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Skeletal Radiology

Multicentric giant cell tumor of skeleton*

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Clinical information

A 29-year-old woman was admitted to our hospital suffering from pain in the right knee and ankle. Seven years before (in 1983) she had undergone curettage in another hospital and autografts for a painful lytic lesion in the distal part of her right femur (Figs. 1, 2). The histologic diagnosis was giant cell tumor. At a routine follow-up in 1985, a bone scan showed uptake of the radionuclide at the distal femur (the operation site), the right proximal femur, and the right proximal tibia (Fig. 3). No symptoms were reported. A further bone scan was done in 1988, when the patient started to complain of knee pain. The three above-mentioned sites showed increased radionuclide uptake, with further increased uptake in the proximal tibia. On radiographs, some abnormalities were identified in the proximal tibia. At the time of admission to our hospital the patient had pain, swelling, and tenderness of the right knee and ankle. The knee had a normal range of motion. A bone scan showed increased uptake of the radionuclide in the proximal femur, the distal femur

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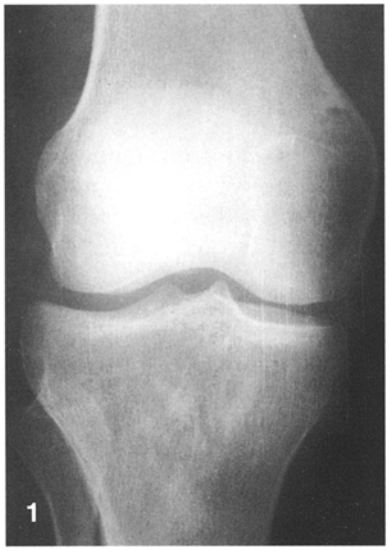


Fig. 1. Anteroposterior radiograph of the distal part of the femur and the proximal tibia in 1983 shows the osteolytic lesion in the medial femoral condyle before surgery and an osteolytic area in the proximal tibia with some sclerotic features

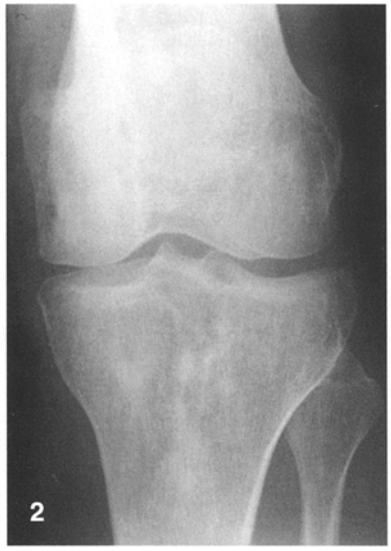


Fig. 2. Anteroposterior radiograph of the knee after surgery in 1984 again shows the lesion in the proximal tibia and an absence of recurrence in the femoral condyle. At that time the patient was asymptomatic

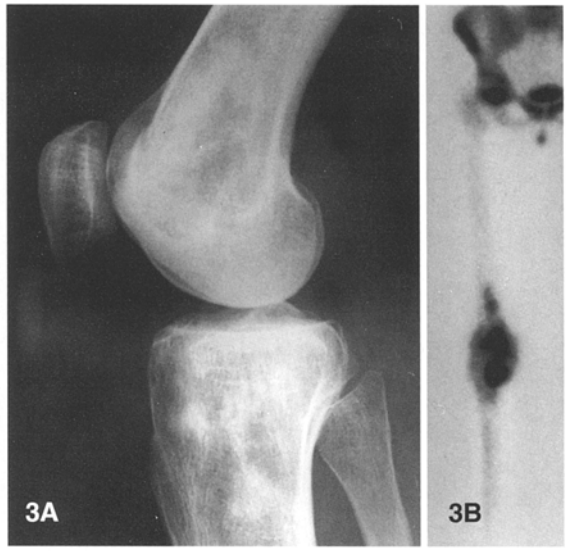


Fig. 3. **A** Lateral radiograph of the knee and **B** bone scan in 1985. Osteolytic areas are evident in both the distal femur and the proximal tibia (A). The bone scan shows increased uptake of radionuclide at both sites. Increased uptake is also visible in the femoral head. At this time the patient started to complain of occasional knee pain

