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CASE REPORT

Ossified soft tissue recurrence of giant cell tumor of the bone: four case reports with follow-up radiographs, CT, ultrasound, and MR images

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Abstract Giant cell tumor (GCT) of the bone is a benign tumor with a high incidence of recurrence. The majority of recurrence occurs in the bone, typically where curettage was performed previously. Soft tissue recurrence is much less common and often shows ossification at the periphery of the soft tissue mass. We report four cases of ossified soft tissue recurrence of giant cell tumor of the bone after surgery at follow-up examination using plain radiography, ultrasound, CT, and MR imagings. Imaging findings of soft tissue recurrence with peripheral or central ossification were reviewed with pathologic correlation. To the best of our knowledge, this is the first report to describe soft tissue tumor recurrence with ossification illustrated and monitored at various imaging modalities over an extended follow-up period.

Keywords Giant cell tumor · Recurrence · Ossification · Magnetic resonance imaging · Ultrasound

Introduction

Giant cell tumor (GCT) of the bone is a benign tumor, but its tumor recurrence after surgery is frequent. The high rate of local recurrence and the occasional pulmonary metastases are the manifestations of the aggressiveness of this tumor [1–6].

The majority of local recurrence occurs in the bone and typically where curettage was previously performed. Recurrence in soft tissue is much less common than in bone and is primarily due to implantation during operations, since complete surgical removal of the tumor with minimal contamination is often difficult [2, 4, 7]. Soft tissue recurrences occasionally show a peripheral rim of ossification surrounding the mass, which is a characteristic of soft tissue recurrence of giant cell tumor of the bone [2, 7–10]. Most previous reports dealt with radiographic and histologic findings of ossified soft tissue recurrence [7, 9], although some did not even show ossification on plain radiography [10]. There have been few reports in the literature that describe ossified soft tissue recurrence using different imaging modalities, except for one report by Ehara et al. [8].

We report four cases of ossified soft tissue recurrence of giant cell tumor of the bone following curettage and/or excision. Follow-up examinations were performed using plain radiography, combined with ultrasound, computed tomography (CT), and magnetic resonance (MR) imaging. Images demonstrated soft tissue recurrence with peripheral or central ossification, which correlated with the pathologic findings.

Case reports

We scanned a database of patients who were diagnosed with giant cell tumor of the bone and received follow-up imaging evaluations at our institution during 13 years and 6 months, from January 2000 to July 2013. The database included patients who underwent surgical treatment at either our institution or elsewhere, with a pathologically confirmed diagnosis. A review of electronic patient records and imaging yielded 129 cases available. Thirty of the 129 cases exhibited tumor

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recurrence at the site of curettage, and four presented with soft tissue recurrence. The Ethics Committee of our institution approved this report, however, did not require written informed consent since this was performed retrospectively.

Case 1

A 23-year-old female presented to the orthopedic clinic with right ankle pain. One year previously at another hospital, she underwent curettage and bone grafting of the medial malleolus of right tibia for giant cell tumor of the bone through an anterior ankle approach.

Plain radiographs taken during the first visit showed a new osteolytic lesion in the medial malleolus that was situated on infero-medial aspect of the previously curetted site. Nodular soft tissue lesions with faint calcification were identified anterior and posterior to the right ankle joint on lateral projection of plain radiograph (Fig. 1a).

CT scan demonstrated a corresponding expansile osteolytic lesion with cortical thinning of the medial malleolus, suggesting intraosseous recurrence. There were approximately five soft tissue masses with a shell-like peripheral hyperdense rim around the ankle joint, located on the same and even on the opposite side of the incision site (Fig. 1b). One of the smaller lesions in the postero-lateral aspect of the ankle showed no definitive peripheral hyperdense rim. The size of masses ranged from 0.3 to 1.3 cm in the longest diameter.

On MR imaging, the soft tissue masses showed inhomogenous low to intermediate signal intensity on T2-weighted images (Fig. 1c), low signal intensity on T1-weighted images, and inhomogenous enhancement following intravenous contrast administration. Considering the patient's history of giant cell tumor of the bone, the suggested radiologic diagnosis was intraosseous recurrence and soft tissue recurrence with ossification.

Ultrasound performed just prior to surgery showed irregularly shaped, inhomogenous hypoechoic masses with focal hyperechogenicity at the periphery.

