Dedifferentiated Chondrosarcoma of Tibial Bone with Knee Pain：A Case Report

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Abstract

We report the case of a 75-year-old woman having knee pain later diagnosed with dedifferentiated chondrosarcoma (DDCS) of the proximal tibial metaphysis. The patient complained of pain in the right knee. Plain radiographs of the right tibia showed irregular sclerotic calcification but no focal cortical thickening or periosteal reaction. In the third year of follow-up, she fractured the right femur in an accident. She developed a swelling of the right knee while admitted for pneumonia in April 2007. MRI revealed an extraosseous soft tissue mass extending into the anterior muscular compartment. Bone biopsy showed high-grade spindle cell sarcoma. Bone scan and chest CT revealed suspicious rib metastases but no pulmonary metastases. She underwent an above-knee amputation in June 2007 after neoadjuvant radiotherapy. She died of metastatic lymphadenopathy, and lung and bone metastases within six months after surgery.

We should have referred the patient to an orthopedic surgeon soon after the ill-defined calcification with a mineralized chondroid matrix and a size of more than 5 cm (radiographically) was noted.(J Inten Med Taiwan 2009; 20: 181-186)

Key Words：Dedifferentiated chondrosarcoma, Knee pain

Introduction

Knee pain is a frequent occurrence in the elderly. Further, it is difficult to distinguish between benign and malignant neoplasms of the bone both radiographically and histologically. Dedifferentiated chondrosarcoma is a fatal malignancy despite aggressive wide resection, or even amputation. The most common localizations are at the femur, humerus, and pelvis[1-4]. Metastases occur early and frequently involve the lungs, lymph nodes, and viscera[1-3]. The prognosis is poor: a 24% five-year survival rate with a median survival of 13 months[4]. Use of adjuvant chemotherapy or radiotherapy does not produce a statistically significant benefit[2,5-7]. Here, we report the case of a 75-year-old female having knee pain later diagnosed with dedifferentiated chondrosarcoma (DDCS) of the proximal tibial metaphysis.

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Case Report

In June 2003, a 75-year-old woman visited our family medicine outpatient service because of intermittent pain in the right knee. She could walk without any assistance. On examination, no effusion, no erythema, a normal range of motion, and slight joint tenderness medial to the right knee was observed. No tenderness of the patella or head of the fibula was found. In the arterial survey, including the dorsal pedis, posterior tibial, and popliteal arteries, pulsation was found to be normal. Her past medical, family, and social histories were reviewed and updated. She denied any weight loss. Routine laboratory investigations such as complete blood count and biochemical parameters including alkaline phosphatase and lactic dehydrogenase levels were within normal ranges during initial evaluation. Plain radiographs of the right knee showed irregular sclerotic calcification but the absence of a ring-and-arc pattern of calcifications over the right tibia. The main intraosseous lesion was at the eccentric proximal tibial metaphysis. There was no evidence of focal cortical thickening or periosteal reaction. The differential diagnosis included bone infarction and enchodroma. Follow-up plain radiographs of the right knee was arranged yearly (Figure 1A-D). In the third year of follow-up, she had a nonpathological fracture of the right femur. We did not arrange for further investigations such as bone scan, CT, or MRI immediately because there were no signs of aggressive growth

