RCR
RADIOLOGY CASE REPORTS

Case Report

Giant cell tumor of the talus: A case report

Dana Galvan, MD, MPH[a], Carola Mullins, MD[b],*, Ellen Dudrey, MD[c], Lisa Kafchinski, MD[d], Shaked Laks, MD[b]

[a] *Transitional Year Department, University of Rio Grande Valley*
[b] *Department of Radiology, Texas Tech University Health Sciences Center El Paso, 5001 El Paso Drive, CSB-A02, El Paso, TX 79905*
[c] *Department of Pathology, Texas Tech University Health Sciences Center El Paso, El Paso, TX*
[d] *Department of Orthopedic Surgery, Texas Tech University Health Sciences Center El Paso, El Paso, TX*

ARTICLE INFO

ABSTRACT

Giant cell tumor is a benign primary bone neoplasm which most often occurs in a periarticular location. Involvement of the bones of the foot and ankle is rare, and there have been a limited number of previous case reports involving the talus. Here we report a case of giant cell tumor of the talus, which was initially radiographically occult in a 43-year-old female, with emphasis on MRI imaging characteristics. The patient underwent surgical excision and curettage. Histological examination revealed the presence of spindle cells admixed with giant cells, confirming GCT. We further provide an overview of the radiological findings of GCT.

Giant cell tumor is a benign bone neoplasm of mesenchymal origin, identified by multinucleated giant cells [1]. GCT is locally aggressive and can destroy adjacent bone and articulations. The most commonly affected bones are the distal femur, proximal tibia, and distal radius, with an epiphyseal predominance in 90% of cases [2]. Presentations are mostly mono-ostotic, however multicentricity may occur in younger patients [3]. Very few cases have been reported in the bones of the feet, an incidence of 1%-2% have been previously reported [4].

GCT is seen between ages 20 and 40 years, with a 56% predominance in females [3]. Although benign, 1%-9% cases may "metastasize" to the lungs. The initial treatment is surgical removal, either en bloc, or more commonly intralesional curettage and the use of adjuvants. Even after resection, GCT has a high recurrence rate [2]. The trigger for GCT is currently unknown. However, a majority of cases have cytogenetic abnormalities of telomeric associations (tas). Involvement of the RANK pathway is also believed to contribute to the pathogenesis of GCT [2].

Introduction

Case report

A 43-year-old female with a past medical history of partial epilepsy presented for 1 month of progressive left ankle pain following a fall. Three months prior to the fall, she had twisted her ankle but did not seek medical treatment. Physical exam revealed mild edema and tenderness of the lateral left ankle. A left ankle radiograph showed a remote avulsion of the tip of the lateral malleolus, but no bone or joint abnormalities were noted. She was diagnosed with an ankle sprain (Fig. 1).

The patient was prescribed a walking boot and physical therapy, without clinical improvement. At her 2 month follow-up visit, the physical exam revealed continued edema on the anterior and lateral aspects of the left ankle, with tenderness but no palpable mass. An MRI performed at this time demonstrated a well-circumscribed lesion of the talar neck with reactive bone marrow edema (Fig. 2).

The patient underwent a CT-guided core needle biopsy which was inconclusive, but images demonstrated a well circumscribed lytic lesion in the talar neck with extension to the articular surface (Fig. 3).

The needle biopsy revealed spindle cells admixed with giant cells and fibrous tissue. However, due to paucity of lesional material, was considered nondiagnostic.

Subsequently, the patient underwent a left talus open biopsy. Intraoperative fluoroscopy was used to confirm location of the lesion (Fig. 5). Frozen section analysis revealed spindle cells admixed with giant cells, fibrous tissue, and bone. No malignancy was detected, and final diagnosis was deferred until the permanent slides could be evaluated (Fig. 4A).

The patient returned to the clinic 2 weeks after open biopsy. Pathology results were reviewed and showed GCT. The patient was counseled for the recommendation of extended intralesional curettage and use of adjuvants to appropriately treat the GCT of bone. She declined to undergo another procedure at that time. The patient was informed that non-treated GCT is progressive in nature and prone to progression with further destruction of the bone. The patient understood but declined further treatment at the time. She was maintained on nonweight bearing precautions and was advanced to weight bearing as tolerated 6 weeks after open biopsy. A radiograph was taken which demonstrated no evidence of fracture.

