



## Cystic presentation of Ewing's sarcoma with indolent clinico-radiologic behaviour

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**Ewing's sarcoma is a high-grade malignant primary bone tumour with aggressive clinico-radiologic features. Rarely, it exhibits a benign pattern, but presentation as a solitary bone cyst in a long bone is rather unusual. The purpose of this paper is to document such a cystic presentation with relatively benign clinico-radiologic course and to review the pertinent literature. A 27-year-old male presented with a pathologic fracture through a radiologically benign appearing solitary bone cyst in the distal tibial metaphysis. The fracture healed on conservative treatment, but the patient presented again a year later with pain and difficulty with weight bearing. Curetting and bone grafting done elsewhere was suggestive of an Ewing's sarcoma, which was later confirmed by a second biopsy. He was treated by standard neoadjuvant chemotherapy followed by wide local excision and reconstruction with an intercalary allograft. At 2 years postoperative follow-up, the patient is without any evidence of local or distant recurrence. Awareness of this atypical presentation is important because it may help in an earlier diagnosis, avoid diagnostic confusion and thus may contribute to improved survival.**

**Keywords :** Ewing's sarcoma ; simple bone cyst ; bone cyst ; cystic presentation of Ewing's sarcoma ; malignant transformation of bone cyst.

features. Although, it may present with a myriad of radiologic appearance (10,11), a benign clinico-radiologic pattern is unusual and presentation as an indolent solitary bone cyst in a long bone is rare (1,2,7,14). The purpose of this paper is to document such a cystic presentation in the tibia and to review the pertinent literature in these cystic types of ES.

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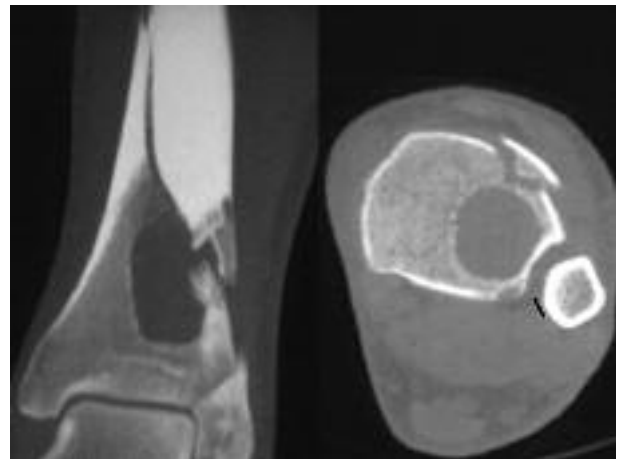
### INTRODUCTION

Ewing's sarcoma (ES) of bone is a high-grade malignant tumour with aggressive clinico-radiologic

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**Fig. 1.** — Initial AP and lateral radiographs of the left distal leg showed an eccentric and predominantly geographic lucent lesion in the distal tibial metaphysis (1A arrows). A geographic margin (arrowheads) was seen supero-laterally. There was a minimally displaced spiral fracture (1B arrowheads).



**Fig. 2.** — Initial CT (coronal and axial) images showed a well defined geographic lesion in the distal tibial metaphysis with a comminuted spiral fracture. The cortical destruction was evident postero-laterally (arrow).

