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CASE REPORT

Metachronous multicentric giant cell tumour of the upper extremity in a skeletally immature girl : A rare presentation

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Giant Cell tumour (GCT) or Osteoclastoma is a benign locally aggressive tumour with a tendency for local recurrence. Long tubular bones (75-90%) are frequent sites of involvement. GCT constitutes 5% of all primary bone tumours. Metachronous multicentric giant cell tumour of bone is a rare entity. Multicentric GCT, in contrast to unifocal GCT, has a tendency to involve the small bones of hands and feet, involving the metaphysis/diaphysis of long bones and tends to occur in a slightly younger population. We report a young girl presenting with metachronous multicentric recurrent benign GCT, with the lesions involving the ipsilateral right hand and distal humerus. She was successfully treated with an aggressive surgical approach (en-bloc resection).

Key words : giant cell tumour ; multicentric ; metachronous ; en-bloc resection.

INTRODUCTION

Giant-cell tumour (GCT) of bone was first described by Cooper and Travers in 1818 (*3*). It represents approximately 5% of all primary bone tumours (*4*). In its most common presentation, GCT is a solitary neoplasm occurring in the meta-epiphysis of a long bone in a skeletally mature individual (*9,20*). The six most common sites of GCT were the distal femur, proximal tibia, distal radius, proximal femur, sacrum, and proximal fibula in Goldenberg's series (*7*). Patients with GCT present with nonspecific symptoms including pain, soft-tissue swelling and limitation of movements at the adjacent joint. GCT presents radiographically as a radiolucent lesion characteristically involving the metaphysis of a long bone, but extending across a closed physis into the epiphysis to abut the articular surface. Often the tumours are located eccentrically within the meta-epiphysis, and they typically have well-defined but non-sclerotic margins. This characteristic appearance often allows a confident radiologic diagnosis. In most of the cases GCT is a benign lesion, but malignancy in these tumours is also known. Hutter *et al* (*10*) and Dahlin *et al* (*5*), proposed a criterion to define a primary and secondary malignant GCT. A primary GCT is a malignant tumour of bone in which sarcomatous tissue is juxtaposed with zones of typical benign giant-cell tissue, and a secondary malignant GCT is a sarco-

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matous lesion occurring at the site of a previously documented benign GCT. The incidence of malignant GCTs in literature ranges from 1.5% for Goldenberg *et al* (*7*) to 7% for Campanacci *et al* (*2*) and 30% for Hutter *et al* (*10*).

The presence of more than one primary GCT (multicentric GCT) in the same patient is very rare. Multicentric GCT represent less than 1% of all GCT's (*4,17,19*). The mechanism by which GCT involves multiple sites is unknown. Multicentric GCT, in contrast to unifocal GCT, has a tendency to involve the small bones of the hands and feet, to involve the metaphysis/diaphysis of long bones and to occur in a slightly younger population (*19*). Multicentric GCT has been reported infrequently in literature (*4,8,17*).

We present a case of metachronous multicentric and recurrent benign GCT of the upper extremity in an adolescent girl, successfully treated with an aggressive surgical approach.

CASE REPORT

A 15-year-old girl presented to the orthopaedic outpatient department in January 2004 with pain and a palpable mass on the dorsal aspect of her right hand. No other swelling was evident on clinical examination. Radiographs revealed an expansile lytic lesion of the 4th metacarpal involving the articular surface of the carpo-metacarpal and metacarpo-phalangeal joints (fig 1). MRI showed an expansile lytic lesion of the entire 4th metacarpal with marked cortical ballooning, erosion and splaying of adjacent soft tissue with no obvious extension across the proximal and distal joint. The patient underwent excision of the 4th metacarpal with reconstruction of the defect with a fibular graft (fig 2). Biopsy from the lesion showed multinucleated giant cells among a background of stromal cells, consistent with a diagnosis of GCT. No malignant features were noted on the pathology specimens.

The patient was doing well until July, 2005 (one and a half years following the initial lesion) when she presented with local recurrence. Radiographs showed recurrence of the tumour with involvement of the 3rd and 5th metacarpal with nearly complete erosion of the fibular graft (fig 3). The recurrence was managed with excision of the 3rd, 4th (grafted fibular strut) and 5th metacarpals and reconstruction with fibular grafts (fig 4). Pathological assessment revealed a typical GCT without malignant features.

