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CASE REPORT

Dedifferentiated parosteal osteosarcoma with giant cell tumor component

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Abstract Dedifferentiated parosteal osteosarcoma is characterized histologically by the admixture of low-grade fibroblastic osteosarcoma and a high-grade component typically resembling conventional osteosarcoma or malignant fibrous histiocytoma. We report an unusual distal femoral dedifferentiated parosteal osteosarcoma in which the dedifferentiated component resembled a giant cell tumor of bone. This phenotype is rarely described in the dedifferentiated component of a dedifferentiated parosteal osteosarcoma. The clinical, radiographic, and pathologic features of this unusual tumor are described to further expand the histologic spectrum of dedifferentiated parosteal osteosarcoma.

Keywords Parosteal osteosarcoma · Dedifferentiated · Giant cell tumor · Femur · MRI

Introduction

"Dedifferentiation" is a well-recognized phenomenon in a variety of low-grade mesenchymal neoplasms, including liposarcoma, chondrosarcoma, and parosteal osteosarcoma [1–3]. Although the most common phenotypes of the dedifferentiated component in dedifferentiated parosteal osteosarcoma include malignant fibrous histiocytoma and conventional osteosarcoma, unusual phenotypes such as rhabdomyosarcoma and telangiectatic osteosarcoma have also been described [4, 5]. Additionally, several cases of dedifferentiated *chondrosarcoma* have been described in the literature in which the dedifferentiated component had the appearance of a conventional giant cell tumor [6–9]. However, giant cell-rich foci occur in dedifferentiated parosteal osteosarcoma, but are rare [8, 10–12]. Herein we describe a case of dedifferentiated parosteal osteosarcoma of the distal femur in which the dedifferentiated component had the appearance of a giant cell tumor.

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Case report

A 33-year-old African-American male presented with a painful mass in the distal left femur. Physical examination revealed a large, firm mass in the supracondylar region of the femur. There was no associated swelling, distal pulses were palpable, and full range of motion was achieved.

Plain radiographs showed a circumferential, largely ossified mass involving the distal femoral metaphysis (Fig. 1a,b). Multisequence magnetic resonance images and an MR angiogram showed a large, complex mass measuring 8.8×7.2×13.0 cm; the popliteal vessels were enveloped by tumor, but patent (Fig. 2a,b). Computed tomography scans demonstrated a mass measuring 7.7×6.8 cm in its largest axial dimension. A portion of the tumor appeared heavily ossified and encompassed the posterior neurovascular bundle. A non-mineralized component was also noted, which extended into the medullary cavity, resulting in a subtle fracture with minimal displacement in the metadiaphysis (Fig. 2c,d). A questionable satellite lesion or skip metastasis was identified in the lateral femoral

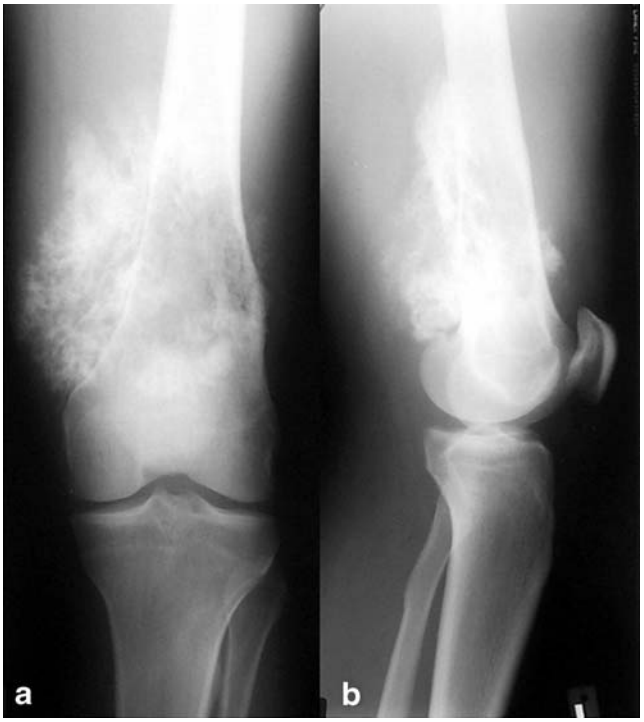

Fig. 1 **a** Posterior-anterior and **b** lateral plain radiographs demonstrate a nearly circumferential, heavily ossified mass involving the distal femoral metaphysis with radiolucent regions deep within the tumor and in the medullary cavity, highly suggestive of dedifferentiation

