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TEST YOURSELF: ANSWER

Proximal tibial pain in a child

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Answer

Intraosseous, osteoblastoma-like phosphaturic mesenchymal tumor with secondary oncogenic rickets.

Discussion

Oncogenic osteomalacia is a rare condition in which mesenchymal-derived tumors secrete fibroblast growth factor 23 (FGF-23) [1]. The condition was described by McCance [2], although Prader discovered the tumoral etiology [3]. FGF-23 is normally secreted by osteocytes and osteoblasts and its action prevents both reabsorption of phosphorus in the renal tubules and the conversion of 25-OH vitamin D to 1,25-OH vitamin D. Elevated FGF-23 causes increased phosphate secretion resulting in rickets or osteomalacia [4, 5]. A similar scenario to oncogenic osteomalacia occurs in autosomal-dominant hypophosphatemic rickets in which gain-of-function mutations in FGF-23 lead to rickets and osteomalacia associated with low serum phosphorus levels [6].

The histopathological spectrum of phosphaturic mesenchymal tumor (PMT) is somewhat varied and, although fairly typical, does not readily lend itself to subclassification [1, 7]. Two groups, however, have subdivided intraosseous PMT into four types. Named according to known tumors that they closely resemble, they are: mixed connective tissue, non-ossifying fibroma-like, ossifying fibroma-like, and osteoblastoma-like PMT [7]. Osteoblastoma-like PMT is an uncommon manifestation with four original cases described in the English, Pubmed-surveyed literature and two revisions of earlier diagnoses [1, 7]. These 6 patients were age 13 to 24 years, 3 were male and 3 were female.

Our patient's plain radiograph of the tibia demonstrated mild physeal widening consistent with rickets. A skeletal survey showed this finding to be consistent throughout the patient's skeleton (Fig. 1). The lesion itself was metaphyseal and lytic compared with the normal bone, but with a sclerotic and well-marginated border; it also demonstrated anterior cortical erosion. A differential diagnosis based upon radiographs alone would include non-ossifying fibroma, an early ossifying fibroma, and, less likely, chondromyxoid fibroma. This lesion demonstrates a narrow zone of transition, little or no periosteal reaction, no soft-tissue mass, and minimal cortical erosion, all of which suggest a non-aggressive histology [8]. Initial management of a patient presenting with these radiographs would be predicated on the lesion's benign characteristics. If the discovery of this lesion were purely incidental and our patient was without symptoms then observation would be a prudent course. A symptomatic lesion indicates that there is either structural weakness of the bone or the lesion is creating products that are chemically stimulating local nociceptors; either situation

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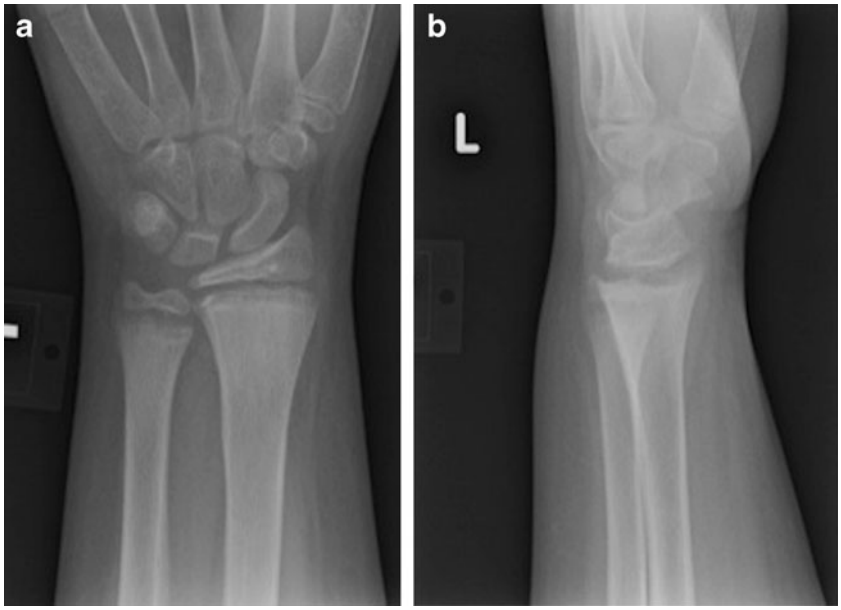

Fig. 1 **a** Anteroposterior and **b** lateral radiographs of the left wrist demonstrating widening of the physes consistent with the patient's diagnosis of rickets

requires further inquiry into the lesion's nature in the form of imaging and biopsy.