The patient was doing well until August 2008 (four and a half years after the initial lesion) when she presented with pain and swelling around her right elbow. Clinical examination revealed a tender swelling over the lower end of the right humerus, involving the elbow joint. Radiographs revealed an expansile lytic lesion in the distal humeral metaphysis, extending into the epiphysis to abut the articular surface, with prominent soft tissue shadow (fig 5 & 6).

Investigatory work-up was done to rule out hyperparathyroidism as a cause of these multifocal and recurrent bony lesions. Results of blood biochemistry, including levels of serum calcium, phosphorus and alkaline phosphatase were normal, and there was no radiographic evidence of hyperparathyroidism. Fine needle aspiration cytology from the lesion revealed features typical of GCT. The lesion was treated by resection-arthrodesis with a free fibular graft. Pathology again was consistent with a GCT of bone. At her most recent follow-up one year after the last surgery, there was no evidence of recurrence (fig 7) and a satisfactory functional outcome was achieved. Metastatic disease to the lungs was not observed on serial radiographs of her chest.

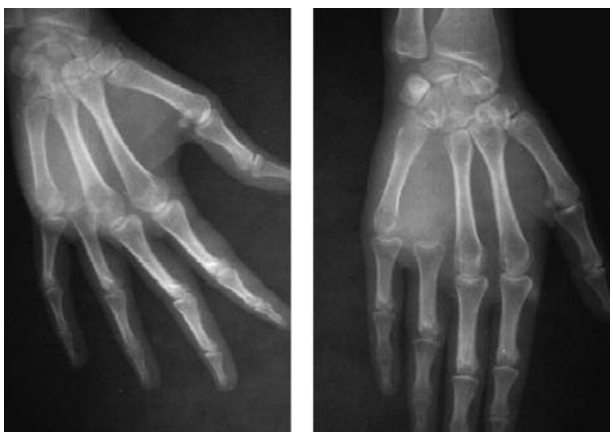


Fig. 1. — Radiograph of the right hand showing an expansile lytic lesion of the 4th metacarpal involving the articular surface of the carpo-metacarpal and metacarpo-phalangeal joint. Note that the whole architecture of the 4th metacarpal is lost.

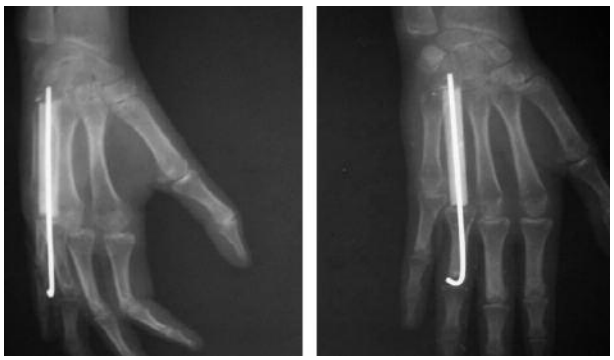


Fig. 2. — Post-op radiograph showing excision of the 4th metacarpal and reconstruction of the defect with a fibular graft fixed with a K-wire.

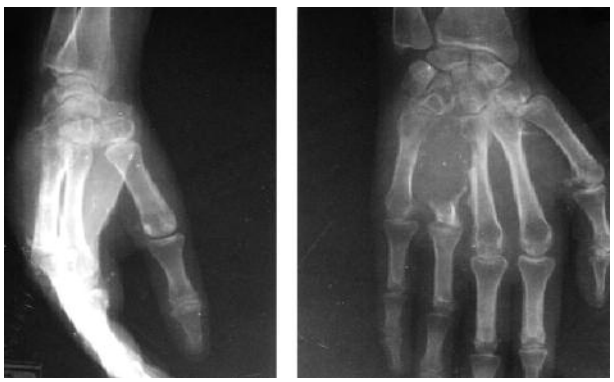


Fig. 3. — Radiograph of the right hand showing recurrence of the tumor with involvement of the 3rd and 5th metacarpal with near complete erosion of the grafted fibula (1 & ½ year following initial lesion).

