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CASE REPORT

Metachronous multicentric giant cell tumour of bone

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Abstract
Metachronous multicentric giant cell tumour (GCT) of bone is rare. We report a case of a 21-year-old man with metachronous multicentric GCTs, with five (including one recurrence) documented lesions reported over a span of 9 years involving various sites, which included the fifth metacarpal bone of the right hand, the intermediate cuneiform bone of the right foot, the left proximal humerus and the lateral malleolus of the right tibia. The radiological appearance of these lesions in these various sites with correlation among clinical history, histopathology and the treatment approach is described in this report. He is undergoing regular follow-up and has now once again presented with recurrence of the right tibial lesion. The case is reported for its rarity.

Keywords Giant cell tumour · Metachronous · Multicentric

Introduction

Giant cell tumour (GCT) is a benign but locally aggressive primary bone neoplasm that accounts for 4–5% of all primary bone tumours. It occurs most commonly in the third to fifth decades of life and affects both males and females, with a slight female preponderance [1, 2]. They usually present as solitary lesions involving the meta-epiphyseal region of long bones. Multicentricity of GCTs is extremely uncommon. We present clinical, radiological and pathological findings of a case of metachronous multicentric GCT (MCGCT) of bone.

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Case report

A 21-year-old man presented to us 3 years back with a painful swelling of the left shoulder for 1 month. It was insidious in onset and progressive in nature. There had been a history of trauma to the site 1 month earlier. Plain radiograph of the left shoulder showed a large expansile lytic lesion in metadiaphysis of the left proximal humerus extending up to the greater tuberosity with foci of cortical breaks (Fig. 1a, b). Magnetic resonance (MR) images of the left shoulder showed the lesion to be iso- to hyperintense on T1-weighted imaging (T1WI), predominantly hyperintense on T2-weighted imaging (T2WI) and short tau inversion recovery (STIR) images (Fig. 1c–f). Six years before the present complaint, he had presented to another hospital with pain and swelling of the right hand of 2 months' duration. Plain radiograph of the right hand performed at that time showed an expansile lytic lesion in the meta-diaphyseal region of the distal aspect of the fifth metacarpal bone extending up to the articular margins, with no evidence of a cortical break (Fig. 2a). On MRI, the mass was hypointense on T1WI and hyperintense on T2WI and STIR images (Fig. 2b–e). Fine needle aspiration cytology (FNAC) of the lesion was suggestive of GCT, following which he underwent excision and reconstruction with a fibular graft (Fig. 3).