The patient was managed for the recurrence by excision of the recurrent soft tissue masses and by curettage and bone cement replacement. Intraosseous recurrence and ossified soft tissue recurrence of giant cell tumor were confirmed pathologically. Microscopic examinations revealed metaplastic bone formation located at the interface of the tumor and the adjacent soft tissue at the periphery of soft tissue masses (Fig. 1d).

Case 2

A 58-year-old man presented with right buttock pain of 5-year duration. Curettage for a bone lesion in the right inferior pubic

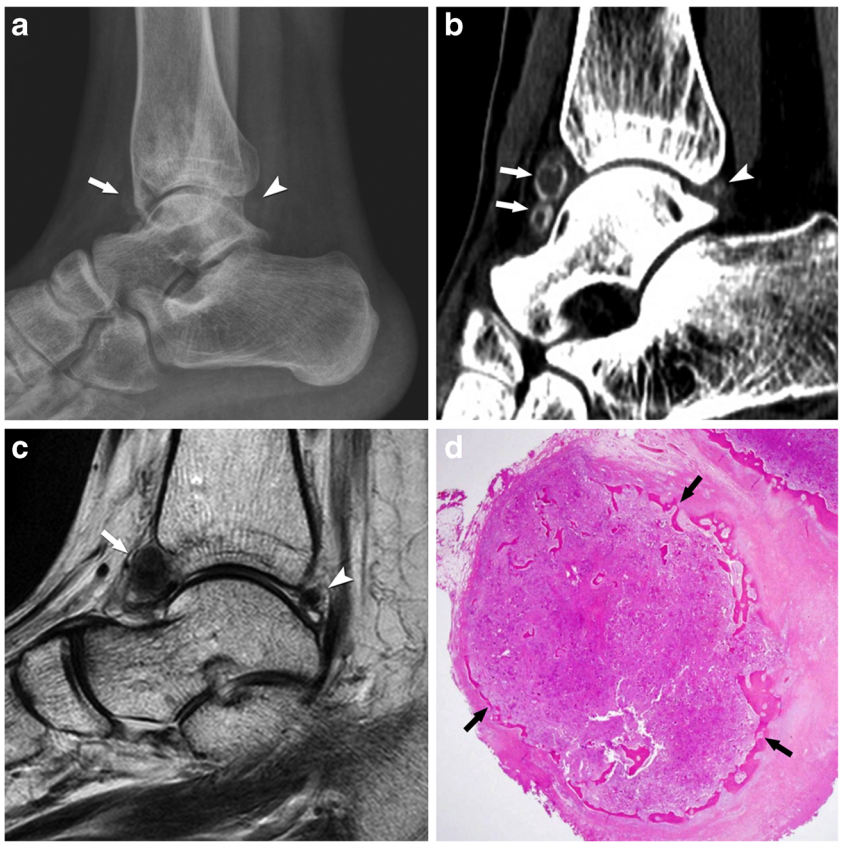

Fig. 1 Case 1. A 23-year-old female with giant cell tumor in the medial malleolus of right tibia. **a** Plain radiograph of lateral projection of the ankle shows soft tissue nodular lesions anterior (*arrow*) and posterior (*arrowhead*) to the ankle joint. **b** On reformatted sagittal CT scan, the soft tissue masses with a shell-like peripheral hyperdense rim are identified around the ankle joint, anterior (*arrows*) and posterior (*arrowhead*) aspect. **c** On sagittal T2-weighted MR image, soft tissue masses reveal inhomogeneous low signal intensity (*arrow* and *arrowhead*). **d** Low-power view of the soft tissue mass demonstrates a thin bony shell (*arrows*) surrounding the soft tissue recurrence of GCT (hematoxylin and eosin stain, ×40)

ramus had been performed 34 months previously. Histologic diagnosis was that of giant cell tumor of the bone. Thirteen months later, the patient was operated on again for intraosseous recurrence at the site of the previous operation.

Fourteen months after the second surgery, the patient complained of a palpable mass in the right buttock area, fluctuating in size. On ultrasound, there was an inhomogeneous hypoechoic mass with a peripheral echogenic portion. Color Doppler imaging showed that linear and focal internal vascularity was present at the periphery of the mass (Fig. 2a).

