

Dedifferentiated Chondrosarcoma: A Case Report And Review Of The Literature

Z Pan, D Sarma

Citation

Z Pan, D Sarma. *Dedifferentiated Chondrosarcoma: A Case Report And Review Of The Literature*. The Internet Journal of Orthopedic Surgery. 2006 Volume 5 Number 1.

Abstract

Chondrosarcoma is a malignant cartilaginous tumor composed of a hyaline cartilage stroma and neoplastic chondrocytes in lacunae. Approximately 10% of chondrosarcomas can dedifferentiate into more aggressive anaplastic lesions, including osteosarcomas, fibrosarcomas, and malignant fibrous histiocytomas. We report a case of a 65-year-old female with a low-grade chondrosarcoma in the left tibia that progressed into a high-grade spindle cell sarcoma two years later. A brief review of the genetic and molecular alterations of such tumors is presented.

INTRODUCTION

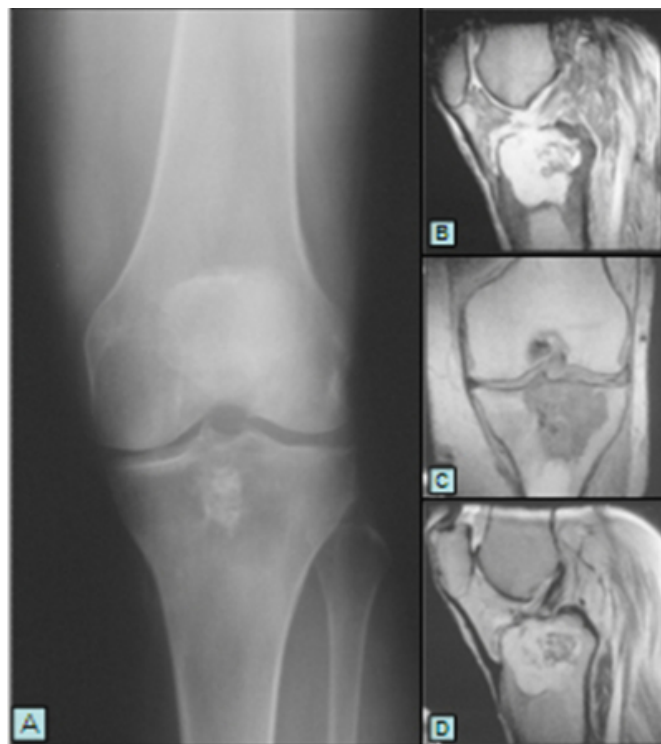
Dedifferentiated chondrosarcoma is a high-grade, aggressive anaplastic sarcoma that progresses from a previous low-grade chondrosarcoma. In our case, this 65-year-old female was initially diagnosed as well-differentiated chondrosarcoma (grade I), and two years later, she was found to have a high-grade pleomorphic spindle cell sarcoma in the same site.

CASE REPORT

A 65-year-old Caucasian female patient had a history of Crohn's disease, melanoma and diabetes mellitus. In October of 2004, the patient presented with a 3-month history of left knee pain that she attributed to some sort of trauma. The radiograph of the left knee showed an intramedullary osteolytic lesion with calcifications in the proximal tibia (Figure 1A). CT scans revealed a poorly demarcated tumor with an eccentric, non-uniform calcification (Figure 1B, 1C and 1D).

Figure 1

Figure 1A: An X-ray showed an intramedullary osteolytic lesion with calcifications in the proximal tibia. 1B, 1C and 1D: CT scans revealed a poorly demarcated tumor with an eccentric, non-uniform calcification.

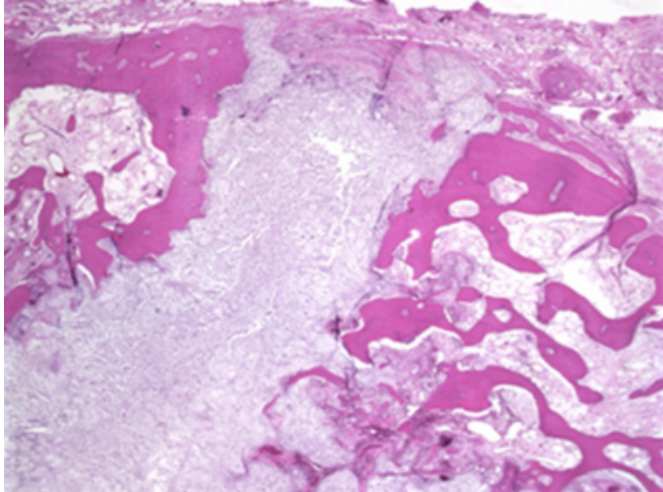


The tumor invaded through the epiphyseal plate with expansion of the articular surface. The patient underwent resection of the tumor with total knee arthroplasty. Grossly, the tumor was lobulated and measured 5.0 cm in greatest diameter with a gelatinous cut surface. Histologically, the

atypical cartilaginous neoplasm penetrated through cortical bone and invaded between bone spicules (Figure 2).