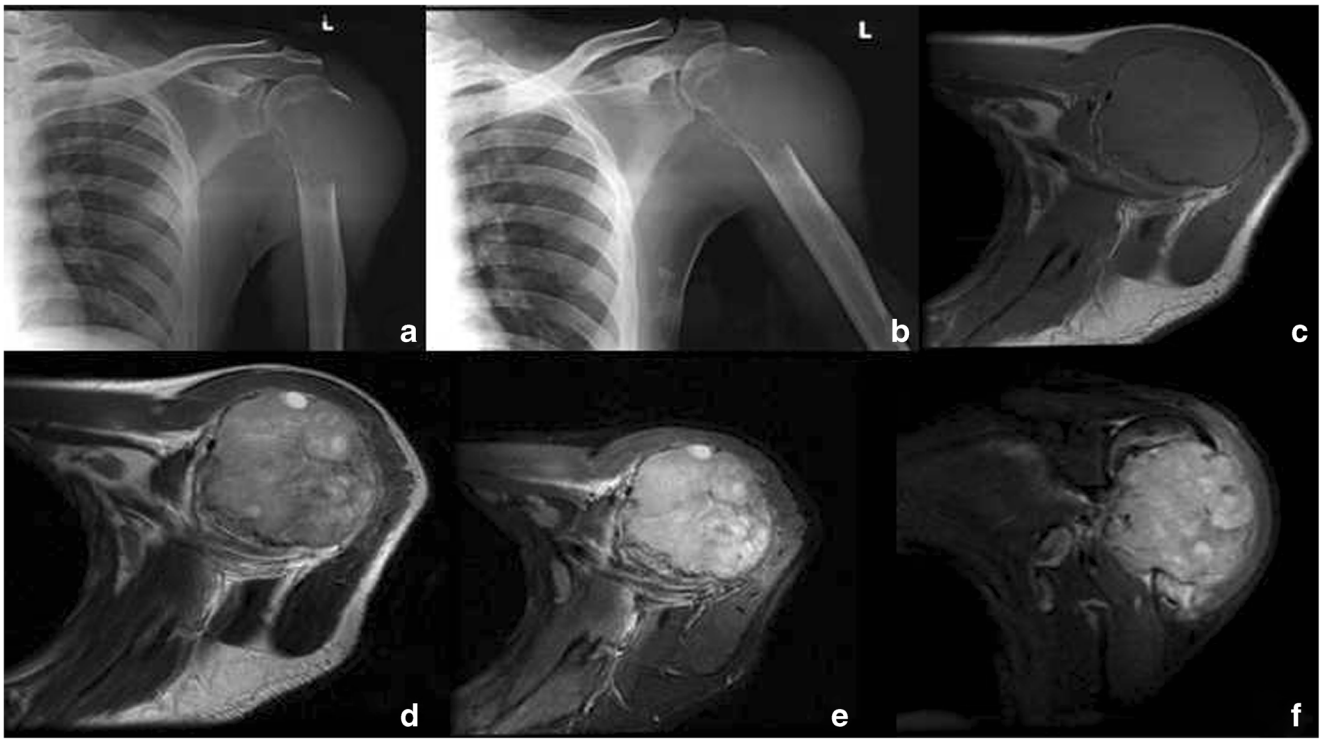


Fig. 1 Radiograph **a** antero-posterior (AP) and **b** oblique views of the left shoulder joint show a large expansile lytic lesion in the meta-diaphysis of the left proximal humerus extending up to the greater tuberosity with foci of cortical breaks. MR images of the left shoulder show the lesion to be iso- to faintly hyperintense on **c** T1-weighted imaging (T1WI), predominantly hyperintense with tiny cystic foci on **d** axial T2WI and **e** axial and **f** coronal short tau inversion recovery (STIR) images displacing the deltoid muscle laterally. The lesion also shows a predominantly solid component with subtle perilesional edema in the bone

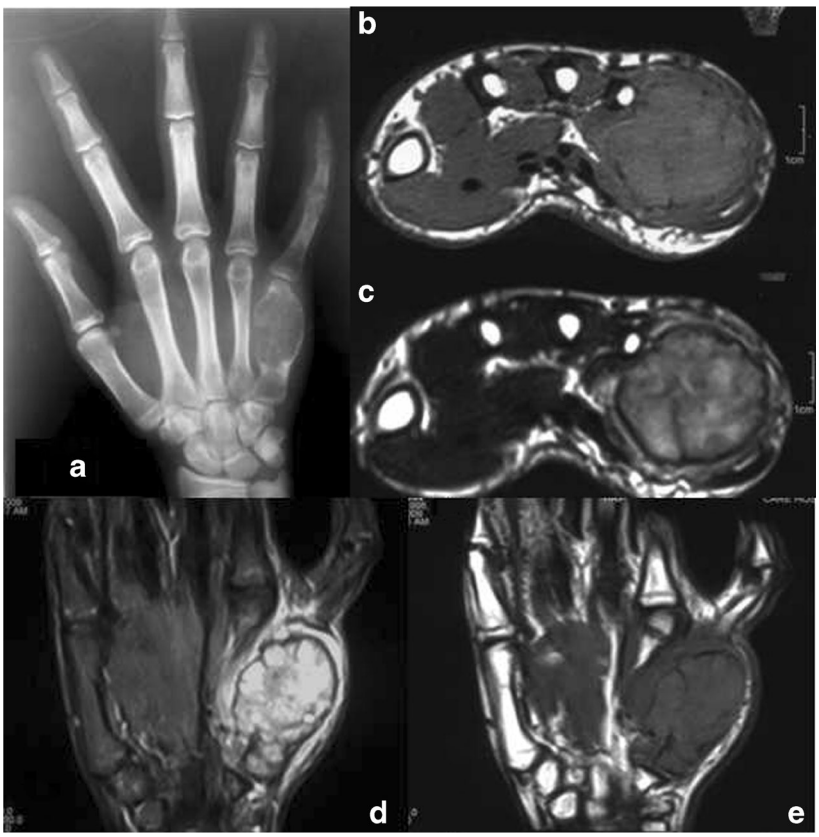


Fig. 2 Radiograph **a** AP view of the hand showing an expansile lytic lesion in the metadiaphyseal region of the distal aspect of the fifth metacarpal bone extending up to the articular margins with no evidence of a cortical break. MRI of the hand shows that the lesion is hypointense on **b** axial and **e** coronal T1WI, hyperintense on **c** axial T2WI and **d** coronal STIR images