On follow-up CT obtained 1 year and 11 months after the second surgery, a new osteolytic lesion with protruding soft tissue mass was observed in the inferior margin of the previous operative site. Again, there was a 3.3×1.5-cm-sized, oval soft tissue mass located in the subcutaneous fat tissue of the right buttock, separate from the right inferior pubic ramus but within the incision site (Fig. 2b), which was seen on the previous ultrasound examination. The mass was surrounded by an irregular hyperdense rim, suggesting calcification or ossification. Despite the patient's history of intraosseous recurrence of giant cell tumor, the differential diagnosis for soft tissue masses included benign soft tissue lesions, such as granuloma. However, CT obtained 4 months later revealed that the soft tissue mass had grown.

Surgery was performed and a diagnosis of recurrent giant cell tumor was confirmed for the intraosseous and soft tissue lesions. Histologic examinations revealed shell-like ossification surrounding the soft tissue mass (Fig. 2c). Metaplastic bone was identified at the interface of the tumor and the adjacent soft tissue.

Case 3

A 26-year-old female was transferred from another hospital with right knee pain. She underwent curettage and bone grafting for a giant cell tumor of the right distal femur had been performed 1 year and 9 months previously.

Plain radiograph taken at the first visit showed new lobulated lytic lesions in the superior and lateral aspect of the cement–bone interface in the right distal femur, representing intraosseous tumor recurrence. A nodular lesion with increased density was observed in the subcutaneous tissue layer, lateral to the bony lesion, and near the incision site (Fig. 3a).

CT obtained 1 month later demonstrated four, soft tissue nodular lesions present in the subcutaneous fat tissue, ranging from 0.3 to 0.5 cm in diameter. One nodule was almost totally opacified, and the others had internal soft tissue density with hyperdense foci at the periphery (Fig. 3b).

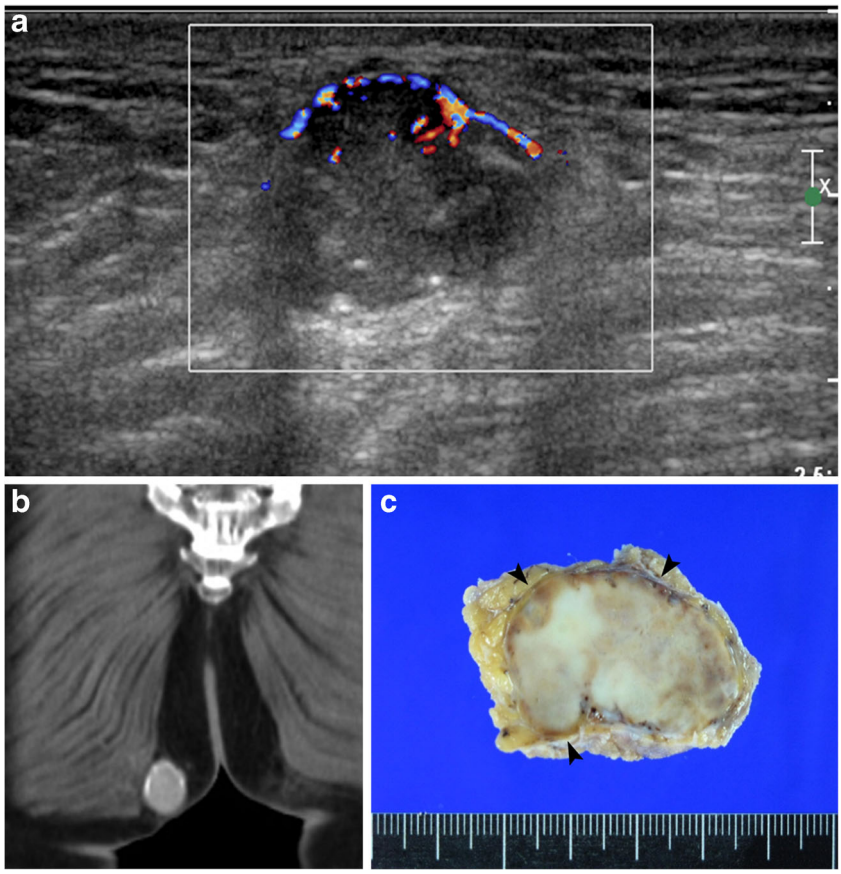

Fig. 2 Case 2. A 58-year-old man with giant cell tumor in right inferior pubic ramus. **a** On ultrasonography obtained 14 months after the second surgery, a palpable soft tissue mass in his right buttock area shows inhomogenous hypoechogenicity with a peripheral echogenic foci at the inferior aspect. Linear and focal internal color signals are present in the peripheral portion of the mass on color Doppler imaging. **b** Reformatted coronal CT scan performed 23 months after the second surgery demonstrates an oval soft tissue mass with irregular peripheral hyperdense rim, suggesting calcification or ossification, in the subcutaneous fat tissue of the right buttock, near the site of incision. **c** Histologic section of the excised mass shows an ossified shell (*arrowheads*) surrounding the soft tissue mass