At 6 months status post open biopsy of the talus, ankle radiographs demonstrated progression of disease as expected (Fig. 6). Intralesional curettage and use of adjuvants was recommended, to which the patient consented.

Follow-up CT shows increase in size of the previously seen lytic lesion now measuring (approximately 2.2 × 2.1 × 2.4 cm (AP, transverse, and CC dimension), (previously measured 1.5 × 1.3 × 1.7 cm) in the medial aspect of the talar neck) (Fig. 7A).

The patient then underwent an extended intralesional curettage and use of adjuvants, including high-speed burr, dilute hydrogen peroxide, sterile water, and argon beam. The talus was then filled with antibiotic impregnated cement with added vancomycin. Postsurgical radiographs demonstrated

Fig. 1 – A remote avulsion lesion of the tip of the left lateral malleolus noted with a well corticated bone fragment.
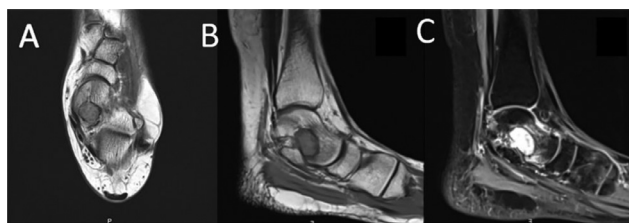
Fig. 2 – MRI of the left ankle. (A) Unenhanced axial TI MRI depicting a well-circumscribed lesion in the medial aspect of the talar neck extending to the articular surface at the level of the medial facet of the subtalar joint. (B) Sagittal T1 MRI with contrast and fat suppression showing enhancement of lesion with a thin sclerotic border. (C) Unenhanced sagittal T2 demonstrates heterogenous hyperintense signal with a thin sclerotic border.

cement-packing of the lesion and mild soft tissue edema (Fig. 7B).

Histological examination from the second procedure, confirmed the presence of multinucleated giant cells (Fig. 4B). Postsurgical treatment plan consisted of denosumab, chest imaging, and regular ankle radiographs, to monitor for pulmonary metastasis and GCT recurrence. At 16 months after the extended curettage, there was no evidence of bone resorption around the cement or GCT recurrence (Fig. 8).

Discussion

Giant cell tumor of the talus has been intermittently described in the past. A search of literature on GCT of the talus in PubMed revealed 28 cases of GCT of the talus, including case reports and case series. Tumors presenting in the bones of the feet have a reported incidence of 1%-2% [4]. However, a previous retrospective case series of 240 cases of GCT, found a GCT talus incidence of only 0.4% [5]. GCT is a benign bone neoplasm with characteristic multinuclear giant cells. The most common presentation is in the early twenties to forties, with a female predominance [3]. The etiology of GCT has not been elucidated completely to date.

Radiographs

The primary diagnosis modality for GCT is radiography. GCT is usually seen in long bones in 85% of cases, with 10% of cases reported in the axial skeleton and 1%-2% in bones of the feet [4,6]. GCT presents as a radiolucent lytic lesion with geographic bone destruction [1,3]. The tumor can develop in the medulla as well as eccentrically. Over time eccentric lesions will grow and become more centered and symmetric, especially in long bones [3]. Most commonly originating in the metaphysis, with extension into the subchondral bone plate and the epiphysis [6,7].

GCT will present with well-defined non-sclerotic margins in 80%-90% of cases, sometimes described as "moth eaten" [7,8]. Sclerotic margins are uncommonly seen [3].