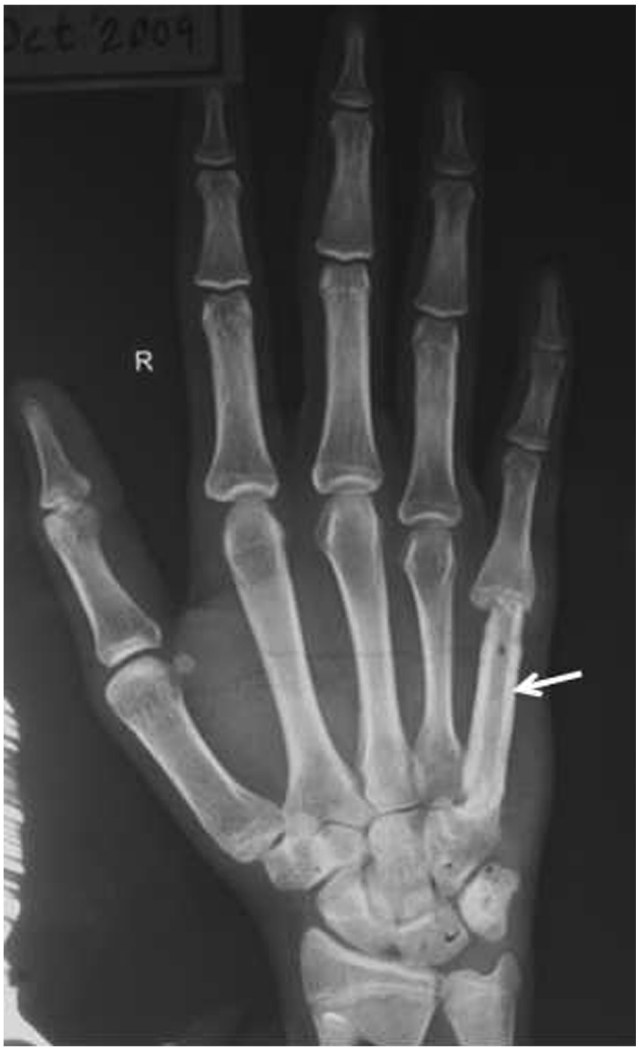


Fig. 3 Radiograph of the hand. AP view showing metacarpal bone excision with a fibular bone graft (*white arrow*)

Two years later, he presented again with pain and swelling of the right foot. Plain radiograph and CT scan of the right foot performed at that time showed a lytic lesion involving intermediate cuneiform bone extending up to articular margins (Fig. 4). He underwent curettage and bone grafting for the foot lesion. Histopathology examination of tissue removed in both the above instances was reported externally as GCT. The histopathology slides of right intermediate cuneiform were reviewed at our institute and confirmed to be GCT (Fig. 5). However, the slides of the right fifth metacarpal lesion were not available for review. Further laboratory investigations at our institute revealed normal serum calcium (10.5 mg/dl), normal serum phosphorous (4.40 mg/dl), normal serum alkaline phosphatase (78 U/l) and normal serum PTH levels (28.30 pg/ml) ruling out the possibility of hyperparathyroidism. Open biopsy of the lesion was consistent with GCT. Later, selective digital subtraction angiography and embolization of the left subclavian artery and subselective artery supplying the left humoral tumour was carried out to reduce the vascularity of the tumour before the surgical procedure (Fig. 6a–c). He later underwent excision of the humeral lesion with placement of a rush nail connecting the acromion, the remaining head of the humerus and the shaft of the humerus (Fig. 6d–f). The histopathological examination of the excised mass was consistent with GCT (Fig. 7). The post-operative recovery was uneventful and the patient was discharged with advice to attend regular follow-up.

He presented again 1 year later with pain and swelling around the right ankle. Plain radiograph of the right ankle showed a well-defined eccentric, slightly expansile lytic lesion involving the subarticular location of the lateral malleolus of the right tibia (Fig. 8a). At MRI, the lesion was hypointense on T1WI (Fig. 8b) and hyperintense on T2WI and STIR images (Fig. 8c–h). There was no cortical break or significant adjacent soft-tissue thickening. The histopathology of the curettage specimen was consistent with giant cell tumour. He was discharged following an uneventful post-operative recovery. Post-curettage radiograph of the right ankle joint showed the curetted area filled with bone chips and no residual tumour (Fig. 9a, b). The patient was undergoing regular follow-up.

More than a year after the last surgery, he again presented with pain in the right ankle joint and imaging performed at this time showed significant lysis of the bone chips, significant soft-tissue thickening anteriorly and subtle fluffy periosteal reaction in the lateral aspect of the distal tibia suggestive of recurrence.

