Imaging of giant cell tumor and giant cell reparative granuloma of bone

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Abstract:
Aims:
o   *Discuss imaging features of giant cell tumor of bone and giant cell reparative granuloma*
o   *Discuss the role of different imaging modalities in diagnosis of giant cell tumor and giant cell reparative granuloma.*
o   *Explain the pathologic basis for radiologic features of giant cell tumor and giant cell reparative granuloma*
o   *Discuss types of malignant giant cell tumors with their imaging features.*
o   *Describe the traditional treatment of giant cell tumors and list the common post operative complications*
Materials and Methods: *This retrospective study of 10 patients was conducted in Shri M.P.SHAH Medical college and GURU GOBIND Singh hospital, Jamnagar.*
Observations: *The most common site for giant cell tumor in our observation was femur; some rare locations for giant cell tumor observed were flat bones like frontal bone and acromion; the single case of malignant giant cell tumor involved the patella. On plain radiography, majority of cases of giant cell tumor showed a well defined, eccentric, lytic lesion with non sclerotic border involving the epi-metaphyseal region of long bones with sub articular extension in patients with closed physis. On MRI, majority of patients showed well defined lesions which appeared hypointense on T1WI and heterogeneous predominantly hyperintense on T2W and STIRWI. The heterogeneous signal on T2WI reflected the inherent tissue inhomogenity.The single case of malignant giant cell tumor in our study, involved the patella in a middle aged female. It presented as expansile lytic lesion involving the patella with destruction of the cortical outline and soft tissue mass replacing majority of the bone. It showed intense enhancement with areas of central necrosis on post contrast scans. It also caused destruction of the anterior tibial cortex with minimal extension into tibial matrix. There was post operative recurrence in one patient who was treated with curettage and cement placement. The single case of giant cell reparative granuloma showed a well defined multiloculated expansile lytic lesion in right temporal bone. On MRI, it appeared hypointense on T1WI and heterogeneous on T2WI and showed homogenous moderate post contrast enhancement*
Conclusion: *Giant cell tumor of bone is typically benign lesion but may demonstrate aggressive imaging features or fluid fluid levels. Traditional treatment of giant cell tumor is associated with high recurrence rate. Giant cell reparative granuloma is a reparative process rather than a true neoplasm. It presents with imaging findings quite similar to giant cell tumor. However, it commonly affects the mandible, maxilla, small bones of hand and feet.*
Key Words: *Giant cell tumor, giant cell reparative granuloma, histopathological correlation, imaging, treatment*
Abbreviations used: *GCT-giant cell tumor, GCRG- giant cell reparative granuloma*

I.   Introduction:

GCT was first described by Cooper and Travers in 1818. [1] GCT is a relatively common bone tumor accounting for 4 to 9.5 percent of all primary bone tumors and 18-23 percent of all benign bone tumors. [2-7]Radiographically, it classically appears as a well defined eccentric lytic lesion with narrow zone of transition but lacking sclerotic border and centered in the meta-epiphysis of long bones with extension into sub articular region. It may be associated with expansile remodeling of bone but classically lacks internal mineralization.GCT is classically benign and solitary. However, multiple lesions have been described (rarely, associated with Paget's disease) and 5-10% lesions are malignant. [2-7]

GCRG of bone is actually a reparative process rather than a true neoplasm. It commonly affects the mandible and maxilla. Second most common site is the short bones of hands and feet. Radiographically, it appears as a well defined expansile lytic lesion centered in the metadiaphysis with sparing of sub articular region. It may show matrix mineralization in contrast to classic GCT.

Histologically, there is prominent and diffuse presence of multinucleated giant cells in a background of mononuclear cells; the nuclei of both the above mentioned cells are indistinguishable – a finding that differentiates GCT from many other pathologies. [8-9]A true GCT should contain a large number of giant cells in a diffuse distribution in a background of mononuclear cells.

II. Materials and Methods:

This retrospective study was conducted in the department of Radio-diagnosis, Shri M.P. Shah medical college and Guru Gobind Singh Hospital, Jamnagar. The patients were first subjected to plain radiography, following which CT scan and MRI were conducted

2.1. Methodology:
Xray: 300 and 500 m.A. Philips M.R.S.
CT scan: G.E. 16 slice CT scanner
MRI: Siemens' Magnatom Essenza 1.5 T

2.2 .Inclusion Criteria:
- Patients presenting with bony complaints.
- Pain/restriction of joint movement due to obvious swelling
- Xray favoring bone tumor
- Pathologic fracture.

