomas with CIC-DUX4 and BCOR-CCNB3 translocations. Skeletal Radiol. 2021; 50:521–529. doi: 10.1007/s00256-020-03589-4. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
28. Meyer J.S., Nadel H.R., Marina N., Womer R.B., Brown K.L., Eary J.F., Gorlick R., Grier H.E., Randall R.L., Lawlor E.R., et al. Imaging guidelines for children with Ewing sarcoma and osteosarcoma: A report from the Children's Oncology Group Bone Tumor Committee. Pediatr. Blood Cancer. 2008; 51:163–170. doi: 10.1002/pbc.21596. [PubMed] [CrossRef] [Google Scholar]
29. Thompson M.J., Shapton J.C., Punt S.E., Johnson C.N., Conrad E.U., 3rd MRI Identification of the Osseous Extent of Pediatric Bone Sarcomas. Clin. Orthop. Relat. Res. 2018; 476:559–564. doi: 10.1007/s11999.0000000000000068. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
30. Shahid M., Albergo N., Purvis T., Heron K., Gaston L., Carter S., Grimer R., Jeys L. Management of sarcomas possibly involving the knee joint when to perform extra-articular resection of the knee joint and is it safe? Eur. J. Surg. Oncol. 2017; 43:175–180. doi: 10.1016/j.ejso.2016.05.018. [PubMed] [CrossRef] [Google Scholar]
31. van Trommel M.F., Kroon H.M., Bloem J.L., Hogendoorn P.C., Taminiau A.H. MR imaging based strategies in limb salvage surgery for osteosarcoma of the distal femur. Skeletal Radiol. 1997; 26:636–641. doi: 10.1007/s002560050302. [PubMed] [CrossRef] [Google Scholar]