Figure 2

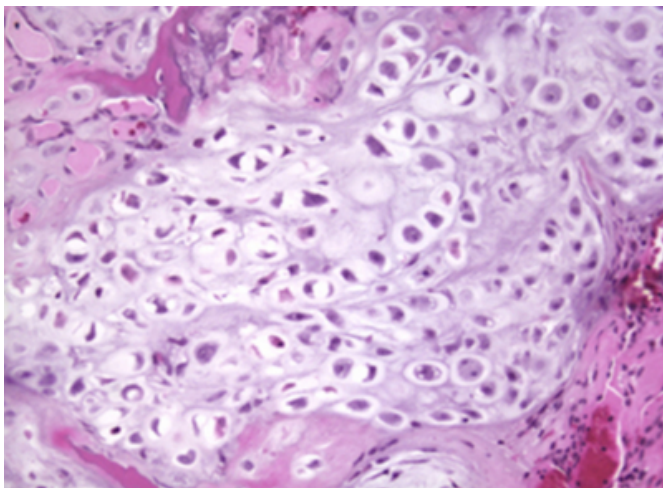
Figure 2: Cartilaginous neoplasm penetrates through cortical bone and invades between bone spicules.



The tumor was composed of disorganized neoplastic chondrocytes with increased cellularity and mild atypia (Figure 3).

Figure 3

Figure 3: Neoplastic chondrocytes showing increased cellularity, nuclear pleomorphism and mild atypia.



Rare binucleated cells were noted, and no mitotic figures were present. Microscopic examination of multiple sections from the tumor did not show any foci of high-grade spindle cell component. Cytogenetic analysis did not reveal any evidence of a consistent detectable numerical or structural chromosomal anomaly of this tumor. A diagnosis of well-differentiated chondrosarcoma (grade 1) was made.

In March 2007, the patient presented with a complaint of

increased pain and swelling of the left knee with difficulty in walking, night sweats and a 40-pound weight loss. Clinical examination of the left knee revealed swelling and warmth with some superficial erythema around the previous prosthesis. Image studies with CT, MRI and bone scan did not show any remarkable lesion or evidence of systemic metastasis. Therefore, a sepsis was suspected. The patient underwent a debridement and irrigation of the left knee prosthesis site. Histology of the left knee tissue around prosthesis demonstrated a high-grade undifferentiated sarcoma. It consisted of highly pleomorphic undifferentiated spindle cells with increased mitoses and large areas of necrosis (Figure 4 and 5).

Figure 4

Figure 4: The recurrent tumor consists of highly pleomorphic spindle cells.

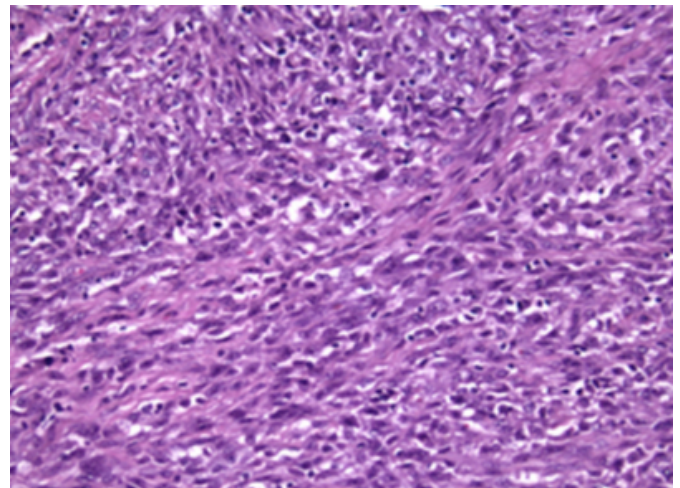
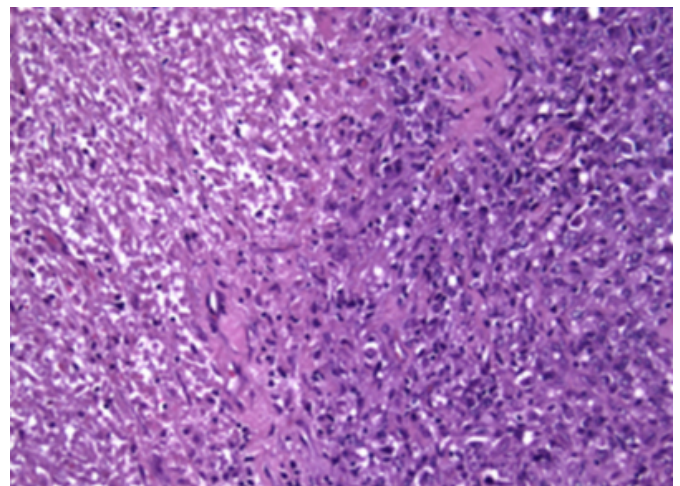


