Case report

Osteofibrous dysplasia: A rare case in 3-day-old female ☆

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ABSTRACT

Osteofibrous dysplasia (OFD) is a nonneoplastic tumor-like lesion, made up of fibrous matrix with immature bone tissue surrounded by osteoblasts, occurring usually in the cortex of tibial diaphysis. OFD is usually seen in the first decade of life and, according to literature, it is rarely seen in the newborn period. Diagnosis of congenital OFD in the newborn is challenging because it is uncommon in this age group and can be confused with other bone benign or malignant lesions. Imaging plays an important role in diagnosis, although histological confirmation is often required. Our report presents a rare case of pathologically confirmed congenital OFD in 3-day-old female which presented with a swelling of her right leg. We will focus on imaging findings of OFD and main differential diagnosis of this lesion in neonatal age.

Introduction

OFD is a benign fibro-osseus lesion that arises almost exclusively from tibial diaphysis, generally presenting with painless swelling of the leg. It has been referred to as "osteitis fibrosa" [1] and then named as OFD by Campanacci and Laus due to its histological resemblance to fibrous dysplasia [2]. Some authors have used "ossifying fibroma" as a synonym for OFD, but in reality, they should be considered as 2 separate pathological entities, since ossifying fibroma is a lesion ob-

served almost exclusively in the jaw of women in the third and fourth decade of life [3]. Typically, OFD occurs in childhood, usually below the age of 10 years, with slight male predilection [4]. The age of presentation ranging from 7 days to 22 years [5]. However, in the literature, only few cases have been described in the neonatal period [6–10]. Diagnosis of congenital OFD is challenging because it is rare and the radiological findings are often nonspecific as they can mimic other neoplastic or nonneoplastic bone lesions. Moreover, in addition to the pathologies from which OFD should be classically differentiated, such as fibrous dysplasia and adamantinoma, other
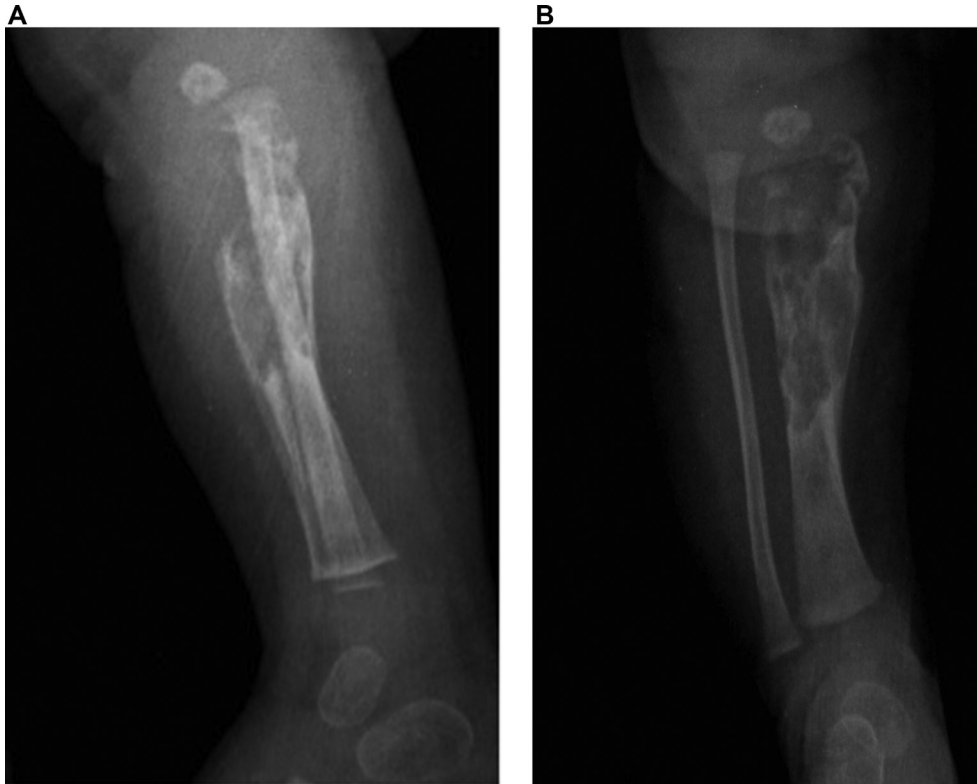
Fig. 1 – First radiographs, anteroposterior (A) and lateral view (B), showing an expansile osteolytic lesion involving the proximal half of diaphysis and metaphysis of tibia that appears swollen. The lesion has a "bubbly" appearance and inner ground glass matrix. Note the well-defined, multi-lobulated sclerotic margins of lesion and internal septa. The cortex is thinned and disrupted in some points suggesting a pathologic fracture (white arrow).

