Dedifferentiated giant cell tumour of bone in the form of low-grade fibroblastic osteogenic sarcoma: case report of a unique presentation with follow-up

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ABSTRACT

Giant cell tumour (GCT) of bone is a locally aggressive benign tumour. It can, however, undergo dedifferentiation, either *de novo* or secondarily after local recurrence or radiation. Whether spontaneously occurring or induced by previous irradiation, this malignant transformation is typically defined as a high-grade anaplastic sarcoma devoid of giant cells. Dedifferentiation of GCT into low-grade-appearing sarcoma has not been reported yet. Here, we describe the first case of dedifferentiated GCT in the appearance of low-grade fibroblastic osteogenic sarcoma with distant bone metastases. This disease progression occurred without previous irradiation. We confirm the aggressive behaviour of this tumour despite the deceptively bland appearance of the malignant component. We also alert others to the importance of recognizing this rare histology to avoid underdiagnosis and subsequent undertreatment.

KEY WORDS

Giant cell tumour, malignancy, osteogenic sarcoma, dedifferentiation

1. INTRODUCTION

Malignant transformation of giant cell tumour (GCT) of bone, also known as dedifferentiation of GCT, is a rare event that occurs in fewer than 1% of all cases [1]. Two forms of malignant GCT can be distinguished: a primary *de novo* type that arises side-by-side with a typical GCT, and a secondary form occurring at the site of previous GCT [1–4]. Nearly all secondary cases are characterized by a history of previous irradiation; spontaneous malignant transformation is exceedingly rare [4,5]. Occurrence of malignancy is important to diagnose, because it entails a worse clinical outcome, including more aggressive local behaviour and a higher risk for metastatic disease [6]. The diagnosis is established by histology, although it is also suspected both clinically and radiographically.

Here, we report a unique case of GCT in which dedifferentiation occurred in the form of low-grade fibroblastic osteogenic sarcoma without prior radiation. Despite the bland appearance of the dedifferentiated component, local recurrence and metastases to distant bone occurred, indicating aggressive behaviour. We also alert others to the importance of recognizing such rare histology to avoid inadequate management.

2. CASE DESCRIPTION

A 47-year-old man presented initially in 1995 with a typical GCT of the right tibia. Histologically, the tumour consisted of bland mononuclear stromal cells with an osteoclast-type giant-cell-rich component. No bone matrix or fibroblastic areas were seen. Local curettage was performed.

The first local recurrence happened in 1998 and showed typical GCT morphology. It was treated with curettage and cementing, and the patient remained disease-free for 8 years.

In 2006, an aggressive recurrence, with a large soft-tissue extension, was observed at the surgical site. Core biopsy led to a diagnosis of recurrent GCT, which prompted a limited local resection of the proximal tibia [Figure 1(A)].

Histologically, in addition to the presence of residual GCT (Figure 2), a second morphologic component was noticed in abrupt transition from the former component [Figure 1(B)]. The new component consisted of an infiltrating fibroblastic process deeply penetrating the cancellous bone, showing prominent paratrabecular predilection, and diffusely producing weakly mineralized immature osteoid matrix not rimmed by osteoblasts (Figure 3). The cellularity was uniformly low, and the fibroblasts were only mildly atypical. The mitotic figures did not exceed 1 per 10 high-power fields, and no necrosis was seen [Figure 4(A)]. Overall, the fibroblastic appearance was reminiscent of fibromatosis.

Because of the unusual histology and the possibility of radical surgical management, an expert opinion was sought, and a diagnosis of malignancy was excluded. The findings were interpreted as reactive fibrosis with stromal calcification; they were considered to represent a reactive phenomenon from the earlier

