Current Concepts in Imaging of Giant Cell Tumor of Bone

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Learning Points for this Article !!

The article describes the current state of the art imaging of giant cell tumor of bone with a focus on both plain radiographs as well as MRI.

Abstract

Giant cell tumor(GCT) of bone is a tumor of giant cell proliferation that usually affects men and women in the thirdand fourthdecades. Typical cases have straight-forward imaging appearances. Atypical cases may resemble many other benign and sometimes malignant lesions. Plain radiographs and magnetic resonance imaging (MRI) are the mainstay of diagnosis, followed by biopsy and histology.Positron emission tomography/computed tomography (CT) has a limited role to play.Aneurysmal bone cyst transformation within GCTs is known. This may change the imaging appearance. GCTs may be multifocal, locally aggressive, and may metastasize to nodes and lungs.Treatment with drugs like denosumab also changes the appearance on radiographs and MRI. Post-operative imaging can be a challenge, and picking up recurrence also requires high-quality radiographs, MRIs, and CT scans.

Keywords: Giant cell tumor, giant cell tumor, bone neoplasm, computed tomography scan, magnetic resonance imaging, plain radiograph.

Introduction

Giant cell tumor (GCT) of bone is an expansile lesion consisting of multi-nucleated giant cells with a tumor that typically involves the epiphysis or epiphysis equivalent of bone [1, 2, 3]. It was first described by Cooper and Travers in1818 [4].

Epidemiology

GCTs occur between the second and fifth decades of life [5, 6, 7] but are known to occur in the pediatric age group [8] and in later decades [9, 10, 11, 12, 13, 14, 15], where they cause diagnostic challenges. The male:female ratio ranges between 1:1.1 and 1:1.5 [6,12, 13, 14, 15]. They affect almost every bone of the body, but the bones of the knee joint are the most commonly affected (50–65%), [6] followed by the distal radius (10–12%), sacrum (4–9%), and proximal humerus (4–8%) [12, 13, 14]. GCTs in uncommon locations often lead to diagnostic challenges.

They are rarely multifocal [16, 17, 18, 19, 20] They are also rarely known to metastasize [21], to the nodes, and the lungs.

Radiology

The following modalities help with the evaluation of GCTs, depending on the location and clinical presentation

1. Plain X-ray
2. CT scan
3. Magnetic resonance imaging (MRI)
4. Positron emission tomography/computed tomography (PET/CT).

Plain radiograph

These are the mainstay of diagnosis. On a plain radiograph, the lesion is expansile, trabeculated, and involves the epimetaphysis of a mature skeleton, extending up to the articular surface (Fig. 1a) [5,12,13]. The zone of transition is narrow to moderate, but a sclerotic rim is not seen [3]. Periosteal reaction is usually not seen, but there may be cortical breaks, if the lesion is locally aggressive [3].The soft tissue extension is usually at the metaphyseal end as the epiphyseal cartilage limitstransarticular tumoral extension(Fig. 2a)[5]. In the SI joints, however, the lesion may extend across the joint(Fig. 3) [16, 22, 23]. In the spine, the body is involved more commonly than the posterior elements [24]. Pediatric GCTs in the immature skeleton may be restricted to the metaphysis, subphyseal in location (Fig. 4) [8].

MRI

On MRI, a GCT shows typically intermediate to low T2 signal (Fig. 1b) [5]. There may be mild marrow edema. Cortical breaks may rarely be seen, more toward the metaphyseal end, and especially in small bones and the spine with extraosseous extension of soft tissue (Fig. 2b). Often, areas of fluid-fluid levels are seen suggesting secondary aneurysmal bone cyst (ABC) transformation (Fig. 5) [25,26]. GCTis the most