Fig. 2 – Coronal (A), sagittal (B) CT- reconstructions confirm the osteolytic nature of the lesion with contextual ground glass component. 3D volume-rendering (C) shows an excellent 3-dimensional representation of the lesion.

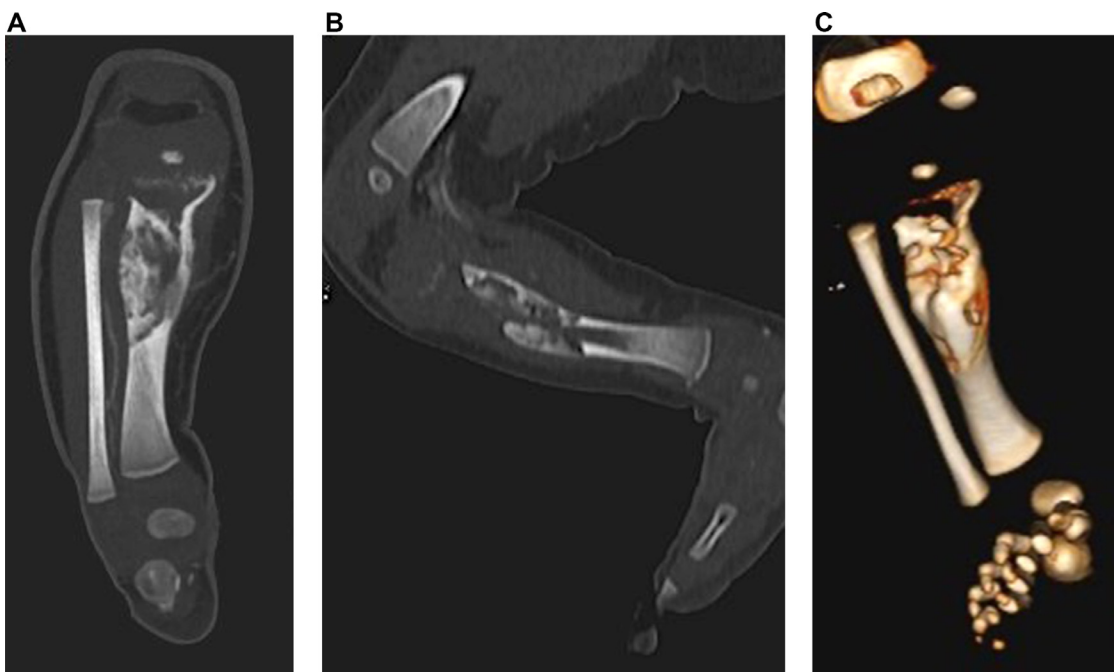**Fig. 3 – Coronal short tau inversion recovery (STIR) (A), coronal T1-weighted (B), coronal (C) and axial (D) T1- weighted post-contrast MRI show an expansile mass with heterogeneous hyperintense signal in STIR, low signal in T1-weighted and heterogeneous enhancement in post-contrast images. Note the thinning of the cortex without any periosteal reaction and involvement of local soft tissue. The axial T1- weighted post-contrast image shows better the cortical location of the lesion that mostly respects the limits of the medullary canal (white arrow).**

pathologies should be considered in the neonatal period. The diagnostic framework is important for a correct therapeutic approach that, compared to other bone pathologies, is conservative because the progression of the lesion is generally slow and halts with the achievement of skeletal maturity.

