Hyperostosis and hyperphosphataemia syndrome: a diagnostic dilemma

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ABSTRACT

The syndrome of hyperostosis and hyperphosphataemia (HHS) is very rare. It can mimic bone infections and tumours. A nine-year-old girl presented with pain in her left lower leg. Radiographs showed patchy sclerosis in the tibial diaphysis. Investigations were normal except for hyperphosphataemia. Open biopsy showed chronic inflammation. Bacterial cultures were negative. Four months later, she had pain in the other leg. On evaluation for hyperphosphataemia, there was increased renal reabsorption of phosphates. She responded to analgesics. In patients between six and 16 years of age, HHS must be considered when there is painful diaphyseal swelling of long bones associated with isolated hyperphosphataemia. The painful episodes can recur. Surgical decompression can be considered if conservative treatment methods are ineffective.

Keywords: bone tumours, hyperostosis and hyperphosphataemia syndrome, hyperphosphataemia, osteomyelitis, painful diaphyseal lesions

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INTRODUCTION

The syndrome of hyperostosis and hyperphosphataemia (HHS) is not common. This can mimic bone infections and tumours,[1,2] and may lead to a delay in diagnosis. We present a case of HHS and review the literature on this subject.

CASE REPORT

A nine-year-old girl, born normally to non-consanguinous parents, presented with pain in the left leg with a six-month duration, and which markedly increased in the last one month. The pain was gradually progressive and very severe, especially at night. She also had associated low grade fever during this period. She had no other bone or joint pain or other systemic symptom. On examination, she had an antalgic gait. There was minimal swelling and tenderness over the mid-shaft of left tibia. On palpation, there was diffuse enlargement of the tibial midshaft. There was no soft tissue swelling or regional lymphadenopathy. Radiographs (Fig. 1a) showed patchy sclerosis involving the medulla in the middle third of the tibial diaphysis. There was periosteal reaction. There were no skip lesions. Bone scintigraphy (Fig. 1b) showed isolated marked increased uptake in the left tibia.

Her other investigations were as follows: total leucocyte count of 7,600/mm^3 (normal 4,000–11,000/mm^3), haemoglobin of 13 g/dL (13–15 g/dL), erythrocyte sedimentation rate of 32 mm/one hour, C-reactive protein was negative, serum calcium 9.9 mg/dL (8.3–10.4 mg/dL), fasting serum phosphorus 8.3 mg/dL (2.5–4.6 mg/dL), serum alkaline phosphatase 159 u/L (50–125 u/L), sickle cell preparation was negative, and serum creatinine was 0.8 mg/dL (0.8–1.2 mg/dL). The differential diagnoses were osteomyelitis, malignant bone tumour, juvenile Paget's disease and osteonecrosis.

She underwent open biopsy which showed abundant new bone formation and chronic inflammation. She had excellent pain relief. The bacterial cultures were negative. She presented again four months later with pain in the right leg with similar characteristics as before. The radiographs (Fig. 2a), blood investigations and bone scintigraphy (Fig. 2b) were similar. The fasting serum phosphate level was persistently high. She underwent detailed evaluation for hyperphosphataemia. Her serum 25 hydroxy vitamin D level (12.9 ng/ml) and parathormone levels (21.1 pg/ml) were normal. Her TmP/GFR (tubular maximum for phosphate/glomerular filtration rate) was > 5 mg/dL (normal 2.5–4.5 mg/dL). A diagnosis of HHS was made and the patient was treated with analgesics.

DISCUSSION

HHS was first described in 1970.[3] Our patient fulfilled all the criteria for this syndrome;[4] these were recurrent episodes of painful swelling of long bones, normal renal function, vitamin D and parathormone levels, and increased renal reabsorption of phosphates. The radiographical features were also consistent with previously reported findings. The painful episodes usually resolved spontaneously.