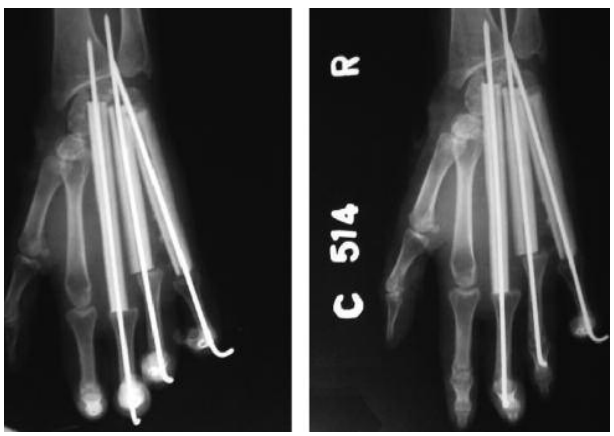
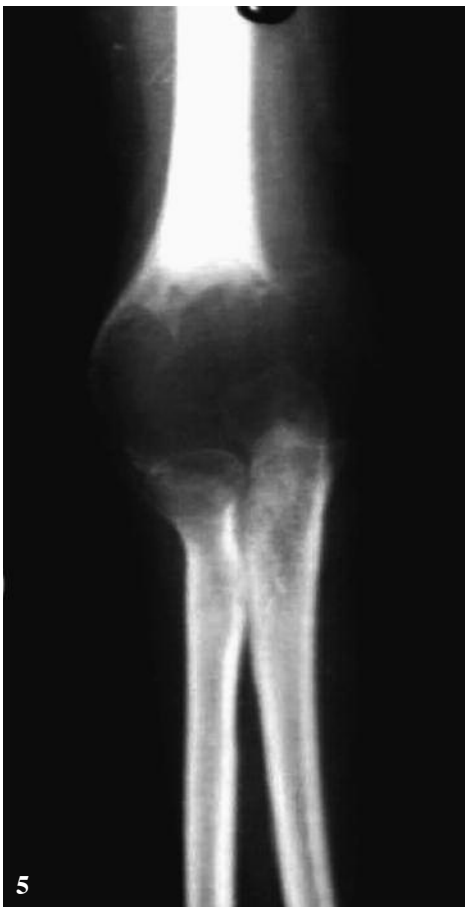


Fig. 4. — Radiograph of the right hand showing excision of 3rd, 4th (grafted fibular strut) and 5th metacarpal and reconstruction with fibular grafts fixed with K-wires.



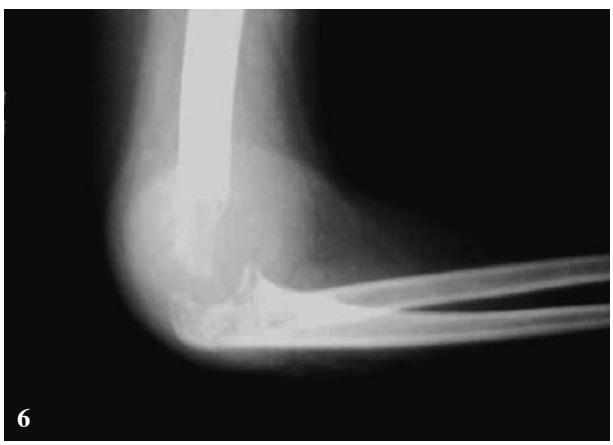


Fig. 5 & 6. — Radiograph of the right elbow (AP and Lateral view) showing an expansile lytic lesion in the distal humeral metaphysis extending into the epiphysis to abut the articular surface, with prominent soft tissue shadow.

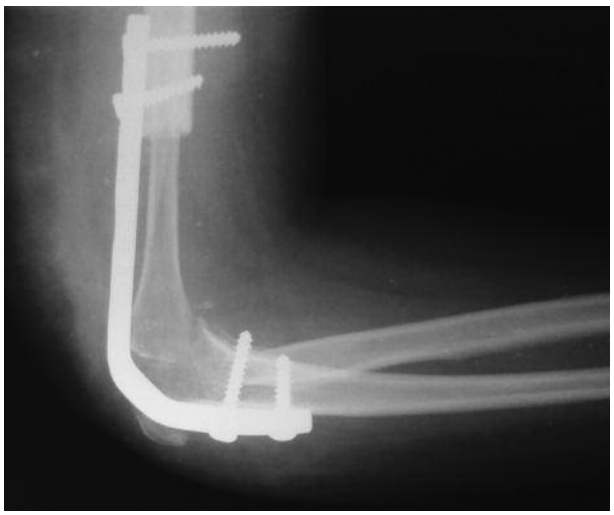


Fig. 7. — Radiograph of the right elbow showing resection-arthrodesis with a free fibular graft without any evidence of recurrence (one year since last operation).