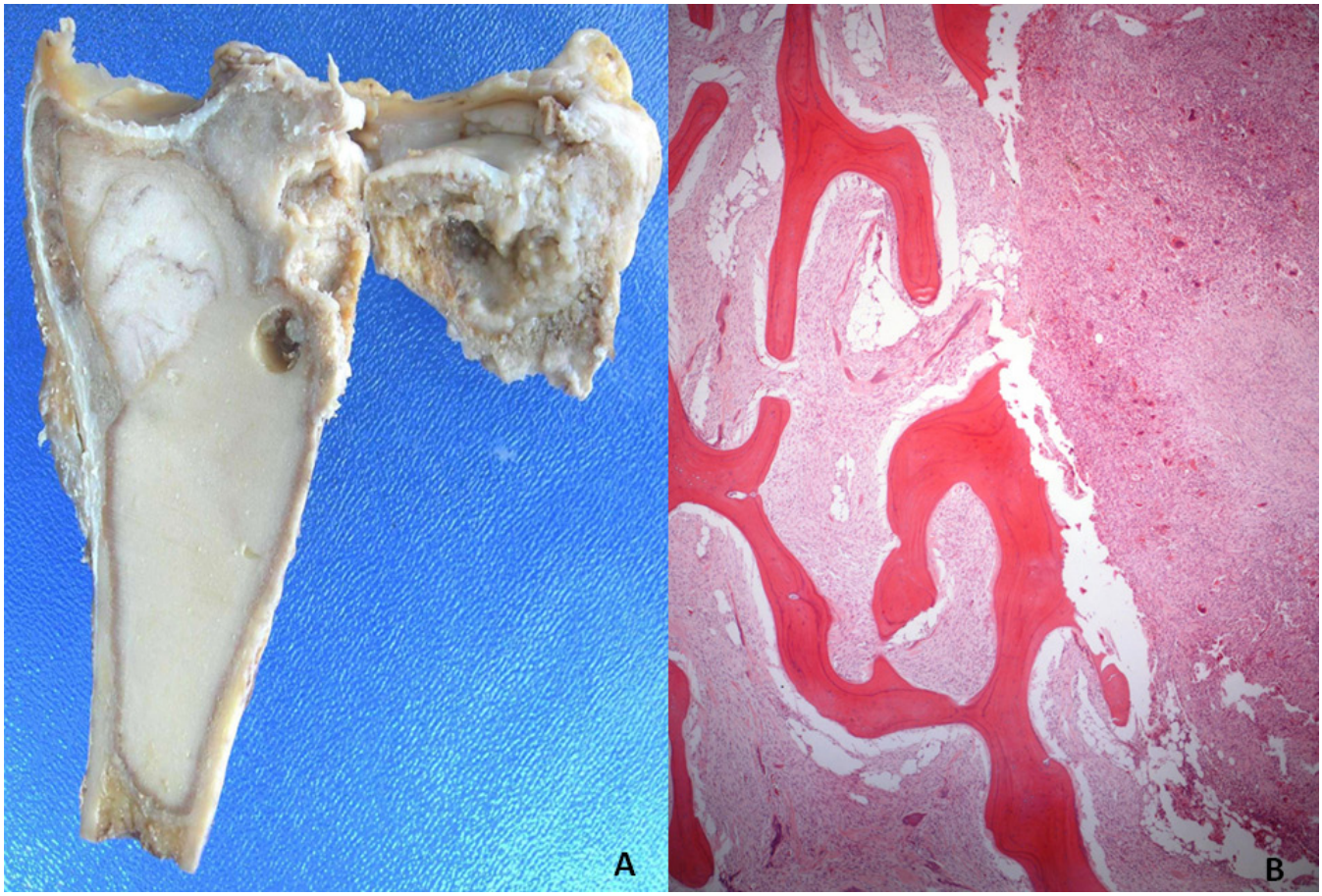

FIGURE 1 *(A) Proximal tibial resection of the 2006 local recurrence (on preoperative biopsy determined to represent a non-malignant recurrence). Note the white-tan appearance of the locally aggressive tumour as compared with the typical brown-tan appearance of giant cell tumour (GCT). (B) Biphasic tumour morphology is apparent upon microscopy examination of the resection. The usual GCT morphology (right side of image) transforms abruptly into a mildly atypical fibroblastic tumour penetrating deeply into bone trabeculae (left side of image). Hematoxylin and eosin stain, 40× magnification.*

