Regression of an ossifying fibroma of the tibia after a fracture involving the lesion. Possible role of the periostina

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Summary

Ossifying fibroma (OF) of the long bones is a benign fibro-osseous lesion typically seen in the first decade of life. OF usually progresses until the age of 10 years, but is occasionally found to regress spontaneously after puberty. The pathogenesis of OF is unknown; however, it has been suggested that the basic defect is in the periosteum. We present the radiological course of an OF of the tibia in a young patient, showing a rapid almost complete regression of the lesion after a tibial fracture at the lesion site. We postulate that the fracture-induced activation of the periosteum in a growing skeleton was fundamental to the regression of the lesion.

KEY WORDS: ossifying fibroma; periosteum, regression lesion.

Introduction

Ossifying fibroma (OF) of the long bones is a rare, benign fibro-osseous lesion, which was first described by Kepson in 1966 (1). OF of the long bones is typically seen in the first decade of life, usually before puberty, and affects males and females equally. The lesion has a predilection for the tibia and fibula, is usually unilateral and rarely bilateral (2, 3). Clinically, it appears as an enlargement of the tibia usually associated with slight anterior bowing, together with pain and inflammation. The occurrence of pathological fracture or pseudoarthrosis in this type of lesions is infrequent (4).
Radiographically, OF presents intracortical osteolysis with a characteristic adjacent sclerotic band associated with an enlargement of the medullary canal. These radiographic features are so typical of OF that diagnosis can be established based solely on radiographic findings, without histologic confirmation. Nevertheless, there are no radiographic criteria to predict the course of the lesion.
Histologically, it is characterized by the presence of benign fibrous tissue with a large amount of irregular-shaped trabeculae rimmed by osteoblasts. A second typical feature is the presence of a so-called zonal architecture with a transition from sparse immature trabeculae of woven bone in the center of the lesion to more mature trabeculae of lamellar bone at the cortex.
Although the pathogenesis of OF is unknown, it has been postulated that it is the result of excessive resorption of bone secondary to defective bone, probably in an attempt at healing by fibrous repair. The basic defect would be located in the periosteum, producing abnormal osteoblasts or an excessive number of osteoclasts (5).
The natural history of OF is progression of the lesion until the age of 10 years. The lesion frequently recurs after curettage or periosteal resection (in approximately 25% of cases). In view of the high recurrence rate, surgery is only recommended when the lesion is rapidly progressive or when the patient sustains repeated fractures (2, 3).
OF occasionally regresses spontaneously after puberty. We present the case of a young patient who showed rapid and almost complete regression of OF of the right tibia, after a tibia fracture at the site of the lesion.

Clinical case

A 20-year-old man consulted because of bilateral knee pain, which exacerbated especially when he was practicing sports. The patient reported sustaining a right tibial fracture at the age of 17 years; the radiographs taken at the time of the fracture (Figure 1 A and B) evidenced altered trabecular structure at the distal diaphysis of the right tibia, bowing of the cortex and alteration of the inner cortex with a sclerotic halo at the periphery. The radiographic findings were indicative of OF (Figure 1), and histologic confirmation was deemed not to be necessary.
The patient had no history of relevant diseases. On examination, he weighed 70 kg, was 172 cm tall, and had a body mass index of 24.1 kg/m^2. Clinical examination revealed no peculiarities in the distal part of his leg. Laboratory assessment of bone mineral metabolism and new radiographic images of both legs and knees were requested. The new X-rays of the right tibia (Figure 2 A and B) showed filling of the OF as soon as 3 years after the first radiograph, which was taken at the time of the fracture. No evidence of bone or joint alterations was observed in either of the knee X-rays. Mineral metabolism laboratory results showed an increase in bone remodeling compared to the reference results for normal adults: serum crosslaps (a marker of bone resorption): 1077 ng/ml and bone alkaline phosphatase (a marker of bone formation): 232 IU/l. These values were thought to be normal for our patient, considering that he was a young adult, and as such was still in the period of peak bone mass-acquisition.

