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Adefovir-associated Fanconi Syndrome Presenting as Repeated Multiple Pathologic Bone Fracture Due to Hypophosphatemic Osteomalacia

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Fanconi syndrome is a generalized dysfunction of the proximal renal tubule that results in impaired reabsorption and increased urinary loss of phosphate and other solutes, such as uric acid, glucose, amino acids, and bicarbonate. Chronic hypophosphatemia may cause osteomalacia, a bone metabolic disease makes the softening of bone induced by defective mineralization of bone, deficiency of available phosphorus and calcium, or overactive resorption of calcium from bones and may have a heterogeneous presentation, ranging from mild muscle weakness and skeletal pain to disabling myopathy, severe bone and joint pain, and bone fractures. The note is that hypophosphatemia, which is one of reasons that cause osteomalacia, is induced by using of adefovir. However, there have been only few case reports. A 35-year old women was presented with progressive multiple bone pain and proteinuria. She has taken adefovir 10 mg/day and lamivudine 100 mg/day since 2005 for chronic hepatitis B. Three years ago, she had an operation for non-traumatic right femur neck fracture. At that time, multiple hot uptake was also shown in knee joints, ribs, and pelvis on 99mTc bone scan. On blood laboratory testing, glucose 80 mg/dl, creatinine was 0.9 mg/dl, potassium 3.8 mEl/l, phosphate 1.5 mg/dl, calcium 9.0 mg/dl, uric acid 1.5 mg/dl, alkaline phosphatase 332 IU/l, intact parathyroid hormone 42.66 pg/ml, 25-OH vitamin D 19.4 ng/ml. ACTH, cortisol, Free T4, TSH, magnesium, aluminium, LH/FSH, E2 were within normal limit. Non-anion gap acidosis and positive urine anion gap were noted. Urinalysis showed a pH of 7.0, protein(+), glucose(+) and b2-microglobulin was 22796.67 ng/ml. At 24-hour urine, it showed glucose 1839.0 mg/day, phosphorus 1305 mg/day, calcium 437 mg/day, protein 309 mg/day, creatinine 846 mg/day, and generalized non-specific hyperaminoaciduria. The tubular resorption of phosphate/GFR was lower than 2 mg/dl, calculated by TmP/GFR, suggesting renal phosphate wasting. Therefore, a diagnosis of adefovir-associated Fanconi syndrome presenting as repeated bone pain and multiple pathologic bone fracture due to hypophosphatemic osteomalacia was made. Adefovir and lamivudine were replaced with entecavir, and a regimen of phosphate and caicitriol was started. After 2 months of treatment, serum phosphate was markedly increased (3 mg/dl) and the patient's bone pain was markedly improved and she was able to perform daily activities and could walk again without using a wheel chair.

Key Words: Adefovir, Fanconi