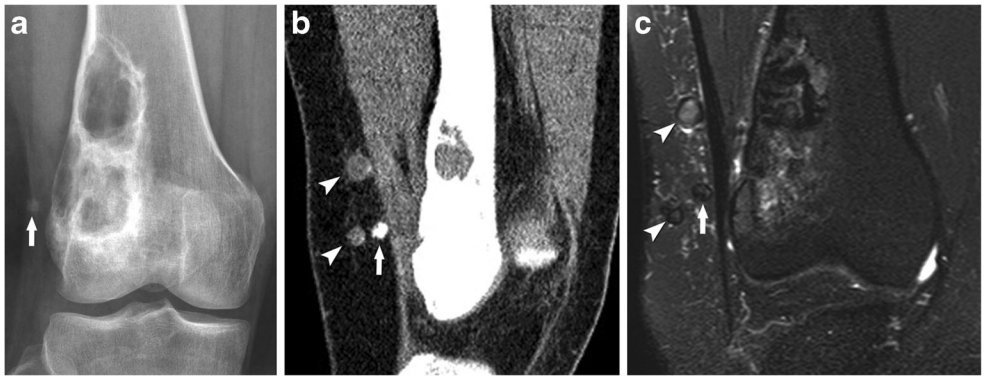

Fig. 3 Case 3. A 26-year-old female with giant cell tumor in the distal femur. **a** Plain radiograph of anterior-posterior projection of the knee shows an increased density nodular lesion in the subcutaneous fat tissue layer, lateral to the bony lesion, near the incision site (*arrow*). Also seen is an irregular area of osteolysis in the superior and lateral aspect of the previously treated bony lesion of the distal femur, at the cement–bone interface, representing intraosseous tumor recurrence. **b** Reformatted sagittal CT scan shows about three soft tissue nodular lesions in the subcutaneous fat tissue. Two of them (*arrowheads*) have hyperdense foci at the periphery, and one nodule (*arrow*) is totally opacified. **c** Three soft tissue nodular lesions (*arrow* and *arrowheads*) in subcutaneous fat layer show inhomogenous low to increased signal intensity on coronal T2-weighted image with fat saturation

Three soft tissue lesions located along the previous incisional site showed inhomogenous low and increased signal intensity on T2-weighted MR images without/with fat saturation (Fig. 3c) and enhancement on contrast-enhanced T1-weighted MR images with fat saturation. The suggested radiologic diagnosis was tumor recurrence rather than postoperative change.

The patient was managed for tumor recurrence by excision of the soft tissue masses and by curettage and bone cement replacement. Microscopic examination of the soft tissue masses showed metaplastic bone formation located at the interface of the tumor and the adjacent subcutaneous fat tissue. The final diagnosis was giant cell tumor with ossification.

Case 4

A 35-year-old female underwent curettage and iliac bone grafting for giant cell tumor in the right distal ulna. On follow-up radiographs and CT after the surgery, a new osteolytic lesion in the distal ulna was found that gradually increased in size. Ten months after the previous surgery, she received a second operation of resection of the right distal ulna for the bony lesion. The lesion was confirmed pathologically as recurrent giant cell tumor.

Follow-up examinations were performed periodically using plain radiography. Ten months later, a focal radiodense lesion was found in the soft tissue near the distal margin of the resected ulna (Fig. 4a). The lesion increased in density and size, finally exhibiting an irregular stellate appearance on radiographs obtained at the 21-month follow-up (Fig. 4b).

Ultrasound obtained at 19-month follow-up showed irregular triangular-shaped, low echoic soft tissue lesion at the site of bone resection. Focal increased color signals in the peripheral portion of the lesion were present on color Doppler imaging (Fig. 4c). Differential diagnosis included soft tissue recurrence of the tumor and postoperative change.

