# An unusual presentation of Ewing's sarcoma in the talus of a preadolescent male: A case report

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August 8, 2023

## Introduction

Ewing's sarcoma (ES) is a highly malignant tumour of bone and/or soft tissue, which is commonly observed during adolescence and young adulthood, and exhibits a distinct propensity for aggressive behaviour.[1] It accounts for approximately 15% of all bone malignancies and primarily affects the metaphyseal region of long bones, representing around 80% of reported cases.[2,3]Furthermore, at the time of diagnosis, around 20% of patients have metastatic spread to distant sites.[4]

Ewing's sarcoma is typically found in the axial and appendicular skeleton, but rarely occurs in the foot, particularly in the talus.[5] It has been reported that the occurrence of ES has not been linked to hereditary or congenital syndromes, environmental factors, or established risk factors. In approximately 90% of cases, the neoplastic cells of Ewing's sarcoma family tumours (ESFT) show a characteristic translocation t(11;22)(q24;q12), while the remaining 10% display a variant translocation, specifically t(21;12)(22;12).[6] Prognostic indicators that result in poor outcomes include tumour size of 8 cm or larger, primary tumour located in the pelvic region, presence of metastases, and age exceeding 15 years at the time of diagnosis.[7]

## Case Presentation

A 12-year-old male presented to the outpatient clinic with chief complaints of pain, fever and swelling around the right ankle for 5 months. He had a history of a fall, resulting in an injury to the right ankle. The patient was managed conservatively with home remedies. However, he continued to experience pain and swelling around the ankle, with incomplete resolution of symptoms. Before presenting to us, he sought consultation with a primary care physician, who referred the patient to a tertiary care hospital due to the presence of a soft-tissue mass with significant swelling observed around the ankle on radiograph.

When the patient was evaluated by us, it was revealed that the pain was constant, aggravated by strenuous activities, and unresponsive to pain medication. It was associated with constitutional symptoms of weight loss, fever, etc. On physical examination, an ill-defined, firm, tender swelling without any overlying skin changes on the right ankle joint was noted *(Figure 1)* . The rest of the physical examination was unremarkable and there was no clinical involvement of other joints. The past medical and family history was not pertinent to the patient's current condition.

The range of motion in the ankle joint was reduced, which elicited terminal pain. The patient had no known contact with individuals diagnosed with tuberculosis (TB). Erythrocyte sedimentation rate (ESR) was 08mm/hour while serum blood tests, including complete blood count (CBC) and antistreptolysin O

(ASO) titres, were within normal range. Moreover, rheumatoid factor (RF) was negative. A repeat radiograph demonstrated an osteolytic lesion of the talus showing periosteal disruption with an indistinct zone of transition, associated soft tissue swelling along the anterior and posterior aspects of the joint and significant osteopenia on the medial side of the right ankle *(Figures 2 and 3)* .

The patient was further evaluated with magnetic resonance imaging of the ankle joint that demonstrated a heterogeneous intramedullary lesion of the talus; predominantly hypointense on the T1-weighted imaging, and hyperintense on the T2-weighted imaging with heterogeneous postcontrast enhancement on contrast-enhanced (C+), fat-saturated (FatSat), T1-weighted imaging. Moreover, the lesion showed significant soft tissue component, abutting anteriorly and posteriorly the adjacent muscles and tendon with loss of fat plane. However, no clear evidence of infiltration was noted *(Figures 4 and 5)* . Based on the clinico-radiological evaluation, a differential diagnosis aneurysmal bone cyst (ABC), unicameral bone cyst (UBC), or tuberculous osteomyelitis or the talus were suggested. For histopathological diagnosis, a biopsy was performed, which revealed small, neoplastic cells. Immunohistochemistry (IHC) stains were positive for cluster of differentiation (CD) 99, NK2 Homeobox 2 (NKX2-2), and special AT-rich sequence-binding protein (SATB2), confirming the diagnosis of Ewing's sarcoma. Cytogenic analysis also revealed 22q12 translocation.

Before the commencement of definitive treatment, which involved surgical resection of the tumour, the patient was referred to another hospital for neoadjuvant chemotherapy but not for radiotherapy. Subsequently, the patient underwent six cycles of chemotherapy. During the surgical operation, a wide margin resection of the right talus and osteotomy of the medial malleolus were performed to enhance visibility of the tumour. The surgery was conducted under general anaesthesia, and following the resection of the talus, a fibular graft was placed in the medial ankle to fill the void. The medial malleolus was then stabilized using K-wires. The wound was closed in layers, and an aseptic dressing was applied. A back slab below the knee was used to immobilize the limb and a Redivac drain was inserted to remove the fluid that collected after the operation. The resected tumour *(Figure 6)* was sent for further histopathological evaluation, which was consistent with biopsy-proven malignancy.

A second surgical procedure was performed to implant a femoral head allograft, obtained from a bone bank. The allograft was secured using K-wires and the wound was closed in layers. Aseptic dressing was applied following the procedure. Additionally, an above-knee back slab was applied for immobilization *(Figure 7)* . The surgical procedure was uneventful, with no intraoperative complications. A blood transfusion of 1 pint was administered. No post-operative complications were observed, and the patient maintained stable vital signs.