2.3. Exclusion Criteria:
- Obvious history of trauma
- Patient in whom radiation/ MRI is contraindicated.

III. Results

A total 10 cases of GCT were studied and the following observations were made.

A total of 10 patients of GCT were studied. There was one patient of giant cell reparative granuloma. Out of all patients of GCT - 8 were males and 3 were females; majority of patients were in their 3rd and 4th decades. The oldest patient was 76 years old and the youngest patient was 20 years old. The most common site for GCT in our observation was femur; some rare locations for GCT observed in this study included flat bones like frontal bone and acromion; the single case of malignant GCT in our study involved the patella. The single case of GCRG involved the temporal bone in a 33 year old male patient. On plain radiography, majority of cases of GCT in our study showed a well defined, eccentric, lytic lesion with non sclerotic border involving the epi-metaphyseal region of long bones with sub articular extension in patients with closed physis. Cortical breech was noted in 3 patients on Xray 6 patients on CT scan. Associated soft tissue mass was noted in 5 patients. Pathologic fracture was noted in one patient. On MRI, majority of patients showed well defined lesions which appeared hypointense on T1WI and heterogeneous predominantly hyperintense on T2W and STIRWI.The heterogeneous signal on T2WI reflected the inherent tissue inhomogenity.The single case of malignant GCT in our study, involved the patella in a middle aged female. It presented as expansile lytic lesion involving the patella with destruction of the cortical outline and soft tissue mass replacing majority of the bone. It showed intense enhancement with areas of central necrosis on post contrast scans. It also causes destruction of the anterior tibial cortex with minimal extension into tibial matrix. There was post operative recurrence in one patient who was treated with curettage and cement placement.

GCRG – The single case of GCRG showed a well defined multi loculated expansile lytic lesion in right temporal bone. On MRI, it appeared hypointense on T1WI and heterogeneous on T2WI.

IV. Discussion:

4.1. Epidemiology:

GCT is a relatively common skeletal tumor. Although, it occurs in all races; there is unusually high prevalence in China and Southern India (State of Andhra Pradesh) [10-12]. Benign GCT affects females more commonly than males with a ratio of 1.1 : 1 to 1.5 : 1.[6,8,11,19-21].Malignant GCTs are more common in males with a ratio of 3:1[5-7].The vast majority of lesions occur in skeletally mature patients in the age group of 20-50 years.[2-7,13].Peak prevalence is in the third decade.

4.2. Lesion location:

Approximately 80 to 99 percent of lesions extend to within 1 cm of sub chondral bone.[3,7,14,15]The lesions arise from the metaphyseal side of the epiphyseal plate.[16,17,13,18,19]The most common location of GCT is around the knee joint 50 – 65 %)[23,2-7,19-22].Common locations in descending order are distal femur, proximal tibia, distal radius, sacrum, proximal humerus.[2-7,25,20-23,26-29]GCT can also occur in patella ,the largest sesamoid bone. Upto15% of GCT occurs in flat bones like pelvis, sacrum, spine and calvaria. Less than 1% GCT occurs in scapula [30]

4.3. Imaging:

Lesions invariably demonstrate geographic bone lysis, most commonly associated with narrow zone of transition and lacking surrounding sclerosis. Although, majority of lesions are eccentrically located, lesions that are large at presentation may be located centrally. [14,15,31]GCT may also have aggressive features such as a wide zone of transition, cortical thinning, expansile remodeling or even cortical bone destruction with or without associated soft tissue mass.[32]Pathologic fracture, which may be complete or incomplete, is seen in 11%–37% of patients [17,20,31]. At radiography, GCTs often demonstrate prominent trabeculation (33%–57% of cases) with a resultant multi loculated appearance (soap bubble appearance) [17, 13, 14, 18, 31]

4.4. Comparison of imaging modalities:

Plain radiograph remains the mainstay of primary diagnosis. However, CT scan and MR imaging allow superior delineation and staging of GCTs.[33,34]CT improves detection of cortical thinning, pathologic fracture, periosteal reaction, and degree of osseous expansile remodeling compared with radiography [14,31]. CT also helps to confirm the absence of mineralization in GCT, although callus formation related to healing pathologic fracture may be seen. The solid portions of GCT demonstrate attenuation similar to that of muscle.

MR imaging is superior to CT in delineating soft-tissue tumor extent because of its improved contrast resolution. Conversely, CT is superior to MR imaging in evaluating periosteal reaction, pathologic fracture, and the absence of matrix mineralization.