On MR imaging at 21-month follow-up (Fig 4d), an ill-defined soft tissue lesion was identified at a site corresponding to the bone resection site, along the extensor carpi ulnaris muscle, measuring 0.9×0.6×2.6 cm. This exhibited intermediate signal on T1-weighted images, intermediate to high signal intensity on fat-saturated T2-weighted images, and inhomogenously enhanced after intravenous contrast administration. Another enhancing soft tissue lesion was observed around the distal resection margin of the ulna (Fig. 4d). After reviewing MR images, soft tissue recurrence rather than postoperative granulation tissue was suggested.

The patient underwent a third operation of soft tissue excision. The soft tissue lesion with irregular central ossification was confirmed as recurrent soft tissue tumor with ossification in central portion of the mass (Fig. 4e). Another soft tissue lesion at the distal margin of the ulna was confirmed as postoperative scar tissue.

Discussion

Giant cell tumors are benign, thus curettage and bone grafting or placement of bone cement (polymethylmethacrylate) has traditionally been the treatment of choice. However, recurrence after surgery is high, ranging 15–25 % up to 40–60 % [11–14], depending on the type of the surgical procedures; marginal resection is associated with a high rate, whereas wide resection has a reduced rate [15–17].

Tumor recurrence usually occurs in the bone, at the previous operative site, which is caused by continued growth of the residual tumor in the bone. Typical radiologic findings of