Less aggressive and early lesions usually do not interfere with the cortex and have defined trabeculation [3,9]. More aggressive GCTs may present with cortical thinning and expansion, leading to periosteal elevation, and extension to surrounding tissues [6,10]. Furthermore, cortical destruction is associated with pathologic fractures during initial presentation [6]. In GCT, tumor matrix mineralization (extracellular space substance between tumor cells) is uncommon [3]. Lastly, GCT exhibits a sharp narrow zone of transition normally located at the lesion margin [2]. However, more aggressive variants may show a wide zone of transition [10].
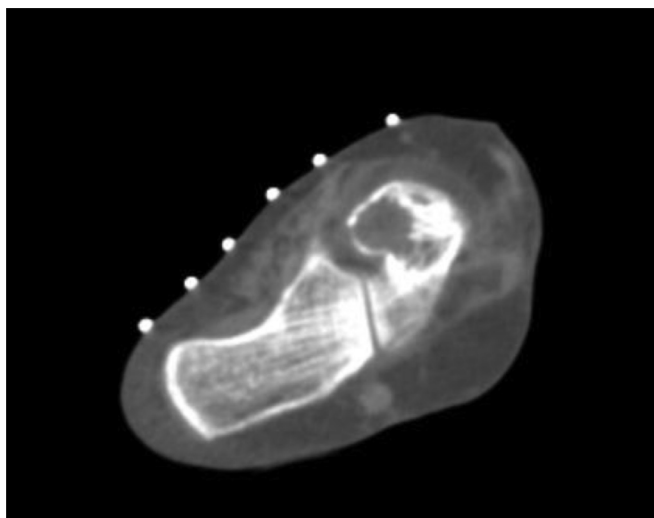

Fig. 3 – CT guided-needle biopsy demonstrating the lytic bone lesion of the talus.
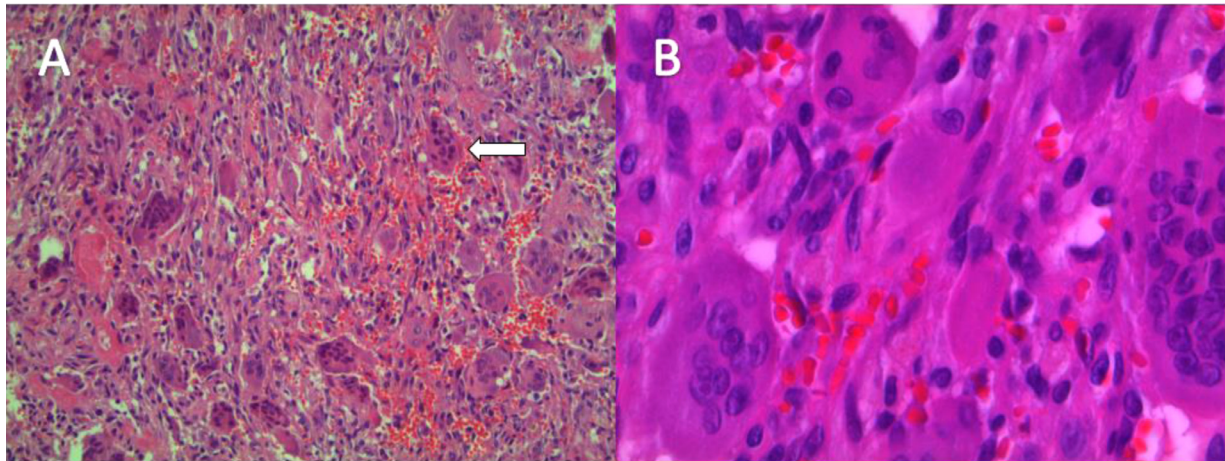
Fig. 4 – (A) Left talus open biopsy specimen with an even distribution of osteoclast-like giant cells (arrow) amongst cytologically bland stromal cells. H&E ⨯100.(B) Left talus, curettage 6 months later. Photomicrograph highlights multinucleate giant cells whose nuclei resemble those of the surrounding stromal cells. H&E ⨯400.

Fig. 5 – Intraoperative bone biopsy with fluoroscopy, revealing lytic lesion on talus.

CT

Staging, operative planning, and lesion progression assessment of GCT is commonly performed through computerized tomography imaging [3]. CT imaging also visualizes certain characteristics such as mineralization, cortical thinning, associated fractures, and extension of the lesion into soft tissues more effectively [2,10]. CT is also favored over MRI for evaluating subtle cortical destruction. The presence of fluid-fluid levels may also be observed, indicating secondary aneurysmal bone cyst formation [3]. Due to the high vascularity of GCT, tumor blush may be exhibited on contrast-enhanced CT [7]. This hypervascularity can lead to intratumoral hemorrhaging that may be seen on CT imaging as well [3].