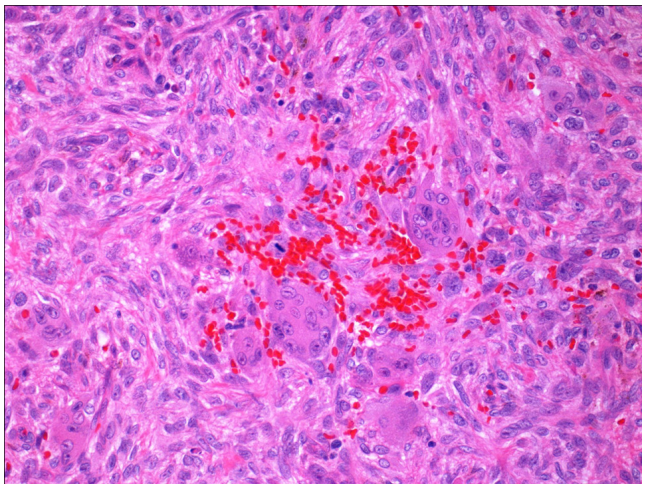

FIGURE 2 *Presence of residual classical giant cell tumour in the recurrent tumour: numerous osteoclast giant cells are admixed with mononuclear histiocytic small cells exhibiting weak spindling. No atypical features are present. Hematoxylin and eosin stain, 100× magnification.*

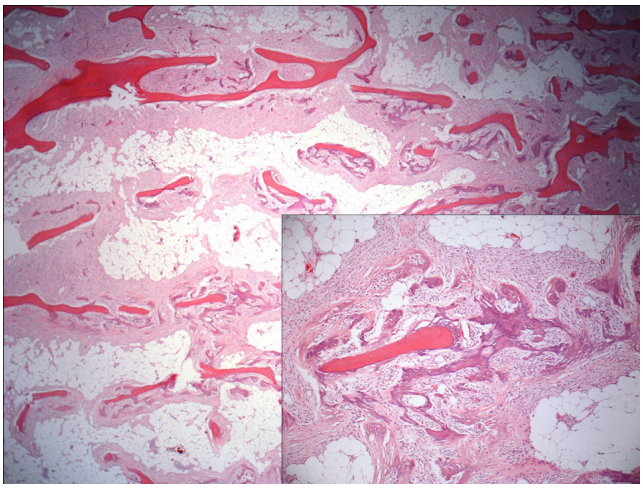

FIGURE 3 *The dedifferentiated component shows extensive infiltration by a low grade fibroblastic osteoid-forming tumour along the cancellous bone. This infiltration was initially interpreted as reactive fibrosis secondary to the earlier cementing. Hematoxylin and eosin stain, 20× magnification.*