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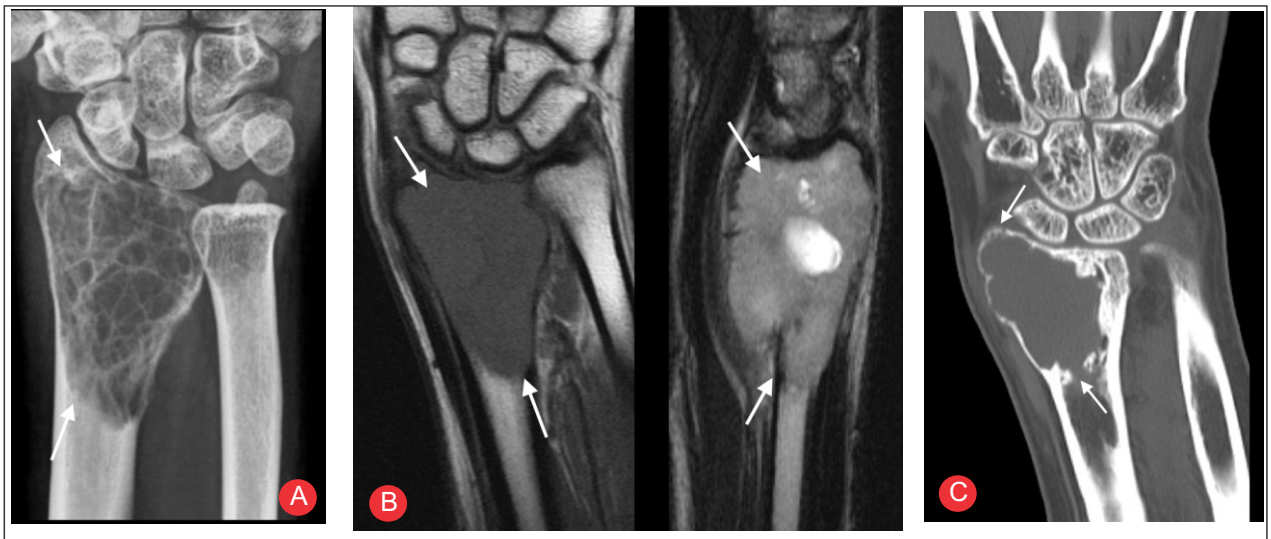

Figure 1: (a-c)Giant cell tumor of the distal radius. Frontal radiograph of the wrist (a) shows a trabeculated osteolytic lesion (arrows) with narrow zone of transition and without a sclerotic rim involving the distal epimetaphysis of the radius. The surrounding cortices appear intact. No periosteal reaction is seen either.Corresponding coronal T1W and sagittal T2W images (b) of the wrist show a T1 low signal and T2 iso to low signal lesion with central T2 high signal area. Corresponding coronal reformatted computed tomography image (c) showsthe lesion without abnormal trabecuation (pseudo-trabeculated appearance).

common lesion associated with secondary ABC [26]. Contrast-enhanced MRI is helpful in these cases in differentiating the secondary ABC component from the intensely enhancing tumoral component which can then be targeted for biopsy [27]. On dynamic contrast studies, the lesion is seen to be hypervascular showing rapid uptake and moderate to rapid wash-out(Fig. 6) [28].

CT Scan

On CT scans, a GCT is expansile but does not show a trabeculated appearance, as the apparent trabeculations on radiographs are due to the ridges created by endosteal scalloping. This "pseudo-trabeculated" appearance (trabeculated on a radiograph but not on CT scan) is often pathognomonic of a GCT (Fig. 1c) [5,6]. As with radiographs and MRI, the lesion extends up to the articular surface and may show cortical breaks and extraosseous extension of soft tissue.

PET/CT (Fig. 7)

PET/CT is not indicated normally. However, when the findings are atypical, it may be performed to help with the diagnosis or staging. On PET/CT, a GCT shows uptake with standard uptake values (SUVs) from 4to 24 [29, 30, 31]. Multifocal lesions are easily picked up on PET.

Differential Diagnosis

The following may pose diagnostic difficulties on plain radiographs and/or MRI.

Benign tumors

1. ABC(Fig. 8a) [5, 32]
This is a lesion more common in the immature skeleton, usually with a sclerotic rim, and shows uninterrupted fluid-fluid levels on MRI across the lesion. ABC is more metaphyseal and may not reach the articular surface. Contrast-enhanced CT/MRI is also helpful in differentiating primary ABC from GCT with secondary ABC transformation as the latter shows enhancing lobular soft tissue component as against a primary ABC which is predominantly cystic with thin enhancing, uninterrupted septae [27].