Case report

A 3-day-old female infant was referred to our medical department to investigate a swelling of her right lower leg. The in-

fant was born by spontaneous vaginal delivery to a 30-year-old mother in full term pregnancy. The mother and infant had no complications during pregnancy and at birth. Familiar history was unremarkable. Physical examination showed a swelling of the right tibial diaphysis without calor or rubor. There were no other pathological physical findings. Laboratory investigations including serum biochemistry, urine and C reactive protein, were normal. The anteroposterior and lateral x-ray showed an expansile osteolytic lesion with areas of contextual ground glass areas occupying almost completely the metaphysis and the proximal half of the diaphysis of left

tibia that appeared enlarged and flared. The contours of the lesion were irregular but relatively well defined with narrow zone of transition (Fig. 1). The cortex was thinned and disrupted in some points with evidence of pathologic fracture (Fig. 1B). The lesion did not affect the epiphysis. There were no signs of periosteal reaction or involvement of adjacent soft tissues. Computed tomography (CT) showed the same findings as x-ray, allowing an excellent representation of the extent of the lesion thanks to 3-D reconstructions and 3D volume-rendering (Fig. 2). Magnetic resonance imaging (MRI) demonstrated a soft tissue mass in the tibial cortex that appeared enlarged and deformed. The lesion revealed heterogeneous hyperintense signal on the T2-weighted images and STIR (short tau inversion recovery) sequences and intermediate-low signal on the T1-weighted images (Figs. 3A and B). Moreover, the lesion showed heterogeneous enhancement on post-contrast T1-weighted image (Figs. 3C and 3D). No restricted diffusion on Diffusion-weighted images was noted. Cross-sectional MRI showed no clear involvement of the medullary cavity (Fig. 3D). Edema of the surrounding soft tissues was associated. Biopsy was performed with pathological result of fibrous stroma and spindle cell proliferation with production of woven bone trabeculae with prominent osteoblastic rimming (Fig. 4A). Scattered cytokeratin-expressing cells were also seen in the stromal cell component (Fig. 4B). Diagnosis of congenital OFD was made. The patient was treated conservatively with plaster immobilization and was discharged. A follow-up radiograph preformed 4-weeks later showed a partial sclerotic remodeling of the lesion with reduction of radiolucent component and cortical thinning (Fig. 5). Actually, the infant is in follow-up.

Discussion

OFD is considered as a benign fibro-osseous cortical lesion histologically formed by fibrous stroma with irregularly shaped, immature trabeculae of woven bone surrounding by osteoblastic rimming.

Immunohistochemical staining shows cytokeratin-positive cells. This is the histologic feature that distinguishes OFD from nonossifying fibroma of the jaw [11].