Discussion

Giant cell tumour is a benign neoplasm of bone with a peak incidence seen between 20 and 45 years of age. GCT shows a slight female preponderance and can arise in association with focal dermal hypoplasia (Goltz syndrome) [3]. GCTs are typically solitary lesions seen in the distal femur, proximal tibia, distal radius and proximal humerus and predominantly involve the epiphysis and adjacent metaphysis. Fewer than 5% of GCTs involve tubular bones of the hands and feet. MCGCT accounts for less than 1% of cases of GCT [2]. Most cases of MCGCT reported in the literature are either single cases or small series [2–15]. In 2006, Hoch et al. published the largest series of 30 cases of MCGCT of bone [2]. A literature review of reported cases of MCGCT worldwide by Dhillon and Prasad in 2007 revealed 101 cases [4]. Hoch et al. [2] classified tumours as “synchronous” when multiple tumours had been discovered at the initial presentation, or when a second tumour had been diagnosed within 6 months of the first, or “metachronous” if the second tumour developed more than 6 months after the first lesion. Accordingly, our patient was considered to

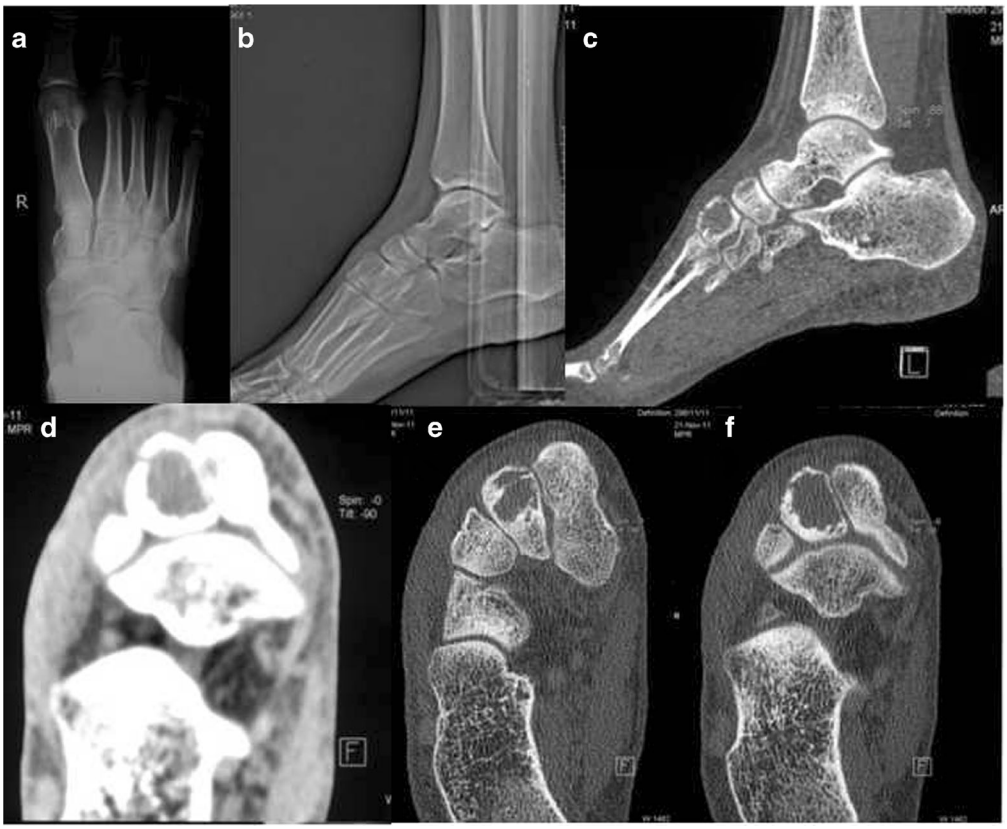


Fig. 4 **a** Radiograph and **b** scanogram of the right foot showing a lytic lesion in the intermediate cuneiform bone (not so clear on the radiograph). **c** Sagittal and **d** coronal CT reformatted images showing the lytic expansile lesion more clearly involving the intermediate cuneiform bone extending up to the articular margins. **e**, **f** Axial CT images in the bone window showing the same. No cortical break was visible

