Osteomalacia and Fanconi syndrome development in Caucasian hepatitis B virus (HBV)-related cirrhosis patient receiving long-time adefovir dipivoxil

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Adefovir dipivoxil is a nucleotide analog reverse transcriptase inhibitor approved to treat adult patients affected by HBeAg-positive and HBeAg-negative chronic hepatitis B and with clinical evidence of lamivudine-resistant hepatitis B virus (HBV) (Peters et al., 2004; Perrillo et al., 2004) as add-on. Adefovir administered at common dosage of 10 mg/day is generally well tolerated and does not cause alterations in creatinine clearance compared to placebo (Marcellin et al., 2003;Hadziyannis et al., 2003). However, a long-time treatment can result in an increase in serum creatinine (Marcellin et al., 2008; Hadziyannis et al., 2006), in the development of renal toxicity (Ha et al., 2009) or in the development Fanconi Syndrome and hypophosphatemic osteomalacia (Wu et al., 2013) associated with muscular weakness 4 years after the beginning of adefovir. We report a case of osteomalacia with Fanconi syndrome and pathologic fracture of the femur related to long-time (67 months) adefovir treatment (10 mg/day) in a 55-year-old man with compensated hepatitis B virus (HBV) cirrhosis (Child 5A) and with a previous normal renal function (estimated Glomerular Filtration Rate before adefovir=78.26 ml/min/1.73 m2; during adefovir treatment=57.38 ml/min/1.73 m2). The patient lamented bone pain, muscle cramps, and asthenia. Biochemical evaluation revealed high levels of serum creatinine, phosphate, alkaline phosphatase and parathyroid hormone level, and low levels of creatinine clearance, phosphorus and potassium. Urinalysis showed high levels of proteins, glucose, potassium, calcium, and phosphate. Cervical, dorsal and lumbosacral spine X-ray showed extensive demineralization of the bones; dual-energy X-ray absorptiometry (DXA) at all sites confirmed a low bone max density. The kidney biopsy showed diffuse and severe tubulointerstitial nephritis with dense lymphoplasmocyte infiltrates. A diagnosis of Fanconi syndrome with hypophosphatemic osteomalacia was postulated and using the Narangio probability scale (Naranjo et al., 1981) we documented a possible association between adefovir and proximal tubulopathy (score=7). Adefovir was dismissed. The patient was switched to entecavir at a dose of 1 mg/day, with suppression of viremia and improvement of osteomalacia and Fanconi syndrome without the development of side effects; is currently being 28 months of follow-up.

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