OFD involves almost exclusively the tibia with unilateral location, most commonly anteriorly within the mid-diaphysis, but can reach the metaphysis, as in our case. Involvement of fibula is described in 12% of cases [12]. Exceptional cases have also been reported in the radius and ulna [13]. Clinical presentation consists of painless fusiform swelling of tibial diaphysis. There may be local tenderness over the tibia. In some cases, the lesion is noted incidentally on x-ray performed for other condition. The biomechanical fragility of dysplastic bone can cause a pathological fracture or progressive bone deformity, typically anterior or anterolateral tibial bowing [8]. In a study, Park et al reported pathological fracture in 12.5% of their patient population [14]. A rare complication can be pseudarthrosis resulting from the local destructive process [5,7,15]. X-ray is the first chief investigation to be performed. Typical radiographic appearance of OFD is well-defined eccentric intracortical osteolytic lesions often with a sclerotic, well circumscribed margins and inner ground-glass density.
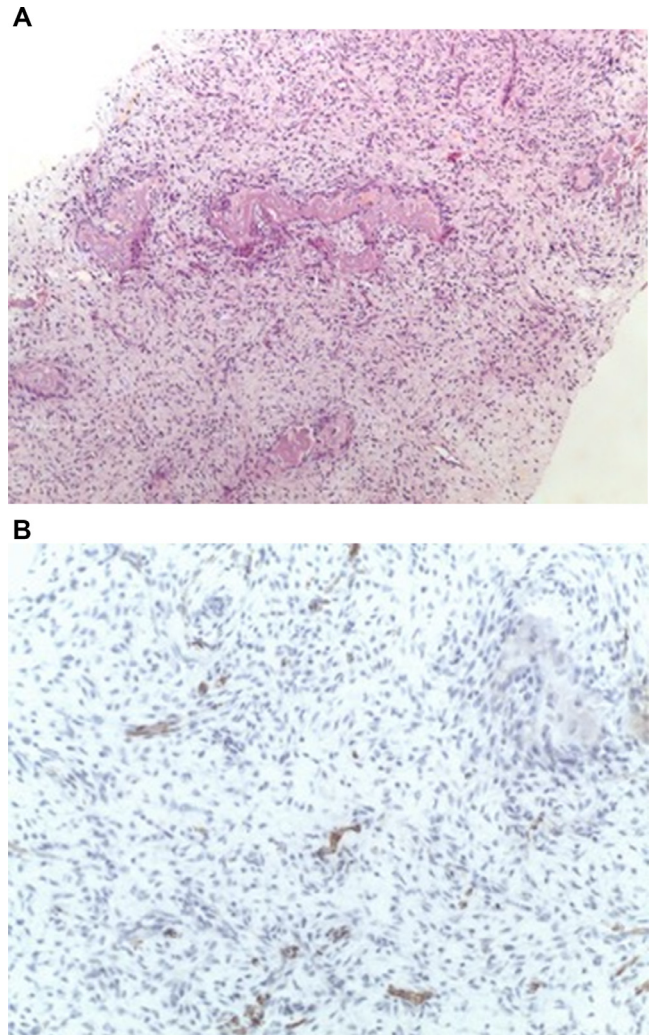
Fig. 4 – Irregular trabeculae of woven bone with osteoblastic rimming and stroma composed of bland spindle cells. Haematoxilin & Eosin x 100 (A). Scattered stromal cells are immunoreactive for Cytokeratin X 200 (B).

It involves almost exclusively the tibial diaphysis with possible spread to the metaphysis. Thus, the process is often centered in the cortex, especially in its anterior side, with consequent cortical expansion and anterior bowing [11,15]. Cortex can also be thinned and disrupted. The lesion can have lobular-to-bubbly appearance with confluence of multiple lytic area. The periosteal reaction is rare and when present is nonspecific and is not aggressive in appearance [5,16]. In minority of cases, the lesion can secondarily encroach the medullary canal, better visualized on cross-sectional images of MRI. However, medullary canal involvement, when present, is usually partial compared to other aggressive lesions. CT confirms the characteristics of the lesion showing better its extension, the ground glass appearance which is related to the presence of fibrous matrix, any pathological fractures and eventual fibular localization [16]. MRI provides additional information especially on tissue characterization, the adjacent soft tissues and the extent of eventual intramedullary involve-
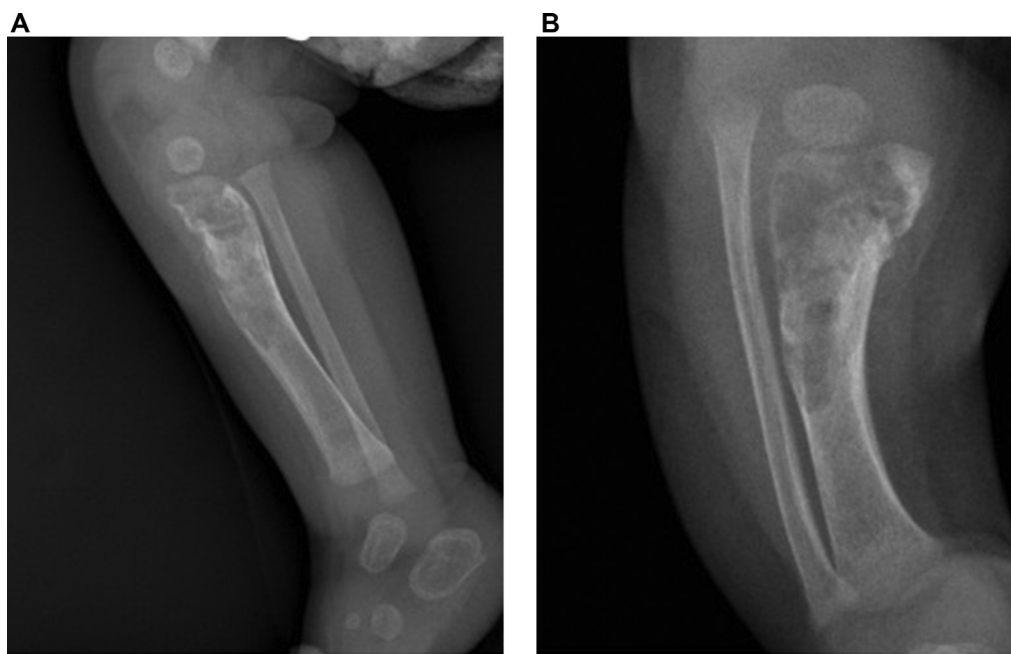
Fig. 5 – Four-week follow-up, radiographs anteroposterior (A) and lateral view (B) show a partial sclerotic remodeling of the lesion with reduction of osteolytic component with increased cortical integrity. Pathological fracture is still evident (white arrow).