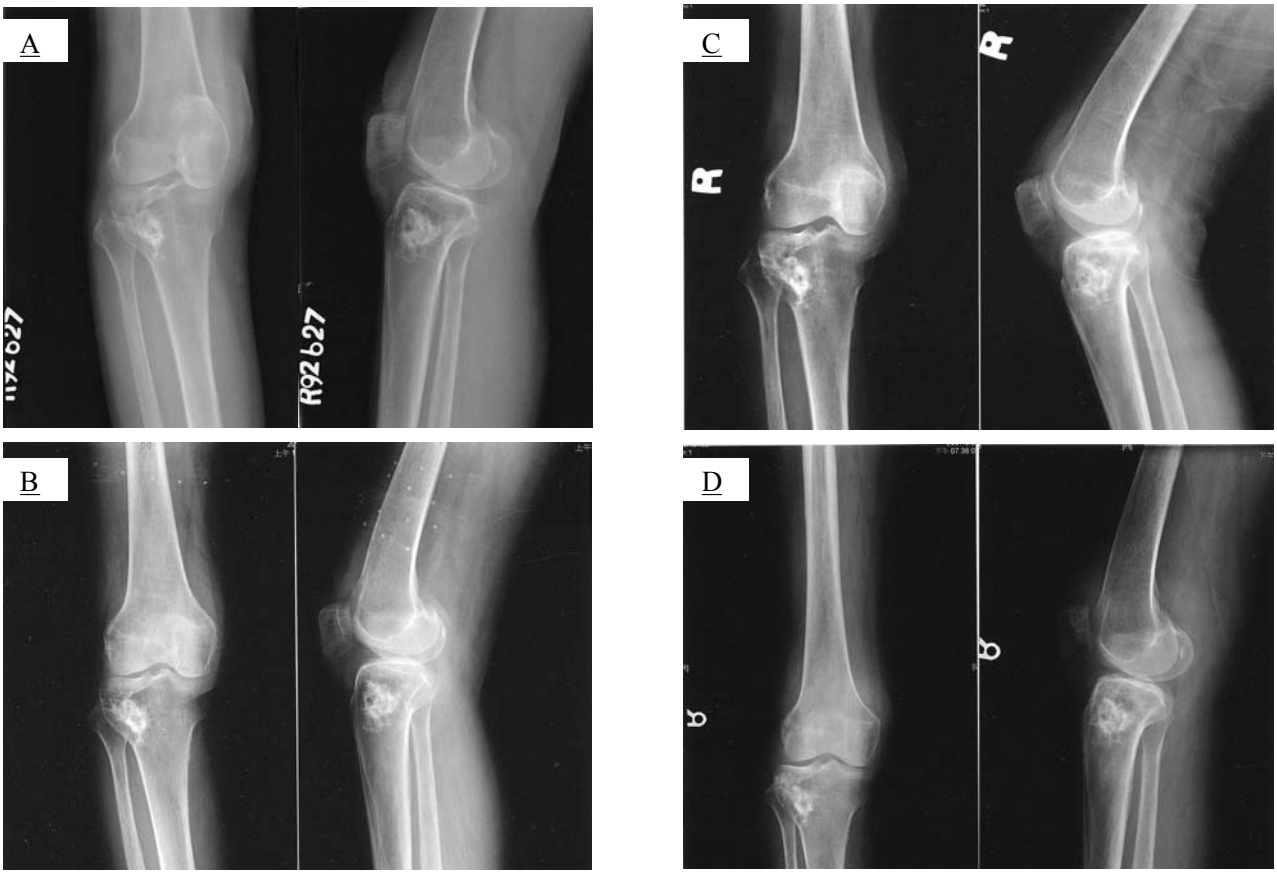

Fig.1A-D. Figure 1A dated on Jun 27 2003; B dated on Nov 4 2005; C dated on Dec 25 2006; D dated on Mar 23 2007.Serial anterior-posterior and lateral radiographs of the right knee demonstrated irregular sclerotic calification lesion located eccentrally within the proximal tibial metaphysis. There was no evidence of focal cortex thickening or periosteal reaction; no significant interval changes within five years follow up.

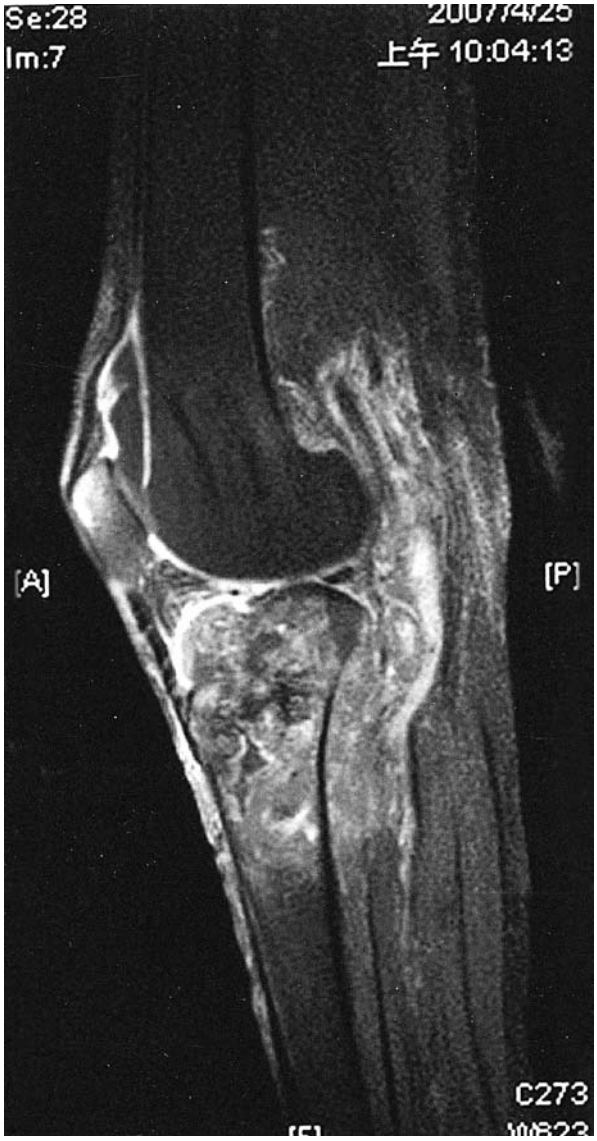

Fig.2. T2-weighted MRI demonstrated the main intraosseous lesion with internal calcification located eccentrically within the proximal tibia. Extraosseous soft tissue extended intraarticular with nodular seeding to the suprapatellar pouch and posteromedial Baker's cyst and extension into the anterior muscular compartment.

