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Hypophosphatemic Osteomalacia with Multiple Bone Fractures: ADV-Induced Fanconi's Syndrome

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A 50-year-old man was referred to our orthopedic clinic with a 24-month history of progressive joint pain involving both knees and ankles. He was diagnosed with chronic hepatitis B (CHB) in 2009 and has been taking adefovir dipivoxil (ADV; 10 mg/day) and entecavir (0.5 mg/day) since 2012. On physical examination, the patient was observed to have an antalgic gait and tenderness involving the bilateral rib cage, back, hips, knees, and ankles. Laboratory tests yielded the following results: dipstick urine protein, 3+ and glucose, 4+; urine pH 7.0; serum phosphate, 1.7 (2.5-4.5 mg/dL); serum total calcium, 9.1 (8.4-10.2 mg/dL); bone-specific alkaline phosphatase, 71.4 (15.0-41.3 IU/L); parathyroid hormone, 31.37 (11-62 pg/mL); 25-hydroxy vitamin D, 11.7 ng/mL; uric acid, 2.3 (3.0-8.3 mg/dL); serum creatinine, 1.10 (0.7-1.7); total CO2 content 21.4 (20-31 mmol/L) and estimated glomerular filtration rate, 77.3 mL/min/1.73 m^2; fractional excretion of phosphate and calcium, 100.62 and 4.50, respectively. A 24-hour urine sample revealed hyperphosphaturia (1,181 mg/day), hypercalciuria (495 mg/day), and proteinuria (1,531 mg/day). Magnetic resonance imaging of both knees revealed microfractures across the femoral and tibial metaphyses (Fig. 1). ^{99m}Tc-DPD (dicarboxypropane diphosphonate) bone scintigraphy revealed increased uptake in bilateral ribs, sacral bone, distal femur, and proximal tibia around the knees, upper end plate of thoracolumbar spines, tarsal bone and 5th toe of the right foot (Fig. 2). Thus, hypophosphatemic osteomalacia due to ADV-induced Fanconi's syndrome was diagnosed. After ADV cessation and phosphate supplementation, the patient reported significant improvement in his symptoms, and laboratory results and bone scintigraphy also showed improvement.

Fanconi's syndrome is characterized by inadequate reabsorption of glucose, amino acids, uric acid, phosphate, and bicarbonate in the proximal renal tubules. This syndrome is categorized as either congenital or acquired by multiple medications and chemicals.[1] ADV, an acyclic nucleotide analog of adenosine monophosphate, was approved for CHB treatment in 2002. An increasing number of studies report nephrotoxicity-inducing osteomalacia related to ADV treatment. Osteomalacia is the inadequate mineralization of bone, most commonly due to the lack of

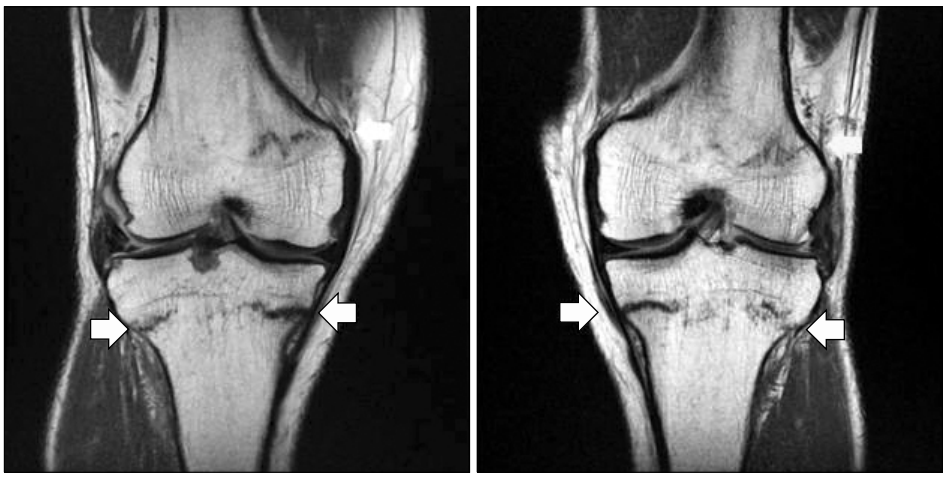

Fig. 1. Coronal T1 weighted magnetic resonance imaging of both knees. Magnetic resonance imaging scans of both knee joints show incomplete nondisplaced microfractures across the femoral and tibial metaphyses.

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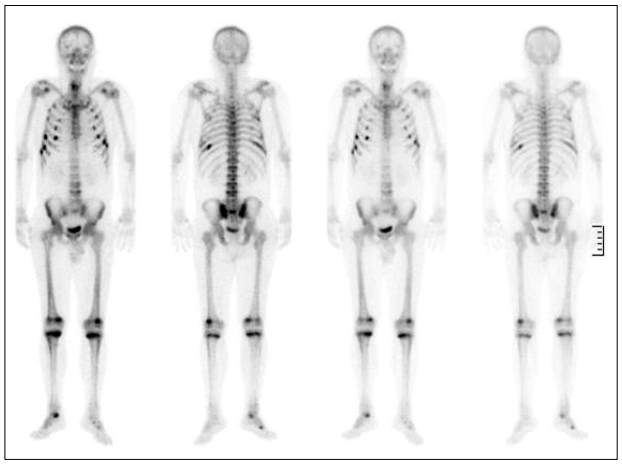

FIG. 2. ^{99m}Tc-DPD (dicarboxypropane diphosphonate) bone scintigraphy. Whole body bone scintigraphy shows increased uptake in bilateral ribs, sacral bone, distal femur, and proximal tibia around both knees, upper end plate of thoracolumbar spines, tarsal bone and 5th toe of the right foot.

vitamin D and sometimes due to phosphate deficiency. Patients with osteomalacia may be asymptomatic until a fracture occurs. Because of the insidious onset and lack of typical symptoms of Fanconi's syndrome, many patients taking low-dose ADV are not diagnosed in a timely manner until multiple fractures occur, as in our case. However, after diagnosis, ADV withdrawal and phosphate supplements can relieve pain, restore renal function, and normalize bone mineralization.[2] Therefore, physicians should be aware of this complication and monitor the urinalysis and serum phosphorus levels, particularly if the ADV treatment period is prolonged.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Izzedine H, Launay-Vacher V, Isnard-Bagnis C, Deray G. Drug-induced Fanconi's syndrome. Am J Kidney Dis 2003;41:292-309.
2. Eguchi H, Tsuruta M, Tani J, Kuwahara R, Hiromatsu Y. Hypophosphatemic osteomalacia due to drug-induced Fanconi's syndrome associated with adefovir dipivoxil treatment for hepatitis B. Intern Med 2014;53:233-7.