Which is your diagnosis?

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Male, three-year-old patient complaining of pain in the left lower limb for one month, without any other associated symptom.

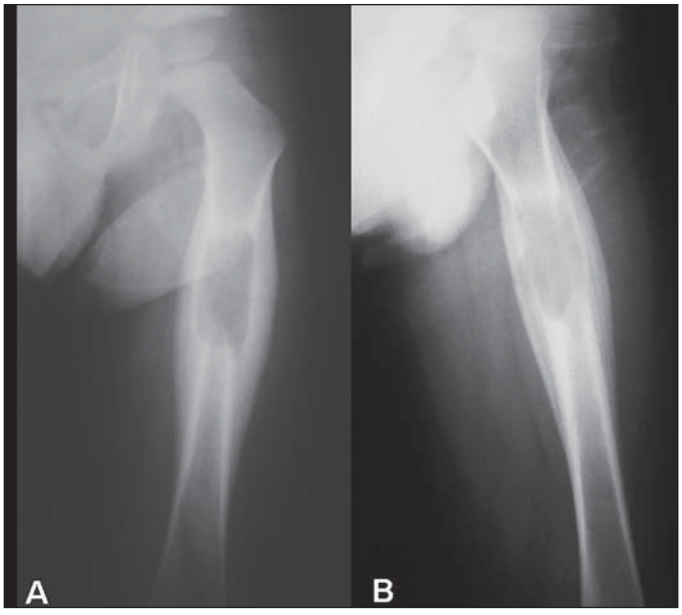

Figure 1. Plain radiograph — anteroposterior (**A**) and lateral (**B**) views.

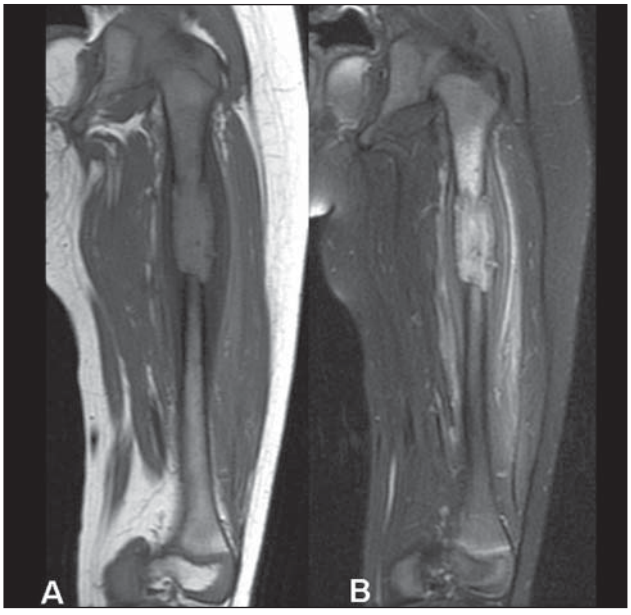

Figure 2. Magnetic resonance imaging — coronal, T1-weighted image (**A**) and T2-weighted image with fat saturation (**B**).

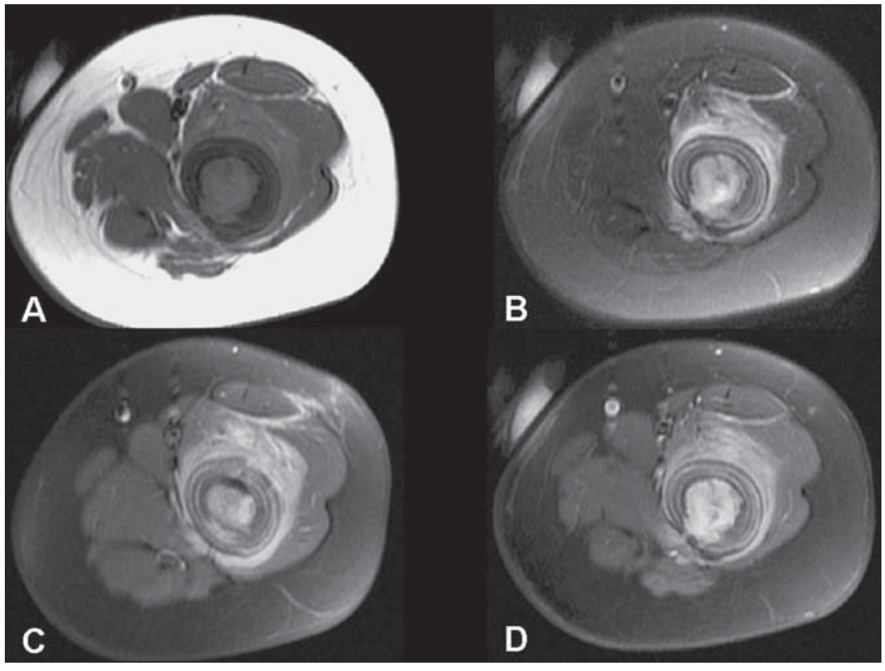

Figure 3. Magnetic resonance imaging — axial, T1-weighted image (**A**), T2-weighted image with fat saturation (**B**) and T1-weighted with fat saturation acquired after paramagnetic contrast agent injection (**C**,**D**).

Images description

Figure 1. Lytic lesion with partially well-defined margins, centrally located in the middle/proximal third of the femoral diaphysis. Lamellar periosteal reaction ("onion peel" pattern) is observed.