have "metachronous" GCT. Patients with multicentric GCTs usually have two or three lesions [5–9] and Park and Jeon reported ten lesions in their case [10]. The time duration between MCGCT may range between 2 years and more than 20 years [11, 16]. As per reported series, MCGCT occurs at a younger age than solitary GCT, with a mean age of 22.5 years [4]. Our patient was 15 years old at initial presentation and had had three lesions diagnosed by the age of 21 years. Although MCGCTs, similar to their solitary counterparts, commonly affect long bones around the knee, it was found that they tend to develop more frequently in atypical sites such as the small bones of the hands and feet and at atypical locations such as the metaphyseal and metadiaphyseal regions in the bone [4] and are common in the immature skeleton [12, 13]. In our patient, too, two of the three lesions affected the small bones of the hands and feet and both metacarpal and humeral lesions involved the metadiaphyseal regions of these bones. Diagnosis of MCGCT is usually based on clinical, serological and radiographic findings [13]. Plain radiographs of GCTs show an expansile, eccentric lesion with lobulated areas of osteolysis and well defined geographic margins with a narrow zone of transition. MRI is the best imaging procedure and is useful in assessing the extent of intraosseous spread and in defining soft-tissue and joint involvement. Large amounts of hemosiderin give areas of low signal intensity on MRI. CT is an alternative for defining intraosseous tumour extension [14].

The pathogenetic mechanism of MCGCT may be different from that of solitary GCT in view of differences in age and site predilection. Although still under debate, suggested mechanisms include direct extension to contiguous bone, metastasis, iatrogenic seeding of tumour cells and multiple independent foci of disease [4]; the latter may be true in our case. As per reported series, individual MCGCT lesions do not differ radiologically or histologically from solitary GCTs. The same was noted in our patient as well. The differential diagnosis for such polyostotic lesions includes multifocal osteomyelitis (a cystic type of tuberculosis), metastasis, multiple myeloma

Fig. 6 **a–c** Selective digital subtraction angiography of the left subclavian artery and the subselective artery branch supplying the left proximal tumour shows significant tumour blush (*red arrow*) which, post-embolization (**c**), is not showing tumour blush (*black arrow*). **d** Post-operative radiograph of the left shoulder shows complete excision of the tumour with a rush nail placed connecting the acromion, the remaining head of the humerus and the shaft of the humerus. **e**, **f** Radiographs of the left shoulder after the fibular graft ▶