In earlier studies, girls have been predominantly

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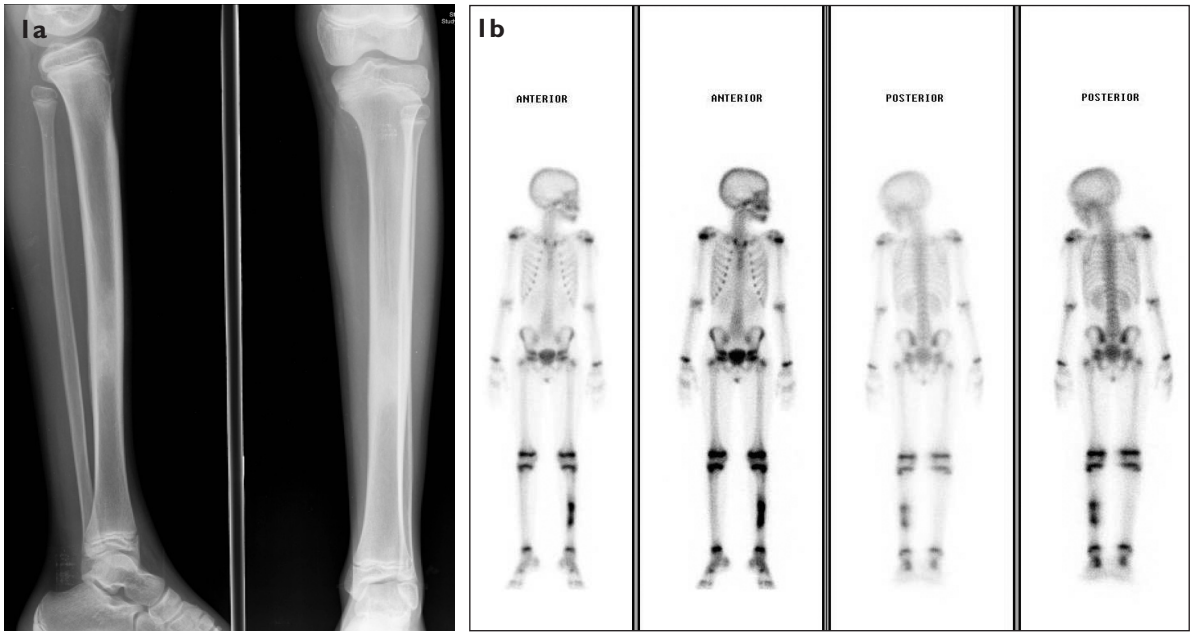

Fig. 1 (a) Lateral (left) and frontal (right) radiographs of the left tibia show sclerosis of mid-diaphysis with periosteal reaction. (b) Bone scintiscans show marked increased uptake over the midshaft of the left tibia.