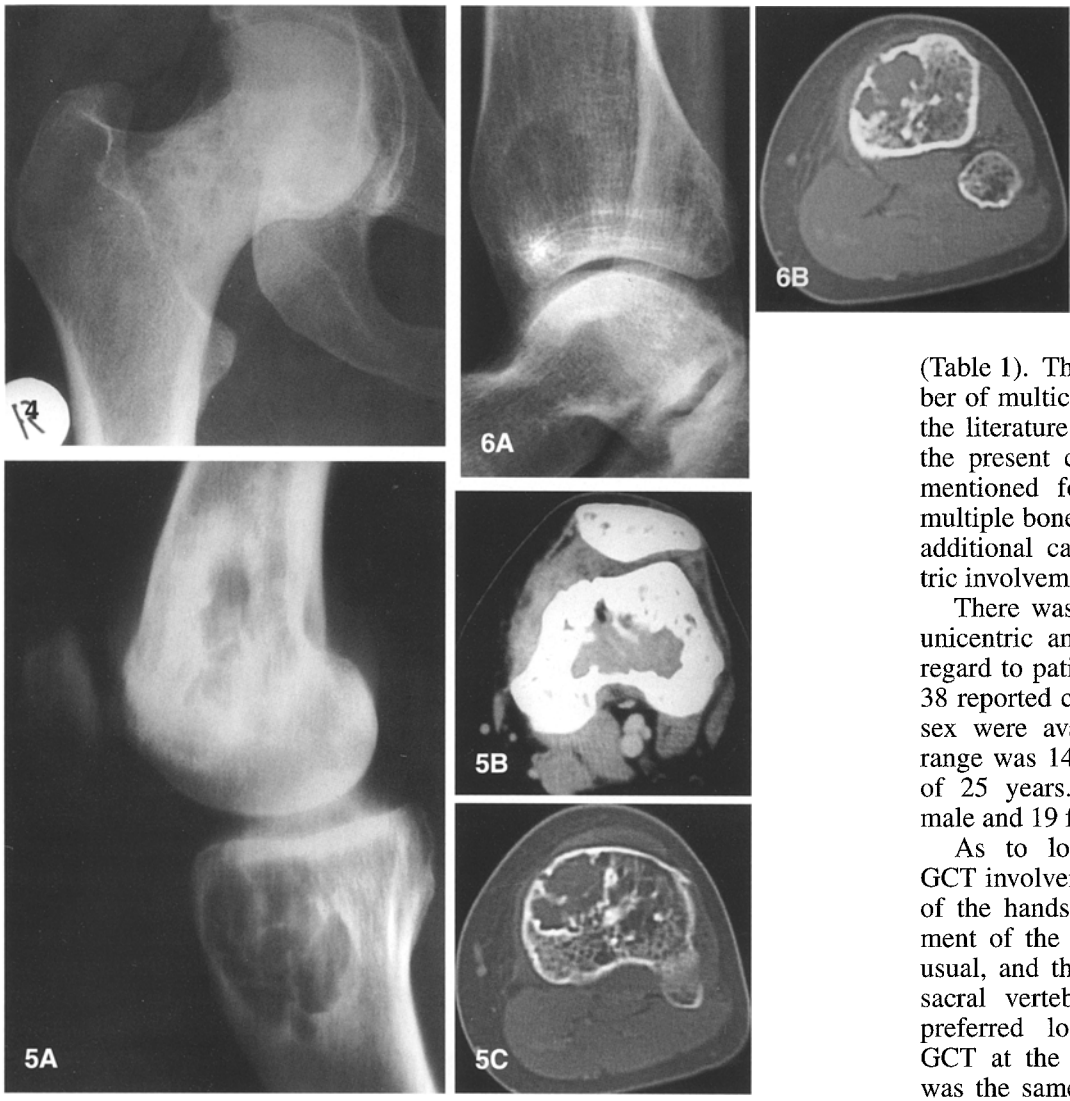


Fig. 4. Anteroposterior radiograph of the proximal femur in 1990 at the time of admission shows an osteolytic area in the femoral head and neck

Fig. 5. **A** Lateral radiograph of the knee, **B** axial CT scan of the distal femur, and **C** axial CT scan of the proximal tibia at the time of admission to our hospital show a recurrent lesion in the distal femur and a lytic area with pseudoseptation in the proximal tibia

Fig. 6. **A** Lateral radiograph and **B** CT scan of the distal tibia at the time of admission clearly show a lytic lesion, which was mildly symptomatic

(site of previous surgery), the proximal tibia, and the distal tibia. Radiographs of the proximal femur showed a lytic lesion, appearently not very active, since it was well defined and contained sclerotic rims of bone (Fig. 4). The hip was asymptomatic. Laboratory tests showed normal serum concentrations of calcium, phosphorus, and parathyroid hormone, and a slight increase in alkaline phosphatase. It was elected not to treat the lesion in the hip, but curettage of the lesions in the proximal and distal tibia was performed (Figs. 5, 6), followed by the placing of autografts and cement in the proximal tibia and cement only in the distal tibia.