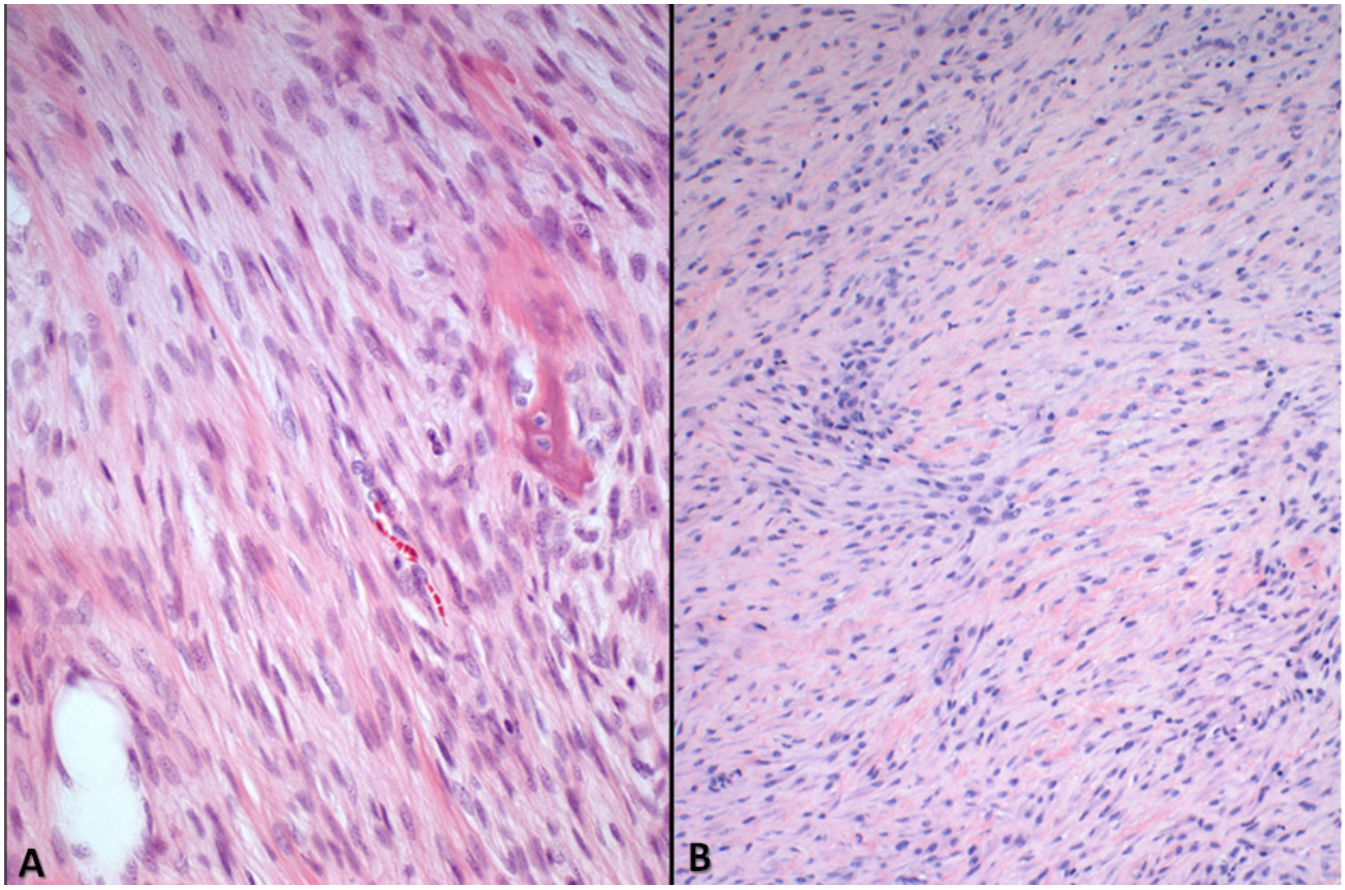

FIGURE 4 In its most recent (2008) aggressive local recurrence, the dedifferentiated tumour is histologically similar to (A) the earlier (2006) recurrence. It features (B) a mildly cellular fibroblastic tumour devoid of giant cells and exhibiting only mild cytologic atypia and sparse mitotic figures. Hematoxylin and eosin stain; (A) 400× magnification, (B) 100× magnification.

cementing. No further treatment was rendered, and the patient remained disease-free for 20 months.

In the summer of 2008, the tumour recurred locally with a large destructive mass involving the right tibia and its adjacent soft tissue and also distantly with several lytic bone lesions in the sternum and humerus.

A core biopsy of the recurring tibial mass [Figure 4(B)] and curettage of the sternal lesion (Figure 5) showed atypical fibroblastic proliferation arranged in vague fascicles, with no evidence of typical GCT morphology. This finding differed from the fibroblastic component observed in the local recurrence of 2006 by virtue of higher cellularity, lack of necrosis, more pronounced cytologic atypia, and average mitotic activity of 2 per 10 high-power fields. No malignant osteoid matrix could be identified in either biopsy, but on computed tomography (CT) and magnetic resonance imaging studies, calcification was highly suggestive. Overall, the histology was consistent with low-grade fibroblastic osteogenic sarcoma. A diagnosis of malignant GCT was made in both the locally recurring tumour and the metastatic sternal lesion.

In retrospect and in light of the foregoing clinicopathologic findings, the earlier infiltrating

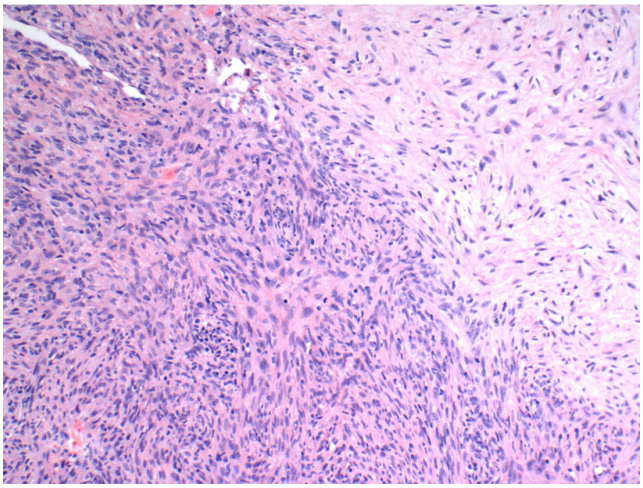

FIGURE 5 The sternal metastasis shows a morphology similar to that of the recurrent tibial tumour, only more cellular, mitotically more active, and displaying moderate cytologic atypia. Hematoxylin and eosin stain, 100× magnification.

bone-producing fibroblastic process in the tibia, which was labelled a reactive process, already represented dedifferentiation. To our knowledge, this is the first case of malignant GCT in which the dedifferentiated component featured a low-grade fibroblastic osteogenic sarcoma.

