Hypophosphatemic Osteomalacia after Low-Dose Adefovir Dipivoxil Therapy for Hepatitis B

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A 40-yr-old male presented with a 5-month history of bone pain involving both knees, ankles, and several ribs with no antecedent trauma. He had an antalgic gait, tenderness involving the bony margins of both knees, but no synovitis. He had a history of chronic hepatitis B infection, receiving lamivudine at a daily dose of 100 mg for 43 months and adefovir dipivoxil (adefovir) at a daily dose of 10 mg for the past 29 months. He had been receiving tramadol hydrochloride intermittently for pain relief.

Investigations revealed a reduced serum phosphate level of 2.0 mg/dl (0.64 mmol/liter), normal serum corrected calcium of 8.8 mg/dl (2.20 mmol/liter), PTH of 39 pg/ml (4.1 pmol/liter), 25-hydroxyvitamin D_3 level of 24.4 ng/ml (61 nmol/liter), and 1,25-hydroxyvitamin D level of 57 pmol/liter. Bone-specific alkaline phosphatase was elevated at 85.4 μg/liter (normal, 3.7–20 μg/liter). The urine deoxypyridinoline/creatinine ratio was elevated at 11 nmol/mmol (normal, 2.3–5.4 nmol/mmol) with an estimated glomerular filtration rate of 60.1 ml/min.

A 24-h urinalysis demonstrated hyperphosphaturia at 1.054 g/d (34 mmol/d) [normal, 0.465–0.93 g/d (15–30 mmol/d)], hypercalciuria at 580 mg/d (14.5 mmol/d) [normal, 100–300 mg/d (2.5–7.5 mmol/d)], glycosuria, and massive aminoaciduria. The 24-h creatinine excretion was normal at 1.41 g/d (12.5 mmol/d) [normal, 1.02–2.03 g/d (9–18 mmol/d)]. Calculated maximal tubular phosphate reabsorption was reduced at 0.3% (normal, 0.8–1.3%).

Magnetic resonance imaging of both knees revealed microfractures across the femoral and tibial metaphyses (Fig. 1). A whole body bone scan showed intense uptake at the subchondral bone of both knees and several bilateral ribs (Fig. 2A).

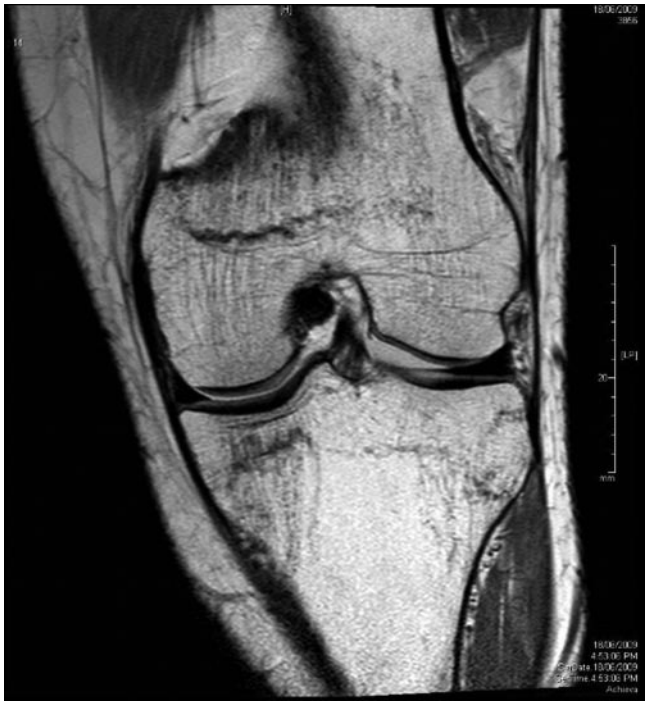

FIG. 1. Left knee coronal proton-density weighted magnetic resonance image. There are incomplete undisplaced fractures across the femoral and tibial metaphyses, consistent with recent insufficiency fractures.

The diagnosis of hypophosphatemic osteomalacia in the context of Fanconi's syndrome secondary to adefovir therapy was made. Fanconi's syndrome is a recognized complication of high-dose adefovir therapy when used in the treatment of HIV (1). However, at the time of writing, there were only two other published reports of hypophosphatemic osteomalacia after low-dose adefovir therapy (2, 3).

Fifteen weeks after cessation of adefovir and after regular phosphate supplementation, the patient reported significant improvement in his knee and other bony pain.

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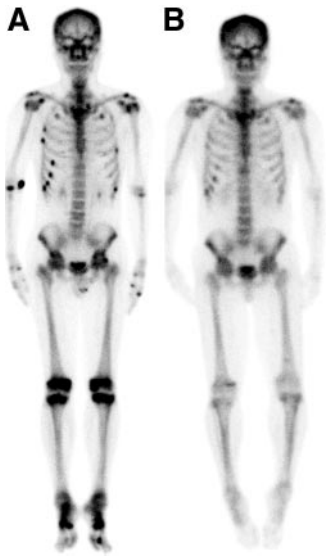

FIG. 2. An initial bone scan (A) demonstrated diffusely increased uptake throughout the skeleton particularly periorbitally consistent with metabolic bone disease. This is supported by the multiple rib fractures and unusual symmetrical uptake in a periarticular pattern in the distal femora and proximal tibiae. A follow-up scan (B) was obtained 15 wk after adefovir was ceased, and the patient receiving phosphate supplementation was compatible with near-complete resolution of the change.

This was associated with near-normalization of his serum and urine parameters (including tubular phosphate reabsorption) and a corresponding reduction in tracer uptake on a repeat bone scan (Fig. 2B).

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