The diagnosis was multicentric giant cell tumor (GCT) of the skeleton (Figs. 7, 8). The differential diagnosis included hyperparathyroidism and other giant cell-rich lesions involving bones.

Discussion

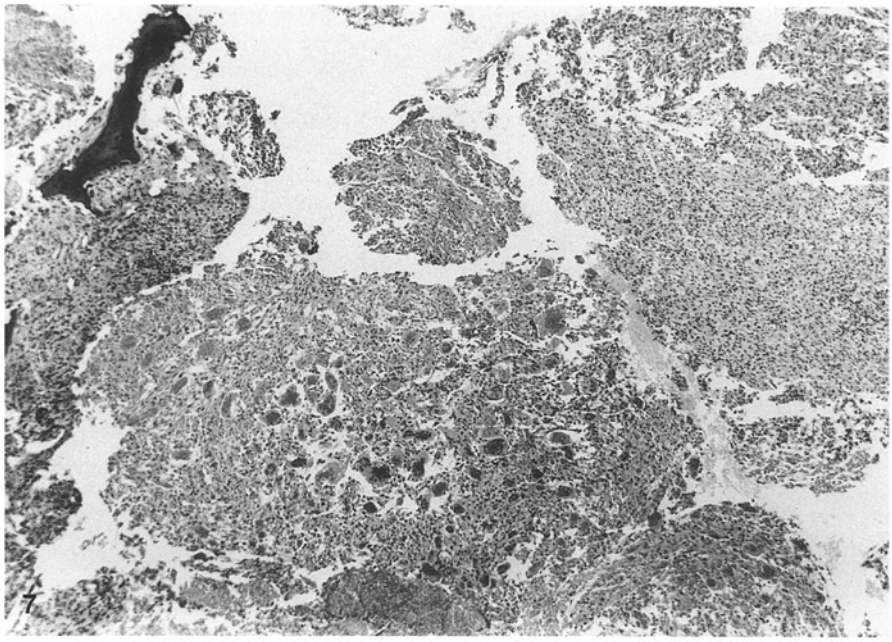
Multicentric GCT is an extremely rare lesion. In 1980 Feldman reviewed the literature and was able to collect 23 cases [1]. Since then 15 additional cases have been reported (Table 1). Therefore, the total number of multicentric GCTs reported in the literature so far is 38 (including the present case). Dahlin and Unni mentioned four further cases with multiple bone involvement, and in an additional case there was multicentric involvement of the radius [8].

There was no difference between unicentric and multicentric GCT in regard to patient age and sex. Of the 38 reported cases, data as to age and sex were available in 34. The age range was 14–62 years, with a mean of 25 years. Fifteen patients were male and 19 female.

As to location, in multicentric GCT involvement of the small bones of the hands was frequent, involvement of the sphenoid and skull unusual, and the thoracic, lumbar, and sacral vertebrae were spared. The preferred location of multicentric GCT at the end of the long bones was the same as in unicentric GCT, but the incidence of metaphyseal involvement was higher (5 out of 35 locations) [9].

In the 38 cases of multicentric GCT, 120 sites were reported. As shown in Fig. 9, the total number of sites per case varied from two to nine. Most patients (15) had two tumor sites, seven patients had three and another seven had four sites. Two patients had five and two had seven tumor sites, while only one had eight and one other nine.

The question of whether multifocal GCT is a multicentric synchronous, metachronous, or metastatic lesion is difficult to answer [1]. In the Mayo clinic series of 11 patients, 3 patients had simultaneous multiple lesions, without any previous history of giant cell tumor, while in the other 8, subsequent lesions appeared later, the interval between the first and the last lesion varying from 4 months to 16 years. Of the 15 cases reported af-



