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Multicentric giant cell tumor: report of five new cases

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Abstract. The typical giant cell tumor (GCT) is a solitary neoplasm that occurs in the epiphysis or epimetaphysis of long bones. GCT is seen with a slightly increased frequency in females, and 70% of patients are between 20 and 40 years of age at the time of presentation. Multicentric giant cell tumor (MGCT; two or more centers) is an unusual variant of GCT. Patients with MGCT are likely to be younger than those with a solitary lesion. The multicentric variety is often of a higher stage at diagnosis and is more often associated with a pathological fracture than the unifocal tumor. We are reporting five new cases of MGCT, with a total of 21 tumors seen over a period of 25 years from 1967 to 1992.

Key words: Giant cell tumor – Multifocal lytic tumors – Giant cell tumor, multiple – Benign bone tumor – Skeletal neoplasms – Bone imaging

Multicentric giant cell tumor (MGCT) is a rare variant of giant cell tumor (GCT) that may result from synchronous, metachronous, or metastatic involvement. There have been 41 cases of MGCT reported in the literature [1–21]. We add five new cases (Table 1). The literature is reviewed, and the features of the new cases are discussed.

Case reports

Case 1

A 22-year-old man sustained a pathological fracture of the proximal phalanx of the left ring finger (Fig. 1A). GCT was diagnosed and the lesion was treated with curettage and grafting. Following multiple subsequent operations for repeated recurrence, the patient eventually underwent ray resection with transposition of the little

finger. Three years after the initial presentation an additional recurrence resulted in amputation of the long and remaining ring finger followed by radiotherapy to the left hand.

Later that year a lytic lesion of the right calcaneus was found, and biopsy showed features of GCT. Routine chemistry studies, including calcium and phosphorus, were within normal limits. Two months later, a curettage of the remaining right calcaneus was performed. At that time, a right lung lesion was also resected as metastatic benign GCT. During the following year, the patient developed lesions of the left fibula and right radius. However, no biopsy was performed on those lesions. One year later, an additional lesion was found in the right calcaneus (Fig. 1B) which required below-the-knee amputation. The man was then free of disease until 11 years after initial presentation when he developed a new lesion on his left calcaneus.

Case 2

This 11-year-old female patient was first seen with a 2-month history of right leg pain and limp. Radiographs of the pelvis revealed an expansile lesion of the right superior pubic ramus (Fig. 2A). She underwent partial resection of the right pubic ramus. Histologic examination revealed GCT. Calcium studies and parathormone levels were normal. She also complained of right ankle pain, and 2 months later a markedly expanded lesion was found in the right ankle. Thus, she was readmitted for curettage of a right distal tibial lesion (Fig. 2B). Biopsy showed a typical benign GCT. At that time, MGCT was diagnosed by several consulting pathologist (Dr. H.D. Dorfman, Dr. D.C. Dahlin). One year after initial presentation, she developed tumors in the middle and proximal parts of the right tibia. Biopsies of these two sites proved GCT. Below the knee amputation was recommended but declined by the mother, and these lesions were treated with liquid nitrogen freezing and cementation. The patient then received radiation therapy to multiple areas of persistent microscopic disease, and eventually underwent resection and cryotherapy of a new lesion in the right femoral neck and intertrochanteric and subtrochanteric areas. Curetted tissue showed features of GCT. Eight months later, she fell, sustaining a pathologic fracture of the right distal femur (Fig. 2C). This lesion was treated with curettage, cryotherapy, and methylmethacrylate cementation. A skeletal survey at this time also disclosed a new lesion in the left femoral neck and base of the femoral head. The patient was admitted 3 years after initial presentation for excision, cryotherapy, and methacrylate fixation of a lesion in the middle third of the right femur. Five and one-half years after initial presentation she was seen for extensive GCT involvement of the right foot including the first through third metatarsals.

