

Case Report

Unusual calcifying fibrous tumor of the distal femur: a case report and review of literature

Lili Chen^{1*}, Qinghua Cao^{1*}, Xiaofang Lu¹, Zhifeng Chen², Xiaoke Zheng¹, Yang Li¹

Departments of ¹Pathology, ²Nuclear Medicine, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China. *Equal contributors.

Received May 18, 2017; Accepted August 1, 2017; Epub September 15, 2017; Published September 30, 2017

Abstract: Calcifying fibrous tumor (CFT) is a rare benign fibrous lesion of uncertain pathogenesis which shows distinct histological features. CFT has a broad anatomy distribution, and it was recently described in the subcutaneous and deep soft tissue, intra-cavity and intrinsic viscera. However, so far, there is no report to describe a CFT occurring in bone. We presented an unusual intraosseous CFT in a 63-year-old female patient with right knee joint pain for 2 weeks. Radiological imaging revealed a well-circumscribed osteolytic lesion with multiple calcifications or ossifications located in the right distal femur. The lesion was curetted totally. Histological examinations demonstrated that the tumor consisted of hyalinized, hypocellular collagen, scattered with fibroblast-like spindle cells, variably prominent chronic inflammatory cells infiltrates, and psammomatous or dystrophic calcifications. The morphologic diagnosis of primary CFT was made by its typical histological features and negative immunostaining for anaplastic lymphoma kinase (ALK). To the best of our knowledge, this is the first reported case of CFT that primarily developed in the bone. Awareness of CFT and its distinctive characteristics are important to avoid a diagnostic pitfall caused by histologic similarities to other spindle cell or calcifying lesions in unusual locations. Despite local recurrences have been reported, CFT still has favorable prognosis.

Keywords: Calcifying fibrous tumor, intraosseous, bone, differential diagnosis

Introduction

Calcifying fibrous tumor (CFT) is a rare benign lesion, and the etiology and pathogenesis of this disease is unclear. Histologically, CFT is characterized as a hypocellular fibroblastic proliferation with variable calcifications, dense hyalinized collagen and patchy chronic inflammatory cells infiltrates. The presence of calcifications, both psammomatous and dystrophic calcifications, is the hallmark of CFT [1]. Although CFT has a unique characteristic, it may easily cause a diagnostic pitfall owing to its rarity and histological similarities to other spindle cell or calcifying lesions. According to available reports, CFTs affect people of wide age range with no sex bias and that have a broad anatomy distribution, including subcutaneous and deep soft tissue of the extremities, trunk, neck, scrotum and breast, as well as intra-cavity and intrinsic visceral such as the gastrointestinal tract and mesentery, peritoneum, pleura, pelvis, mediastinum, adrenal gland and gallbladder [2-5]. However, to the best of our knowl-

edge, CFT arising in the bone definitely has not been reported yet. Herein we describe firstly an intraosseous CFT occurring in right distal femur of an older female patient. The purpose of this report is to show the distinctive features of CFT and avoid the diagnostic pitfalls caused by microscopic similarities to other spindle cell or calcifying tumors in bone.

Case presentation

Patient and clinical management

A 63-year-old Chinese female patient presented with pain of right knee joints for 2 weeks. The patient had been referred to a local hospital, and undergone radiological examination including plain radiographs and magnetic resonance imaging (MRI). Plain radiographs revealed an osteolytic lesion with multiple patches of calcification and osteosclerosis in the lower part of the right femur (**Figure 1A, 1B**). Cortex of the bone was integrate without any soft-tissue mass. The plain radiographs find-

An intraosseous calcifying fibrous tumor of bone



Figure 1. Posteroanterior (A) and lateral (B) radiograph of the right knee showed an osteolytic lesion with multiple patches of calcification and osteosclerosis in the lower part of the right femur. Cortex of the bone was intact without any soft-tissue mass.