MR imaging of GCT frequently reveals a relatively well-defined lesion with a low-signal-intensity margin representing either osseous sclerosis or a pseudo capsule .However, more invasive and aggressive growth may also be seen .The solid components of GCT demonstrate low to intermediate signal intensity at T1- and T2-weighted MR imaging in the vast majority of cases.[35]This feature can be useful in excluding other subarticular lesions such as large solitary subchondral cyst, intraosseous ganglion, Brodie abscess, and clear cell chondrosarcoma that demonstrate high signal intensity at T2-weighted MR imaging. The cause of this appearance has been reported as hemosiderin deposition, although we believe it is more likely related to increased cellularity or high collagen content [35,36,37]

ABC components in GCT are relatively common (14% of lesions) [2-7,34,35,38-44]. In addition, GCT is the most common lesion associated with secondary ABC. The ABC regions frequently exhibit fluid levels at both modalities. These ABC areas demonstrate low attenuation at CT, low or high signal intensity at T1-weighted MR imaging, and markedly increased signal intensity at T2-weighted MR imaging.[38-44]At advanced imaging, the solid components of GCT are easily distinguishable from the ABC areas. Recognition of and distinction between the cystic (ABC) and solid areas of a GCT can be vital for patient treatment for two important reasons: first, to prevent misdiagnosis of the lesion as a primary ABC, which should contain only cystic components; and second, to allow biopsy to be directed at the solid portions of the lesions, which harbor diagnostic tissue, as opposed to ABC regions, which yield nonspecific blood. Contrast-enhanced CT or MR imaging can also help distinguish cystic from solid regions. Cystic areas enhance with a thin and delicate peripheral and septal pattern. In contrast, the solid regions of a GCT enhance diffusely, reflecting the hypervascular tissue seen at pathologic analysis.

4.5. Malignant GCT:

Malignant giant cell tumor is a term used to describe a heterogeneous group of giant cell–containing lesions that are capable of malignant behavior and of producing pulmonary metastases [45, 46]. **Benign metastasizing GCT** is a form of malignant GCT in which the metastases demonstrate a histologically benign appearance identical to that of conventional GCT [7].These pulmonary mets may either remain stable or regress spontaneously. The term **malignant GCT** most frequently refers to a tumor in which there is de novo malignant transformation of a formerly benign GCT. It can either be primary or secondary. A secondary malignant GCT of bone is defined as "a sarcomatous growth that occurs at the site of a previously documented GCT, usually after previous radiation therapy and less commonly after a long latency period or repeated resections". The final type of malignant GCT is **osteoclastic (giant cell) sarcoma.** Pathologically, this lesion is defined as "a highly malignant tumor composed of anaplastic stromal and anaplastic osteoclast-like giant cells in which there is no evidence of tumor osteoid, bone or cartilage,"[7]

The radiologic appearance of malignant GCT invariably includes cortical permeation and an associated soft-tissue mass, findings that reflect its aggressive behavior [46]

4.6. Histo-pathological Appearance:

Histologically, there is prominent and diffuse presence of multinucleated giant cells in a background of mononuclear cells; the nuclei of both the above mentioned cells are indistinguishable – a finding that differentiates GCT from many other pathologies.[8,9]A true GCT should contain a large number of giant cells in a diffuse distribution in a background of mononuclear cells.

4.7. Treatment:

Definitive treatment consists of intralesional surgical resection. Historically, curettage and bone grafting has been the treatment of choice for GCT, although marginal resection is associated with a high recurrence rate of 40%–60% [2-7,24]Wide resection shows a reduced recurrence rate (7%)[47-54]however, this treatment often causes significant compromise of limb function, which may be difficult to justify in treatment of a benign lesion. Newer surgical treatments emphasize methods of extending surgical margins without use of wide resection to maintain limb function and limit recurrence[45,46].Curettage and filling the void with polymethylmethacrylate(PMMA) is associated with a 25 % recurrence rate[48].Curettage with high-speed burring of the cavity combined with a thermal or chemical adjunct to extend the surgical margin has resulted in improved local control [48-51]For large and highly destructive GCTs, either primary or recurrent, wide resection and reconstruction with allograft or metal prostheses is often used. Because of the risk of secondary sarcomatous transformation, radiation therapy is generally reserved for tumors that are deemed inoperable.

