Case Report

Reflex sympathetic dystrophy in hypophosphataemic osteomalacia with femoral neck fracture: a case report

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Abstract

We report a male patient who presented with suspicion of skeletal metastases based upon an abnormal 99mTc bone scan, which showed increased uptake at both femoral heads, left femoral neck, and several ribs. The images also suggested reflex sympathetic dystrophy, subcapital fracture of the left femur, and rib fractures. A diagnosis of hypophosphataemic osteomalacia was finally made.

KEY WORDS: Hypophosphataemic osteomalacia, Femoral fracture, Reflex sympathetic dystrophy.

Osteomalacia (OM) is a metabolic bone disease with multiple causes. It is usually related to alterations in calcium and phosphate metabolism, but also to enzymatic or bone matrix disturbances, drug therapy, hepatic and renal diseases [1]. It has also been associated with bone fractures [1, 2], reflex sympathetic dystrophy (RSD) [3, 4], and other bone diseases [5].

We present a patient with a femur fracture and RSD of the lower limbs, in whom hypophosphataemic OM was diagnosed.

Clinical case

A 36-yr-old male presented to our service in April 1993 with suspected skeletal metastasis. The symptoms started in May 1992 in the form of progressive pain and weakness of the shoulder and hip girdles and painful ribs on movement and breathing. The patient also presented with asthenia, anorexia, and a weight loss of 3 kg. He was treated with non-steroidal anti-inflammatory drugs and also received a 3-week course of glucocorticoids 6 months before his first admission, without symptomatic improvement. In March 1993 he had been attending another hospital. Full blood counts, erythrocyte sedimentation rate (ESR), general biochemistry (including calcium) and protein electrophoresis were normal. The only abnormalities detected were hypophosphataemia (2.01 mg/dl; normal range: 2.5–4.5) and hydroxyprolinuria (60.8 mg/24 h/m²; normal range: 6–22). Alkaline phosphatase was 133.4 IU/l (normal range: 35–135). X-rays showed mild vertebral collapse of T4, patchy osteoporosis of both femoral heads, and a subcapital fracture of the left femur. 99mTc bone scan showed increased uptake in both femoral heads, the left femoral neck and several ribs. In April 1993 the patient was transferred to our service. He denied personal or family history of OM or rickets, gastrointestinal symptoms, use of laxative drugs, antacids or diuretics, alcohol abuse or recent trauma.

Physical examination revealed decreased breath sounds of the right chest and tender right hemi-abdomen. Neurological examination was normal, except for painful proximal weakness in all four limbs. Musculoskeletal examination revealed tenderness of the ribs and iliac spines, pain and reduced movement of the lumbar spine and hips, and tenderness of C6–T4 and L3–L5.

Blood tests were normal, except for phosphate 0.47 mmol/l (normal range: 0.84–1.47 mmol/l), alkaline phosphatase 2 microkat/l (normal range: 0.6–1.6), pH 7.29, pCO₂ 57.9 mmHg, bicarbonate 28.4 mEq/l and base excess of 1.1 mEq/l. Urinary hydroxyproline was 23.87 mmol/24 h/m² and pH 5. Parathyroid hormone was 2 pmol/l (normal 1.1–4.6). Calcium, phosphate and alkaline phosphatase levels are shown in Table 1. The phosphate:calcium index showed a renal tubular defect in the re-absorption of phosphates (Table 2). Given the clinical and radiological suspicion of OM, a bone biopsy was performed following tetracycline labelling. The biopsy confirmed the presence of OM. Renal phosphate loss was considered to be the cause of hypophosphataemia in the absence of any other congenital or acquired cause.

Pelvic X-ray and magnetic resonance imaging (MRI) suggested RSD in both hips. Abdominal ultrasonography and thoracoabdominal computed tomography (CT) were normal.

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Phosphate:calcium index measurements

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<th>Serum (mmol/l)</th>
<th>Urine (mmol/l)</th>
<th>Urine (mmol/day)</th>
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<tr>
<td>Calcium</td>
<td>2.21</td>
<td>1.48</td>
<td>1.78</td>
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<tr>
<td>Phosphate</td>
<td>0.61</td>
<td>31.5</td>
<td>37.8</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.082</td>
<td>9.88</td>
<td>11.86</td>
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<tr>
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<th>UPO4V/GFR&lt;sup&gt;a&lt;/sup&gt;: 0.26 mmol/l GFR (normal 0.06–0.25)</th>
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<tr>
<td></td>
<td>Tubular re-absorption of phosphate: 0.57 (normal 0.82–0.95)</td>
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<td>Phosphate clearance 40 ml/min (normal &lt;10)</td>
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<td></td>
<td>TmP/GFR&lt;sup&gt;b&lt;/sup&gt;: 0.36 mmol/l (normal 0.8–1.35)</td>
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<sup>a</sup>UPO4V/GFR, urinary excretion of phosphate per unit of glomerular filtration.
<sup>b</sup>TmP/GFR, renal threshold phosphate concentration [6].