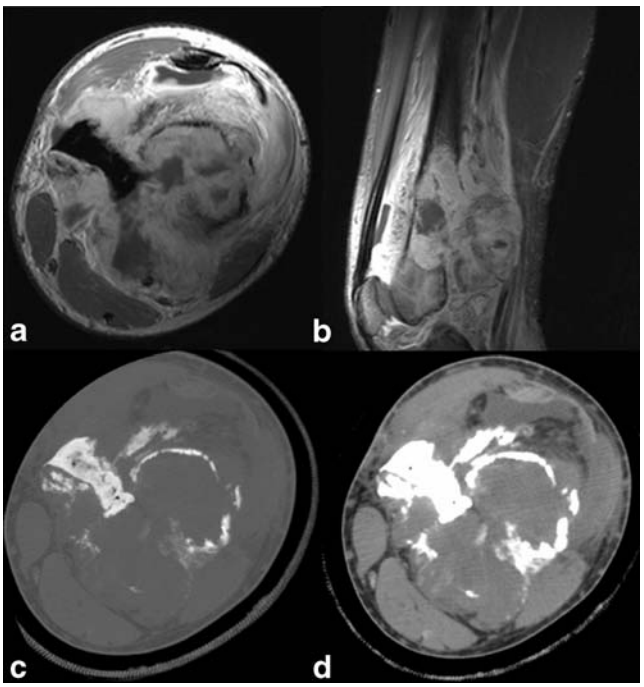

Fig. 2 **a** Axial and **b** sagittal T1-weighted MRI shows the heterogeneous nature of the tumor, which involves the medullary cavity and surrounding soft tissue. The CT scan (**c**, bone window, **d**, soft tissue window) highlights the heavy ossification in areas of the tumor and its destructive nature

condyle. A technetium scan showed intense uptake in the lesion, but no other sites of disease were detected (Fig. 3). Staging computed tomography scans of the chest showed a 0.5-cm nodule in the right middle lobe and a smaller nodule in the right lower lobe, which were concerning for metastatic disease.

The patient initially underwent needle biopsy of the lesion, which yielded a diagnosis of "low-grade fibroblastic osteosarcoma." Because of the radiographic suspicion of a high-grade component, the patient subsequently underwent incisional biopsy, which again showed "low-grade fibroblastic osteosarcoma." Following incisional biopsy, the patient sustained a pathologic fracture of the distal femur after falling down the stairs at home.

The patient underwent excision of the distal femur with resection of the neurovascular bundle. The specimen consisted of the distal 20.0 cm of left femur, including adjacent soft tissue and the overlying biopsy tract. Coronal sections demonstrated a large, poorly demarcated mass measuring approximately 14.5×10.5×10.2 cm (Fig. 4). The

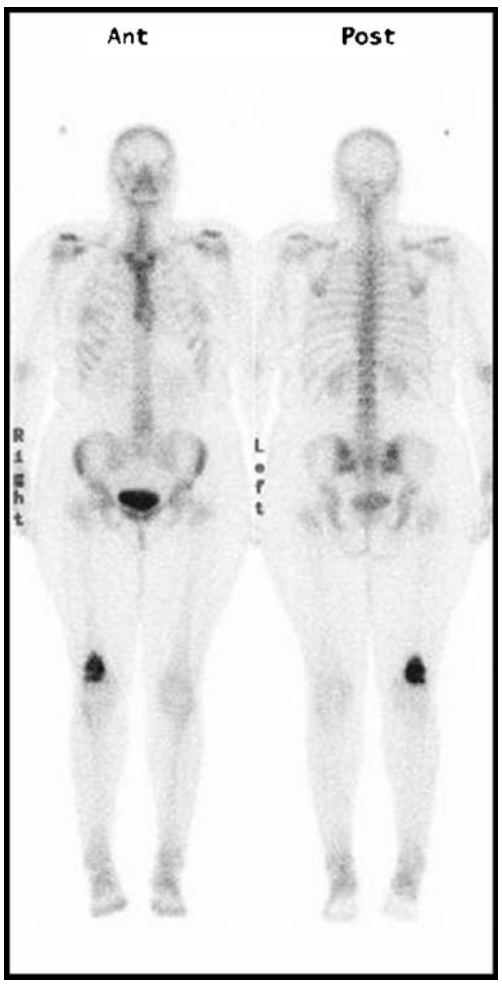

Fig. 3 Technetium bone scan reveals intense uptake within the lesion with no additional sites of involvement

