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CASE REPORT

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Multifocal, metachronous, giant cell tumor of the lower limb

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Abstract A case of multifocal giant cell tumor in a skeletally immature male with documented metachronous disease of the lower limb is described followed by a review of the literature including treatment options and their outcomes.

Keywords Giant cell tumor · Lytic lesions of bone · Multicentric · Metachronous · Radiographs

Introduction

Multicentric presentation is an uncommon variation of the well-known giant cell tumor (GCT) of bone, representing fewer than 1% of all cases. It is even more unusual when metachronous lesions are identified and the skeleton is immature. We present a case of multifocal giant cell tumor (MGCT) of bone in a skeletally immature male. The tibia, femur and navicular were involved at presentation with subsequent metachronous involvement of the medial cuneiform, calcaneus and two sites in the talus.

Case report

Our case involves a 16-year-old white male who presented in June 1998 with left foot and ankle pain of 6 months' duration. The onset was associated with playing basketball; however, no injury was sustained. Physical examination revealed swelling and pain over the distal left tibial metaphysis as well as pain to palpation over the midfoot. There were no signs or symptoms of infection.

Initial radiographs of the left ankle, dated May 30, 1998, showed a lytic lesion of the distal tibia prompting further evaluation (Fig. 1). Subsequent MR imaging of the ankle on June 5, 1998, showed a 3 cm well-defined lesion of the anterolateral distal tibia with low signal intensity on T1-weighted images and intermediate signal on T2-weighted and inversion recovery images. There was adjacent bone marrow edema. Another lesion with low signal on T1-weighted images and high signal on T2-weighted images was shown involving most of the navicular (Fig. 2). A radiographic skeletal survey was performed on June 22, 1998 and identified a third lytic lesion in the distal left femur (Fig. 3). On June

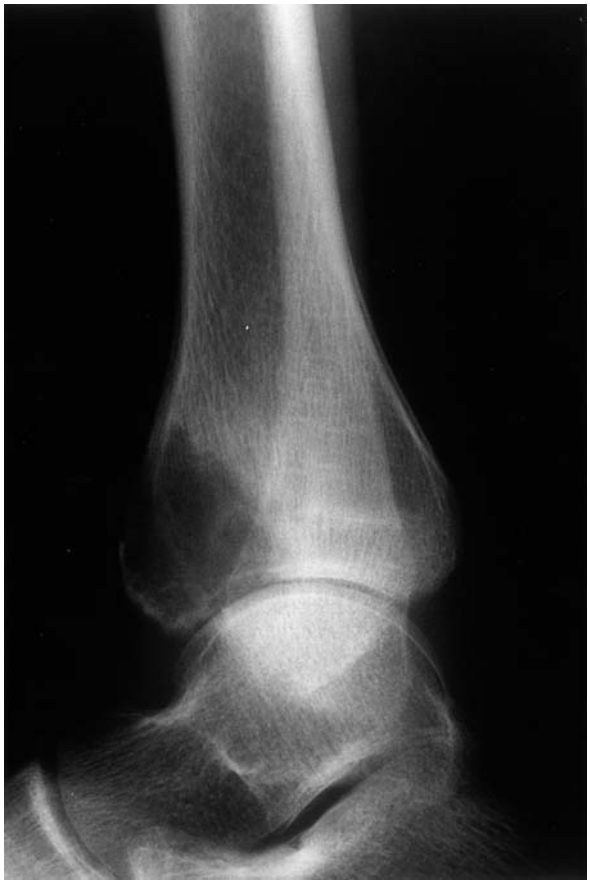

Fig. 1 Lateral radiograph of the ankle showing a lytic lesion of the distal tibia