2. Chondroblastoma (Fig. 8b) [1, 3, 32]
This is an epiphyseal tumor with a sclerotic rimwith extensive surrounding edema and an occasional calcified matrix as well, only when large, does it create diagnostic difficulties.

3. Desmoplastic fibroma(Fig. 8c) [33, 34]
This is an uncommon tumor that involves the metaphysis but does not reach the articular surface and shows significant T2 low signal.

4. Ganglion cyst(Fig. 8d) [5]
It is usually easy to diagnosis, though the location is usually epiphyseal, subarticular, and may extend into the metaphysis. It shows T2 bright signal.

5. Brown tumor[32,35]
This may on occasion create diagnostic dilemmas, though brown tumors usually are not restricted to the epimetaphysis and

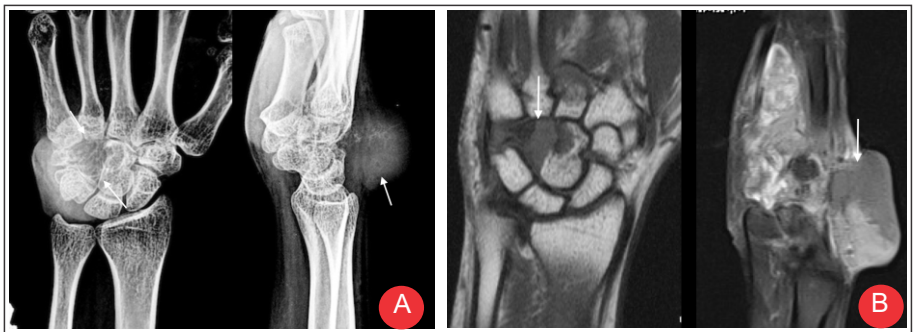

Figure 2: (aand b) Giant cell tumorof the hamate.Frontal and lateral radiographs (a) of the wrist show an expansile, trabeculated, osteolytic lesion (arrows) involving the hamate with a soft tissueabnormality (arrow) seen along the dorsal as well as the palmar aspects. Corresponding coronal T2W and sagittal post contrast fat saturated T1W images (b) of the wrist show an enhancing T2 low signal lesion (arrow) involving the hamate with an associated large soft tissue component (arrow) along the dorsal as well as the palmar aspects. Transarticular extension is not seen.

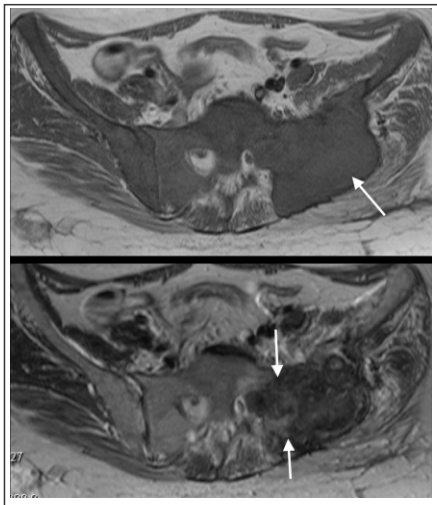

Figure 3: Giant cell tumor of ilium. Axial T1 and T2 W images of the pelvis show a low T2 signal intensity lesion (arrows) involving the left ilium with transarticular extension across the left sacroiliac joint to involve the adjacent sacrum.

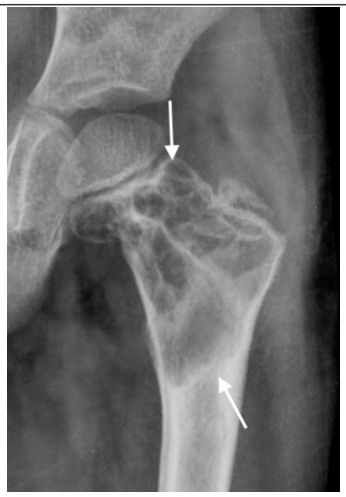

Figure 4: Pediatric giant cell tumor. Frontal radiograph of the left hip in an immature skeleton shows a giant cell tumor involving the proximal femoral metaphysis and extending up to the physeal plate but without transphyseal extension.