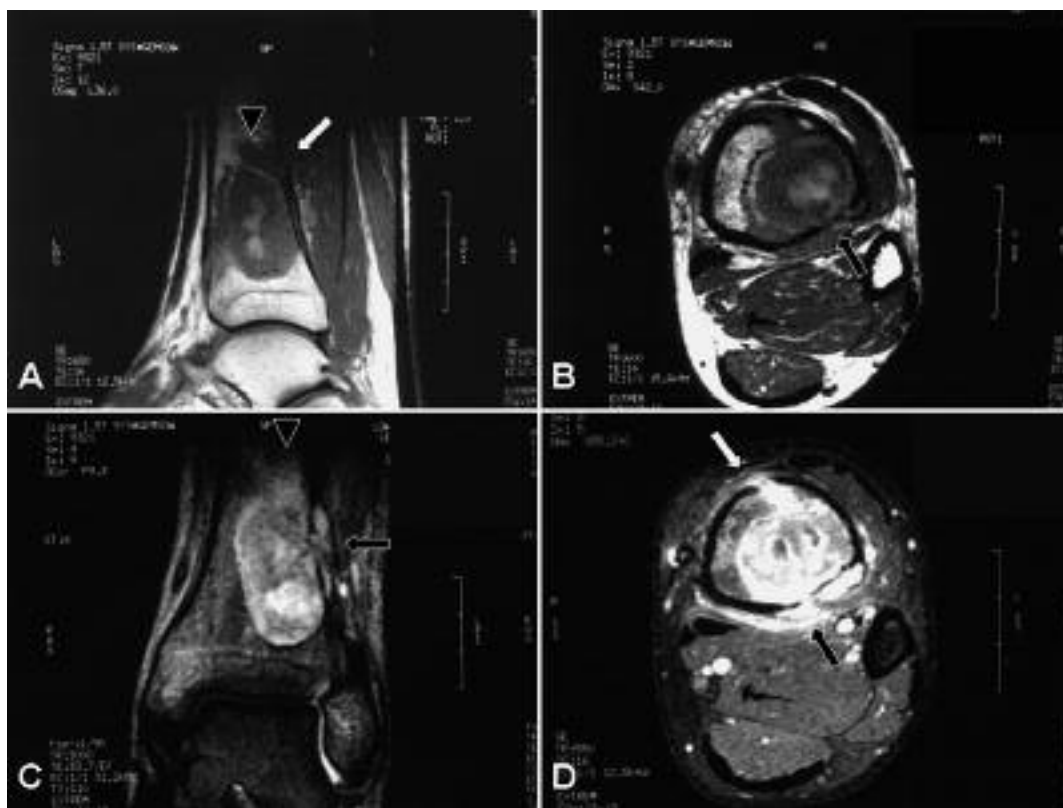
## CASE REPORT

A 27-year old male athlete sustained a fracture of the left distal tibia while participating in martial arts. He denied any prior constitutional symptoms, pain, swelling or limitations of activities. He denied any other significant medical history in himself or his immediate family. Radiological examinations showed a pathologic fracture through a simple bone cyst appearing lesion in his distal tibia (figs 1-3) and he was treated with a cast for three months at a different institution. Radiographs at 3 months showed interval healing of the cyst and the fracture (fig 4). He was symptom free thereafter and gradually resumed unrestricted activities, including sports. One year after the injury, he again started having insidious onset pain and difficulty in weight bearing. Radiographs showed progressive lucency at the previous site (fig 5). Because of the history and the risk of another pathologic fracture, the lesion was curetted and grafted with allograft at the same institute. The lesion did not have a typical fibrinous lining as in a simple cyst but no solid tumour mass was appreciated. The histology showed small blue round cells without rosette formation, immunohistochemically positive for CD 99 (fig 6), but negative for cytokeratin and leucocyte common

antigen. A preliminary diagnosis of an Ewing sarcoma was made. At this time the patient was referred to us, about 16 months after his initial pathologic fracture.

On examination, he was a healthy-appearing man in no acute distress, with unremarkable general physical examination. There was a well-healed 7 cm scar on the antero-lateral aspect of the distal leg. There was no overlying warmth, erythema, induration, tenderness, bruit, soft tissue mass, dilated vein or significant regional lymphadenopathy. The distal neurovascular status was intact. He had an almost full active range of motion at the knee and ankle. A surveillance CT scan revealed no other focus of disease. A Tc 99m MDP triple phase bone scan showed this isolated area of increased uptake with a central photopenic area. Laboratory test results were non-contributory. A bone marrow aspiration from the iliac crest was normal.

Lack of correlation between clinico-radiologic and histologic features led to diagnostic uncertainty and concern over sampling error. Additionally, the patient was confused as to appropriate treatment due to consultations from his previous health care providers, three of whom were orthopaedic surgeons and none believed the lesion to be an ES. The lesion was rebiopsied openly with fluoroscopic



**Fig. 3.** — Initial MRI (A) sagittal T1-weighted : TR 650, TE 16 ; (B) axial T1-weighted : TR 600, TE 14 ; (C) coronal fat-saturated proton density : TR 3000, TE 33.7 ; and (D) axial post-contrast T1-weighted : TR 550, TE 16 showed complex heterogeneous internal signal characteristics. The margin was indistinct superiorly with associated marrow oedema (arrowheads). There was cortical destruction and soft-tissue enhancement postero-laterally (black arrows). The pathologic fracture was noted (white arrows).

guidance to sample the suspicious radiologic lucent area. The  $2.5 \times 2.0 \times 0.6$  cm biopsy material mainly consisted of the bone graft but scant tumour tissue was identifiable with the same previous characteristics (fig 6) and ancillary studies confirmed the diagnosis of an ES.