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Table 1. Patient data and tumor chronology

Case	Age (years)	Sex	Date	Bone involvement
1	23	M	Nov 1979 June 1982 May 1983 May 1983 Nov 1992	Left proximal phalanx: epi., meta. Right calcaneus Left proximal fibula Right distal radius Left calcaneus
2	11	F	Nov 1978 Jan 1979 Nov 1979 Apr 1980 Dec 1980 Dec 1980 Dec 1982 May 1983	Right pubis Right distal tibia: epi., meta. Right mid tibia: dia. Right proximal tibia: epi., meta. Right proximal femur: epi., meta. Right distal femur: meta., dia. Left femur head and neck: epi., meta. Right mid femur: dia. Right metatarsal I–III
3	17	F	Aug 1967 Aug 1973 1990	Right proximal humerus: meta., dia. Right distal radius: epi., meta. Right distal radius
4	10	F	1985 1991	Left distal femur: meta., dia. Left proximal tibia: epi., meta.
5	27	M	1978 1990	proximal radius distal humerus: epi., meta.

Epi., epiphysis; meta., metaphysis; dia., diaphysis

Fig. 1A, B. Case 1: a 22-year-old man presenting with a pathologic fracture of the ring finger. **A** Posteroanterior radiograph reveals an expansile, lytic lesion of the base of the proximal phalanx which extends to the articular surface. The medial cortex is interrupted. **B** Five years after initial presentation, a lateral radiograph of the calcaneus shows an additional lesion with pathologic fracture (arrow)

Fig. 2A–C. Case 2: an 11-year-old girl. **A** Anteroposterior radiograph of the pelvis. The lesion involves the right superior pubic ramus. The cortex is extremely thinned and is interrupted. **B** Two months later, a lesion of the right distal tibia was noted. Again, the cortex is discontinuous. **C** Two years after initial presentation, the patient presented with a pathologic fracture of the right distal femoral metadiaphysis. (**A**, **B** reproduced with permission from [22])

Case 3

A 17-year-old female sustained a pathological fracture of the proximal right humerus following a fall (Fig. 3A). The lesion was curetted and diagnosed as a GCT. Block resection of a local recurrence was performed 17 months later. She remained asymptomatic over

the subsequent 4 years, and then returned with a GCT of the distal right radius (Fig. 3B). This was treated with excision, curettage, and grafting with bank bone. Another recurrent GCT of the distal right radius occurred 23 years after the initial presentation. A consulting diagnosis of MGCT was made (Dr. H.D. Dorfman).

Fig. 3A, B. Case B: a 17-year-old girl presented with a pathological fracture through the surgical neck of the right humerus (A). B Four years later she presented with a giant cell tumor of the right distal radius

Case 4

A ten-year-old girl had direct trauma to the distal third of the left thigh when she fell on concrete while playing ball. Radiographs revealed a pathological fracture through a well-defined cystic lesion of the distal femur (Fig. 4A). A skeletal survey at the time failed to reveal additional lesions, and the patient was treated with casting. Six years later, she returned with pain and swelling. An expansile lesion was seen radiographically involving the left distal femur in the region of the earlier fracture. Biopsy revealed GCT, and the lesion was packed with bone graft. Postoperative films then revealed a lytic lesion in the proximal part of the left tibia (Fig. 4B). This lesion was also biopsied and proven to be GCT. Because of increasing pain and evidence of soft tissue extension of the femoral tumor, the distal femur and proximal tibia were resected and replaced with a custom endoprosthesis. Histological examination of the resected specimen confirmed the diagnosis of GCT within the distal femur and proximal tibia. Multicentric GCT was diagnosed by consulting pathologists (Dr K.K. Unni, Dr H.D. Dorfman).

Case 5

A 27-year-old man presented with an expansile lesion of the proximal metaphysis and epiphysis of the radius. The proximal part of the radius was resected, and the diagnosis of GCT was made (confirmed by pathologist's report). Laboratory studies revealed

normal calcium and phosphorus levels. Fifteen years later (age 42) the patient returned with an expansile lesion in the distal part of the humerus of the same arm (Fig. 5), and biopsy documented GCT. This lesion was curetted and packed with methylmethacrylate cement. The patient has done well for 2 years with no evidence of recurrence or additional tumors.