4.8. Imaging in Post treatment recurrence

Radiologic evaluation of recurrence typically reveals new areas of bone destruction at the previous resection margin or resorption of intralesional bone graft material [48,55-60].On MRI ,the recurrent lesion follows the signal intensity of the primary lesion.
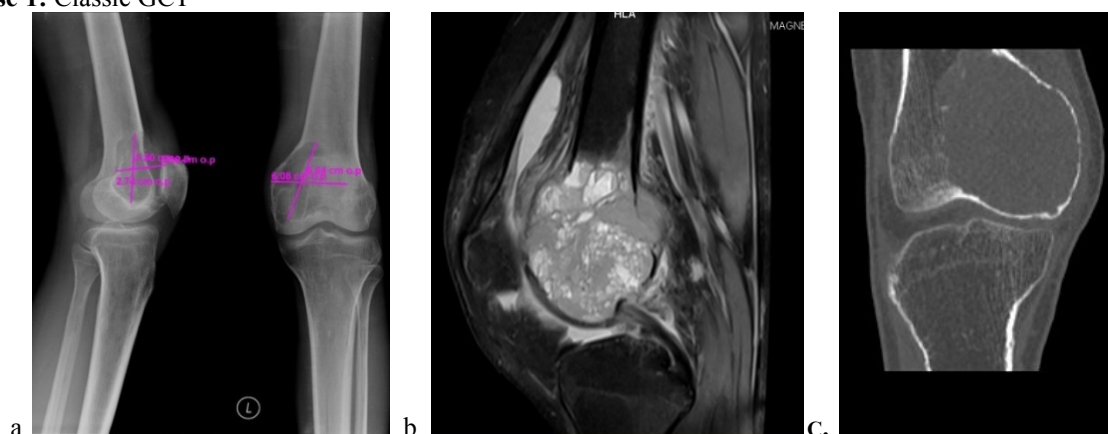
4.9. Giant cell reparative granuloma

GCRG is a reactive inflammatory process secondary to trauma and intraosseous hemorrhage and predominantly affects children and young women. [61,62]It arises from the periosteal connective tissue, whereas GCT originates in the connective tissue of the bone marrow.[62]
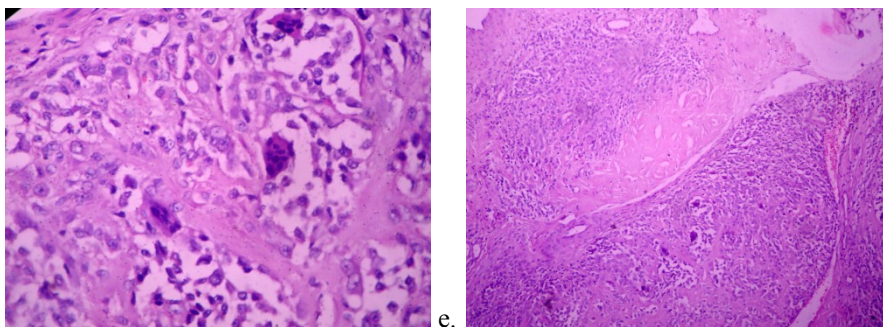
Radiologic appearances of GCT and GCRG are indistinguishable. Histologically, abundant multinucleated giant cells are evenly distributed in GCT [61,64] whereas they are unevenly distributed and contain fewer nuclei in GCRG. [63,65].

GCRG occurs in many bones, with the mandible, maxilla, and the small bones of the hand and feet being the most common sites. Extragnathic GCRG has another peak of occurrence in the 50- to 80-year range, with the most common site in the craniofacial region being the temporal bone. [61,65].