Figure 5

Figure 5: Necrotic area in the recurrent tumor.

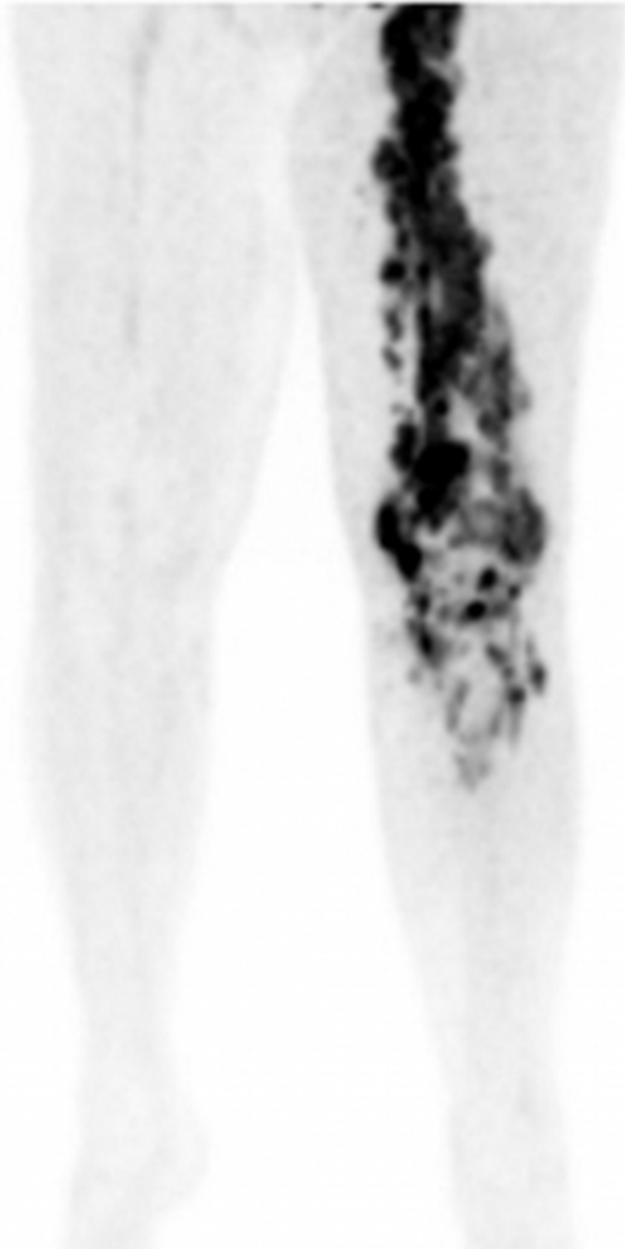


There was no cartilaginous tissue. This appeared to be a

dedifferentiation of the previous low-grade chondrosarcoma. A subsequent PET scan revealed multiple mass lesions along the left thigh and pelvis (Figure 6).

Figure 6

Figure 6: A subsequent PET scan revealed multiple mass lesions along the left pelvis and the left thigh.



DISCUSSION

Dedifferentiated chondrosarcoma is a highly malignant variant of chondrosarcoma. Histologically this tumor consists of an underlying cartilaginous component (either benign or malignant) juxtaposed to a high-grade non-cartilaginous component with a typically abrupt transition between the two tissue types. The cartilaginous component

in the dedifferentiated tumor may constitute a very small proportion, so a diagnosis of dedifferentiated chondrosarcoma often requires careful histological evaluation of the entire tumor. In our case, the patient had a history of low-grade chondrosarcoma, and two years later, she had a high-grade pleomorphic undifferentiated spindle cell sarcoma in the same location. Therefore, the patient clearly had a dedifferentiated chondrosarcoma although there was no residual low-grade tumor noted in the biopsy specimen after extensive sampling.