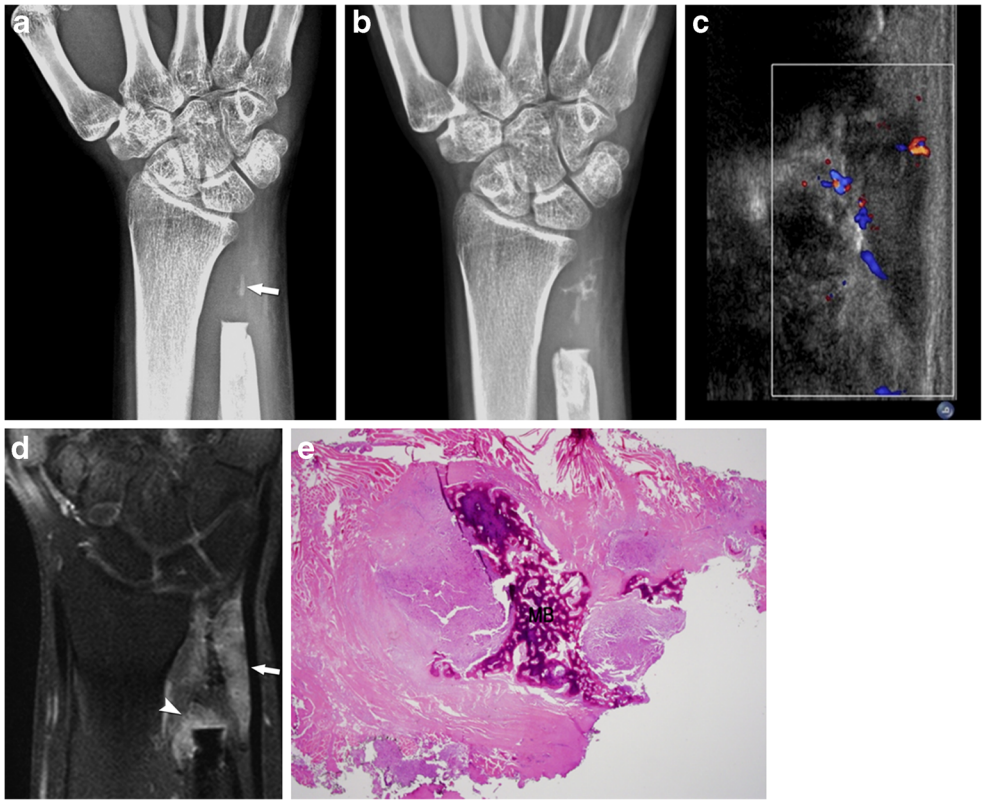

Fig. 4 Case 4. A 35-year-old female with giant cell tumor in right distal ulna. **a**, **b** On serial follow-up radiographs of anterior-posterior projection of the wrist taken 10 months (**a**) and 21 months (**b**) after the second operation, a focal radiodense lesion (*arrow*) in the soft tissue, near the distal margin of the resected ulna, is gradually increasing in density and size, forming an irregular stellate appearance. **c** Ultrasonography obtained at the 19-month follow-up shows a triangular low echoic soft tissue lesion distal to the bone resection site. Focal color signals are present in the peripheral portion on color Doppler imaging. **d** 21-month follow-up MR imaging reveals an ill-defined soft tissue mass along the extensor carpi ulnaris muscle (*arrow*), showing inhomogenous enhancement on post-contrast T1-weighted image with fat saturation. Another enhancing soft tissue lesion around the distal resection margin of the ulna (*arrowhead*) was confirmed as postoperative scar tissue. **e** Low-power image of the excised soft tissue lesion along the extensor carpi ulnaris muscle shows a centrally located ossification (*MB* metaplastic bone formation) within a soft tissue recurrence of GCT (hematoxylin and eosin stain, ×40)

recurrence are new areas of bone destruction at the resection margin or adjacent to resorption of intralesional bone graft material at follow-up imaging evaluation [2, 17–20]. Evaluation for tumor recurrence is best identified by comparing follow-up images with the initial baseline postoperative images and careful inspection of images is fundamental. Recurrence in soft tissue can be observed but is less frequent. The presumed cause of soft tissue recurrence is implantation of the tumor into surrounding soft tissues at the time of surgery. Such soft tissue contamination may occur even in the absence of surgery, if the tumor is associated with cortical disruption or pathologic fracture [2, 8, 9]. In one case (case 1) with soft tissue recurrence around the ankle joint, masses were even located on the opposite side of the incision site, as well as the same side. In this instance, micro-cortical disruption could be responsible since cortical disruption or pathologic fractures were not evident on the pre-operative images.

An accurate rate of incidence for soft tissue recurrence has not yet been determined. Cooper et al. [7] reported 17 instances of soft tissue recurrence in their review of 1,100 cases of giant cell tumor. All of the cases in the review demonstrated radiographically visible ossification. They reported an incidence rate of 1.5 % (17/1,100); however, this was not the rate of soft tissue recurrence itself but that of soft tissue recurrence with ossification. Yang et al. [10] reported that the incidence of soft tissue recurrence was 1.9 % (2/106). Their pathological examinations determined that two cases exhibited ossification that was not identified radiographically. We found four cases after reviewing 129 cases of giant cell tumors of the bone. All of them had ossification that was visible at imaging and was confirmed pathologically. Hence, the incidence rate of ossified soft tissue recurrence in our series was 3.10 % (4/129).

The clinical symptoms of soft tissue recurrence are non-specific. A history of giant cell tumor of the bone can be the most significant finding to reach a correct diagnosis when a new soft tissue lesion occurs near the previous operative site at follow-up. As such, imaging evaluations are an effective method for monitoring tumor recurrence. Comparisons of serial plain radiographs are essential, particularly for the detection of intraosseous recurrence [2, 17–20]. Soft tissue

recurrence is strongly suggested if an ossified peripheral rim is detected in the soft tissue on plain radiographs [2, 7–10]. However, ossification may not occur in all soft tissue recurrences, in which occasion the recurrent soft tissue masses could be better evaluated by cross-sectional imaging regardless of the presence of ossification. CT may provide more information about the soft tissue lesions than plain radiographs and is a sensitive method for detecting the presence of ossification within the soft tissue masses. MR imaging has superior soft tissue contrast which provides simultaneous and detailed evaluation of soft tissue and bone. Recurrent masses show inhomogenous low to intermediate signal intensity on T2-wieghted images and are enhanced following intravenous contrast administration. An ossified rim was observed as a rim of low signal on all pulse sequences. However, metal artifacts, which are common post-operative findings, impede interpretation by deteriorating the operative site. Repeated MR examinations over long follow-up periods may be costly. In such an instance, ultrasound could be an alternative follow-up examination over long follow-up periods, particularly after recurrent surgeries. It enables detection of new lesions and monitoring of pre-existing lesions in a cost-effective manner. Recurrent soft tissue masses were inhomogeous hypoechoic, with intralesional vascularity at color Doppler imaging. The ossified rim was presumed to be focal hyperechogenicity at the periphery.