ment. On MRI, the lesion demonstrated intermediate to high signal on the T2w sequences and intermediate signal on the T1w sequences, like other lesions with fibroblastic matrix. Superimposed hemorrhagic, cystic, myxoid change and cartilaginous differentiation can contribute to heterogeneous signal intensity on the T2w image. Furthermore, OFD shows a relatively well-enhanced pattern in Gadolinium-enhanced T1w sequences, reflecting the rich fibrovascular stroma [17–19]. OFD should be classically distinguished from adamantinoma and fibrous dysplasia (FD) due to histological and radiological similarities [20–22]. Some Authors consider OFD as part of a spectrum of OFD-like adamantinoma and adamantinoma consequently as different stages of the same pathology [23]. Adamantinoma is a rare primary malignant bone tumor with a worse prognosis and requires an extensive surgical approach due to its locally aggressiveness and the possibility of distant metastases. As OFD, adamantinoma in most cases occur in the tibial diaphysis of young patients, especially in the second and third decades. Histologically, the presence of nests or strands of epithelioid cell is the key to differentiating adamantinoma from OFD [11,24]. However, needle biopsy sampling may not be sensitive enough due to intralesional heterogeneity and can underestimate aggressive lesions. Khanna et al. showed the importance of diagnostic imaging and radiologic-pathologic correlation in presence of equivocal biopsy results. In their series, radiological signs of aggression such as complete or almost complete involvement of the medullary cavity, extension to the adjacent soft tissues, skip lesion in the ipsilateral fibula and a "moth-eaten" bord are found in the adamantinoma. However, these findings may also appear in OFD, as a partial medullary involvement [20]. Moreover, well differenti-

ated adamantinomas may lack these aggressive features. A report on the MRI findings of the adamantinoma by Van der Woude et al. shows that the signal strength characteristics of OFD are not specific to those of differentiated adamantinoma [25]. FD is found predominantly in children and young adults, can be monostotic or polyostotic and involve any bone. It has intramedullary location unlike OFD. The cortex is usually thinned but intact and the deformity of involved bone is rare. Histologically, osteoblastic rimming of bony trabeculae is absent in fibrous dysplasia [24].