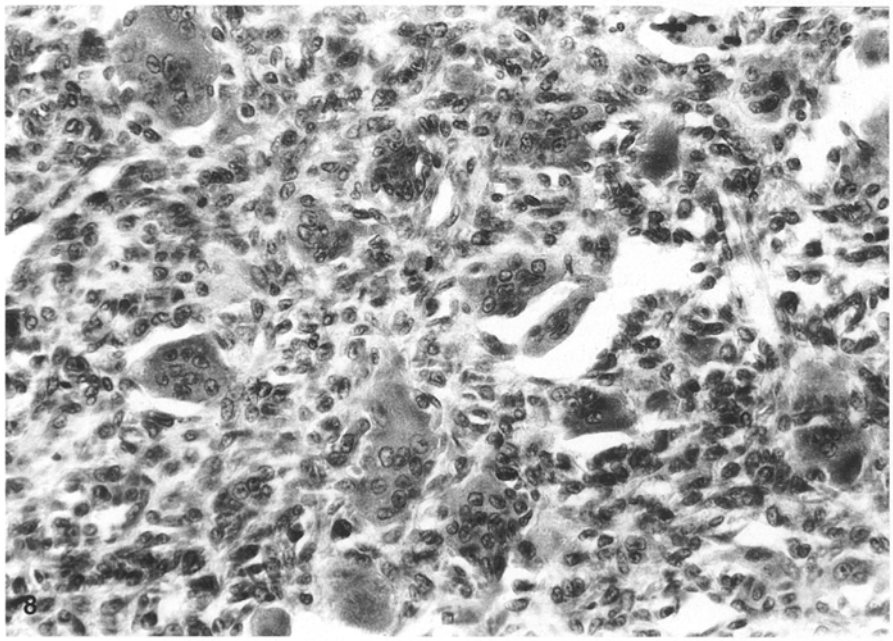


Fig. 7. Low-power micrograph of the tumor specimen show areas of giant cell tumor and host trabecular bone. (H&E, ×60)

Fig. 8. At a higher magnification, proliferating cells with round oval nuclei are seen surrounding multinucleated giant cells. No fibrous stroma is detectable between the cells. Nuclei of the mononuclear and multinucleated cells are similar. (H&E, ×400)

ter Feldman's review [1], 3 were synchronous and 12 metachronous. In the last group, the interval between the first and the last lesion varied from 3 months to 21 years.

Radiographically, multiple GCT involving the end of the long bones showed expanded eccentric nonmineralized radiolucency. This coincides with the radiographic appearance of solitary GCT. In flat bones or the small bones of the hand, the radiographic features were less distinctive.

Histologically there were no differences between solitary and multicentric GCT. Oval round cells forming giant cells were the consistent histologic pattern. Multifocal GCT should be differentiated from other multifocal giant cell-rich lesions by combined clinical, roentgenographic, biochemical, and histopathologic studies. More specifically, hyperparathyroidism has to be excluded by biochemical blood and urine tests. The possibility of preexisting systemic conditions in which GCT of bone is known to arise, such as Paget's disease, must also be considered. In the literature, four cases of multiple GCT of bone associated with Paget's disease have been reported [10].

There are some other primary osseous tumors with a giant cell component that may be multicentric, such as fibrosarcoma, osteosarcoma, angiosarcoma, and chondroblastoma [9].

Our case, with metachronous tumor behavior, had a 7-year history between the first diagnosis and the last lesion. The patient was in the most common age group. The radiographic appearance of the lesion was consistent with a diagnosis of stage 2 GCT in the distal femur, proximal tibia, and distal tibia. The lesion in the proximal femur was not treated. The imaging studies showed a nonaggressive lesion that in this clinical setting was suggestive of an involuting GCT. The lesion was latent; no surgical treatment was performed, and it was decided just to monitor the patient. In the other two locations material for histologic evaluation was available and GCT was diagnosed. As the lesion was painful, a thorough curettage was considered adequate for tumor control.

As Sim et al. [9] pointed out, from the therapeutic standpoint multicentric GCT represents a challenge to the surgeon because each lesion has to be treated separately according to surgical stage and location.

In *summary*, a case of multicentric metachronous GCT was presented. The clinical and radiographic features of multicentric GCT as reported in the literature and in the present case were discussed. The multiple bone involvement made therapeutic assessment difficult. The surgical stage as well as the location of each lesion were important in planning surgery.