2.1 Imaging Features

The right knee radiograph performed 8 years after the initial curettage was non-contributory. Given the patient's symptomatology, a multiplanar, multi-sequential contrast-enhanced magnetic resonance imaging study was performed. That study revealed a new lesion surrounding the area of curettage at the proximal tibial aspect (Figure 6). The abnormality was heterogeneous, being mainly hypointense on T1-weighted and hyperintense on T2-weighted images with intense post-gadolinium enhancement. Extraosseous intra-articular tumoural extension, with an associated joint effusion, was present. A complementary CT imaging study demonstrated local lytic bone expansion and cortical destruction. However, no intra-lesional matrix was seen. The overall imaging features were in keeping with aggressive local tumoural recurrence. The CT imaging of the chest showed 3 minute right upper lobe nodules, with no associated thoracic wall abnormalities.

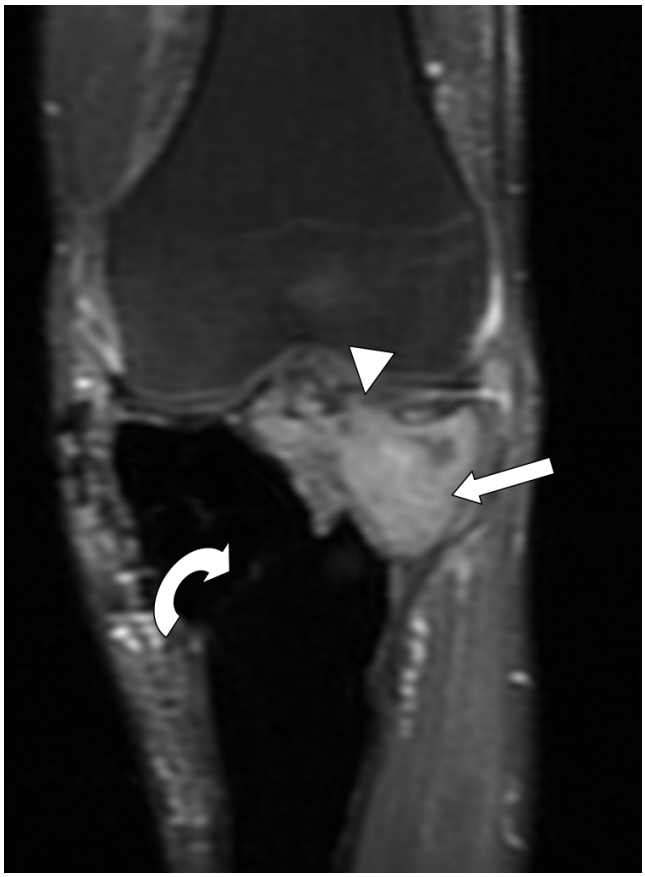

FIGURE 6 Coronal fat–saturated T1-weighted magnetic resonance image of the patient's left knee at presentation in 2006. An enhancing soft-tissue tumoural recurrence can be seen at the proximal tibia (regular arrow) with intra-articular extension (arrowhead). Note the region of low signal intensity, a result of earlier cementing (curved arrow).

The CT imaging study performed during the patient's 2008 presentation was extremely limited: prosthesis-related artefacts extensively obscured the images, although periprosthetic ossifications were identified. Despite hardware-related degradation of the complementary magnetic resonance images, a very large heterogeneous multi-lobulated periprosthetic mass lesion was seen. The lesion demonstrated multi-compartmental involvement and revealed signal-intensity changes in keeping with internal necrosis and hemorrhage. These findings were consistent with extensive local tumoural growth.

The CT images of the chest showed a new aggressive lytic sternal lesion and new right upper and right lower lobar pulmonary nodules. Imaging by combined positron emission tomography and CT revealed metabolically active lytic lesions of the sternum, right scapular glenoid fossa, and right sacral bone (Figure 7).

The lung and distant bone lesions were considered metastatic in nature, given the clinical context and imaging appearance.