ODF can mimic other rare lesions with osteolytic radiographic appearance in the neonate include Langerhans-cell histiocytosis (LCH), Chondromyxoid fibroma (CMF), giant cell tumor of bone, nonossifying fibroma (NOF), intraosseous neurofibromas, infantile myofibromatosis (IMF), osteomyelitis and malignant tumor such us Ewing's sarcoma. Localized LCH, also known as eosinophilic granuloma, may involve the skeleton that is the most common location for single-lesion LCH. In long bones it arises from diaphysis or metadiaphysis and respects growth plates and has an aggressive appearance in the early phase with endosteal scalloping, periosteal reaction, intracortical tunneling and associated soft tissue mass. However, below 2 years of age the multisystem form is more common [26]. NOF is the most common type of nonneoplastic fibrous bone lesion, very common in children and adolescents, characterized by spontaneous healing with growth. NOF presents as multiloculated lucent lesions with a sclerotic rim, located eccentrically in the metaphysis, adjacent to the physis [27]. CMF is rare, benign cartilaginous neoplasms that occur in during second and third decades. CMF is lobulated or oval eccentric lytic lesion with well-defined, lobulated scle-

rotic margin. It arises in 25% of cases from the tibia but involves mostly metaphyseal region with possible extension to the epiphyseal line [28]. Giant cell tumor of bone is relatively common bone tumor occurring only with closed growth plate and thus, is typical of young adult. In 50%-65%, it arises around the knee, in distal femur or proximal tibia, abutting articular surface. In addiction it has well-defined but non-sclerotic margin [29]. IMF is a rare mesenchymal disorder characterized by a fibrous proliferation of the skin, bone, muscle, and viscera, usually occurs before age 2. Common findings of bone lesions are well-defined lytic lesions with, or without, sclerotic borders. However, a solitary lesion of the bone can also occur, but is extremely rare [30]. Neurofibromatosis can cause congenital pseudarthrosis of the tibia that can mimic the radiological appearance of OFD pseudarthrosis [31]. Neonatal osteomyelitis is characterized by systemic and local clinical sign of infection. The radiological appearance is characterized by destructive lesions with marked periosteal reaction in the metaphysis and frequent joint involvement [32]. Malignant tumors of bone, including Ewing's sarcoma, are exceedingly rare in the newborn and infant. The appearance of these tumors is very variable, but they usually have clearly aggressive appearance. Common findings include permeative aspect and lamellated periosteal reaction. In our case, the clinical presentation with painless swelling of the tibia without other symptoms and radiological features (such us predominant cortical involvement, regular and sclerotic margins with narrow zone of transition, absence of periosteal reaction) led us to hypothesize OFD. However, biopsy and histology of the lesion were required to rule out the possibility of other condition, including malignancy, to allow an adequate therapeutic approach [33]. Nonsurgical treatment is recommended for ODF by most authors because of progressive remodeling of the lesion up to spontaneous regression after bone maturation and the high incidence of recurrence after surgery, especially during the first years of life [34]. Surgery might be delayed as long as possible and considered only in those lesions which are large [35]. According to the literature, we have chosen a conservative approach. The 1-month follow-up x-ray showed partial remodeling of the lesion. We expect a further progressive remodeling of the lesion until a possible regression in the subsequent radiographic controls.

Conclusion

Although congenital OFD is uncommon, it might be considered in differential diagnosis of neonatal bone tumor or tumor-like lesions involving unilateral lower leg, especially with tibial diaphysis localization. Congenital OFD should be distinguished from juvenile adamantinoma, FD, localized LCH, CMF, GCG, NOF, IMF, neurofibromatosis, osteomielitis and malignant tumors. Imaging can suggest the diagnosis when radiological appearance is typical. However, biopsy is need because in many case imaging findings are nonspecific, especially in presence of atypical features such as complete intramedullary involvement, pathologic fracture with prominent perilesional reactive change and even pseudoarthrosis. In conclusion, diagnostic imaging is important for the follow-up of the lesion as treatment is conservative.

Patient consent

According to guidelines of the Radiology Case Reports Journal, "formal consents are not required for the use of entirely anonymized images from which the individual cannot be identified for example, x-rays, ultrasound images, pathology slides or laparoscopic images, provided that these do not contain any identifying marks and are not accompanied by text that might identify the individual concerned."

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