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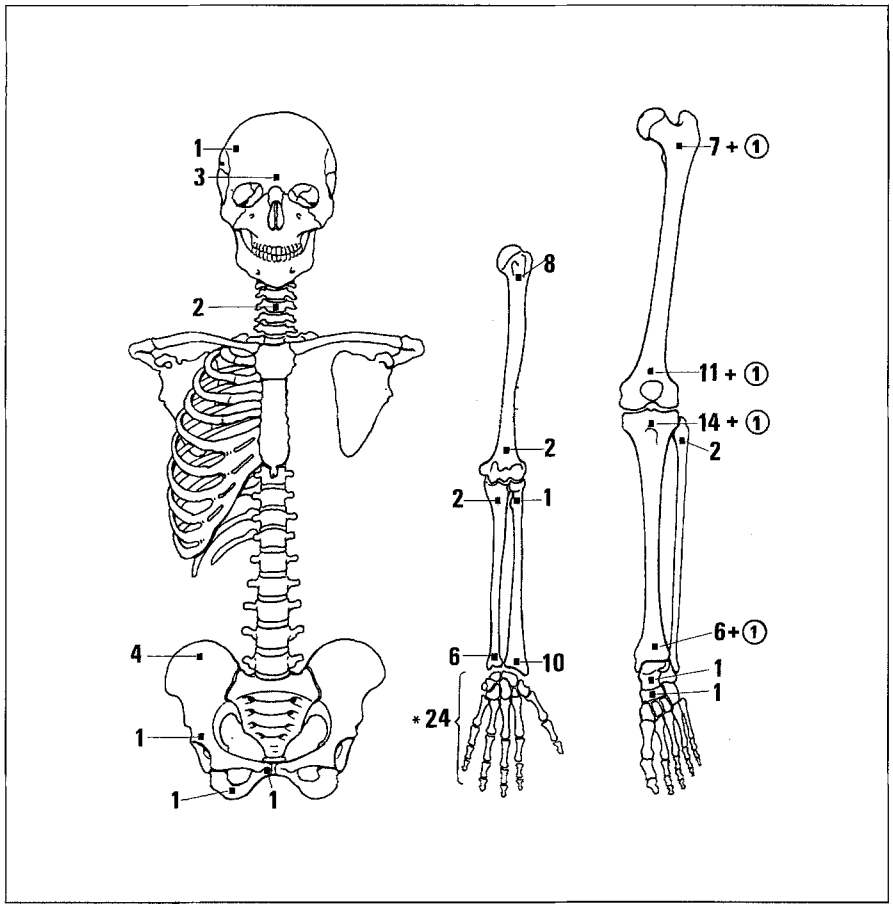

Fig. 9. Distribution of tumor sites in 38 cases of multicentric giant cell tumor of bone (37 reported in the literature plus the present case). Sites involved in the present case are *circled*. The figure shows the distribution of 112 sites. Eight further sites involved (not specified more closely) were: hemipelvis 1, humerus 1, radius 2, femur 3, tibia 1 (these are not included in the figure, since the part of the bone involved was not reported). * The distribution of the 24 sites in the hand was: carpus 4, metacarpus 8, phalanges 11; plus 1 "hand" (not specified more closely)

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Table 1. Patient sex and age and tumor sites in the 15 cases of multicentric giant cell tumor reported since Feldman's 1980 review [1]

Year	Reference	No. of cases	Patient sex	Patient age (years)	Total no. of sites	Sites
1980	Peimer et al. [2]	5	M	19	3	LM, LP, LF
			M	30	7	RPU, RDH, RM, RP, LC, LM, RC
			F	20	4	LP, LP, LH, LR
			F	17	2	RT, LP
			F	18	2	LR, RP
1986	Wu et al. [3]	1	F	17	3	Sp, RPT, LDR
1987	Gaur et al. [4]	1	F	38	3	RPT, RDF, LP
1987	Mittal et al. [5]	1	M	20	5	LPH, RPT, RDF, RPF, RI
1989	Williams [6]	1	M	26	3	LDF, LPH, RH
1989	Mirra [7]	2	M	24	2	PFi, DR
			F	9	2	DT, IB
1989	EMSOS revision[a]	3	M	32	4	DR, PFi, H, C
			F	34	2	PT, DT
			F	31	2	PH, DR
	Present case	1	F	29	4	RDF, RPT, RDT, RPF

LM, Left metacarpus; LP, left phalanx; LF, left femur; RPU, right prox. ulna; RDH, right distal humerus; RM, right metacarpus; RP, right phalanx; LC, left carpus; RC, right carpus; LH, left humerus; LR, left radius; RT, right tibia; Sp, sphenoid; RPT, right prox. tibia; LDR, left distal radius; RDF, right distal femur; LPH, left prox. humerus; RPF, right prox. femur; RI, right ilium; LDF, left distal femur; RH, right hemipelvis; PFi, prox. fibula; DR, distal radius; DT, distal tibia; IB, innominate bone; H, hand; C, calcaneus; PT, prox. tibia; DT, distal tibia; PH, prox. humerus; RDT, right distal tibia.

[a] Unpublished data: 3 multicentric cases out of 677 cases of giant cell tumor