## Discussion

Primary malignant bone tumours arising in the foot are exceedingly uncommon. In the case of Ewing's sarcoma (ES), the lytic lesions initially present with clinical symptoms such as pain, swelling, and occasionally fever (particularly in the presence of metastatic disease),[8] which was seen in our case too. Consequently, a significant number of patients with ES initially receive a misdiagnosis of tendinitis or osteomyelitis and are treated accordingly.[9,10] Around 20% of patients exhibit a concomitant history of trauma.[11] According to Yang et al.,[12] the median duration of delay in reaching the final diagnosis from the onset of symptoms is 52 weeks. In our case, this problem did not manifest. ES typically originates from the diaphysis or meta-diaphyseal region of the long bones and commonly involves the pelvic bones and ribs. Infrequently encountered locations include the cranial bones, scapula, vertebra, as well as the phalanges and metatarsals of the hand and feet.[13] Foot involvement in ES is observed in a minority of cases, ranging from 0.93% to 4.2%. When the foot is affected, the most common sites of involvement are the calcaneum (heel bone) and the metatarsals (bones of the midfoot).[14,15] However, talus involvement is an exceedingly rare occurrence, with the first case reported by Cohen et al. in 1953.[16]

Clinical imaging is normally performed when the patient fails to show improvement after receiving antibiotics and/or analgesics. In such cases, initial radiological imaging, performed in two planes, may reveal indications of tumour-related osteolysis and periosteal reactions. The presence of these radiographic findings suggests

a potential diagnosis of primary malignant tumour.[17] Furthermore, the plain radiographs often exhibit a distinctive pattern known as a "permeative" or "moth-eaten" appearance, which indicates a destructive osteolytic lesion. This pattern is most commonly seen in long bones. In the foot and ankle, bone destruction tends to be more prominent than periosteal reactions and may manifest with an atypical presentation that resembles a benign lesion. The classical periosteal reaction referred to as "onion skin peel" is predominantly observed in tumours affecting the diaphysis.[18] Additional radiological imaging is necessary and magnetic resonance imaging (MRI) is employed for detailed assessment. MRI imaging is useful in determining the extent of the tumour and provides precise details regarding its relation to adjacent blood vessels and nerves.[17] In modern medical practice, PET/CT has become the predominant investigation for evaluating metastases, enabling the detection of both skeletal and visceral metastatic spread and eliminating the necessity for bone marrow biopsy.[19] Common sites of metastasis encompass the lungs, bones, liver, brain, and distant lymph nodes.[4]In our case, extensive bony and visceral metastases were not seen.

Relying solely on radiologic imaging is inadequate for establishing a definitive diagnosis of ES. Therefore, histopathological confirmation is essential.[17] Although the gold standard method for obtaining tumour specimens is an incisional open biopsy, a minimally invasive procedure such as a core needle biopsy yields an adequate quantity of tissue in the majority of cases. Microscopically, the tumour is composed of sheets of small, round blue cells, exhibiting a high nuclear-to-cytoplasmic ratio.[13] Supplementary investigations, such as immunohistochemical (IHC) markers and molecular genetics, play a critical role in narrowing the differentials and ultimately leading to a final diagnosis. The CD99, an IHC marker, demonstrates positive expression in over 90% of ES cases. However, it is also observed in various other conditions, including lymphoblastic lymphoma, small-cell osteosarcoma, and mesenchymal chondrosarcoma, among others. Hence, the presence of FLI-1 immunoreactivity in a suspected primary small round cell bone tumour greatly supports the diagnosis of ES.[20] Moreover, laboratory findings in cases of ES include elevated erythrocyte sedimentation rate (ESR) and levels of lactate dehydrogenase (LDH), moderate anaemia, or leucocytosis.[9]

Treatment of ES depends on modern multimodal therapeutic regimens, involving a combination of chemotherapy for systemic control and radiotherapy and surgery for local control.[8,9,21] In cases of foot involvement, where there is no evidence of metastasis, amputation is the preferred surgical procedure over limb salvage.[12,22] The reason includes poor tumour compartmentalization in the foot, but, in our case, adequate bone resection was achievable and no challenges were encountered during bony and soft tissue reconstruction. Although Ewing's sarcoma has the worst prognosis amongst all osseous foot malignancies, with the shortest median time to death,[12] patients presenting with metastatic ES have notably poorer outcomes and, as a result, are usually managed with a treatment regimen involving chemotherapy and radiation therapy, while avoiding surgical interventions.[23] The five-year survival rate for patients with localized disease is significantly higher, at approximately 80%, in contrast to those with bony metastasis, where survival rates range from 30% to 19%.[24] Given the favourable prognosis in our case, the tumour board did not recommend a palliative chemotherapy and radiotherapy.

**Keywords:**

Bone malignancy; adolescence; metastatic spread; foot involvement; prognostic indicators; gene translocation

**Key Clinical Message:**

The presentation of Ewing's sarcoma of the talus is extremely rare and is a commonly misdiagnosed entity, affecting the overall prognosis of the patient.

**Funding Information:**

No funding was obtained for this case report.

**Conflicts of Interest Statement:**

The authors have no conflicts of interest to declare.

**Author Contributions:**

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