Enthesopathy as the presenting feature of X-linked hypophosphatemia

A case report

John Chalmers

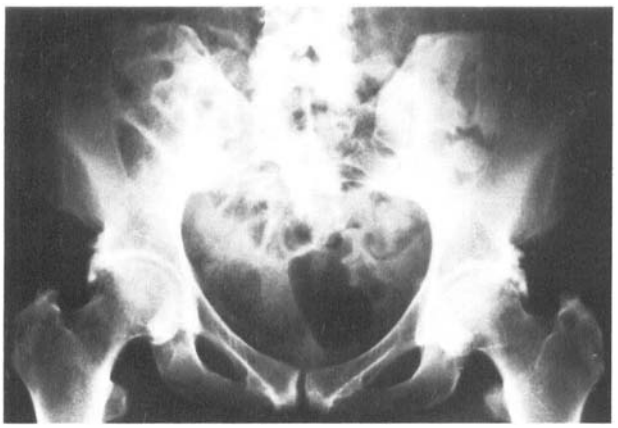
X-linked hypophosphatemia has a wide spectrum of clinical presentation. I describe a woman in whom diffuse enthesopathy was the only manifestation. The diagnosis was established from the family history. The severity of the enthesopathy did not relate to the severity of the biochemical changes.

Princess Margaret Rose Orthopedic Hospital, 41–43 Frogston Road West, Edinburgh EH10 7ED, UK
Tel +44–31 447 1586. Fax–31 445 3440. Submitted 92-07-19. Accepted 92-10-08

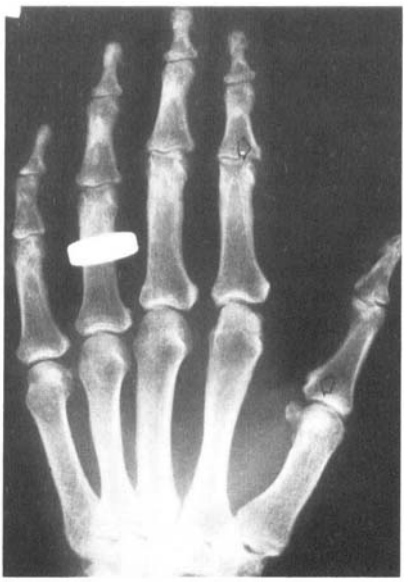
A housewife, aged 49, sustained minor injuries as a result of a fall in a bus. Radiographs showed enthesopathies involving the hips, the trochanters, and the ankle and tarsal joints. Further radiographs showed these features to be widespread affecting both shoulders and hands (Figure 1), but not the spine.

The patient had had no previous illness and the bones were undeformed and of normal density. She had widespread slight limitation of joint movements and a number of small bony prominences could be felt around her finger and ankle joints. Clinical examination was otherwise normal. Biochemical examination

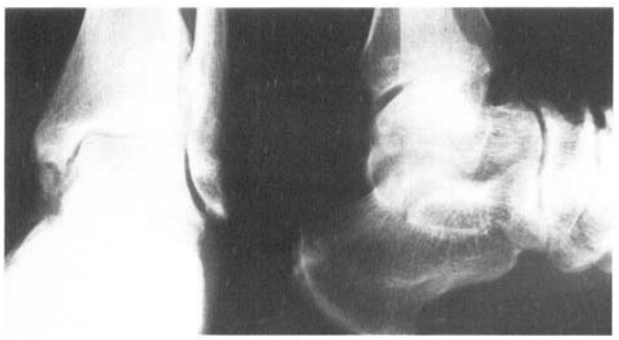
Figure 1. A 49-year-old woman with X-linked hypophosphatemia.



Prominent enthesopathic changes are present around the hips and trochanters. The sacro-iliac joints and lumbar spine are unaffected.



Small bony projections (arrows) occur in relation to many of the hand joints.



Bone proliferation is present at the tip of the medial malleolus, around the talus and at the inferior tibiofibular joint.