Magnetic resonance imaging revealed cortical disruption with heterogeneous signal on T1- and T2-weighted images, no marrow edema on T2-weighted images, and minimal contrast uptake. In this case, MRI is not particularly helpful in narrowing the differential diagnosis as all of the aforementioned diagnoses can demonstrate mixed high- and low-signal images. The bone scan shows a modest increase in uptake at the lesion compared with normal bone. The needle biopsy submitted for consultation showed nodules and sheets of eosinophilic matrix, focally calcified and focally polarizable in a pattern similar to woven bone, as the dominant feature. Rather bland small spindle-shaped cells were present at the periphery of the matrix or as isolated cells or strands within it. Mitoses were rare and necrosis was absent. Occasional multinucleated giant cells were seen. The biopsy was interpreted as concerning for osteosarcoma, but because of the relatively bland histopathology and the clinical and imaging features that suggested an indolent tumor, a repeat needle biopsy was recommended, which revealed a similar histopathological appearance (Fig. 2). Additional consultation resulted in PMT being proffered as the most likely diagnosis with a suggested conservative but complete resection that might further help to clarify the nature of the tumor.

In our patient, dual-energy X-ray absorptiometry (DEXA) scanning confirmed the diagnosis of rickets with a whole-body bone mineral density of 0.64 g/cm^2, corresponding to a Z-score of −3.8 SD. The initial FGF-23 level was 332 RU/ml (normal <230). Before resection of his tumor he was started on calcitriol 0.25 mcg twice daily and phosphate 250 mg four times daily to treat his bone pain and rickets. The tumor was resected en bloc via a hemicortical osteotomy followed by allograft and plate reconstruction (Fig. 3). Pathological examination of the resected specimen showed that the lesion was confined to the bone and that the margins of resection were free of tumor (Fig. 4). Histopathology was similar to that observed in the needle biopsies (Fig. 5). The final pathological diagnosis was phosphaturic mesenchymal tumor, osteoblastoma-like variant, which was