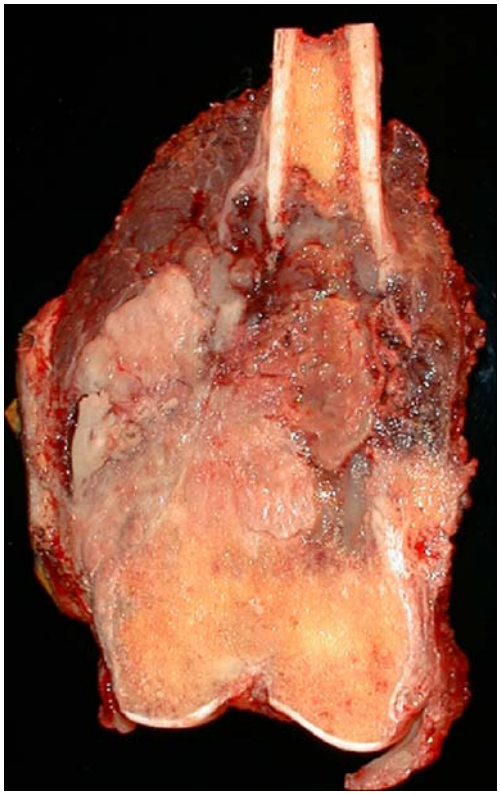

Fig. 4 A coronal section through the specimen illustrates a large, poorly demarcated, destructive tumor with heavily ossified and fleshy regions as well as a pathologic fracture proximally

lesion involved the extraosseous soft tissue posterior and medial to the femur and extended into the medullary cavity medially. The tumor had two distinctly different gross appearances. Approximately one-third of the tumor had a firm, tan, heavily ossified appearance and was associated with the surface of the femur. The remainder, including a large proportion of the soft tissue mass and the entire intramedullary component, was tan, fleshy, and contained large areas of hemorrhage and necrosis. A pathologic fracture was present near the proximal border of the mass. Histologically, the heavily ossified areas of the tumor had the appearance of a low-grade fibroblastic osteosarcoma (Fig. 5a,b), characterized by trabeculae of woven bone embedded in a bland fibroblastic stroma with no significant cytologic atypia or mitotic activity. The majority of the hemorrhagic, fleshy component of the tumor had the appearance of a giant cell tumor, including diffusely, evenly dispersed multinucleated giant cells and intervening mononuclear stromal cells, both of which had similar nuclear features (Fig. 5c). However, this component also contained microscopic foci in which significant nuclear enlargement, nuclear hyperchromasia, and numerous mitoses, including abnormal forms, could be easily identified, along with abundant hemorrhage and necrosis (Fig. 5d,e). No extracellular osteoid matrix was identified within the giant cell component. A final diagnosis of high-grade dedifferentiated parosteal osteosarcoma with a "malignant giant cell tumor" component was rendered.

A megaprosthesis was utilized for reconstruction, and a femoral-popliteal bypass with interpositional saphenous vein graft was used to reconstruct the popliteal artery. The patient died 7 months after resection with radiographic evidence of extensive presumed metastatic disease in the lungs, which had progressed considerably when compared with the presenting staging studies. However, the patient's metastatic disease was not confirmed histologically.