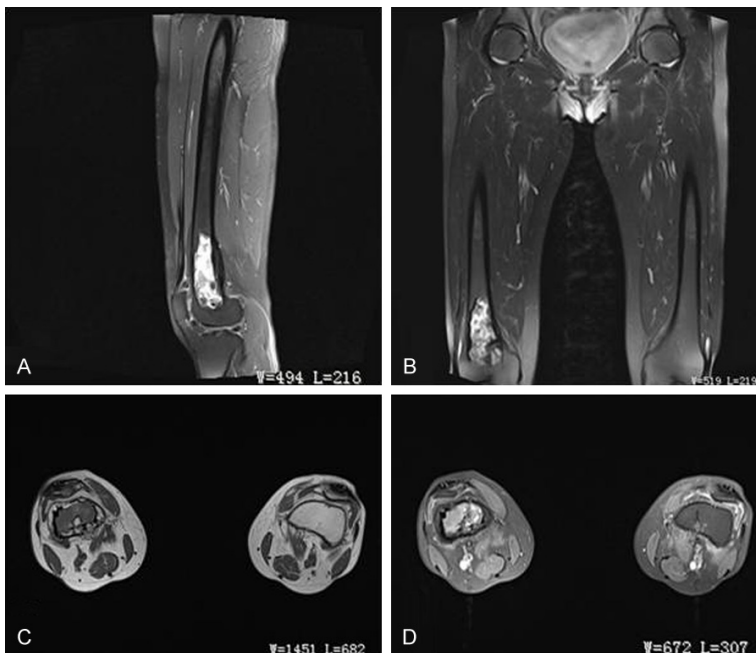


Figure 2. Sagittal Proton density weighted image (A) and coronal T2-weighted fat-suppressed MR images (B) showed that the lesion had a clear edge and mixed high signal intensity without any soft-tissue mass. Axial T1-weighted (C) and contrast enhanced fat-suppressed T1-weighted (D) images demonstrated that the lesion had mixed equal signal on T1-weighted images and significantly heterogeneous enhancement on contrast enhanced fat-suppressed T1-weighted image. Focal high signal intensity with obvious osteosclerosis of the adjacent bone cortex could be seen.

ings were suggestive of benign tumor. MRI showed a clear edge and mixed high signal intensity on T2 and Proton density weighted

images and mixed equal signal on T1 weighted images (**Figure 2A, 2B**). Osteosclerosis could be found mostly at the margin of the lesion and in part of the adjacent cortex without any soft-tissue mass. There was focal high signal intensity with marginal osteosclerosis of the adjacent bone cortex on T1-weighted images (**Figure 2C**). Significantly heterogeneous enhancement of the lesion could be found on fat-suppressed T1 weighted images (**Figure 2D**). Osteochondroma was initially suspected in the image findings. As a result, the patient was referred to our hospital for further examination and treatment.

The patient denied trauma and family history. Physical examination of the body and the laboratory results, including tumor markers, were found within normal limit. Biopsy was performed to confirm the histologic diagnosis, while the sample showed collagenous stroma with spindle cells and multiple calcifications. With no features of malignancy, the lesion was totally curetted by surgery.

Histological findings

The surgical specimens were routinely fixed in 10% neutral buffered formalin after tumor curettage. The masses were grayish white, firm, fragmented and about 5 cm in diameter. Under microscopic examination, the neoplasm mainly consisted of hypocellular hyalinized fibrous tissue with scattered dystrophic and psammomatous calcifications (**Figure 3A, 3C**), and focal lymphoplasmatic infiltration, which mirrored the findings of the previous biopsies. The sparsely spindle cells had oval to elongated vesicular

An intraosseous calcifying fibrous tumor of bone

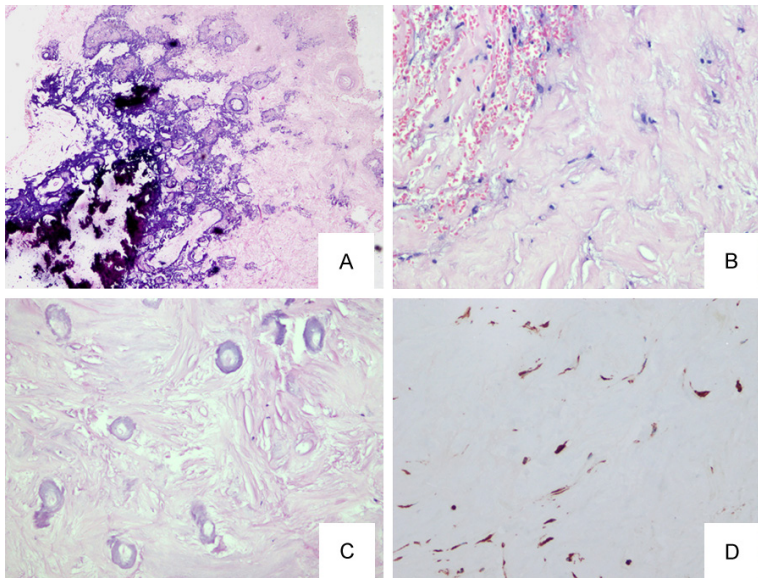


Figure 3. Photomicrograph of the lesion of distal femur. A. Low magnification showed paucicellular spindle neoplasm merging with areas of calcifications. B. High magnification showed that the lesion was composed of dense, hyalinized collagenous fibrous tissue with associated inflammatory cells. C. Hypocellular hyalinized collagen with scattered psammomatous calcifications. D. Immunohistochemical staining showed spindle cells positive for vimentin diffusely.

nuclei with fine chromatin, small inconspicuous nucleoli, and small amount of cytoplasm (**Figure 3B**). There were no coagulative tumor necrosis, cellular atypia, mitotic figures or any sign of malignancy found in the lesion. Immunohistochemical analysis demonstrated that the spindle cells were strongly and diffusely stained with antibodies to vimentin (**Figure 3D**), focally stained with antibody to CD34, but not response to anaplastic lymphoma kinase (ALK). Ki-67 highlighted a low nuclear proliferative rate (less than 1%). The Congo red and Methyl violet stains were negative for amyloid. Based on the above characteristic morphological and immunohistochemical findings, the lesion of distal femur was diagnosed as CFT according to WHO diagnostic criteria [2, 3].