DISCUSSION

Giant cell tumours are typically seen in young and middle-aged adults, with 80% of tumours occurring in patients between the ages of 20 and 50 years, and peak prevalence in the third decade of life (*12*). GCT is not common in skeletally immature individuals. The treatment for GCT of bone is basically surgical resection.

The presence of more than one primary GCT in the same patient is rare (*4,8,17*). Multifocal GCTs account for less than 1% of all patients presenting with GCT (*4*). The lesions may present synchronously or metachronously. Most multicentric GCT's are synchronous, occurring within a poorly defined period of time from the initial tumour (*8*). Sixty eight percent of cases of multicentric GCT occur with a disease-free time interval shorter than 4 years (*8*). In the case reported, discovery of the metacarpal lesion preceded that of the distal humeral lesion by 4.5 years ; at initial presentation there was no clinical sign of involvement of any other site besides the 4th metacarpal. Involvement of multiple bones poses difficulty in therapeutic assessment (*1*). Other primary osseous lesions may have a multicentric presentation : fibrosarcoma, osteosarcoma, chondroblastoma, hyperparathyroidism, infection, eosinophilic granuloma, Paget's disease, multiple and metastatic carcinoma (*20*). The aetiology of multifocal GCT is uncertain. Solitary benign GCTs may metastasize to the lung or undergo malignant transformation (either *de novo* or following radiation therapy) ; however, there does not appear to be any increased risk of pulmonary metastases in patients with multifocal tumours, and pathologic analysis of multifocal GCT reveals findings identical to histologically benign solitary tumours (*12*). This suggests that the multifocality of some GCTs is not a metastatic phenomenon, but rather represents the separate development of the tumour at multiple sites.

A literature review suggests that the average age of presentation of patients with multifocal GCTs is younger than that of patients with solitary lesions (*20,22*), although multifocal GCTs have been described in patients as old as 62 years (*18*). The patient presented here was 15 years old at the time of initial diagnosis. Cummings *et al* (*4*), in a review of 29 cases of multicentric GCT, found that approximately 80% of the patients were 25 years old or younger at the time of initial diagnosis. The youngest patient in their series was 10 years old.

While the knee is the most common site of involvement in patients with multifocal GCT, there is an increased prevalence of involvement of the small bones of the hands and feet (*12*). There is also an increased prevalence of diaphyseal (rather than the usual epiphyseal) extension of the tumour in multifocal cases. This may be particularly true in children who still have open physes, which may act as barriers to epiphyseal spread.

Multifocal GCTs must be differentiated from other multiple lesions that present certain similarities for the most part roentgenographically, by clinicoradiological, biological and histological studies (*7,15,20*). In our patient, multifocal GCT presented no special problems in diagnosis. Each lesion exhibited the typical histopathological pattern of GCT, while most of the lesions also had roentogenographic features consistent with GCT. Brown tumours may mimic GCTs pathologically. Hence, a metabolic workup should be obtained when multifocal GCT is considered. Metabolic workup was normal in our patient.

GCT is an infrequent and unpredictable bony lesion (*6*). Although numerous attempts have been made to predict the behaviour of GCT, there are no definite biological or histological parameters to determine the prognosis or aggressiveness of this lesion (*11*). In GCT local recurrence is more frequently observed in the first three years after treatment. The patients with multiple local recurrences are more likely to develop metastases (*16*). Local recurrence is associated with a 6% incidence of metastatic disease, whereas in patients without local recurrence, this incidence is less than 1% (*16*). Multifocal lesions also appear to be more locally aggressive than their solitary counterparts and have higher rates of recurrence, as in our case in which there was recurrence of the metacarpal lesion even after en-bloc resection. Recurrence of solitary type GCT of bone has been reported to be expected in 10 to 60% of cases ; the rate depends on the type of treatment, the anatomic location, and the cortical integrity of the involved bone (*7, 21*). The multicentric variety is often of a higher stage at diagnosis and is more often associated with a pathological fracture than the unifocal tumour (*9*). En-bloc resection is the most successful surgical technique for treating both multicentric and solitary lesions (*7*). The recurrence in our case was treated by en-bloc resection and there was no evidence of further recurrence.

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