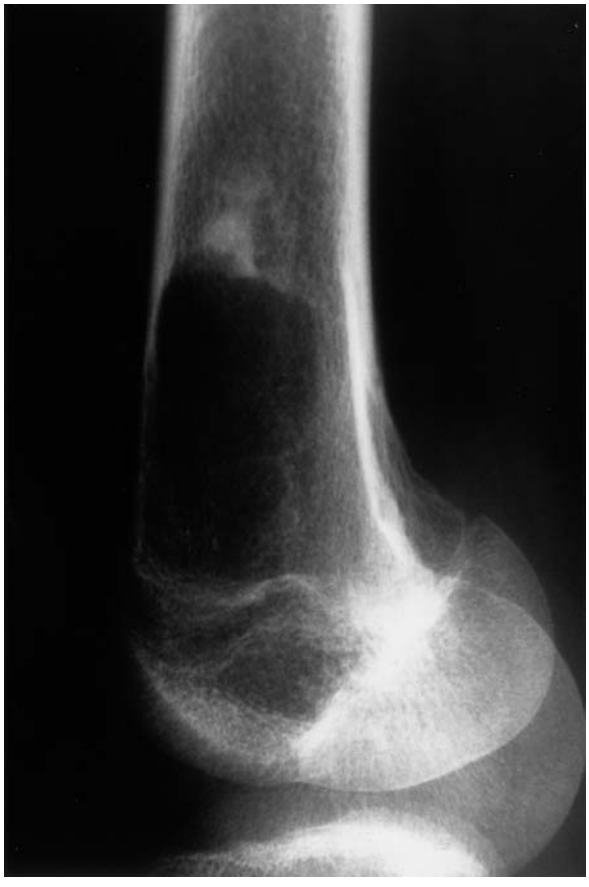

Fig. 3 Lateral radiograph showing a lytic lesion of the distal femur

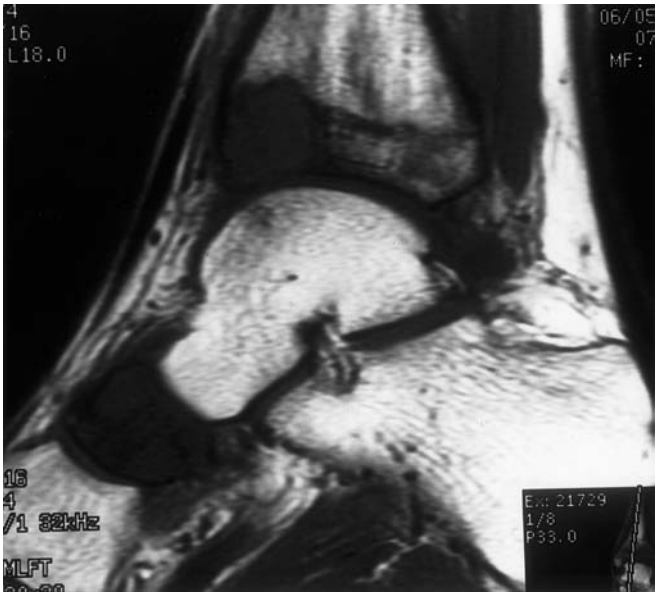

Fig. 2 Sagittal T1-weighted MR image showing tumor involving the navicular and distal tibia

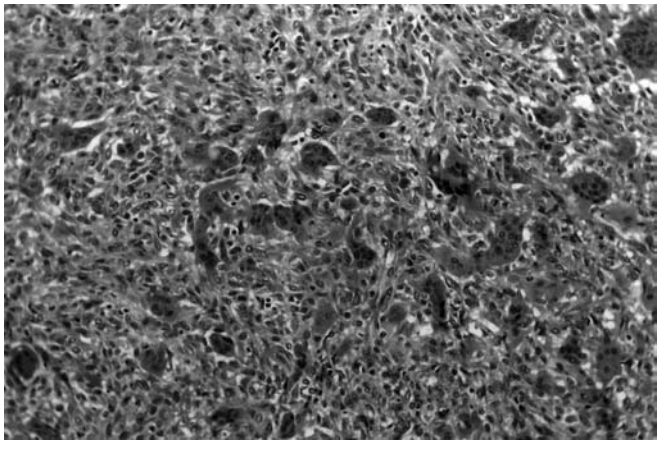

Fig. 4 Histologic section of the distal tibia lesion showing spindle cells characteristic of giant cell tumor of bone with multinucleated giant cells and mononuclear stromal cells (H&E, ×200)