In the report by Cooper et al. [7], ossification was seen at the periphery of the soft tissue implants in 16 cases. Ossifications varied in thickness from a barely visible shell to a thick rind. One exceptional case reported to show ossification in a central location within the soft tissue mass. In our series, two cases (case 1, 2) showed shell-like peripheral ossification surrounding the soft tissue masses present near to the previously curetted intraosseous lesion. One lesion of case 3 was observed as a small, totally ossified soft tissue mass and other lesions showed fine and focal peripheral ossification. In the remaining case (case 4), ossification was located in the central portion of the soft tissue lesion instead of the peripheral rim. This ossification was discovered during the initial follow-up after surgery and was observed as a faint irregular shape that became more prominent, gradually increasing in size, forming a stellate appearance over time. This is a finding that has not been previously described at serial follow-up imaging of soft tissue recurrence of giant cell tumor.

Pathologically, such ossification is considered to be the result of metaplastic bone formation, especially when localized to the periphery of a lesion. It has been suggested that these tumor cells, when exposed to an extraosseous environment different from that of intraosseous giant cell tumor, stimulate osteoblastic differentiation and bone formation. In this mechanism, transforming growth factor β1 (TGF-β1) and transforming growth factor β2 (TGF-β2) released from neoplastic stromal cells and osteoclastic-like giant cells may act in a paracrine manner to influence mesenchymal progenitor cell function [9, 21]. This theory may also explain a similar characteristic peripheral rim of calcium detected in pulmonary metastases from benign giant cell tumor [1, 3, 5, 22].

Given this appearance of soft tissue recurrence with ossification, the main differential diagnosis is heterotopic ossification. Previous operation can be a major causative factor for heterotopic ossification. Hematoma, which may be associated with a pathologic fracture if present, can be another causative factor. Heterotopic ossification tends to be apparent earlier than soft tissue recurrence, about 3-6 weeks after surgery. With time, the lesion matures and often attaches to the adjacent bone, appearing blended with cortex [1, 7, 8, 23]. By contrast, recurrent soft tissue masses are usually present several months or years after the primary surgery and grow constantly [1, 7, 8]. These different time courses and growing patterns are the important features of differentiation.

In a clinical setting of post-operative status, postoperative scar or granulation tissue can be included in the differential diagnosis. Postoperative fibrosis has been reported to show low signal intensity on both T1-, T2-weighted MR images and little or no enhancement following intravenous contrast enhancement [24]. However, its imaging findings may have a broad spectrum, which can lead to difficulty in making an accurate diagnosis. In one case (case 4) of our series, two separate soft tissue lesions were found at follow-up; one was located more distally, at the resection site of the ulna, and the other was around the distal resection margin of the ulna. Both lesions shared similar imaging findings, including inhomogenous enhancement on post-contrast T1-weighted MR images, except for the presence of irregular central ossification. The distal soft tissue lesion with central ossification was confirmed as soft tissue tumor recurrence, whereas the other lesion without ossification was confirmed as postoperative scar tissue.

When nodular calcifications of soft tissue are detected, granulomas may be suggested as a possible diagnosis. This lesion usually results from injection or foreign bodies [25]. Diagnosis could be made when foreign bodies are identified on plain radiographs, more effectively on CT and even on ultrasonography, although it is difficult to identify radiolucent foreign bodies, such as wooden splinters, on plain radiographs. In this situation, the clinical information may play a role in facilitating the differentiation.

Also, most of our cases had concomitant intralesional (bone) and soft tissue recurrences. As such, an adjacent bone lesion representing presence of intraosseous recurrence may be an additional indication of soft tissue recurrence of giant cell tumor.

In summary, giant cell tumor is generally benign, however, and may be aggressive and recur after surgical resection. Tumor recurrence is most often found in bones and occurs less frequently in the soft tissue. Ossified soft tissue masses

near a previous operative or incisional site, combined with a clinical history of giant cell tumor of the bone, are characteristic of soft tissue recurrence of giant cell tumor of the bone, although infrequent. Ossification of soft tissue is commonly identified at the periphery, and occasionally, albeit rarely, in the central portion. These findings were detected and monitored by plain radiography, CT, MR imaging, ultrasound, and correlated with pathologic examinations. For follow-up examinations after surgery, plain radiography is essential. However, CT, MR imaging, and ultrasound could provide sensitive and detailed information for the diagnosis of soft tissue recurrence as well as intraosseous recurrence. Recognition of these appearances enables early and accurate diagnosis of locally recurrent tumors with more confidence during follow-up examinations of patients treated for giant cell tumor of the bone.

Conflict of interest There are no conflicts of interest to disclose.

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