Microscopic findings

Review of case 1 (two specimens from different locations, seven from recurrent GCT and one from metastatic GCT), case 2 (seven specimens from different locations and two recurrent GCT), case 3 (two specimens from different locations and two recurrent GCT), and case 4 (two specimens from different locations) show features of a typical benign GCT with numerous multinucleated giant cells scattered in hypercellular spindle-shaped or ovoid to round mononuclear stromal cells. The nuclei of the stromal cells and multinucleated giant cells are similar in appearance and show no atypia. Occasional mitosis is present. In case 5, only the recurrent lesion was available for review, and the lesion is typical of GCT.

Discussion

Like conventional unifocal GCT, MGCT lesions are typically located in the distal part of the femur, proximal part of the tibia, and distal part of the radius. Both unifocal and multicentric GCT appear radiographically as an eccentric lytic process.

MGCT is a rare occurrence. A review of the literature discloses 41 cases of MGCT with a total of 148 tumors. Recurrent lesions may present as late as 16 years following the discovery of the first tumor. A higher incidence of MGCT is seen in patients with tumors of the hand and wrist [16]. Patients with polyostotic Paget's disease are also reported to have an increased incidence of MGCT [23].

The tumors of MGCT may be synchronous (lesions which are remote from one another but discovered within a short period of time and at similar stages of development) or metachronous (lesions which occur at different times and in different locations). Metachronous tumors may be metastatic or may represent a second, independent focus of disease. Metastatic involvement of other

Fig. 4A, B. Case 4: a 10-year-old girl presented with a pathologic fracture of the distal left femur (A). B Five years later, the patient underwent curettage and bone grafting for recurrent tumor. The immediate postoperative film shows an additional lesion in the proximal tibia

Fig. 5. Case 5: a 44-year old man, 17 years following resection of the proximal radius for giant cell tumor. Anteroposterior radiograph reveals an expansile lesion in the distal humerus of the same arm

bones or the lung does not imply a malignant process. The tendency of GCT to invade blood vessels locally may result in "benign GCT metastasis" [12]. Benign GCT may undergo spontaneous malignant degeneration, although malignant degeneration most frequently occurs following irradiation [24]. Primary malignant GCT, in which the giant cell lesion exhibits an aggressive and clinically malignant biological behavior from the onset, is extremely rare [25]. The diaphyseal involvement seen in case 2 could be accounted for on a metastatic basis. Multiple bone involvement may also result from direct tumor extension (including seeding at the time of surgery or as a result of pathologic fracture). GCT is capable of extending along fascial planes and directly crossing the joint space to a neighboring bone [1, 7]. When MGCT affects contiguous bones or involves both sides of the joint space, direct tumor extension must be considered. Case 4 may be an example of direct extension of tumor.

Epiphyseal involvement is essential to the radiographic diagnosis of GCT in the skeletally mature patient. Lesions may, however, be confined entirely to the metaphysis in skeletally immature patients [12, 26]. Metaphyseal GCT in skeletally immature individuals has, in fact, been considered as evidence for a metaphyseal origin of all GCT [26]. Three of the patients in this series developed their first tumor while skeletally immature (cases 2, 3, and 4). The initial tumor found in two of these cases (cases 3 and 4) was confined to the metaphyses of a long bone. The first tumor found in case 2 involved portions of the pelvis.

In all patients with MGCT, it is essential to exclude other possible causes of multiple lytic lesions, including multiple brown tumors of hyperparathyroidism, giant cell reparative granuloma, Paget's disease, metastatic disease from an unknown primary, multifocal infection, and eosinophilic granuloma. In all cases presented, hyperparathyroidism was excluded by calcium and phosphorus determinations. The patient in case 2 had a parathormone assay in addition to routine calcium and phosphorus. Giant cell reparative granuloma usually occurs in the small bones of the hands and feet and the jaw. Histologically, the stromal components contain more collagenous tissue and the nuclei are more spindle-shaped than in GCT. None of the patients had a clinical presentation which suggested infection, and there was no radiographic evidence of Paget's disease in any of the five cases. All of our five patients are still alive without any major complication.

MGCT of bone is rare. A careful exclusion of other diseases should be undertaken. The addition of five new cases of MGCT to the literature underscores the necessity of being aware of this condition. It is important to understand that many of these lesions may present in unusual locations and the lesions of MGCT tend to be aggressive with frequent local recurrences.

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