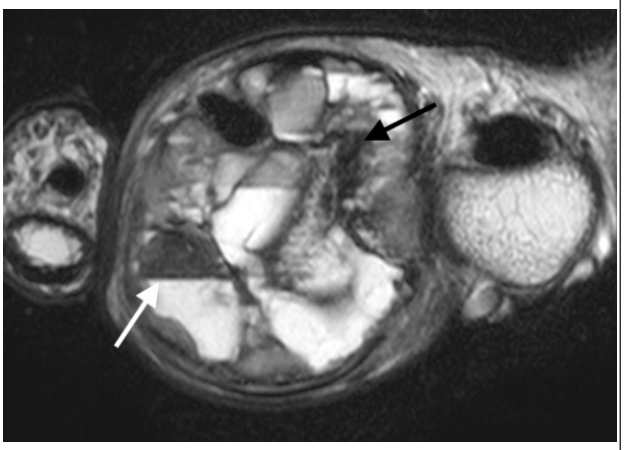

Figure 5: Giant cell tumor with secondary aneurysmal bone cyst transformation. Axial T2Wmagnetic resonance imaging shows a giant cell tumor involving the second metacarpal bone with internal fluid-fluid levels (white arrow) suggestive of aneurysmal bone cyst transformation. Low signal soft tissue component of the giant cell tumor (black arrow) is also well seen.

often show T2 bright signal. Almost invariably, the patients have hyperparathyroidism and other stigmata of osteomalacia and/or osteoporosis.

6. Giant cell reparative granuloma (GCRG)[5].

This may pose diagnostic difficulties in the jaws as well as sometimes in the appendicular skeleton. GCRG is often called a solid ABC in the appendicular skeleton.

Malignant tumors

1. Clear cell chondrosarcoma [1,3] This is probably the most difficult lesion to differentiate from a GCT. A clear cell chondrosarcoma is usually epimetaphyseal and has a moderate zone of transition. It may also have ABC transformation on MRI, though the lesion is usually T2 bright.

2. Metastasis/myeloma/plasmacytoma(Fig. 9) [1, 3] These are usually metaphyseal or diaphyseal and have narrow-to-moderate zones of transition on radiographs. Expansile lesions are typically seen with metastases from thyroid and kidney. In patients above the age of 35–40, metastasis/plasmacytoma should be the first diagnosis.

Guided Biopsies

LargeGCTs can be biopsied under fluoroscopy/C-arm guidance, but smaller ones and those that are difficult to approach may require CT scan guidance. All biopsies must be performed along the plane of the expected surgical incision[36]. A J-needle or core biopsy using a coaxial technique is the best way to achieve a diagnosis.

Post-treatment Imaging

1. Recurrence A large percentage of GCTs (80–90%) are known to recur within the first 3years of treatment[2,5,6]. Recurrence is usually appreciated on follow-up plain radiographs where new areas of osteolysis can be seenat resection margins or resorption is seen within the cement or the bone graft material(Fig. 10a) [37, 38, 39]. On MRI and CT scan, these are usually seen as T2 low signal areas and show progression on follow-up studies. Soft tissue deposits may be seen, both intra- and peri-articular (Fig. 10b).

2. Denosumab[40,41] Denosumab is a monoclonal antibody that targets the receptor activator of nuclear factor K-B [RANK] ligand and stops the osteoclastic activity of the GCT cells. Patients on denosumab have increasing sclerosis and reconstitution of the cortical bone that is best appreciated on radiographs. MRI may, however, show the same findings as before treatment with a diffusely enhancing hypointense mass [41]. PET/CT usually shows decreased uptake within the lesion post-treatment.

3. Malignant transformation This is

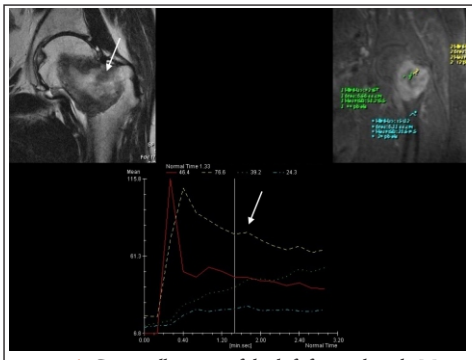

Figure 6: Giant cell tumor of the left femoral neck. Mean curve analysis of a dynamic contrast-enhanced magnetic resonance imagingshows intense early enhancement within the tumor with washout (arrow), closely paralleling the arterial enhancement and washout.