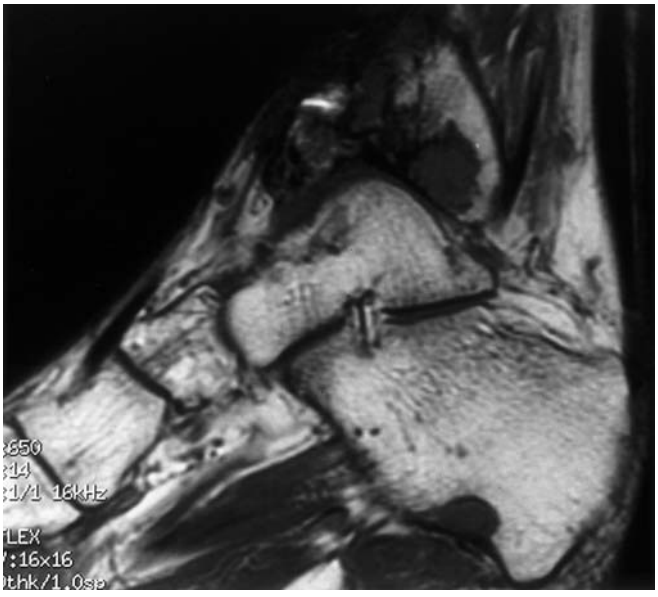

Fig. 5 Sagittal T1-weighted MR image showing new lesions in the posterior tibia and plantar aspect of the calcaneus

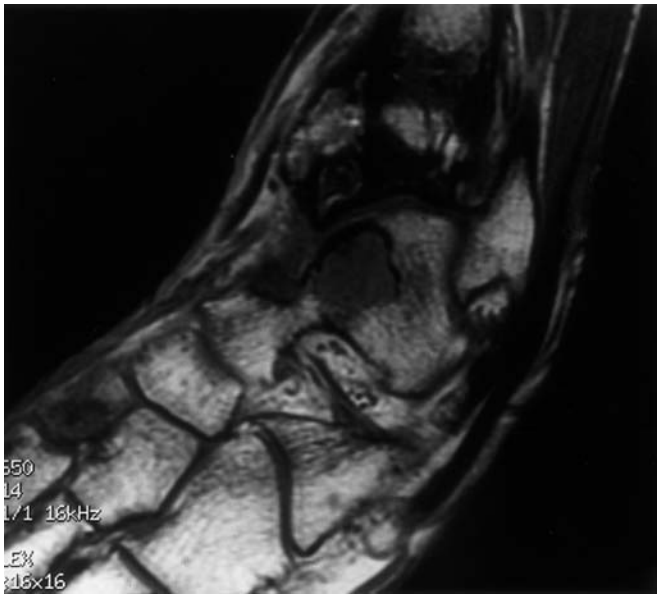

Fig. 6 Oblique coronal T1-weighted MR image showing new lesions in the cuneiform and the talus

23, 1998, open surgical biopsy was performed of the tibial and navicular lesions. The cortical bone was soft with an underlying cystic cavity. The pathologic specimens showed soft, brown, friable tumor. Histologic examination at both sites revealed multinucleated giant cells, mononuclear stromal cells and spindle cells characteristic of giant cell tumor of bone (Fig. 4). There were no mitoses, atypia, or other malignant features. Cultures were negative. Extensive laboratory investigation was also performed and was negative, including specific testing for episodic hyperparathyroidism. A chest radiograph on June 22, 1998 was normal. No CT imaging of the chest was performed.

Given the unexpected pathologic diagnosis, a biopsy of the distal femoral lesion also was performed. Following this, a more extensive mechanical debridement was performed at all three anatomic sites in August 1998. The lesions were irrigated with hot saline and packed with iliac crest bone graft and Osteoset pellets.

In January 1999, a CT scan of the left ankle was obtained. There was evidence of tumor recurrence in the posterior distal tibia. Also noted was a solitary 7 mm lytic lesion of the lateral talar dome which was not present on prior images and which was felt to represent a new tumor focus. Additional debridement and grafting of the distal tibia was performed in February 1999. The talar lesion was not addressed surgically at this time.