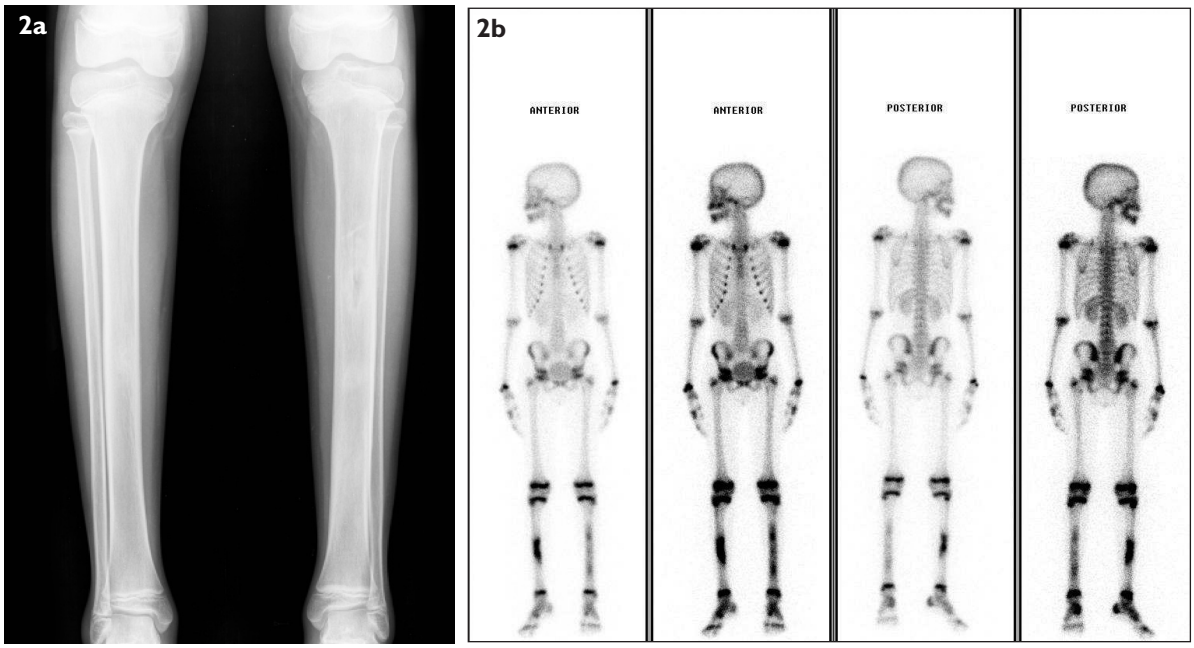

Fig. 2 (a) Radiograph of both tibiae shows bilateral midshaft sclerosis. (b) Bone scintiscans show marked uptake on the right side and less uptake on the left side, compared to the previous scintiscan.

affected by this condition.[5] Geographically, this has been mainly found in the Middle East. This is the first time this condition is being reported from India. Though the presentation of this condition mimics osteomyelitis and bone neoplasms, the elevated serum phosphate level along with other normal parameters help in the diagnosis of this condition. This syndrome should be considered as part of the differential diagnosis for osteomyelitis, neoplasms and vaso-occlusive crises. Familial occurrences have also been documented.[4] This girl had a younger sister aged six years and a younger brother aged 13 months. Both the siblings did not have any similar episode. They have not been evaluated for hyperphosphataemia.

In 2005, Frishberg et al identified a recurrent mutation in uridinephosphorylase-N-acetyl-alpha-D-galactosamine: polypeptide N-acetylgalactosaminyltransferase 3 (GALNT3), which encodes a glycosyltransferase responsible for initiating O-glycosylation in patients with HHS.[1] This mutation is found in patients who have familial tumoural calcinosis. Tumoural calcinosis also has been found to be associated with this condition.[4,6] DNA

analysis was not done in this patient. In the previous reports, the exact location of the lesion in the bone has not always been mentioned. However, this seems to exclusively affect the diaphysis when long bones are involved. All the radiographs so far shown in the previous reports show only diaphyseal involvement in the long bones.[2-5,7,8] In our patient, histopathological examination showed abundant new bone formation and chronic inflammatory infiltration. There was a focus of cortical fibrosis, in contrast to medullary fibrosis reported by Nakamura.[8]

As reported by Nakamura, we also observed excellent pain relief after biopsy,[8] which may be due to the decompressive effect. Though in some reports where biopsies have been avoided, we recommend surgical decompression when the pain is very severe or not responding to analgesics. Our patient had excellent pain relief after the biopsy during the first episode. The painful episodes are known to recur over a period of time in the same or different sites. This was also seen in this patient. The treatment of hyperphosphataemia has been shown to have no influence in the course of this disease.

In conclusion, HHS should be considered in patients between six and 16 years of age, and who present with a painful swelling of the long bones involving the diaphysis and isolated hyperphosphataemia. Early and accurate diagnosis will help avoid multiple invasive investigations. The painful episodes can recur. Surgical decompression is an option when conservative measures fail.

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