Approximately 10% of chondrosarcomas can dedifferentiate into more anaplastic lesions. In most cases, the dedifferentiated components are osteosarcomas, followed by fibrosarcomas and malignant fibrous histiocytomas [1]. A controversy, whether the dedifferentiated and cartilaginous components are derived from a common precursor cell, or they represent separate genotypic lineages (collision tumor) remains. Recent studies have shown compelling evidence that both components are derived from a single precursor. In these studies, the low-grade chondrosarcoma component and the high-grade dedifferentiated chondrosarcoma component from the same cases were dissected separately, and then these two components were investigated using loss of heterozygosity (LOH) analysis, comparative genomic hybridization (CGH), DNA flow cytometry, and p53 analysis. Both components showed p53 overexpression and an identical somatic 6 bp deletion in exon 7 of p53. Combination of the CGH and LOH results revealed that both components had lost the same copy of chromosome 13. These studies confirmed that the high-grade malignant non-cartilaginous component arises from the previous cartilaginous component [2, 3, 34].

Although the two components in dedifferentiated chondrosarcoma show a monoclonal origin with many similar genetic and molecular changes, certain genotypic alterations are not shared. In chondrosarcoma, structural aberrations in chromosomes 1 and 9 and trisomy or tetrasomy of chromosome 7 are among the more frequently observed aberrations, and methylation of p16INK4 and E-cadherin are also noted. These similar changes can also be observed in the high-grade component. However, the high-grade anaplastic component shows severe aneuploidy, LOH at additional loci, and amplification and deletion of several chromosome parts. Significant genetic alterations in the anaplastic component include overexpression of p53, Rb and FHIT, and H-ras mutation [5, 6, 7], and these changes may be responsible for the progression of low-grade

chondrosarcoma to high-grade anaplastic sarcoma.

Despite radical surgical treatment, the prognosis of dedifferentiated chondrosarcoma is unfavorable with a five-year survival rate of 10%, and there is very little benefit from adjuvant chemotherapy [8].

CORRESPONDENCE TO

Deba P Sarma, MD Department of Pathology Creighton University Medical Center Omaha, NE 68131 E-mail: debasarma@creighton.edu

References

1. Staals EL, Bacchini P, Bertoni F. Cancer. Dedifferentiated central chondrosarcoma. 2006 Jun 15; 106(12): 2682-91.
2. Bovee JV, Cleton-Jansen AM, Rosenberg C, Taminiau AH, Cornelisse CJ, Hogendoorn PC. Molecular genetic characterization of both components of a dedifferentiated chondrosarcoma, with implications for its histogenesis. . J Pathol. 1999 Dec; 189(4): 454-62.
3. Aigner T, Unni KK. Is dedifferentiated chondrosarcoma a 'de-differentiated' chondrosarcoma? J Pathol. 1999 Dec; 189(4): 454-62.
4. Bridge JA, DeBoer J, Travis J, Johansson SL, Elmberger G, Noel SM, Neff JR. Simultaneous interphase cytogenetic analysis and fluorescence immunophenotyping of dedifferentiated chondrosarcoma. Implications for histopathogenesis. Am J Pathol. 1994 Feb; 144(2): 215-20.
5. Ropke M, Boltze C, Neumann HW, Roessner A, Schneider-Stock R. Genetic and epigenetic alterations in tumor progression in a dedifferentiated chondrosarcoma. Pathol Res Pract. 2003; 199(6): 437-44.
6. Sakamoto A, Oda Y, Adachi T, Oshiro Y, Tamiya S, Tanaka K, Matsuda S, Iwamoto Y, Tsuneyoshi M. H-ras oncogene mutation in dedifferentiated chondrosarcoma: polymerase chain reaction-restriction fragment length polymorphism analysis. Mod Pathol. 2001 Apr; 14(4): 343-9.
7. O'Malley DP, Opheim KE, Barry TS, Chapman DB, Emond MJ, Conrad EU, and Norwood TH. Chromosomal changes in a dedifferentiated chondrosarcoma: a case report and review of the literature. Cancer Genet Cytogenet. 2001 Jan 15; 124(2): 105-11.
8. Dickey ID, Rose PS, Fuchs B, Wold LE, Okuno SH, Sim FH, Scully SP. Dedifferentiated chondrosarcoma: the role of chemotherapy with updated outcomes. J Bone Joint Surg Am. 2004 Nov; 86-A (11): 2412-8.

Author Information

Zenggang Pan, M.D., Ph.D.

Department of Pathology, Creighton University Medical Center

Deba P. Sarma, M.D.

Department of Pathology, Creighton University Medical Center