Due to a previous intralesional procedure, sub-optimal placement of skin incision and a solitary distal lesion, an option of primary amputation after neoadjuvant chemotherapy was offered to the patient. The patient refused this and the option of neoadjuvant chemotherapy followed by a resection and allograft reconstruction of the bone defect was discussed. Radiation was the other option but was not favored due to the location of the lesion. The patient underwent four cycles of neoadjuvant

chemotherapy, restaging, wide local excision of the tibia and reconstruction with an intercalary allograft (fig 7), and subsequent adjuvant chemotherapy as per protocol (6). The excised specimen did not show any focus of tumour cells. Postoperatively he was started with non-weight bearing ankle motion, followed by partial weight bearing gradually over the next one year. At 2 years follow-up, there has been no complication including local or distant recurrence. Radiographs suggest partial healing of the bone-allograft junction (fig 8). The plan is to take out the syndesmotic screw. Currently, he has  $5^\circ$  degrees of dorsiflexion and  $20^\circ$  of plantar flexion at the ankle. He still uses a support for walking, has mild to moderate pain with prolonged activities and no longer participates in sports.



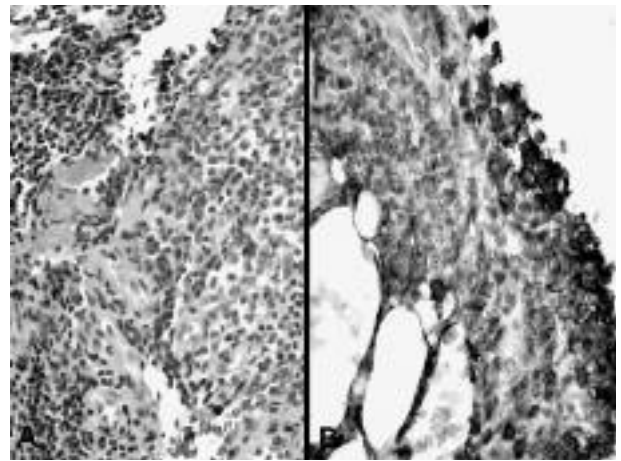
**Fig. 4.** — AP and lateral radiographs 3 months later showed interval healing of the pathologic fracture without significant displacement or angulation. Increased sclerosis in the supero-lateral aspect of the lucent lesion reflected healing in this region as well (arrowheads). The overall margins and size of the lesion appeared stable.



**Fig. 5.** — AP and lateral radiographs at 13 months showed healed fracture but the lesion showed progressive lucency. Moreover, the supero-lateral margin of the lesion was less distinct and cortical thinning in this region was more prominent (arrowheads). There was minimal extension of the lesion toward the distal articular surface at its posterior-inferior aspect (arrows).

## DISCUSSION

Ewing sarcoma family of tumours (ESFT) is a high-grade malignant tumour that typically presents with aggressive clinico-radiologic features. How-



**Fig. 6.** — (A) The histology showed a cluster of small round blue cells (Haematoxylin and Eosin, 400 $\times$ ), which (B) were immunohistochemically positive for CD99.



**Fig. 7.** — Intraoperative photograph showing the reconstruction after wide local excision of the tumour. The tibial allograft was turned upside down and telescoped into the native bone (for additional intrinsic stability) along with fixation with an interlocking nail and allograft powder at the junction. The native ankle joint was preserved (\* is on the talus).

ever, ES of bone may exhibit a benign radiologic pattern in less than 2% of the cases, a sharp endosteal margin in 10% of cases and in up to 27% of these tumours may have at least one radiological atypical feature (10,11). Simple bone cysts tend to recur after attempts at surgical treatment, but their natural history is considered to be benign. Moreover 2% of simple bone cysts may exhibit a moth-eaten pattern of bone destruction and 1% may



**Fig. 8.** — AP and lateral radiographs at 2 years follow-up showing partial healing of the allograft-bone junction.

show irregular cortical destruction (10). Further, both malignant changes in an unirradiated simple bone cyst, and association of ES with other benign conditions have also been described (4,5,8,12,15).