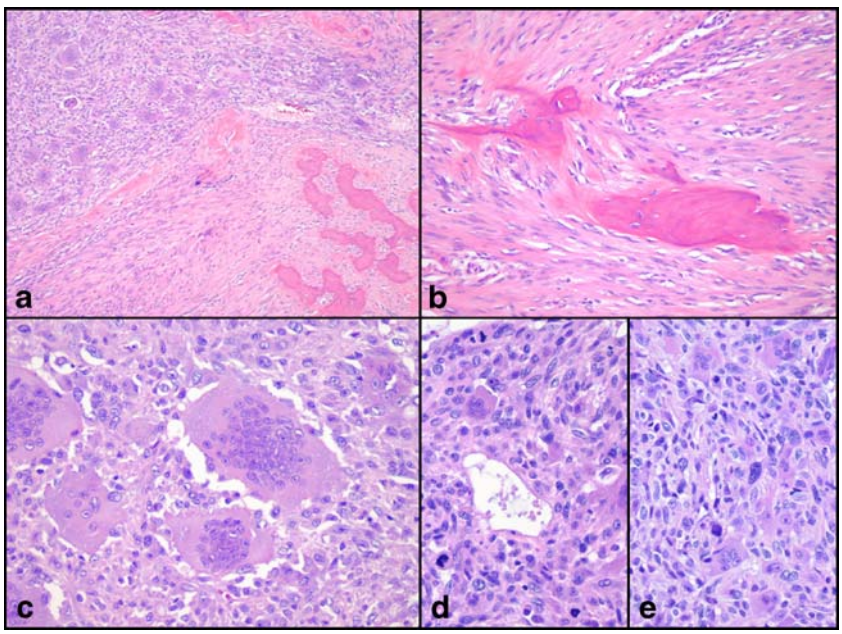

Fig. 5 **a** Low-power photomicrograph showing the interface between the low-grade fibroblastic osteosarcoma and the area of dedifferentiation. **b** Higher magnification of the low-grade fibroblastic osteosarcoma. **c** The dedifferentiated component was composed predominantly of a "typical" giant cell tumor, with identical nuclear features in both the mononuclear stromal cells and the multinucleated giant cells. **d**, **e** Focally, the dedifferentiated component showed numerous mitotic figures, including abnormal mitoses, and significant cytologic atypia

Discussion

Parosteal osteosarcoma is the most common form of surface osteosarcoma, accounting for approximately 5% of all osteosarcomas. Most parosteal osteosarcomas are low-grade and remain confined to the surface of the bone and adjacent soft tissues. However, a small percentage of parosteal osteosarcomas invade the underlying medullary cavity and/or progress to a higher grade sarcoma (i.e., "dedifferentiate"). The term "dedifferentiated parosteal osteosarcoma" was first introduced in 1984 by Wold et al. [13], although descriptive reports of this entity were reported in the literature prior to this [14]. Dedifferentiation has been reported to occur in 16–24% [10, 13, 15] to 43% [16] of parosteal osteosarcomas.

Typically, parosteal osteosarcomas appear radiographically as lobulated, radiodense lesions that attach to the cortical surface, often with a lucent cleft between the tumor and the underlying bone [15, 17]; occasional tumors will completely encompass the involved bone. Most parosteal osteosarcomas arise from the metaphyseal region of long bones (distal femur, proximal tibia or proximal humerus). Occasionally, they involve the diaphysis of the long bones. The majority of parosteal osteosarcomas are confined to the surface of the involved bone; however, some of the larger tumors, as well as dedifferentiated lesions, are capable of invading through the cortex into the medullary cavity. The prediction of histologic grade and the presence of dedifferentiated foci based on imaging studies has been well-described by Bertoni et al., Futani et al., and Jelinek et al. [18–20]. The presence of radiolucent regions deep within the tumor and distinct from the ossified regions of the mass is highly suggestive of a higher grade, dedifferentiated component.

Based on the extensive mineralization seen within the lesion on radiographic studies, the primary differential diagnosis was osteosarcoma, including both surface and central variants. Because the mineralization was localized to the posteromedial surface component of the tumor, there was a strong suspicion that this represented a parosteal osteosarcoma with extensive dedifferentiation. Although multiple biopsies showed only low-grade fibroblastic osteosarcoma, examination of the entire tumor confirmed that the large, mineralized mass was composed entirely of low-grade fibroblastic osteosarcoma, and the unmineralized areas had giant cell tumor-like features. No osteoid was identified within the giant cell tumor-like foci. The lack of osteoid in the giant cell component, coupled with the discrete mass of low-grade fibroblastic osteosarcoma on the surface of the femur, led to the diagnosis of dedifferentiated parosteal osteosarcoma as opposed to a central giant cell-rich osteosarcoma with soft tissue extension.