Figure 2. Diaphyseal lesion presenting hyposignal on T1-weighted sequence, and hypersignal on T2-weighted sequence with fat saturation. Proximal, medullary hypersignal adjacent to the lesion is observed. Also, lamellar periosteal reaction is observed, besides hypersignal in soft tissues surrounding the lesion, corresponding to edema.

Figure 3. Lesion with hyposignal on T1-weighted, and hypersignal on T2-weighted sequences, demonstrating erosion of the posterior cortical bone. After paramagnetic contrast agent injection, an intense enhancement of the lesion, periosteum and soft tissues is demonstrated.

Diagnosis: Langerhans' cell histiocytosis.

COMMENTS

Langerhans' cell histiocytosis covers a spectrum of diseases characterized by the idiopathic proliferation of atypical histiocytes and formation of granulomas resulting in focal or systemic alterations[1].

Eosinophilic granulomatosis, also known as a localized presentation of the disease, presents an involvement restricted to bones or lungs, corresponding to 70% of cases of Langerhans' cell histiocytosis. It is the most benign expression of the disease, besides being the most favorable in terms of prognosis[2,3].

In these cases, Langerhans' cell histiocytosis may affect any bone, although the incidence is higher in flat bones. More than 50% of eosinophilic granulomas present like a lytic lesion with a destructive component. Although less frequently, periosteal reaction and permeative pattern may be present[4–6]. The skull is the most affected region, with the calvaria, particularly in the parietal region, being more frequently affected than the skull base. The mandible, ribs and pelvis are other frequent sites of involvement[5].

Approximately 25%–35% of monostotic lesions affect long bones, especially femur, humerus and tibia, most frequently in the diaphyseal region (58%), followed by the metaphyseal region (28%), metadiaphyseal (12%), and rarely the epiphyseal region (2%)[4,5,7].

The majority of patients are asymptomatic, although pain, edema and, less frequently, a pathological fracture may occur in the site of the lesion[4]. Fever and leukocytosis also may be present. Langerhans' cell histiocytosis may affect patients at any age, although there is a prevalence of cases in persons less than 15 years old, with a slight male preponderance[8].

Two other clinical syndromes are part of the Langerhans' cell histiocytosis spectrum: Hand-Schüller-Christian disease, a chronic and recurrent presentation corresponding to 15%–20% of cases, affects multiple bones (predominantly the skull) and the endothelial-reticular system, and is most frequently found in male children between one and five years of age. The acute, fulminant presentation of Langerhans' cell histiocytosis, also known as Letterer-Siwe disease, corresponds to 10% of cases and occurs predominantly in children younger than two years of age without sex predilection. There is a systemic bone and endothelial-reticular involvement, rapidly progressing to multiple organs dysfunction[5,9,10].

Histologically, the three clinical syndromes are characterized by atypical Langerhans' cells which, associated with polymorphonuclear cells, lymphocytes, and mainly eosinophils, lead to the formation of granulomas. In the early phase of the disease, aggregate of Langerhans' cells are found, frequently associated with eosinophils, although their presence is not essential for the diagnosis. In the chronic phase, the findings include lesions with few Langerhans' cells, associated or not with the presence of eosinophils[11,12]. Electronic microscopy can detect Birbeck granules, cytoplasmic structures found exclusively in Langerhans' cells, and currently the definite diagnosis is immunohistochemically determined by the presence of CD-1 and S-100 markers[10,13].

Imaging findings in cases of Langerhans' cell histocytosis are quite variable, and may present any radiographic feature, sometimes mimicking malignant diseases.

Plain radiography is the primary method of investigation, and the most typical finding is a lytic lesion, with well- or ill-defined margins and bone destruction, usually centrally located in flat bones or in the diaphyseal region of long bones. Cortical bone destruction or expansion may be found, and the periosteal reaction is generally compact, although lamellar periosteal reaction may be found in young children.

The evaluation by means of computed tomography allows confirming the presence of the lesion, defining the extent of cortical destruction and the degree of involvement of soft tissues. Additionally, this method is useful in cases where the bone lesion is situated in anatomically complex regions such as mastoid process, atlantoaxial joint, and posterior elements of vertebral bodies[6,10].

Magnetic resonance imaging presents a high sensitivity, however its specificity is low. The lesion of eosinophilic granuloma presents iso/hyposignal on T1-weighted images, and hypersignal on T2-weighted images, and possibly enhancement after contrast agent injection. Magnetic resonance imaging also is useful for defining the extent of bone marrow and soft tissues involvement[13,14].

The most significant prognostic factors in these cases are the patient's age and the lesion extent, the prognosis being worst in children younger than two years old, and in case of large lesions[15,16]. Spontaneous resolution of focal bone disease may occur in some cases.

The treatment for solitary lesions of long bones resulting from eosinophilic granulomas consists of curettage of the area and implantation of bone or methacrylate graft, or corticoid injection[17].

The most significant differential diagnoses in this context are acute osteomyelitis and Ewing's sarcoma0[10,18].

In cases of osteomyelitis, radiological alterations can be visualized 10 to 12 days after the onset of the disease, when

edema of soft tissues can be observed. After 10 to 14 days, an ill-defined, focal area of rarefaction in the metaphysis, with a "piecemeal" pattern of the bone marrow, progressing to lytic destruction and associated focal periosteal reaction.

Ewing's sarcoma is a metaphyseal tumor that affects both flat and long bones, characterized by a lytic lesion with ill-defined margins, cortical invasion and periosteal reaction which can be lamellar, interrupted or present with Codman's triangle. Sclerotic lesions may be observed in 25% of cases.

Differentiation, in these cases can be achieved by means of biopsy.

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