In April 2000, follow-up radiography and MR imaging of the ankle again showed abnormalities of the talus suspicious for tumor. The lateral lesion had increased to 17 mm on MR imaging compared with 7 mm at the January 1999 CT examination. A new 3 mm medial dome lesion was seen with normal marrow intervening between the two lesions. In the calcaneus, a 12 mm lesion was seen at the attachment of the plantar fascia. Abnormal signal was also identified in the medial cuneiform (Figs. 5, 6). The initial study of June 1998 showed no signal abnormalities in either the calcaneus, talus or cuneiform, therefore confirming metachronous disease. Two foci of lobular enhancement had also developed in the distal tibia on the margin of the graft site consistent with recurrence. At this point the patient became non-compliant and biopsy of the talus, cuneiform and calcaneus was not performed.

Discussion

The diagnosis of multifocal, metachronous giant cell tumor is unusual and often difficult to document. Given the proximity of the bones involved in our case, we were fortunate in documenting a normal-appearing calcaneus and talus at the June 1998 examination to have for comparison with the April 2000 MR imaging findings. This allowed us to definitively diagnose metachronous disease, essentially excluding the possibility of synchronous disease where a "second" site is involved at the time of presentation but remains asymptomatic and is therefore not imaged in the initial evaluation.

GCT comprises approximately 5% of bone biopsy specimens [1, 2]. Solitary tumors usually involve the distal femur, proximal tibia, proximal humerus and distal radius. In contrast, MGCT often involves the small bones of the hands and feet in addition to the solitary locations [1, 3]. Multifocal lesions are more likely to be confined to the metaphysis and diaphysis when a long bone is involved in contrast to the traditional metaepiphyseal location [1]. Although MGCT accounts for fewer than 1% of GCT cases, it is an important entity to recognize. It has been shown to occur more frequently in younger patients and has a more aggressive course, including an increased incidence of pathologic fractures in some studies [3]. Other series state no difference between unicentric and multicentric GCT with regard to age or sex [4]. It is important to exclude other diseases in the radiographic differential including brown tumors, multifocal infection, metastases, giant cell reparative

granulomas, eosinophilic granuloma and enchondromas. An endocrine evaluation to exclude episodic hyperparathyroidism is imperative since brown tumors can have similar histologic features to GCTs [1].

If a single GCT is diagnosed in the small bones of the hands or feet it may be appropriate to counsel these patients on the possibility of this representing multifocal disease. In our opinion, a skeletal survey to detect asymptomatic lesions or a scheduled screening protocol including radiographs or bone scan may be beneficial as this could lead to tumor resection at an earlier stage. MGCT is shown to have more aggressive characteristics than conventional GCT [5]. Therefore, early detection may decrease the number of pathologic fractures and possibly decrease the overall morbidity of this unusual disease.

Several approaches have been utilized in the treatment of MGCT. Conventional treatment with curettage alone or curettage and grafting was found to be ineffective, with a 90% recurrence rate in one series of 15 patients [5] and similar results in all cases reviewed. The majority of patients in our review required repeat curettage for recurrences until en bloc resection or amputation was eventually performed depending on the anatomic site [1, 2, 3, 5, 6, 7]. More recently there have been changes in the surgical management of GCT. Orthopedic oncologists have incorporated phenol/alcohol application, polymethylmethacrylate, cryosurgery and laser to create a zone of bone necrosis through the cytotoxic effects of such treatments [8]. McDonald et al. [9] showed that curettage with adjunctive phenol and acid alcohol therapy in 80 patients reduced the recurrence rate to 34% compared with the historical rate of 40–60% in conventional GCT. It is encouraging that this new management could decrease the recurrence rate and the need for en bloc resection and/or amputations in patients with MGCT, therefore preserving function and quality of life.

Conclusion

Although MGCT remains an uncommon tumor, its aggressive nature and relatively typical presentation warrants recognition of this entity by the radiologist. Diagnosis of a GCT in an atypical location should lead to routine screening by radiographs or bone scan since there is a known association with multifocal disease and early detection of tumors may decrease the overall morbidity.

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