or destruction of the surrounding cortex, neither was there any periosteal reaction or cortical breakthrough during this period of follow-up. However, in April 2007, she developed a painful swelling of the right knee while admitted for pneumonia at the General Internal Medicine division. MRI revealed an extraosseous soft tissue mass extending into the anterior muscular compartment; the main intraosseous calcification was located at the eccentric proximal tibial metaphysis with an intra-articular extension, nodular seeding of the suprapatellar pouch, posteromedial Baker's cyst, and posterolateral popliteal cyst. No invasion of the popliteal vessels was seen (Figure 2). The patient was referred to an orthopedic surgeon for bone biopsy: the specimen showed high-grade spindle cell sarcoma with focal chondroid differentiation and calcification. The histological grading was based on the modified French Federation of Cancer Center (FNCLCC) system[8]. Bone scan and chest CT revealed no lung metastases but suspicious rib metastases. After neoadjuvant radiotherapy, she underwent an above-knee amputation in June 2007. Bone tumor pathology confirmed the diagnosis of dedifferentiated chondrosarcoma through the biopsy samples and the resected tumor. The lesion measured 12 × 10 × 10 cm. The specimen from the lesion showed the characteristic bimorphic pattern of DDCS, with a high-grade sarcomatous component juxtaposed to a low-grade cartilaginous

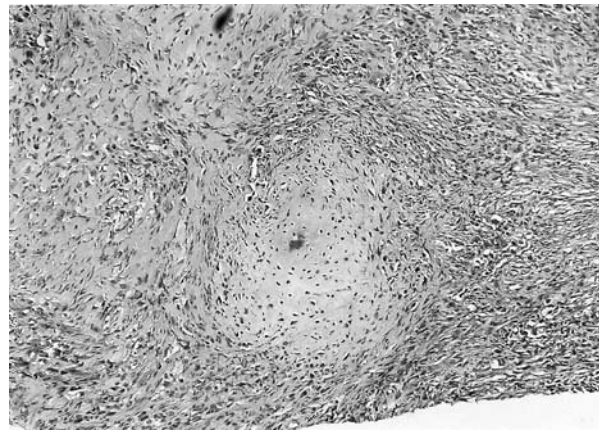

Fig.3. At magnification level of ×100, atypical spindle cells intermingling with oval shaped cells containing pleomorphic nuclei and eosinophilic cytoplasm. According to FNCLCC system, tumor was rated as grade 3 with total scores above 6. The specimen established the diagnosis, dedifferentiated chondrosarcoma with focal chondroid differentiation and leiomyosarcomatous component.

lesion (Figure 3). The section margins were negative for malignancy. Three months after surgery, follow-up imaging showed right inguinal lymph node, lung, and bone metastases. The patient decided she would rather receive hospice care than further radiotherapy and chemotherapy. She expired on November 26, 2007.

Discussion

What was wrong with our initial diagnosis and management during the five-year follow-up? We researched related journal articles on DDCS and sought the advice of a biomedical engineer. We discuss our findings as follows:

DDCS and several rare subtypes such as mesenchymal and clear cell chondrosarcomas constitute 10-15% of all chondrosarcomas 9. DDCS is mostly seen in the elderly (＞60 years)[1-3]. Metastases occur early and frequently involve the lungs, lymph nodes, and viscera[1-3]. Staals et al., in 2007, classified DDCS into central lesions (those arising in enchondromas) and peripheral lesions (those arising in osteochondromas); they found no difference in the survival between both classes of lesions[10].

Three mechanisms for the origin of DDCS have been proposed. The widely accepted theory is that the high-grade noncartilaginous component arises within a longstanding lower-grade chondrosarcoma. A second hypothesis is that the noncartilaginous sarcoma results from a malignant transformation in the inflamed fibrous pseudocapsule of a lower-grade chondrosarcoma. The third theory is that malignant cell lines arise simultaneously in a chondrosarcoma with differing ability to differentiate[2,3,6,7,11]. In the clinical and radiographic follow-up of our patient over five years, we could not deduce whether the DDCS originated from an enchondroma; besides, we did not have an initial bone biopsy specimen to prove that this was the case. Few studies have shown that p53 overexpression and mutations are mostly found in the high-grade anaplastic component. There were two cases that exhibited H-ras oncogene mutations [12].

The most frequently reported symptoms are pain, soft tissue masses, and pathologic fractures[2-4,7,13]. No statistically significant correlation has been found between the clinical symptoms and the benign or malignant nature of the neoplasm[2,3,7,13]. Further, no relationship has been found between the duration of prior symptoms and length of survival after diagnosis[2].