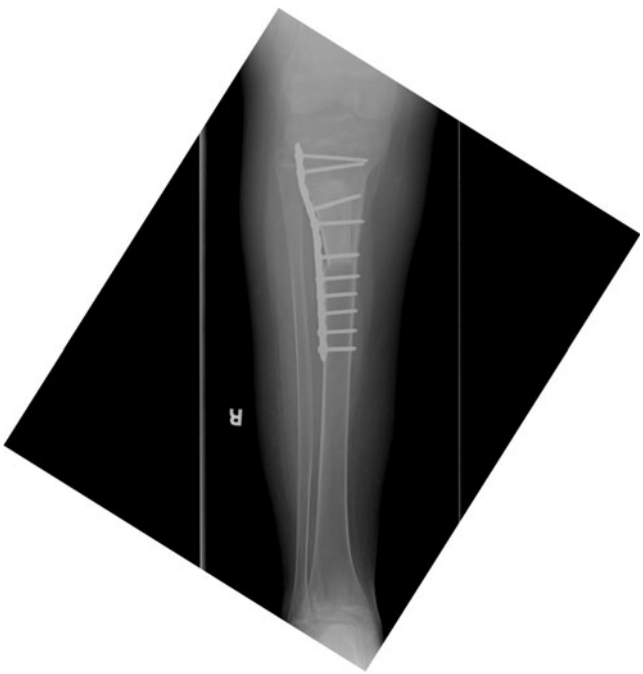

Fig. 2 Anteroposterior radiograph of the tibia 1 month after operation

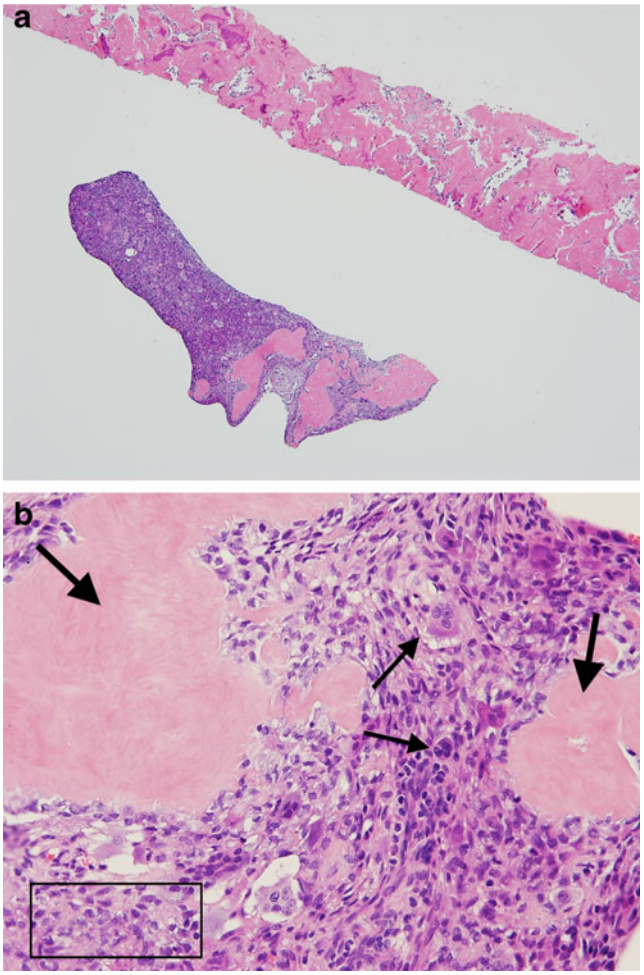

Fig. 3 **a** Low-power (×40, H and E) histological image showing hypocellular, focally calcified osteoid-like matrix with interspersed cellular areas and **b** high-power (×400, H and E) histological image showing small, spindle-shaped, bland lesional cells (*box*) combined with rare multinucleated giant cells (*small arrows*) surrounded by an osteoid-like matrix (*large arrows*)

histologically benign. Immediately following tumor excision, calcitriol and phosphate supplements were discontinued and he was started on calcium and vitamin D supplements. Two weeks after his operation the FGF-23 level was <50 RU/ml.

One year following his operation the patient has no pain; hip, knee, and ankle range of motion are symmetrical to the contralateral side. He walks with a normal, plantigrade gait and participates in all activity except contact sports. His FGF-23 level remains <50 RU/ml.

Definitive treatment for oncogenic osteomalacia is surgical removal of the tumor, after which serum FGF-23 levels return to normal [9]. When resection is not feasible, patients may be managed pharmacologically. Treatment is identical to that for patients with hypophosphatemic rickets and includes phosphate and

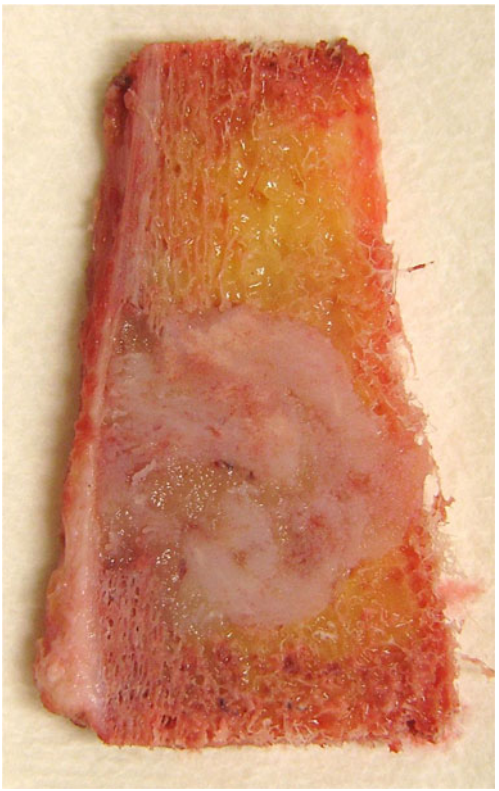

Fig. 4 Coronal section through a specimen resected in a hemicortical fashion with an irregular but well-marginated gray mass. The cortex at the zone of lesion abutment demonstrates cortical erosion (left aspect of the photograph)

1,25-OH vitamin D supplements [10]. After tumor resection, phosphate supplementation is discontinued; however, patients should continue calcium and 1-25-OH vitamin D supplementation until bone density is restored.

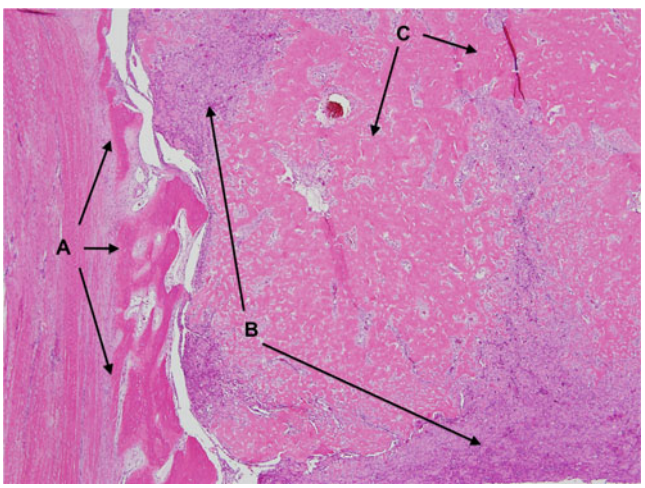

Fig. 5 The cortex is infiltrated and eroded, but not penetrated by the tumor (*A*). Cellular areas (*B*) representative of the initial biopsy specimens interspersed with extensive osteoid-like matrix (*C*) (×40, H and E)

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Conflicts of interest None.

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