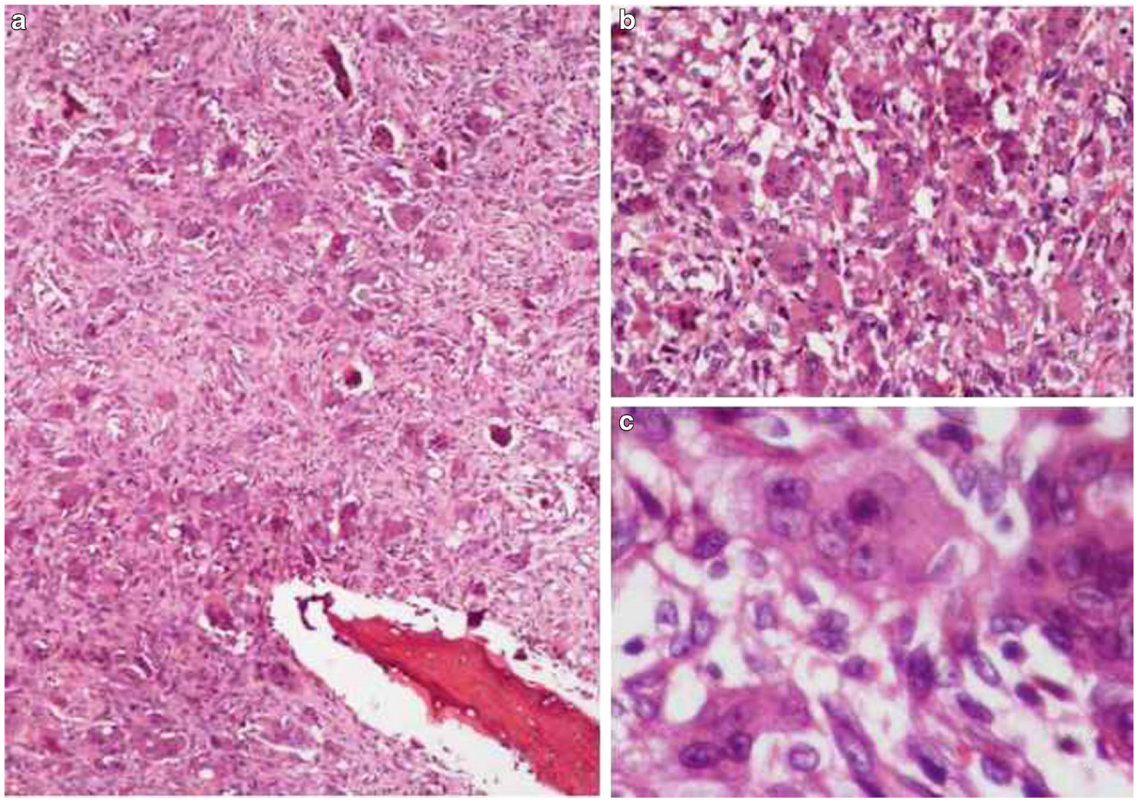
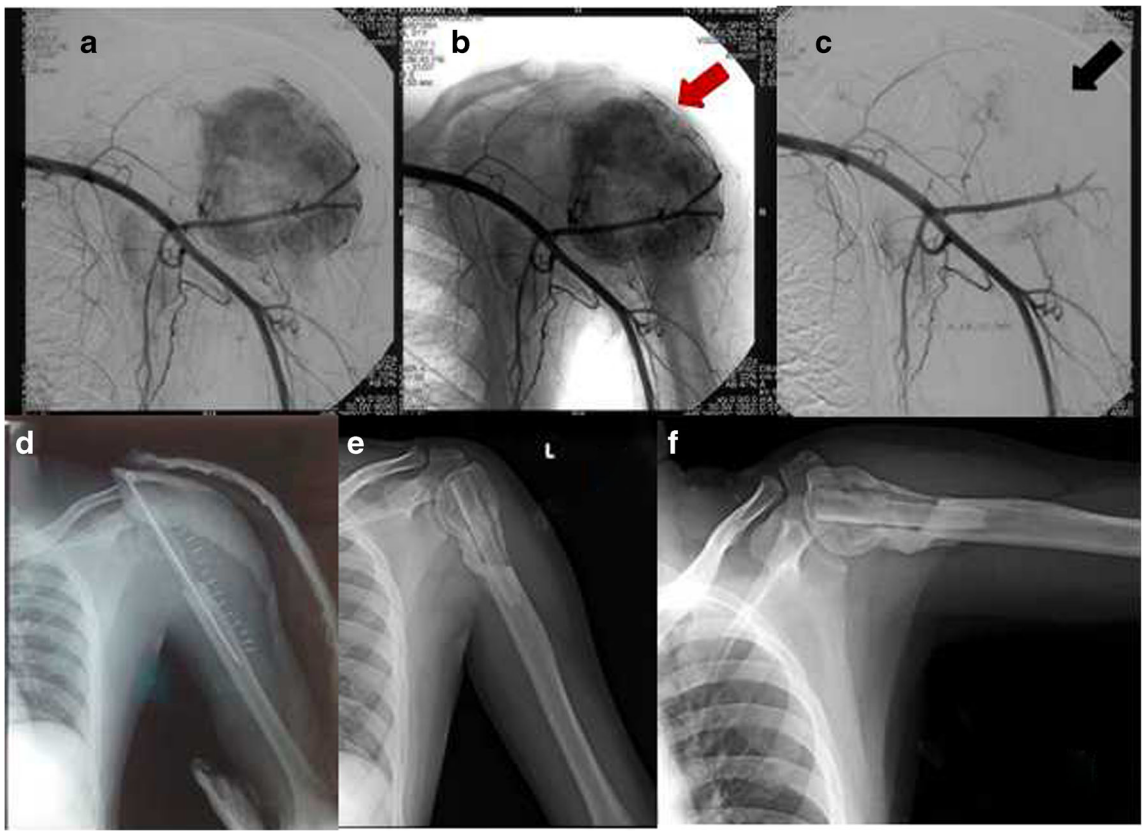


Fig. 5 Sections show a lesion comprising mononuclear spindle cells admixed with multinucleated osteoclastic giant cells in spatial arrangement. The nuclei of the giant cells resemble those of the adjacent mononuclear cells. (H&E: **a** ×40, **b** ×100, **c** ×400)