V. Illustrations:
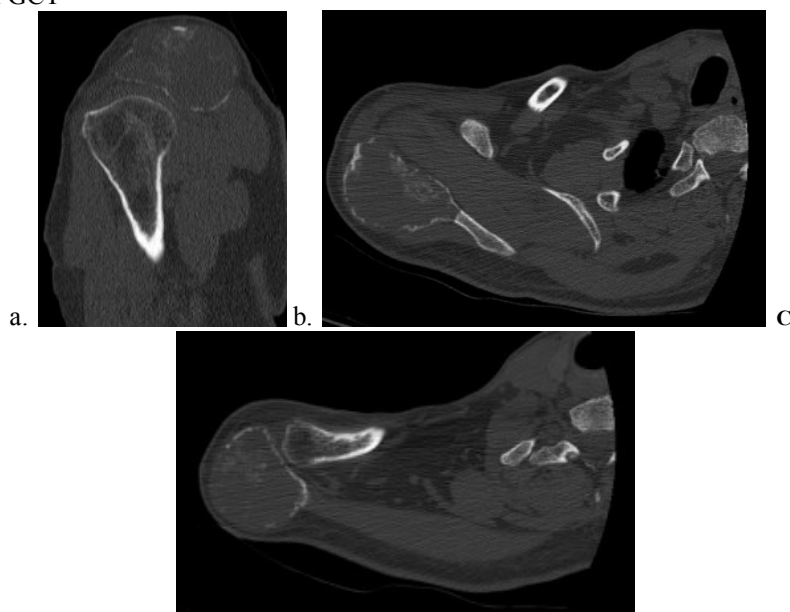
Case 1: Classic GCT

a.   b.   **c.**

a, c : Well defined eccentric lytic lesion with non sclerotic margin involving the subarticular region of femur b: MRI – PDFS image –well defined cystic solid lesion in subarticular location of femur. The solid components appear hypointense on PDFS d,e: Even distribution of multinucleated giant cells in a background of mononuclear cells.

Case 2: Acromion GCT

a,b.c: Sagittal, axial and coronal reformatt plain CT images reveal well defined lytic lesion in subarticular location of acromion process of right scapula causing expansile remodeling and cortical erosion.
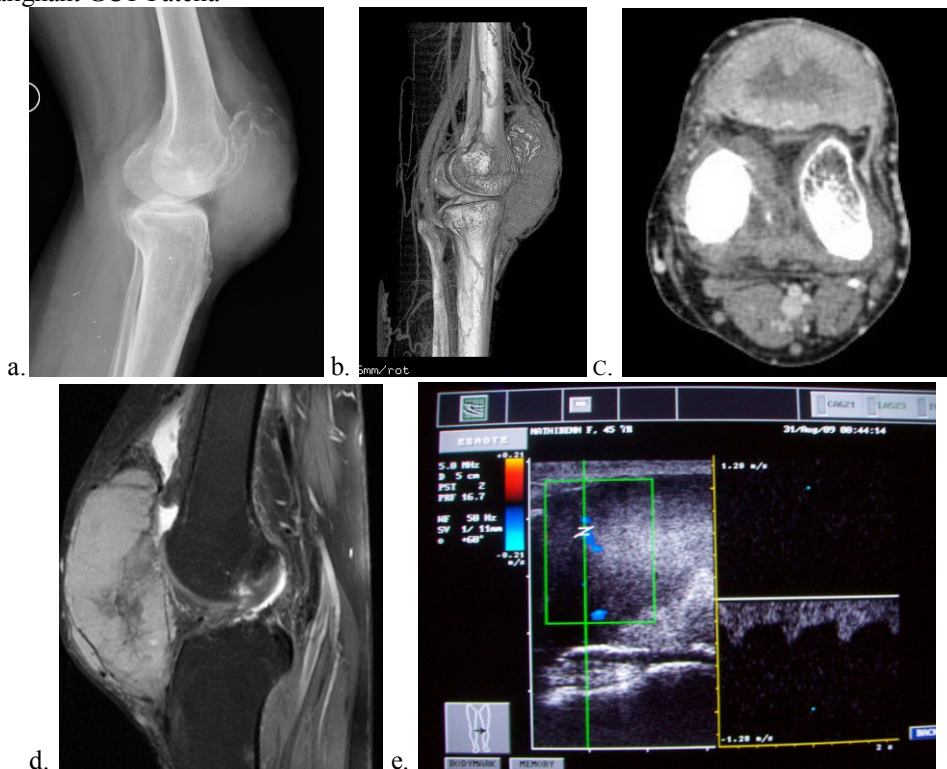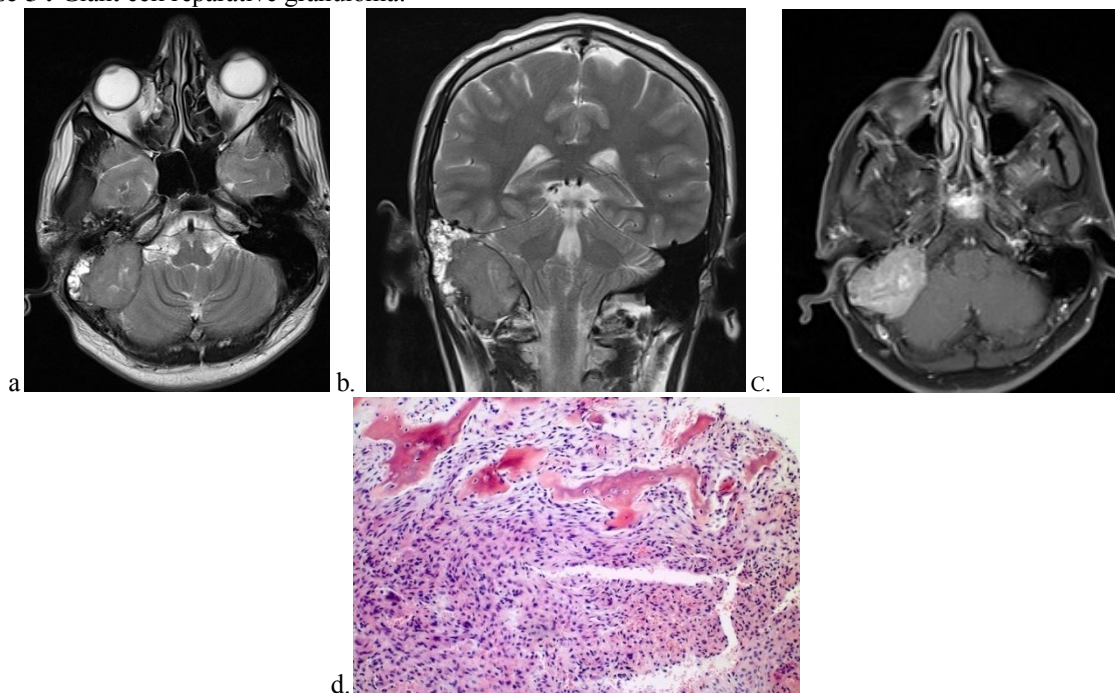
Case 3: Recurrent GCT