Dedifferentiated foci may be identified in the primary tumor or within local recurrences [13, 15]. The presence of dedifferentiation may be associated with permeation of the tumor into the medullary cavity and surrounding soft tissues. Approximately 50% of patients with dedifferentiated parosteal osteosarcomas develop distant metastases [15, 21]. The patient described herein presented with a Musculoskeletal Tumor Society stage III dedifferentiated parosteal osteosarcoma. The prognosis of dedifferentiated parosteal osteosarcoma, regardless of the histologic appearance of the dedifferentiated component, is similar to that of conventional intramedullary osteosarcoma.

The most common histologies of the dedifferentiated component of a dedifferentiated parosteal osteosarcoma include malignant fibrous histiocytoma, fibrosarcoma, and osteosarcoma. Unusual high-grade phenotypes include rhabdomyosarcoma, telangiectatic osteosarcoma, and giant cell-rich osteosarcoma [4, 5, 12]. We are aware of only two cases of dedifferentiated parosteal osteosarcoma in which the dedifferentiated component resembled a giant cell tumor, similar to what has been described in several examples of dedifferentiated chondrosarcoma with a giant cell tumor-like component [6–9, 11]. In both cases, the dedifferentiated component was giant cell-rich, but did not produce osteoid, unlike a giant cell-rich osteosarcoma. The first case was reported in Dahlin and Unni's textbook, although no details of the case are provided [11]. The lesion was described originally as a low-grade parosteal osteosarcoma that recurred as a "highly malignant sarcoma with...an abundance of benign giant cells." Mirra also illustrated a case of "dedifferentiated parosteal osteosarcoma, benign giant cell-rich variant" in his textbook [8]. The patient, a 69-year-old woman, had a low-grade parosteal osteosarcoma removed from the mandible 41 years prior to developing dedifferentiation within a local recurrence in the region of the parotid gland. No follow-up information was given

Table 1 Reported variants of dedifferentiated parosteal osteosarcoma with giant cells

Variant	Cytologic atypia/mitoses	Osteoid	Histology of dedifferentiated component
"Conventional" [10, 13]	Prominent	+/–	Malignant fibrous histiocytoma with giant cells
Giant cell-rich [10, 18]	Prominent	+	Giant cell-rich osteosarcoma
Giant cell tumor-like [8, 11, current case]	Focal	–	Giant cell tumor

+/–, variable, depending on differentiation; +, present; –, absent

for the patient. A third case has been described as a "giant cell-rich parosteal osteosarcoma" by Sciot et al. [22]. This case differs from the two previous cases and the present case in that the tumor was not felt to be dedifferentiated, but rather a low-grade tumor with abundant giant cells; however, no follow-up was reported.

Large numbers of giant cells may also be seen in dedifferentiated parosteal osteosarcomas with a high-grade component that resembles giant cell-rich osteosarcoma (Table 1). Shuhaibar and Friedman first reported this phenomenon in 1998 [12], describing a tumor that contained areas that resembled a conventional giant cell tumor as well as areas that resembled giant cell-rich osteosarcoma. Bertoni et al. reported 29 cases of dedifferentiated parosteal osteosarcoma, 3 of which showed giant cell-rich osteosarcoma morphology in the high-grade dedifferentiated component [10]. Similar to the case described by Sciot et al. [22], the tumor reported herein demonstrated extensive areas that resembled a conventional giant cell tumor of bone, with only focal areas that contained significant cytologic atypia and prominent mitotic activity. However, no osteoid matrix was identified within the tumor, distinguishing this case from those reported as "dedifferentiated parosteal osteosarcoma with foci of giant cell-rich osteosarcoma."

Despite the relatively bland appearance of the dedifferentiated component of the tumor described here, the designation of this unusual dedifferentiated parosteal osteosarcoma as "high grade" seems justified based on the patient's rapid clinical progression and demise. Although clinical data are limited for reported cases of dedifferentiated parosteal osteosarcoma and dedifferentiated chondrosarcoma with giant cell tumor-like features, most of these tumors behave aggressively. Therefore, it is important to be aware of radiographic and pathologic features of this unusual variant of dedifferentiated parosteal osteosarcoma, not only to avoid a misdiagnosis of a giant cell tumor of bone, but to understand the potential for aggressive clinical behavior, despite the deceptively benign appearance of the tumor.

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