A cystic presentation of ES in an unirradiated bone is quite unusual but has been reported (1,2,7,14). Renius *et al* (11) noted the radiologic cystic component of ES in their series of Intergroup Ewing's Sarcoma Study (IESS) in 1984, but they did not comment on its clinical course. Steinberg (14) in 1985 was the first to report the association of ES with a simple bone cyst. He reported an 8-year old boy with pain and a pathologic fracture through the cyst in the distal fibula after a trivial trauma. The fracture healed on conservative treatment. The lesion was prophylactically curetted and bone grafted two months later. The histopathology was consistent with an ES and he underwent a below knee amputation, a fibulectomy and adjuvant chemotherapy. He was reported as disease-free at 5-years follow-up. Bhagia *et al* (1) described a similar painful lesion in the proximal humerus of a 9-year old boy. He presented with a recurrence three years after an initial curetting and bone grafting of a histopathologically confirmed simple bone cyst. However, a second biopsy as well as review of the previous curettings showed presence of malignant small

round cell tumour. He was being planned for a neoadjuvant chemotherapy and endoprosthesis replacement surgery at the time of writing. Hammoud *et al* (7) reported a painful proximal fibular lesion in a 10-year old girl. The lesion was biopsied because of pain and unusual location for a bone cyst, and was subsequently treated with neoadjuvant chemotherapy and resection of the proximal fibula. She was reported as disease-free at 3-years follow-up. Although not typical of a simple bone cyst, Ehara *et al* (2) reported a 29-year old male with a painful cystic expansion in the peritrochanteric region of the femur with a pathological fracture. He was treated by internal fixation followed by radiation and chemotherapy. One year later the implant was removed due to infection and at that time no tumour was found histologically after curetting. However the fracture did not heal and the initial cystic-expansile radiologic finding did not regress at almost 5 years follow-up. Interestingly, none of these cases, including ours, had any evidence of local recurrence or systemic macro-metastasis at the time of reporting, suggesting a relatively indolent clinico-radiologic course of this cystic variety of ES.

It is not clear whether the above mentioned cases were primary presentation of an ES or a simultaneous or subsequent secondary sarcomatous change of the cyst. Three morphologic patterns have been described for masses that consist of more than one tumour type: collision, composition (composite), and combination (9,13) but aetiology of such association is unclear. Johnson *et al* pointed out the presence of parietal nubbins of tissue which project out into the bone cyst or lay in the adjacent bone marrow and may undergo malignant transformation (8). They found four different tissue patterns in these foci, any one of which can predominate: angiomatous, myxomatous with foci of chondroid, fibrillary with foci of osteoid, and undifferentiated mesenchymal with cells ranging from lipoblasts to xanthoma cells to mature fat cells. In their cases of malignant transformation of bone cysts, diagnosis included fibrosarcoma, malignant giant cell tumour or osteosarcoma, chondrosarcoma, rhabdomyosarcoma and liposarcoma. However none of their patients had histological proof of the initial simple bone cyst.

The majority of the ES cases occur in the first two decades of life with 95% of the patients being between 4-25 years of age with a slight male predominance (11). Because most patients with apparently localized disease at diagnosis have subclinical micrometastatic (systemic) disease, multi-drug chemotherapy as well as local disease control with surgery and/or radiation therapy is currently indicated in the treatment of all patients (6). Ewing Sarcoma has a strong potential to metastasize and in a recent study, 27% of patients presented with distant macrometastasis (3). Radiologically, the typical lesion in a long bone is medullary based, diaphyseal or metadiaphyseal in location with poor margination, aggressive periosteal reaction and an associated soft tissue mass (11). Ewing Sarcoma is a high grade tumour by definition and, unlike osteosarcoma, does not have low grade variants to explain the course in the cases discussed here (15). Because it is a rapidly growing neoplasm, ES can undergo large zones of necrosis. The necrotic zone may be centrally located and may become cystic leading to a radiologic interpretation as a simple bone cyst or clinically mimicking purulence (7). The relatively older age, cystic metaphyseal presentation with no periosteal reaction or soft tissue mass, and a relatively stable clinical course over a period of more than a year in our case is unusual for an ES. No tissue suggestive of a simple bone cyst was evident and thus we believe our patient's disease to be a primary ES, where the biological course reflected the imaging findings rather than the histological diagnosis. We do not suggest that ES should always be included in the differential of a bone cyst, but mean to document some discordant features of ES in its clinical course and sequential imaging findings that still remain unresolved and seemingly irreconcilable. Due to this, treatment for ES was started almost 17 months after the initial detection of the lesion in our case. Awareness of this atypical presentation is important because it may help in an earlier diagnosis, avoid the problem of diagnostic confusion, and thus may contribute to improved survival.

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