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Case report

Dedifferentiated chondrosarcoma with "adamantinoma-like" features: A case report and review of literature

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ABSTRACT

Dedifferentiated chondrosarcoma is defined by the presence of a low grade malignant cartilaginous component juxtaposed to a high grade malignant non-cartilaginous sarcomatous components. Only 4 cases in which the high grade component showed epithelial differentiation have been reported in the literature; three featured a squamous and the one a glandular epithelial component. Here we describe a case of dedifferentiated chondrosarcoma exhibiting epithelial "adamantinoma-like" basaloid features. The patient underwent wide resection of the proximal tibia and post-operative chemotherapy and died 8 months after the diagnosis due to lung and bone metastases.

1. Introduction

Chondrosarcoma is a malignant tumor characterized by the presence of chondrogenic differentiation. The majority of cases are represented by primary conventional central chondrosarcoma (75%). More rarely (15%) the neoplasm develops in a pre-existing osteochondroma (secondary peripheral chondrosarcoma). In addition to conventional form several rare subtypes are recognized such as periosteal chondrosarcoma, clear cell chondrosarcoma, mesenchymal chondrosarcoma and dedifferentiated chondrosarcoma. This latter represents less than 10% of all chondrosarcoma and morphologically is characterized by two components: a low-grade malignant chondrogenic tumor juxtaposed with high-grade malignant non-cartilaginous neoplasm [1]. The high-grade component most often exhibits the morphology of an undifferentiated pleomorphic/spindle cell sarcoma or of a high-grade osteosarcoma [2–4]. Rarely, the presence of rhabdomyosarcomatous, leiomyosarcomatous, and angiosarcomatous differentiation has been reported [1–3]. Previous studies have demonstrated that both components share the same genetic alteration of *IDH1* gene indicating a common precursor cell with early diversion of the two components [5,6]. Unfortunately, *IDH1* gene aberrations seems to affect approximately half of cases. Dedifferentiated chondrosarcoma commonly affects the femur and pelvis of elderly patients and it is associated with a worse prognosis when compared with conventional variants [1].

To date only 4 cases of dedifferentiated chondrosarcoma featuring epithelial differentiation (three squamous and one glandular) have been reported [2–4,7].

We describe herein a case of dedifferentiated chondrosarcoma arising in the tibia of a 78-year-old man, in which the dedifferentiated component exhibits adamantinoma-like features.

2. Case report

In February 2014 a 78-year-old Caucasian man presnted at our institution with medicament resistant pain of the left knee of recent onset treated as osteoarthritis. Clinical history was non informative. Clinically tenderness of the soft tissue of the left knee was observed not associated with swelling. Motion in flexion and extension of the left lower limb was limited. Pain increased at full weight bearing. A radiograph of the knee showed a cartilage-like lesion in the tibia with thickened, scalloped cortex associated with numerous round calcifications. A "secondary" ill-defined lesion was observed causing breakage the cortex (Fig. 1A). CT scan and MRI confirmed the presence of two components with soft tissue involvement in the posterior aspect of the proximal tibia (Fig. 1B–D).

Bone scan and total body CT showed a small lesion in the upper left pulmonary lobe. A CT-guided biopsy of the tibial lesion

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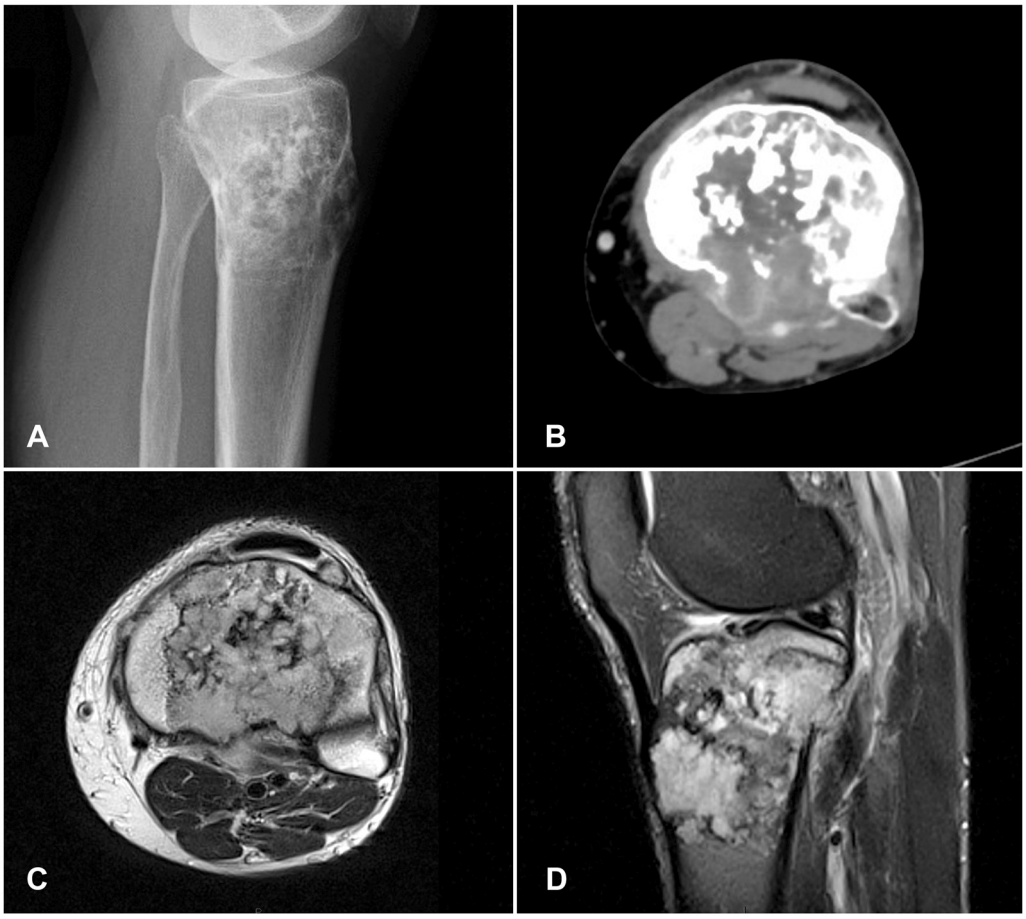