MRI

For more specific tumor characterization, MRI may be used. GCT demonstrates homogenous, low to intermediate signal lesion on T1-weighted images [3]. T1 is preferred for intramedullary tumor characterization [9]. Gadolinium administration will result in heterogenous enhancement of solid components [11]. T2-weighted imaging will demonstrate a heterogenous hyperintense lesion. This sequence is preferred for extraosseous involvement [3,11]. Additional findings can include low signal intensity for hemosiderin deposition most identifiable on gradient echo sequences and fluid-fluid levels in secondary bone cyst formation [3,13].

Findings of other talus lesions

Previous cases of GCT of the talus have also presented as a radiolucent lytic lesion on radiographs, with most taking up the whole talus or body [12,14–16]. Most cases displayed cortical thinning with a case showing multiple radiolucencies indicating osteolytic lesions have also been reported [12,14–17]. Expansion of the lytic lesion was also commonly seen [12,14]. Other radiographic findings included, narrowed joint spaces and narrow zone of transitions. CT was beneficial for ruling out extension into soft tissues, ligaments, and capsules, as well as further characterizing cortical destruction and joint space preservation [12,16]. For cases with MRI findings, these were consistent with hypointense lesions in T1 and hyperintense lesions in T2. Enhancement of solid components was also commonly seen [14]. One case described the tumor as a solid cystic mass with multiple trabeculations, leading to a heterogenous hyperintensity on T2 [14].

Radiographic differentials

Differentials for radiolucent lesions that should be considered for radiographs include chondroblastoma, chondromyxoid fibroma, enchondromas, and chondrosarcoma. Osteosarcomas and osteoblastomas are less commonly mistaken for GCT [8]. Defining characteristics of chondroblastoma include internal matrix calcification with a thin sclerotic border usually seen in the epiphysis of bones. Chondromyxoid fibroma arises will be

Fig. 6 – Weight-bearing ankle radiograph after open biopsy demonstrating progression of Giant Cell Tumor.

a lobulated lucent lesion in the metaphysis with a scalloped sclerotic border [18]. Enchondromas are lytic lesions usually located in the metaphyseal region that lack aggressive features, such as a periosteal reaction, endosteal scalloping [19]. Lastly, chondrosarcomas are malignant lesions that have a unique ring-and-arc calcification pattern from chondroid matrix mineralization [20].

Pathological differentials

The most prominent characteristic of GCT pathologically is the presence of multinucleated giant cells uniformly scattered with mononuclear stromal cells [10]. Immunostaining will be positive for CD45, CD68, and cathepsin K with some staining for antihistone H3.3 G34W antibody [21].However, there are other bone lesions that contain osteoclast-like giant cells include chondroblastoma, chondromyxoid fibroma, aneurysmal bone cyst (ABC), Langerhans cell histiocytosis, and giant cell-rich osteosarcoma [18]. Chondroblastoma will have polyhe-
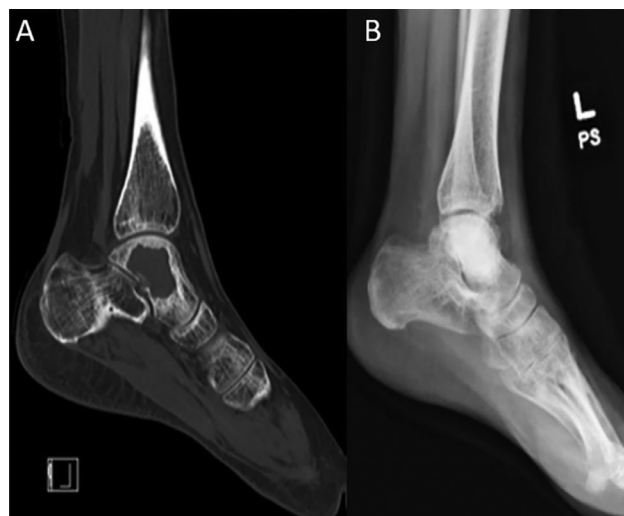

Fig. 7 – (A) Unenhanced sagittal helical CT showing an interval increase in size of the 2.4 cm well-circumscribed lytic lesion, status post open biopsy. (B) Nonweight-bearing ankle radiograph immediately status postcurettage, use of adjuvants and cementation of talar lesion soft tissue edema and ankle joint effusion from surgery.