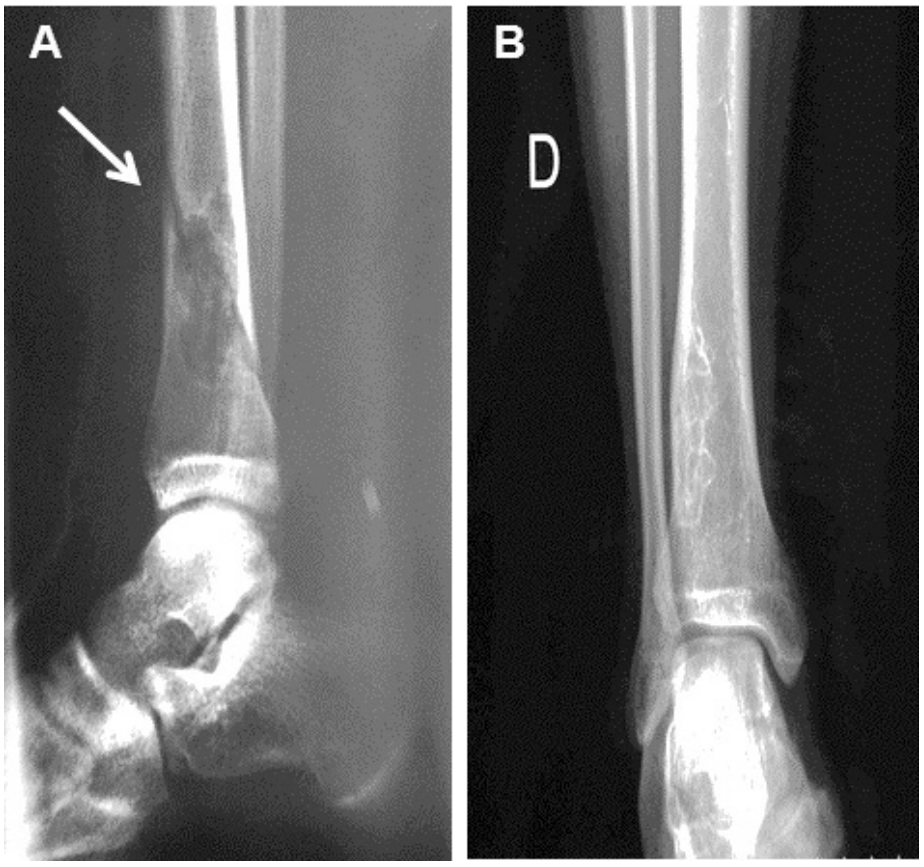

Figure 1 A and B - Lateral and antero posterior X-rays of the ankle taken at the time of the fracture (patient was 17 years old). A radiolucent lesion with well defined and sclerotic borders with multilobular appearance can be observed in the distal diaphyseal-metaphyseal region of the tibia. A bowing of the inner surface of the tibia is observed. The image is compatible with ossifying fibroma. Tibial fracture line (arrow) was observed.