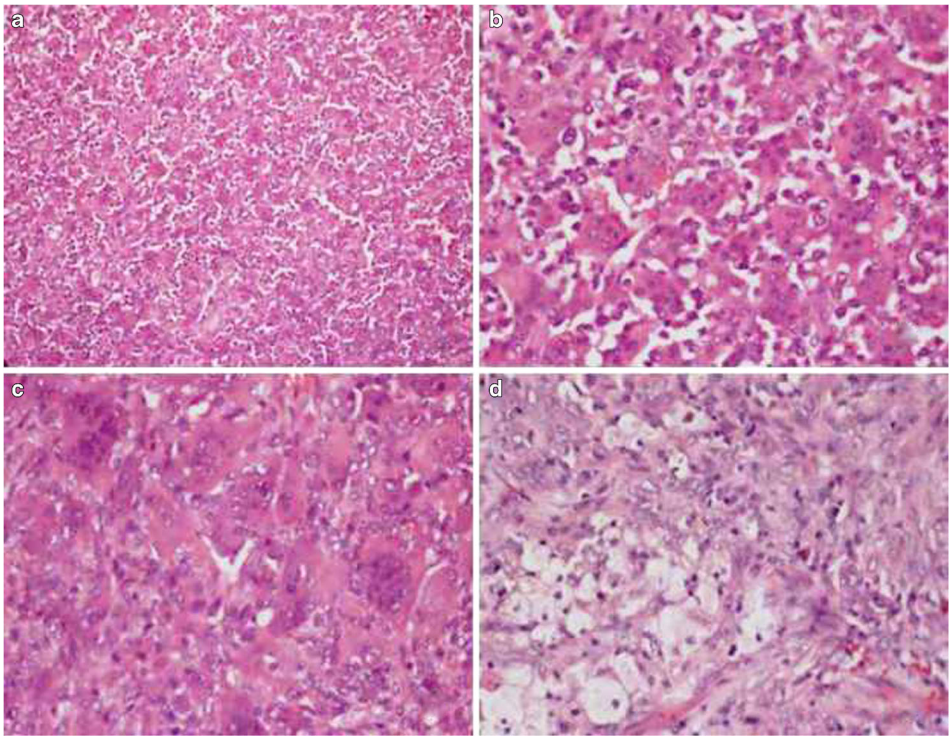


Fig. 7 Sections show a lesion comprising spatially arranged mononuclear spindle cells admixed with multinucleated osteoclastic giant cells. The giant cells show many nuclei, which resemble those of adjacent mononuclear cells. Focal areas showed collections of foamy cells. (H&E: **a** ×40, **b** ×100, **c** ×200, **d** ×200)

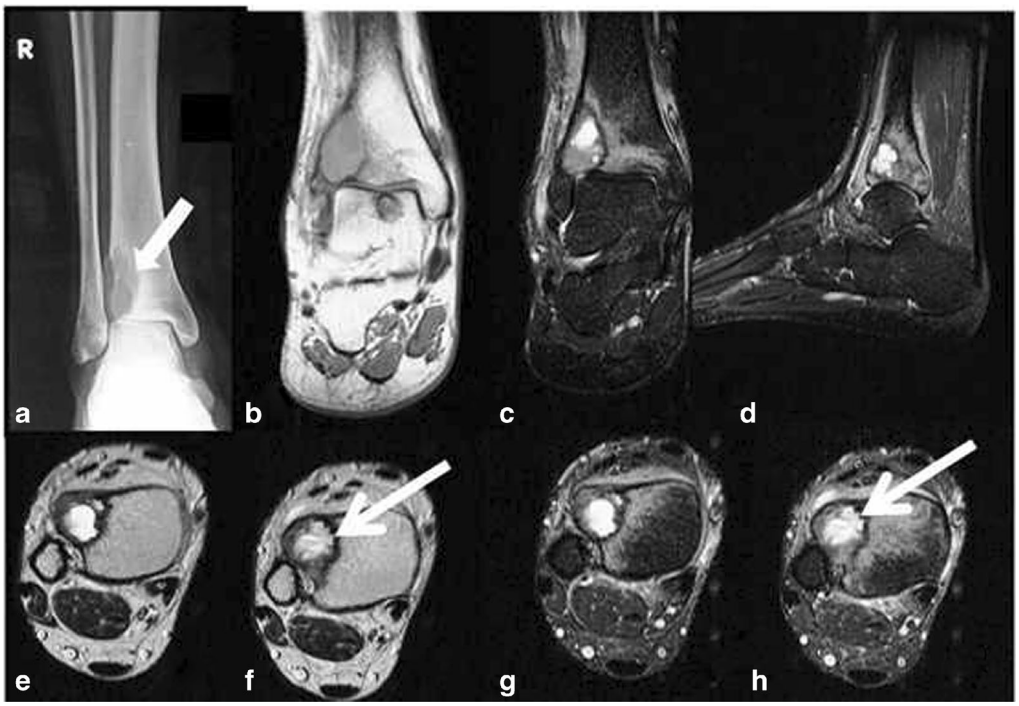


Fig. 8 **a** Radiograph of the right ankle, AP view showing a well-defined eccentric lytic, slightly expansile lesion (*thick white arrow*) noted in a subarticular location of the lateral malleolus of the right tibia, the transition zone is narrow, few septations are seen within and no periosteal reaction is noted. MRI of the right ankle shows that the lesion is hypointense on **b** axial T1WI, hyperintense on **c** coronal, **d** sagittal, **g**, **h** axial STIR, **e**, **f** axial T2WI with fluid–fluid levels (*thin white arrow*). No cortical break or significant adjacent soft-tissue thickening was seen