The left subcapital femoral fracture was treated by internal fixation. OM was treated with inorganic phosphate at a daily dose of 1.8 g, with 25(OH) vitamin D 16 000 IU (0.266 mg) weekly. After a month the patient had partially recovered, but the hypophosphataemia persisted, and he became intolerant to the treatment in the form of diarrhoea. The daily phosphate dose was reduced to 1.2 g. When the diarrhoea remitted, the phosphate dose was slowly increased to 2.8 g/day with complete disappearance of pain and weakness within a few months.

At the same time as the diarrhoea, the patient developed painful swellings of the knees and ankles. X-rays showed patchy osteoporosis, and RSD of the knees and ankles was diagnosed. He improved completely with rest.

After 5 yr the patient remains asymptomatic, and continues to receive the same treatment. Radiological assessment during follow-up showed evolution towards remission. Biochemical parameters were normal, except for phosphate, which remained low throughout follow-up. No neoplasia was detected during this period.

Discussion

OM is an infrequent condition in southern Europe because of the abundance of sunlight, and the vitamin supplementation of certain foods. Calcium, phosphate and vitamin D deficiency is only found in special circumstances [7].

Hypophosphataemic OM has many causes [1]. In the absence of a history of drug use or the intake of toxic products, tubular diseases with phosphate loss are among the main causes of hypophosphataemic OM. Serum calcium and PTH tend to be normal. Many tubular diseases present with phosphaturia and hypophosphataemia. Fanconi’s syndrome and phosphaturia, either alone or associated with glycosuria and/or aminoaciduria, are the most important [8]. X-linked hypophosphataemic vitamin D-resistant rickets presents with hypophosphataemia and phosphaturia, but it appears early after birth [8, 9].

In Fanconi’s syndrome there is a defect in the proximal tubules. The condition presents with metabolic acidosis and a combination of glycosuria, phosphaturia, aminoaciduria, hyperuricosuria and mild hypercalciuria [2]. We did not determine glycosuria, aminoaciduria and uricosuria; as a consequence, we did not have
enough data to diagnose a specific cause of the hypophosphataemia. The acidosis was thought to be due to hypoventilation as a consequence of thoracic pain.

Non-familial hypophosphataemic OM begins in adulthood and is due to renal wasting of phosphate, in isolation or with aminoaciduria, mainly glycineria, and in some cases also with glycosuria [2, 10]. The disease is usually associated with neoplasia, mainly of mesenchymal origin, normally vascular, and frequently benign [2, 10]. In some cases, however, there is no evidence of tumour even after many years [11]. The pathogenesis is unknown, but a humoral factor has been identified [12] which may favour the loss of phosphate by the kidney. In our patient a thorough examination failed to detect any neoplasia, and none has appeared after 5 yr.

In the literature, there are no studies in large series of the treatment of hypophosphataemic OM with renal loss of phosphate. Replacement is the treatment of choice when the cause is irreversible or when complete removal of the cause is not possible. The phosphate dose is variable, but usually high. However, clinical improvement can be achieved without complete correction of the biochemical or histological defect [2, 3, 11]. The addition of vitamin D is a standard practice, and its indication is clear in cases of vitamin D deficiency. When serum vitamin D or its metabolites are normal, vitamin D supplementation corrects intestinal calcium absorption and reduces the secondary hyperparathyroidism associated with phosphate treatment [13]. Phosphate and vitamin D doses must be adapted to clinical response, and to serum levels of calcium, phosphate and alkaline phosphatase [2].

OM-associated RSD is frequent but poorly understood. It may be the first, or the most important, manifestation of the OM. As in our case, the lower limbs are most frequently involved [3]. Huaux et al. [4] diagnosed RSD in five of 24 patients with OM. They observed that 66% of their patients with OM secondary to tubular defects had RSD, but only 5.5% of those in whom OM was secondary to vitamin D deficiency. The same authors indicated that the cause of RSD could be the delay in the repair of the microfractures that appear in osteomalacic bone. The chronological coincidence and the fact that treating the OM is the only way to heal the RSD suggest a close relation between the two diseases [3, 4].

Bone fractures are recognized complications of OM [1, 2]. Sometimes, they appear due to evolution of Looser pseudofractures and, in others, due to minimal trauma upon the pathological bone [1]. Pseudofractures appear in fewer than half of OM patients, and only a few of them become complete fractures, most frequently in the ribs [1]. The fracture can be the first manifestation of OM [2]. Weakness of the bone structure could be the cause of fractures in OM, as suggested elsewhere [9].

In conclusion, we present a patient with hypophosphataemic OM with a femoral fracture and, within a few months, RSD of the hips, knees and ankles which healed with rest and treatment of the OM. The femoral fracture required internal fixation.

Acknowledgement

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References