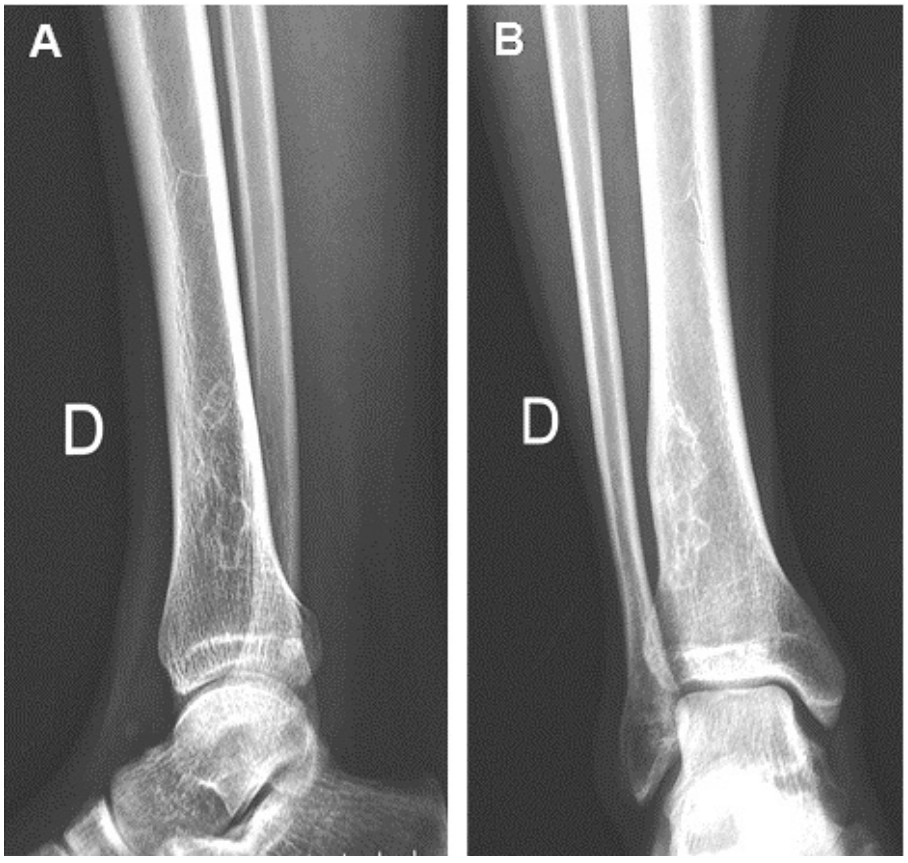

Figure 2 A and B - Lateral and antero posterior X-rays of the ankle taken 3 year after the previus study. Compared to the previous images, the lesion shows greater density and filling and the bowing is less marked. The image is compatible with ossifying fibroma undergoing ossification.

Discussion

OF is a rare, benign bone disease, that occasionally regresses after puberty. In the case of the patient presented here, diagnosis was an incidental finding due to a fracture at the lesion site. Three years after the fracture almost complete remission of the lesion was observed.

It has been postulated that the periosteum plays a main role in the pathogenesis of OF (5). The periosteum is a complex structure composed of an outer fibrous layer predominantly consisting of collagen that lends structural integrity, and a highly cellular inner layer of mesenchymal progenitor cells that possess the potential to differentiate into osteoblasts or fibroblasts (6). The periosteum is particularly active during the period of skeletal growth, contributing to the determination of bone diameter and muscular strength, and in fracture consolidation, playing a fundamental role in the processes of bone regeneration (7). The osteoblastic potential of the periosteum varies with age and with localization. It is greater during growth and in certain bones such as the tibia, where its osteogenic capacity is greater as compared to that of the periosteum of other bones of the skeleton (8).

We postulate that certain factors, which were present in the patient discussed here, combined to enable filling of the OF lesion. One of such factors may have been the tibial fracture at the same site as the lesion, which allowed not only detecting the lesion unknown to the patient until then, but also stimulating the periosteum to initiate healing of the bone injury.

Immediately after a fracture, a series of molecular events are triggered. These events lead to the formation of hematoma and inflammation, followed by a repair phase which includes angiogenesis, cartilage formation, and remodeling (9). Periostin, a protein of the extracellular matrix expressed in the periosteum among other tissues, is elevated during the initial stages of the bone healing process, specifically during recruitment of osteoblastic progenitors in the fracture callus, as well as during osteoblast differentiation and bone formation (10). Thus, periostin plays an active role in the early stages of bone regeneration.

Another factor that may have favored the filling of the lesion is the fact that the fracture occurred during the period of skeletal growth. The periosteum is specially active during growth. Periostin is regulated by growth hormones and factors. The latter would seem to act on pre-osteoblasts, favoring their proliferation and differentiation into osteoblasts (11, 12). On the other hand, hormones such as estrogen and parathyroid hormone would have an antiapoptotic effect on undifferentiated cells in the periosteum (13).

Lastly, the somewhat elevated levels of bone remodeling markers were attributed to the stage of acquisition of peak bone mass of our patient. Periostin levels do not correlate with levels of bone formation or resorption markers in growing animals (7). Therefore, periostin would not reflect bone remodeling, but rather, ontogenic ossification.

In summary, we herein present the case of a young patient who showed rapid, and almost complete, regression of an OF in his right tibia. Because the defects of the periosteum may have been involved in the pathogenesis of OF, we speculate that the fracture healing process and the fact that patient's skeleton was still growing may have contributed to the rapid filling of the lesion. In the light of current knowledge, both events have been identified as activators of the periosteum. OF could be an interesting model to study the relation between periostin and the regression of fibro-osseous lesions.

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Conflicts of interest

All Authors have no conflicts of interest.

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