Radiographs are important not only for detection but also to decide on follow-up analysis with MRI or histology. DDCS may have a wide range of radiographic appearances. Radiographic studies include evaluation for the presence of bone destruction, cortical thickening, and cortical endosteal scalloping; the presence and pattern of periosteal reaction; matrix mineralization; the presence and features of soft tissue masses; pathologic fracture; and the presence of bimorphic features[3-4,14]. Geirnaerdt et al. reported that clinical symptoms and morphological radiographic features do not improve the ability to differentiate between enchondromas and central grade I chondrosarcomas[13]. Localization in the axial skeleton and a size greater than 5 cm were found to be reliable predictors of malignancy [13].

Dynamic contrast-enhanced MRI has greater sensitivity: a soft tissue mass presents as an intermediate signal intensity with T2-weighted pulse sequences; if more prominent, diffuse contrast enhancement suggests a more aggressive type of chondrosarcoma[3,15]. CT can detect matrix mineralization in complex anatomic areas, and is recommended for the pelvis and other flat bones where it might be difficult to discern the pattern of bone destruction and the presence of matrix mineralization[9]. MRI is used to depict the extent of intraosseous and soft tissue involvement[9]. Bone scan is not suited for differentiating enchondroma

from chondrosarcoma because technetium uptake increases even in benign lesions[16]. Aggressive chondrosarcoma subtypes, such as mesenchymal and DDCS, may demonstrate intraosseous lytic areas, bone destruction with a moth eaten to permeate pattern, and large soft tissue masses, besides ill-defined areas of matrix mineralization [9,13].

The most important factors affecting survival are early recognition of the radiographic features, adequate histological sampling, and wide-margin resection of the lesion. The prognosis of DDCS is poor despite adequate wide resection and adjuvant systemic therapy[2,4,7,9]. Grimer RJ et al. found no evidence that diagnosis prior to treatment affected outcome, although it did provide the patient with an opportunity to have neoadjuvant chemotherapy in some cases[17]. In the literature, no relationship was found between histological subtype and patient outcome[2,4,17]. Our patient underwent an above-knee amputation after neoadjuvant radiotherapy, and all resection margins were free of malignancy. However, she died of lymph node, lung, and bone metastases within six months of surgery. For all grades and subtypes of nonmetastatic chondrosarcoma, surgery is the only effective form of treatment; the most optimal type of surgical management is still debated [2,4,9,17].

The role of adjuvant chemotherapy in DDCS remains unclear[5,9] : one study seemed to show an effect on survival[2], which was not confirmed by others[4,7,17]. Chondrosarcoma is relatively radioresistant. Radiotherapy can be considered in the case of incomplete resection, or when resection is not feasible or would cause unacceptable morbidity [9].

An accurate method for differentiating a benign bone tumor from a malignant bone tumor is necessary. For this patient, we should have arranged an MRI and referred her to an orthopedic surgeon when the ill-defined calcification with mineralized chondroid matrix was noted and a lesion greater than 5 cm was seen on the radiographs. Health status is often a limiting factor, because the patients with DDCS have an average age of 60 years and frequently have significant comorbidities. Our patient refused adjuvant chemotherapy and decided to receive hospice palliative care.

In conclusion, we suggest that any bone lesion showing features of intraosseous chondroid matrix mineralization and tumor bimorphism should raise the level of suspicion for dedifferentiation.

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脛骨的去分化型軟骨肉瘤併膝痛：病例報告

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摘 要

老年人常抱怨膝痛。我們提出一個七十五歲女性膝痛，最後診斷爲脛骨的去分化型軟骨肉瘤的案例。病患於2003年6月27日主訴右膝疼痛來門診求助。由X光片發現脛骨近端不規則鈣化，無皮質破壞或骨膜增厚，也無骨膜反應。鑑別診斷包括脛骨骨梗塞、軟骨瘤。追蹤第三年，患者因意外發生右股骨骨折。直到2007年4月患者因肺炎住院時，右膝出現紅腫熱痛。安排核磁共振攝影，發現有軟組織增生。轉介骨科，進一步安排骨穿刺細胞學檢查，結果爲高度惡性肉瘤。骨骼同位素掃瞄及肺部電腦斷層檢查懷疑肋骨轉移，並無肺部轉移。患者先接受術前放射線治療，於2007年6月進行膝蓋以上截肢手術，病理診斷爲去分化型軟骨肉瘤。手術後發現有右腹股溝淋巴結、骨及肺部轉移。病患於術後6個月死亡。因骨腫瘤的惡性度難以從組織學及放射線學檢查區分。我們學習到當X光片發現不規則鈣化且大於五公分時，應及早轉介骨科，做完整的腫瘤評估。