dral chondroblasts, amorphous chondroid, and chicken wire pattern calcification. Few giant cells can be found scattered in chondroid matrix. Chondroblastoma will stain positive for S100 and have sometimes been found to express DOG1 [18]. ABCs have giant cells and macrophages lining cystic blood-filled spaces. Histologically, chondromyxoid fibroma has very few giant cells with fibrous tissue bands surrounding stellate cell lobules. Chondromyxoid fibroma will stain for S100, SOX9, and collagen III and express smooth muscle actin [18]. Langerhans cell histiocytosis have characteristic Langerhans cells, which are ovoid cells with a lobulated nuclei. They will contain intracytoplasmic tennis racquet-shaped inclusion bodies or Birbeck granules. The bone lesion will also contain some giant cells and eosinophil polymorphs that may form eosinophil abscesses. Langerhans cell histiocytosis will be positive for S100, CD68, HLA-DR, and Langerin [18]. Lastly, giant cell-rich osteosarcoma will present with a high number of giant cells which are evenly distributed, most characteristic by atypical mitoses and nuclear pleomorphism representing malignant features [18].

Treatment and prognosis

The prognosis of GCT is favorable, only 5% of cases show pulmonary metastasis. Malignant transformation usually may occur after radiotherapy [22]. Treatment often consists of extended intralesional curettage that may include adjuvants such as phenol, high-speed burr, dilute hydrogen peroxide, sterile water, argon beam, and liquid nitrogen [7]. After curettage, reconstruction may be done with bone grafts and cementation [22]. Recurrence occurs in up to 20% of cases. A second intralesional curettage is then indicated [7]. In cases

Fig. 8 – Postextended curettage weight-bearing ankle radiograph demonstrating cement packing with no resorption or GCT recurrence at 2-year follow-up.

where surgery is not an option, radiation therapy or denosumab treatment may be used [22].

Although GCT of the bone is most often benign, there is a small risk of malignant transformation [18]. Follow-up chest radiographs are routinely performed to rule out lung metastases (seen in 1%-6% of GCT cases) [10].

Overall, GCT is a benign bone malignancy that has favorable prognosis after appropriate surgical intervention. Clinical signs include pain and edema over the ankle, at times with tenderness as well [16]. Early presentations may be associated with a sudden fracture. Therefore, suspicion should arise after a pathological fracture in an unusual location, to ensure early detection. The earliest recognition will often occur with a radiograph showing a lytic lesion. Further characterization of a lytic lesion is recommended when found in unexpected areas such as the talus. Careful search for other lesions is warranted, since GCT of the talus may be multicentric in small bones [16]. Further imaging to confirm the presence of GCT benefits from MR imaging. T1-weighted MRI will demonstrate a hypointense or isointense lesion that will be hyperintense on T2-weighted imaging. CT imaging is often preferred to investigate cortical destruction, extension into soft tissues, and for surgical staging and planning. After resection, repeat imaging for the appearance of pulmonary metastasis or GCT recurrence is highly encouraged.

REFERENCES

[1] Turcotte RE. Giant cell tumor of bone. Orthoped Clin North Am 2006;37(1):35–51. https://doi.org/10.1016/j.ocl.2005.08.005.

[2] Sobti A, Agrawal P, Agarwala S, Agarwal M. Giant cell tumor of bone-an overview. Arch Bone Jt Surg 2016;4(1):2–9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4733230/ Accessed May 19, 2019.

[3] Purohit S, Pardiwala DN. Imaging of giant cell tumor of bone. Indian J Orthop 2007;41(2):91–6. doi:10.4103/0019-5413.32037.

[4] Wilde GE, Gakhal MS. Radiological reasoning: imaging of a talar mass. AJR Integr Imaging 2011;196:WS47–52. doi:10.2214/AJR.09.7195.

[5] Minhas MS, Khan KM, Muzzammil M. Giant cell tumour of foot bones—25 years experience in a tertiary care hospital. J Pakistan Med Assoc 2015;65(11):S-67-S-71.

[6] Van der Heijden L, Dijkstra PD, van de Sande MA, Kroep JR, Nout RA, Van Rijswijk CSP, et al. The clinical approach toward giant cell tumor of bone. Oncologist 2014;19(5):550–61.

