Multiple vertebral fractures in HIV-infected patient: case report and differential diagnosis

Academic author: **Thiago Quadrante Freitas**

Academic advisor: **André Silva Franco, Camila Nobre Bulhões, Rosa Maria Rodrigues Pereira**

VP, a 45 year-old patient treating for HIV since 1994, was referred to the Rheumatology Division by the Infectious Diseases Department in 2010 due to a history of decrease in height, diffuse bone pain, and low bone mineral density (BMD). The HIV infection was diagnosed 20 years earlier and had been treated with tenofovir, atazanavir, and lamivudine/ritonavir since 1994. He developed several comorbidities, including dyslipidemia, polyneuropathy, and right hip osteonecrosis.

He presented with diffuse bone pain despite heavy analgesia, important height loss (previously 183 cm to 169 cm in 2010), and low BMD in bone densitometry (February/2010: femur Z-score: -1.9; L1-L4 Z-score: -2.2). Physical examination was unremarkable, apart from significant kyphosis and scoliosis. Cervical, thoracic and lumbar spines radiographs confirmed such alterations and showed multiple vertebral fractures. Laboratory workup (February/2010) showed total calcium 9mg/dl (reference values[RV]: 8.6-10.2), phosphorus 1.2 mg/dl (RV: 2.7-4.5), vitamin D 13ng/dl (RV: 30-100), PTH 96pg/ml (RV: 16-87), alkaline phosphatase 403U/l (RV: 35-104), gamma-GT 32U/l (RV: 5-36), creatinine 1,19mg/dl (RV: 0.7-1.2). Additionally, a whole-body bone scintigraphy demonstrated increased activity in shoulders, sternum, ribs, thoracic spine, sacroiliac joints, and eight other spots.

Bone impairment is well described in people living with HIV and taking antiretrovirals due to direct and indirect effects of both the virus and the medications on bone and immune cells. This report aims to present a differential diagnosis to such classical bone loss mechanism and its treatment, since inadequate therapy could lead to clinical worsening.

At first, for this patient, osteoporosis secondary to HIV, antiretroviral therapy and/or low dietary calcium intake were the main hypotheses. Nonetheless, laboratory analysis discarded such diagnoses since he presented with normocalcemia, hypophosphatemia and high alkaline phosphatase, besides low BMD, all compatible with hypophosphatemic osteomalacia, which could be due to phosphate loss or malabsorption. Urinary testing revealed pH 8 (RV: 5-6), and 24-hour phosphaturia 2550mg/24h (RV: 400-1300); with a venous gasometry demonstrating pH 7.33 (RV: 7.35-7.45), pCO2 55mmHg (RV: 35-45), bicarbonate 28.7mmol/L (RV: 23-27), sodium 138mEq/L (RV: 135-145), and chloride 108mEq/L (RV: 98-107), directing the diagnosis towards proximal renal tubular acidosis induced by tenofovir.

Tenofovir-induced tubule dysfunctions have an estimated prevalence of 17% in HIV-infected patients on tenofovir, and may appear years after treatment initiation. Approximately 0.5% develop hypophosphatemic osteomalacia, especially if its use is concomitant with ritonavir-boosted protease inhibitors and non-steroidal anti-inflammatories. The most common clinical finding is diffuse bone pain due to multiple stress fractures, and should be suspected by the presented laboratory findings, that rule out osteoporosis, preventing wrong treatment with bisphosphonates, which depletes even more phosphorus, leaving no substrate with which to mineralize the bone, worsening pain and fractures.

This patient was treated with phosphorus, vitamin D and bicarbonate supplementation, besides tenofovir discontinuation. Following, bone densitometries from 2012, 2015 and 2016 showed a femur Z-score of -0.1; 0.8 and 0.8, respectively, with normalization of phosphatemia (2.7mg/dl), phosphaturia (1100mg/24h), and alkaline phosphatase (75U/l), besides pain relief and no new fractures.

Therefore, clinicians should be alert to hypophosphatemic osteomalacia in patients with low BMD receiving tenofovir, since it can be easily mistaken and incorrectly treated as osteoporosis, worsening bone pain, fractures and hypophosphatemia.

Keywords: Bone mineral density; HIV; Osteoporosis.