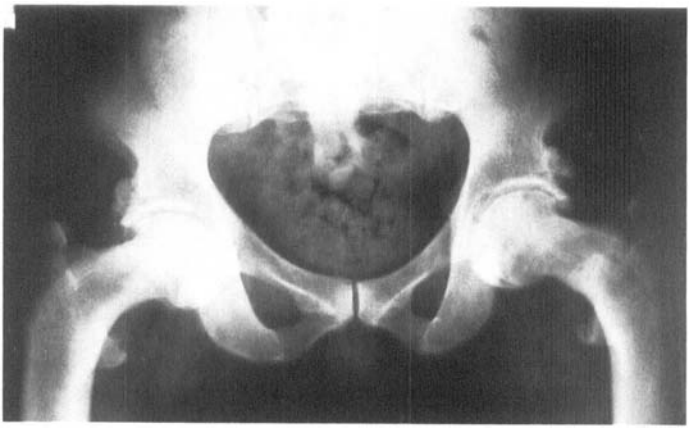


Figure 2. The patient's father shows similar enthesopathic changes around the hip and trochanters. In addition, there is a Looser zone in the left femoral neck and coxa vara.

gave normal values for alkaline phosphatase (59 units/L) and calcium (2.26 mmol/L). Her phosphate level was marginally low, ranging from 0.62 to 0.78 mmol/L.

The diagnosis of X-linked hypophosphatemia was established from the family history. The patient's father had presented 12 years earlier, aged 54, with multiple skeletal pain affecting his hips, back and knees and a generalized feeling of tiredness and muscle weakness. In the father's case, biochemical investigations gave consistently low values for plasma phosphate and evidence of a renal phosphate leak, his TmP/GFR being 0.3 (normal range 0.7–1.4) Plasma calcium and alkaline phosphatase and 25-hydroxy vitamin D values were normal. The father's bone biopsy specimen revealed nonspecific osteomalacia and diffuse radiographic enthesopathic changes were present, similar to those in his daughter (Figure 2), but in his case there was also involvement of the spine. His daughter (the subject of this case report) was screened at that time and was found to have a marginally low TmP/GFR (0.56). However, this finding was discounted in the absence of any other abnormality and a diagnosis of idiopathic hypophosphatemic osteomalacia was made. The family history was otherwise normal. The patient had one daughter aged 3 who was developing normally and had a normal plasma phosphate level.

Discussion

X-linked hypophosphatemia (XLH), although one of the commoner forms of vitamin D-resistant rickets, is a distinctly rare inherited disorder. Clinical involvement ranges from minor and unimportant hypophosphatemia to florid rickets with stunted growth or osteomalacia (Winters et al. 1958, Burnett et al. 1964, Stickler et al. 1970). As an X-linked dominant disorder, the disease tends to be more common in women but more severe in the male.

Enthesopathy is well recognized as one of the radiographic features of XLH. In a study of 26 patients Polisson et al. (1985) found two thirds to be affected, the incidence increasing with age from none under the age of 10 to 100 percent in the over-forties. A similar incidence was found by Hardy et al. (1989) who found that women had a slightly higher incidence than men. The most common sites of involvement recorded in these two papers were the ankle (75 percent), followed by the trochanters, the pelvis and the hands and wrists. In a series of 6 cases, Burnstein et al. (1989) noted proliferative changes in the annulus fibrosis in all cases which looked like those in the father of the patient.

Other radiographic features include altered bone density which, in contrast to vitamin D-deficient osteomalacia, is more often increased than decreased (Hardy et al. 1989).

The origin of the enthesopathic changes in XLH is obscure. It is not related to the severity of the biochemical changes, which in this case were so minimal that the diagnosis could not have been established without the family history; nor is it associated with the presence of osteomalacia or its treatment (Polisson et al. 1985). The enthesopathy may be entirely symptomless, as in this case, but may contribute to the high incidence of arthrosis which has been noted in XLH (Hardy et al. 1989).

The incidental finding of otherwise unexplained enthesopathy warrants a careful screening of the patient and the family for evidence of hypophosphatemia.

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