The post-operative recovery was uneventful. The patients were discharged from hospital and on a regular follow-up for 6 months. No recurrence of the tumors was observed within the periods of follow-up.

Discussion

CFT is a rare benign entity of unknown etiology and it was originally described as a “childhood

fibrous tumor with psammoma bodies” in the soft tissues of the extremities in 2 children by Rosenthal and Abdul in 1988 [5]. Subsequently, Fetsch *et al.* proposed a new term of calcifying fibrous pseudotumor with analysis of 10 cases of similar pathologic features in their reports, which occurring not only limitedly in children, but also adults [1]. Considering the recognition of its presumptive neoplastic characteristics, the nomenclature calcifying fibrous tumor was used for this entity in the World Health Organization (WHO) classification system in 2002 [3]. We have reviewed CFT reported in English literature in recent 2 decades. It revealed that the tumor had a wide age range and both sexes were equally affected [6, 7]. Initially, CFT was considered

a lesion of subcutaneous and deep soft tissue, whereas subsequent reports have widened spectrum of its anatomic locations including intra-cavity and intrinsic visceral [2-5].

CFT usually presents as a solitary, painless mass or site-specific symptoms. Sometimes, it is asymptomatic and may be detected incidentally. Some patients with multifocal lesions have been described in the pleura, abdominal cavity and other locations as well [8-11]. Even though CFT generally behaves in a benign fashion, local recurrence has been noted in a subset of patients with the same morphology as the primary lesion [1, 6, 12]. However, recurrence occurs mainly in cases of incomplete resection, and any sign of malignant transformation has not been reported to date. Thus, complete local excision with clear margins appears to be appropriate treatment to prevent recurrence in most cases.

Microscopically, CFT is characterized by a proliferation of sparsely bland spindle cells embedded in hyalinized stroma with various degrees of calcification as well as a lymphoplasmatic infiltrate. Calcification presents in the form of psammomatous bodies or dystrophic calcifica-

An intraosseous calcifying fibrous tumor of bone

tions. Immunohistochemical staining shows that the spindle cells are positive for vimentin and factor XIIIa, and negative for anaplastic lymphoma kinase (ALK) in most cases. However, cases of CFT with focally positive to CD34 and smooth muscle actin (SMA) have also been reported [6, 10, 11]. In the present case, factor XIIIa was not done on the lesion of distal femur. Actually, according to the characteristic appearance of CFT with positive expression of vimentin and CD34, the diagnosis of CFT could be made regardless of the expression level of factor XIIIa.

Taking into consideration the morphological resemblance, the diagnosis of CFT often presents a challenge to the pathologists, especially while occurring in rare sites. The differential diagnosis of CFT in soft tissue usually includes fibromatosis, inflammatory myofibroblastic tumor, calcifying aponeurotic fibroma, and solitary fibrous tumor. However, CFT occurring in bone should mainly differ from desmoplastic fibroma, tumoral calcinosis, inflammatory myofibroblastic tumor, calcifying aponeurotic fibroma, and solitary fibrous tumor. Desmoplastic fibroma is a locally aggressive neoplasm of bone composed of bland spindle cells and abundant collagen, and it may involve any bone. In contrast to CFT, lack of the psammoma bodies or dystrophic calcifications, being positive for SMA, actin, desmin and nuclear β -catenin and negative for factor XIIIa are the diagnostic features. Tumoral calcinosis is a rare benign clinical condition resembling a neoplasm. It is characterized by tumor-like calcium deposits, usual hyperphosphataemia with normal serum calcium and alkaline phosphatase values, usually located in the soft tissues around the large joints. Histopathology findings show deposition of amorphous substance with evidence of calcifications related to a foreign body granulomatous reaction. These features can help to distinguish tumoral calcinosis from CFT. It has been reported that CFT may be the late, sclerotic phase of the inflammatory myofibroblastic tumor (IMT) [13]. However, infiltrate of inflammatory cells and myxoid background can be observed in IMT. Immunostaining for anti-ALK is detectable in approximately 50% of IMTs, whereas the expression of ALK is consistently negative in CFT [4, 6, 14]. Calcifying aponeurotic fibroma is a benign tumor that occurs most commonly in the distal extremities of young children. Its histopathological features

include scattered calcification foci surrounded with nuclear palisading and chondroid areas with proliferative plumps of fibroblasts around. Lack of chondroid areas with surrounding fibroblasts can separate it from CFT. In addition, calcifications and inflammation, which are hallmarks of CFT, are not commonly observed in solitary fibrous tumor. Positive immunostaining of CD34 and CD99 in spindle cells is also useful to distinguish solitary fibrous tumor from CFT.