a: Development of a new area of radiolucency at the cement bone interface with pathological fracture b: Axial plain CT scan images revealing cortical erosion and pathological fracture

Case 4: Malignant GCT Patella

a. Expansile lytic lesion of patella with complete destruction of cortical outline and complete destruction of cortical outline with soft tissue replacing the bone b. Sagittal reconstruction CT image showing soft tissue mass replacing the patella c. Post contrast axial CT image showing moderate peripheral enhancement of the lesion with central necrosis d. Post contrast Sagittal MRI image showing moderate enhancement of the lesion e.Arterial Doppler image showing arterial flow within it

Case 5 : Giant cell reparative granuloma:

a,b: Axial and coronal T2WI showing a well defined mass lesion involving the right temporal bone;it appears isointense to the cortex on T2WI.c:Post contrast axial image showing intense enhancement of the lesion d:Uneven distribution of giant cells in a background of mononuclear cells

VI.   Conclusion :

GCT and GCRG of bone often have a characteristic radiographic appearance. A diagnosis of GCT is suggested by a non mineralized, lytic, eccentric meta epiphyseal lesion involving a long bone and extending to subarticular bone in a skeletally mature patient. GCRG has a similar radiographic appearance but most commonly affects the mandible, maxilla, hands, or feet. CT and MR imaging are useful for staging these lesions and particularly for defining their soft-tissue extent. These modalities also allow detection of cystic (secondary ABC) components, frequently with fluid levels, seen in some GCTs. However, there are both solid and cystic components in GCT, allowing distinction from primary ABC, which contains only cystic regions. Biopsy must be directed at the solid regions of GCT, which harbor diagnostic tissue. Unlike in many musculoskeletal neoplasms, the solid components of GCT demonstrate low to intermediate signal intensity at T2-weighted MR imaging. This feature can be helpful in diagnosis, particularly in lesions in unusual locations, and in distinguishing GCT from other subarticular lesions (large solitary subchondral cyst, intraosseous ganglia, Brodie abscess). GCT is typically solitary, whereas multiple GCTs rarely occur and may be associated with Paget disease. Malignant GCT is unusual, accounting for 5%–10% of all GCTs. These lesions most commonly arise as secondary lesions following irradiation of benign GCT. Surgical resection is currently associated with a lower recurrence rate (2%–25%) than has been historically seen (40%–60%) as a result of extension of surgical margins with a variety of methods. The spectrum of radiologic features of GCT and GCRG of bone reflects their pathologic appearance. Recognition of these features usually allows prospective diagnosis, helps guide therapy, and facilitates early detection of recurrence, thereby improving clinical case management.

Acknowledgements:

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