[7] Raskin KA, Schwab JH, Mankin HJ, Springfield DS, Hornicek FJ. Giant cell tumor of bone. J Am Acad Orthop Surg 2013;21(2):118–26. doi:10.5435/JAAOS-21-02-118.

[8] Stacy GS, Peabody TD, Dixon LB. Mimics on radiography of giant cell tumor of bone. Am J Roentgenol 2003;181(6):1583–9.

[9] Mavrogenis AF, Igoumenou VG, Megaloikonomos PD, Panagopoulous GN, Papagelopoulos PJ, Soucacos PN. Giant cell tumor of bone revisited. SICOT-J 2017;3(54). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5598212 Accessed May 19, 2019.

[10] Chakarun CJ, Forrester DM, Gottsegen CJ, Patel DB, White EA, Matcuk GR. Giant cell tumor of bone: review, mimics, and new developments in treatment. 2013; 33(1). https://doi.org/10.1148/rg.331125089.

[11] Pereira HM, Marchiori E, Severo A. Magnetic resonance imaging aspects of giant-cell tumours of bone. J Med Imaging Radiat Oncol 2014;58(2014):674–8.

[12] Sharma S, Wani IH, Gupta N, Mahajan N, Salaria AQ. Giant cell tumor of talus: a case report. Cases J 2009;2(1):74 Published 2009 Jan 21. doi:10.1186/1757-1626-2-74.

[13] Wan JMC, Magarelli N, Peh WCG, Guglielmi G, Shek TWH. Imaging of giant cell tumour of the tendon sheath. La radiologia medidca 2010;115:141–51. https://link.springer.com/article/10.1007%2Fs11547-010-0515-2.

[14] Khatoon Z, Tariq R, Kureshi SB, Ahmed R. Giant cell tumor: rare sites. Pakistan J Radiol 2012;22(1). https://pdfs.semanticscholar.org/0e85/04e6443043516fd3ad3a30035695528488c0.pdf Accessed May 20, 2019.

[15] Bapat MR, Narlawar RS, Pimple MK, Bhosale PB. Giant cell tumour of talar body. J Postgrad Med 2000;46(2):110–11. http://www.jpgmonline.com/article.asp?issn=0022-3859;year=2000;volume=46;issue=2;spage=110;epage=1;aulast=Bapat Accessed May 20, 2019.

[16] Bhattacharyya A, Das R, Darwani R. Giant cell tumor of the talus: a case report and review of literature. Foot Ankle Online J 2010;3(88):2. http://faoj.org/2010/08/01/giant-cell-tumor-of-the-talus-a-case-report-and-review-of-literature/ Accessed May 20, 2019.

[17] Mondal S, Banik R, Sarkar A, Saha B. Giant cell tumour of the talus: a rare case report. IOSR-JDMS 2015;14(2):72–4. http://www.iosrjournals.org/iosr-jdms/papers/Vol14-issue2/Version-3/P014237274.pdf Accessed May 20, 2019.

[18] Orosz Z, Athanasou NA. Giant cell-containing tumors of bone. Surg Pathol Clin 2017;10(3):553–73.

[19] Ferrer-Santacreu EM, Ortiz-Cruz EJ, Díaz-Almirón M, Pozo Kreilinger JJ. et al Enchondroma versus chondrosarcoma in long bones of appendicular skeleton: clinical and radiological criteria—a follow-up. J Oncol 2016;216. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4791495/.

[20] Murphey MD, Walker EA, Wilson AJ, Kransdorf MJ, Temple HT, Gannon FH. Imaging of primary chondrosarcoma: radiologic-pathologic correlation. AFIP Arch 2003;23(5):1245–78. https://pubs.rsna.org/doi/full/10.1148/rg.235035134.

[21] Skubitz KM. Giant cell tumor of bone: current treatment options. Curr Treat Options Oncol 2014;15(3):507–18. https://link.springer.com/article/10.1007%2Fs11864-014-0289-1 Accessed May 20, 2019.

[22] Puri A, Agarwal M. Treatment of giant cell tumor of bone: current concepts. Indian J Orthop 2007;41(2):101–8 Accessed May 20, 2019. doi:10.4103/0019-5413.32039.