Herein we presented an intraosseous CFT for its rarity of site. To the best of our knowledge, this is the first case of CFT that primarily developed in the bone. The differential diagnosis of CFT in usual locations is difficult and diagnosis should be made cautiously. As CFT occurring in the bone may be confused with other spindle cell or calcifying lesions, we could not ignore it due to its rarity. Although CFT has favorable prognosis, long-term follow-up is suggested as local recurrences might occur infrequently.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Yang Li, Department of Pathology, The First Affiliated Hospital, Sun Yat-sen University, 58 Zhongshan Road II, Guangzhou 510080, China. Tel: +86 20 8733 0890; Fax: +86 20 8733 1780; E-mail: li_yang_yang99@aliyun.com

References

- [1] Fetsch JF, Montgomery EA, Meis JM. Calcifying fibrous pseudotumor. *Am J Surg Pathol* 1993; 17: 502-8.
- [2] Nascimento AF. Calcifying fibrous tumor. In: *World Health Organization Classification of Tumours of Soft Tissue and Bone*. Lyon: IARC Press; 2012. pp. 69.
- [3] Montgomery E. Calcifying fibrous tumor. In: *World Health Organization Classification of Tumours of Soft Tissue and Bone*. Lyon: IARC Press; 2002. pp. 77-8.
- [4] Agaimy A, Bihl MP, Tornillo L, Wünsch PH, Hartmann A, Michal M. Calcifying fibrous tumor of the stomach: clinicopathologic and molecular study of seven cases with literature review and reappraisal of histogenesis. *Am J Surg Pathol* 2010; 34: 271-8.
- [5] Rosenthal NS, Abdul-Karim W. Childhood fibrous tumor with psammoma bodies: clinicopathologic features in two cases. *Arch Pathol Lab Med* 1988; 112: 798-800.

An intraosseous calcifying fibrous tumor of bone

- [6] Nascimento AF, Ruiz R, Hornick JL, Fletcher CD. Calcifying fibrous "pseudotumor": clinicopathologic study of 15 cases and analysis of its relationship to inflammatory myofibroblastic tumor. *Int J Surg Pathol* 2002; 10: 189-96.
- [7] Qian J, Rubio A, Powers JM, Rosenblum MK, Pilcher WH, Shrier DA, Stein BM, Ito M, Iannucci A. Fibroosseous lesions of the central nervous system: report of four cases and literature review. *Am J Surg Pathol* 1999; 23: 1270-5.
- [8] Bajpai J, Rekhi B, Iyer K, Samar A, Mahajan A, Jambhekar NA. Multifocal calcifying fibrous tumor of the mesentery: an unusual case report with literature review and therapeutic implications. *J Cancer Res Ther* 2011; 7: 500-2.
- [9] Farah RB, Dimet S, Bidault AT, Benbraheim C, Ndiaye N, Lazure T, Gayral F, Buffet C, Pelletier G. Multiple peritoneal calcifying fibrous tumors revealed by ischemic colitis. *Ann Diagn Pathol* 2007; 11: 460-3.
- [10] Suh JH, Shin OR, Kim YH. Multiple calcifying fibrous pseudotumor of the pleura. *J Thorac Oncol* 2008; 3: 1356-8.
- [11] Mito K, Kashima K, Daa T, Kondoh Y, Miura T, Kawahara K, Nakayama I, Yokoyama S. Multiple calcifying fibrous tumors of the pleura. *Virchows Arch* 2005; 446: 78-81.
- [12] Maeda A, Kawabata K, Kusuzaki K. Rapid recurrence of calcifying fibrous pseudotumor (a case report). *Anticancer Res* 2002; 22: 1795-7.
- [13] Van Dorpe J, Ectors N, Geboes K, D'Hoore A, Sciote R. Is calcifying fibrous pseudotumor a late sclerosing stage of inflammatory myofibroblastic tumor? *Am J Surg Pathol* 1999; 23: 329-35.
- [14] Sigel JE, Smith TA, Reith JD, Goldblum JR. Immunohistochemical analysis of anaplastic lymphoma kinase expression in deep soft tissue calcifying fibrous pseudotumor: evidence of a late sclerosing stage of inflammatory myofibroblastic tumor? *Ann Diagn Pathol* 2001; 5: 10-4.