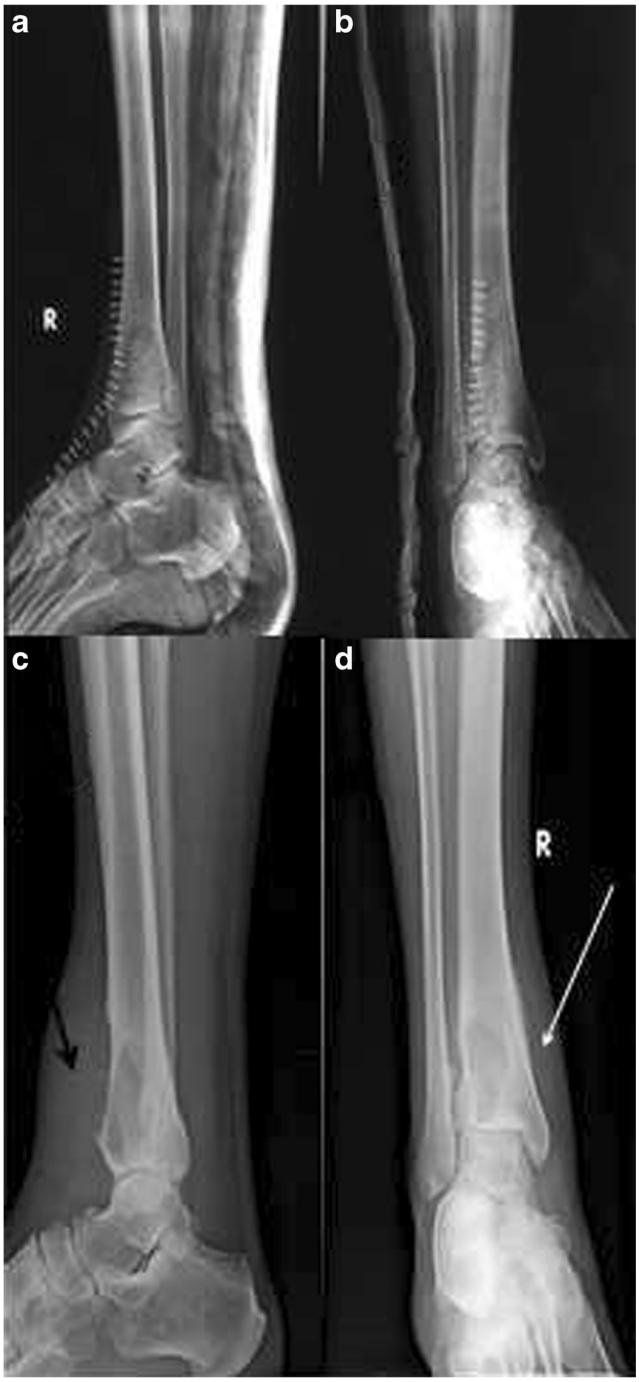


Fig. 9 **a**, **b** Radiographs of the right ankle joint post-curettage and bone chips of the lesion. **c**, **d** Follow-up radiographs showing significant lysis of the bone chips, significant soft-tissue thickening anteriorly (*black arrow*), subtle fluffy periosteal reaction (*white arrow*) in the lateral aspect of the distal tibia. These features are suggestive of recurrence of giant cell tumour with significant soft-tissue thickening and subtle periosteal reaction

[15] and brown tumours (hyperparathyroidism) [17]. Laboratory investigations ruled out the possibility of brown tumour in our patient and clinical presentation in our patient was inconsistent with the other listed conditions. Current treatment modalities are similar for solitary GCT and MCGCT and include intralesional curettage or wide resection with reconstruction of the defect [14]. MCGCTs do not behave any differently with regard to recurrence (and metastases) compared with solitary GCT [3]. Risk of metastasis is comparatively higher for MCGCTs (5–10%) than for solitary GCT (1–2%) [4]. Even though our patient had recurrence of the right tibial lesion, he has had no metastases to date.

Conclusion

Although extremely uncommon, GCTs can present as multicentric metachronous lesions. Such lesions can occur at a young age and can involve small bones of the hands and feet, which is uncommon for solitary GCTs. Hence, bone scan screening is recommended in cases of GCT occurring in younger patients, at atypical locations (small bones of the hands and feet) and those involving meta-diaphyseal regions, to ensure early diagnosis of MCGCT.

Compliance with ethical standards

Sources of support None.

Conflicts of interest None declared.

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