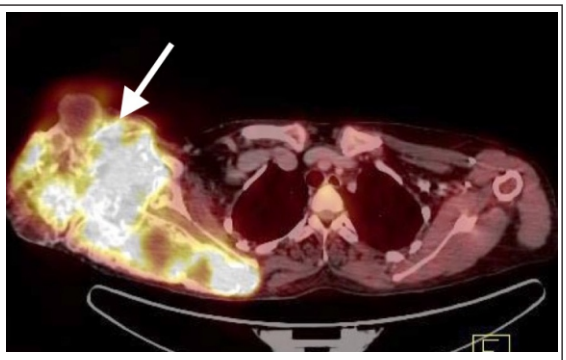

Figure 7: Giant cell tumorof scapula.Positron emission tomography/computed tomography scan shows intense FDG uptake (SUVmax: 24) (arrow) within the lesion

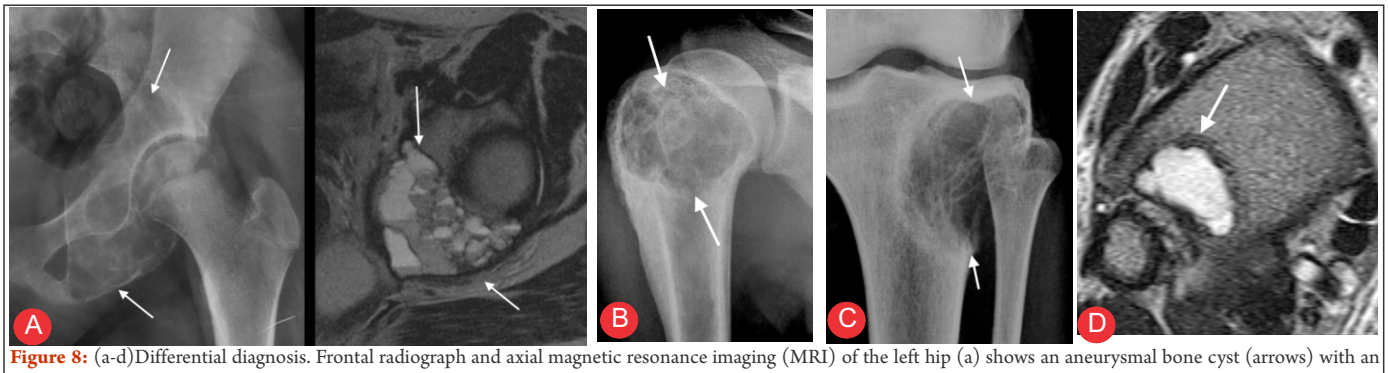

Figure 8: (a-d)Differential diagnosis. Frontal radiograph and axial magnetic resonance imaging (MRI) of the left hip (a) shows an aneurysmal bone cyst (arrows) with an expansile, trabeculated lesion on the plain radiograph and complete fluid-fluid levels on the MRI. Plain radiograph (b) of the right humerus shows a large chondroblastoma (arrow) in the epimetaphysis with sclerosis and periosteal reaction. Plain radiograph (c) of the left tibia shows a trabeculated, expansile lesion (arrows) not reaching up to the articular surface. Axial T2W MRI (d) of the ankle shows a tibial ganglion cyst (arrows).