3. DISCUSSION

Malignancy arising in GCT of bone is histologically suspected when a high-grade sarcoma is observed either in close contact with a typical GCT or in a patient with a known history of GCT [2,3]. The current literature describes this malignant transformation mainly as a high-grade spindle or pleomorphic sarcoma with or without osteoid production [1–5,7–9]. Dedifferentiation exhibiting low-grade morphology has not yet been reported. This lack of reports is likely a result of the extreme rarity of such examples or of the difficulty in recognizing such a histology as malignant, given that typical GCT commonly displays cytologic atypia, mitotic activity, and prominent fibrohistiocytic change.

Dedifferentiation is an event that occurs only rarely in some types of musculoskeletal neoplasms. Well-differentiated liposarcoma, low-grade skeletal chondrosarcoma, periosteal osteogenic sarcoma, and skeletal chordoma are among the entities recognized as most being capable of such behaviour [10–13].

Although dedifferentiation usually takes the form of a high-grade undifferentiated sarcoma, it can sometimes exhibit low-grade histology. When such histology is encountered, confirmation that dedifferentiation has occurred can be very challenging to diagnose [11,12].

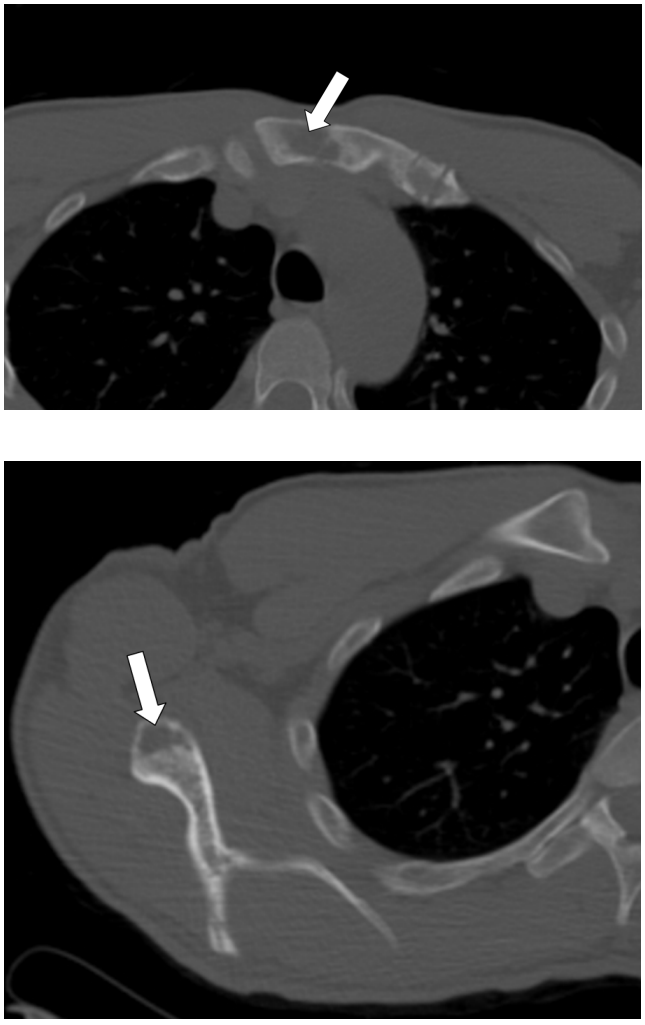

FIGURE 7 Selected transverse computed tomography images demonstrate aggressive lytic lesions of the sternum (arrow, upper panel) and the right scapular glenoid (arrow, lower panel).

Although the malignant component was deceptively bland in our case, its abrupt transition from typical areas of GCT was evident. That finding, in our opinion, is very important and, in itself, should raise ample concerns regarding the possibility of dedifferentiation. The presence of extensive bone matrix production in the 2006 recurrent tumour is consistent with osteosarcomatous differentiation. This histology has not been described in malignant transformation of GCT of bone; the few examples in the literature describe only high-grade osteosarcoma [1,4,8,14].

4. CONCLUSIONS

Our case unequivocally proves dedifferentiation despite deceptive histology. It also confirms the aggressive behaviour of such histology by demonstrating both local recurrence and distant bone metastases, and it reveals that prior local treatment such as cementing can make interpretation of otherwise worrying changes in histology difficult.

Regardless of whether our case provides sufficient evidence to formally expand the definition of malignancy arising in GCT of bone, it does show that dedifferentiation should not be eliminated based on the absence of aggressive high-grade histology. Therefore, in such examples, we recommend close observation during follow-up appointments, a high index of suspicion, and perhaps a more aggressive surgical approach.

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