Fig. 1. On radiograph a cartilaginous lesion with scallopped cortex and a "secondary" lesion destroying the cortex (A) are visible. CT scan (B) and MRI scan (C, D) confirming the two components.

was performed. Histological diagnosis was dedifferentiated chondrosarcoma. The lesion was composed of a low-grade cartilaginous tumor juxtaposed to a high grade spindle cell sarcoma (Fig. 2A–B). In consideration of the patient's age, no neoadjuvant chemotherapy was advised and the patient underwent a resection of the proximal tibia (Fig. 2C) with wide margins and reconstruction with a modular mega-prosthesis.

Following surgery, the patient underwent two cycles of chemotherapy with ifosfamide (2,5 mg/m^2 daily for 3 days). After 5 months rapid progression of the disease occurred with a local recurrence in the soft tissues, left humerus pathological fracture, associated with increased volume of the lung mass. Multiple vertebral lesions with spine cord involvement appeared that led to palsy of the lower limbs. The soft tissue recurrence was removed with marginal resection margins. The histological examination of the surgical specimen revealed again the presence of a low-grade chondrogenic proliferation associated with a high-grade malignant sarcomatous component (Fig. 2D). Interestingly, this latter was composed of a spindle cells proliferation associated with nests of epithelioid cells arranged in a basaloid "adamantinoma-like" pattern (Fig. 2E–F). The dedifferentiated component was focally positive for high molecular weight cytokeratin (34βE12) (Fig. 2G), cytokeratin CAM 5.2 (Fig. 2H), cytokeratin MNF116, and EMA, while was negative for cytokeratin AE1/AE3 and cytokeratin 20. Immunohistochemical staining for IDH1 was negative as were the results of the molecular analysis of *IDH1/2* genes. Moreover, real time RT-PCR failed to demonstrate the presence of SYT-SSX, type 1 and type 2 fusion transcripts, excluding a diagnosis of synovial sarcoma. Final diagnosis of dedifferentiated chondrosarcoma with epithelial ("adamantinoma-like") features was therefore made. The patient died 8 months from first surgery.

3. Discussion

Dedifferentiated chondrosarcoma is a rare neoplasm, representing approximately 10–15% of central chondrosarcomas [1]. The latest WHO classification [5] defines it as a highly malignant variant of chondrosarcoma, characterized by a biphasic histological appearance, featuring areas of low-grade chondrosarcoma juxtaposed to a high-grade, non-chondrogenic sarcoma.

The high-grade dedifferentiated component generally has the features of an undifferentiated pleomorphic/spindle cell sarcoma or osteosarcoma [2–5]. Rare examples of heterologous rhabdomyosarcomatous, leiomyosarcomatous, angiosarcomatous differentiation, have been reported [2–5]. Only four cases exhibiting epithelial features in the dedifferentiated component have been described so far. The first case [2] was a 68-year-old woman presenting with a lesion in the left proximal humerus. The patient received a Tikhoff-Linberg resection. Histologically the lesion was composed of lobules of well-differentiated cartilaginous tissue permeating the host bone and associated with large areas of keratinyzing squamous cell carcinoma. The patient died 3-and-a-half years after the onset of symptoms, with no clinical evidence of either a primary tumor relapse or metastasis but with undetermined mental problems (the patient refused a CT-scan of the head). The second case was a 53-year-old woman presenting with a lesion in the right femoral diaphysis, treated with hemipelvectomy followed by chemotherapy (paraplatine 450 mg once a month)