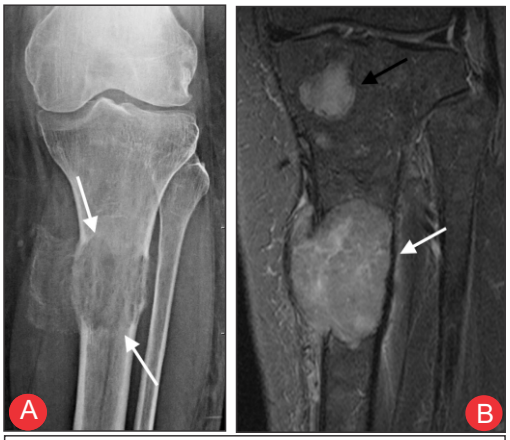

Figure 9: (a and b) Metastases from thyroid carcinoma. Plain radiograph (a) of the knee joint and proximal leg shows an osteolytic lesion (arrow) with wide zone of transition and associated soft tissue component involving the proximal tibial diaphysis.Post-contrast fat-saturated T1W magnetic resonance imaging (b) shows the soft tissue component well (white arrow)with another metastatic deposit in the proximal tibial epiphysis (black arrow).

controversial, and many people believe that malignant GCTs are malignant sarcomas that are just giant cell rich. However, there are published reports of malignant GCT [42]. In patients with recurrence, the GCTs may simulate high-grade sarcomas due to their aggressive behavior.

Unusual Features

1. Lung metastases (Fig. 11) [21] These are uncommon, but when they occur, the diagnosis should be confirmed with image-guided biopsy.
2. Multifocal lesions [16, 17, 18, 19, 20] These are uncommon and often create diagnostic dilemmas, simulating brown tumors or myeloma.

Conclusions

GCT is a common bone tumor that is easy to diagnose when it presents with typical findings. However, it may be locally aggressive, multifocal, metastasize, and present in unusual locations where the diagnosis may create difficulties. The judicious use of radiographs and MRI, image-guided biopsy, and on occasion PET/CT helps in the diagnosis and management of GCTs.

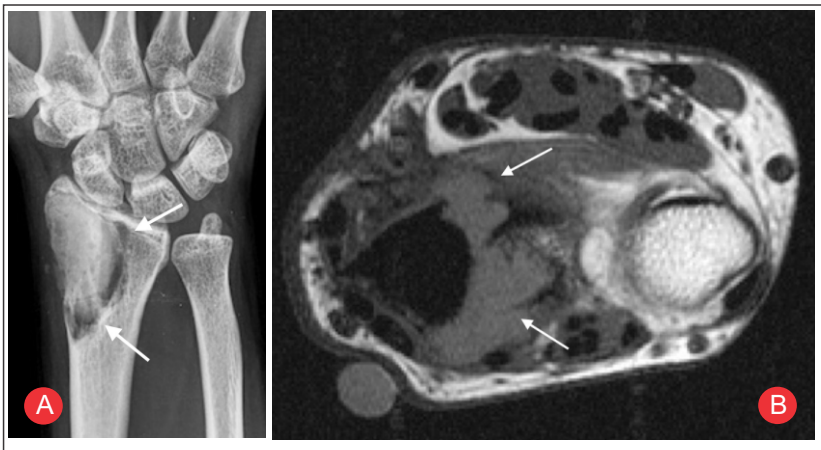

Figure 10: (a and b) Recurrence. Plain radiograph (a) of the wrist following curettage and cementing shows areas of osteolysis around the cement, best appreciated medially (arrows). Axial T1W magnetic resonance imaging (b) shows low soft tissue medially (arrows).

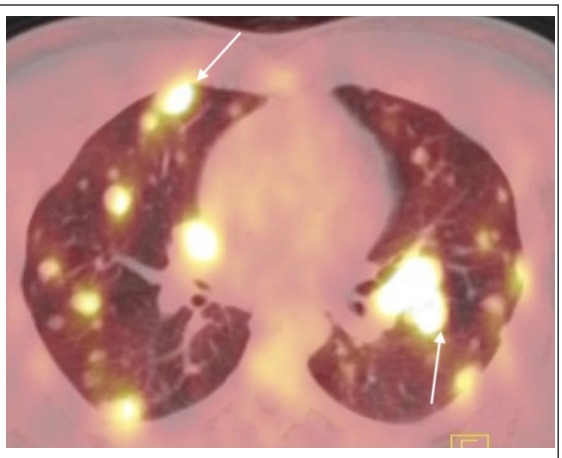

Figure 11: Metastases from giant cell tumor(GCT). Positron emission tomography/computed tomography scan of a patient with a left distal femoral GCT shows multiple metabolically active metastatic lung nodules (arrows).

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