

Navigating Tenofovir-Associated Osteoporosis: Lessons from a Case Study

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ABSTRACT

Tenofovir Disoproxil Fumarate (TDF) is one of the drugs in the initial first-line antiretroviral regimen for the treatment of HIV infections with a rare side effect of bone toxicity. We describe a case of an HIV-positive man who had been using TDF for 9 years and had presented to the emergency room with multiple fractures. The bone fracture investigation identified reduced bone mineral density and severe osteoporosis. TDF was discontinued, and treatment was focused on controlling the bone disease through vitamin D and calcium supplementation. After the new treatment regimen, the patient exhibited a slow improvement in his bone mass density (BMD). Long-term follow-up is still required to assess subsequent changes in BMD and fracture healing. This abstract provides a concise overview of the mechanisms underlying tenofovir-induced bone loss and highlights current management strategies.

Keywords: Tenofovir Disoproxil Fumarate; Drugs; HIV

INTRODUCTION

Case: 54 White M with a past medical history of Anxiety, Depression, Migraine with aura, varicella, and HIV on efavirenz-emtricitabine-tenofovir (ATRIPLA) 600-200-300 mg daily. The patient was on Atripla for nine years, following which he presented to the hospital with right-sided hip pain after a trivial fall while getting out of the car and was found to have a femoral neck fracture on X-Ray, which was fixed with open reduction and internal fixation with IM nail. The younger age of presentation prompted further evaluation with DEXA scan, which showed osteoporosis in the lumbar spine and the femoral neck. His PTH, Vitamin D, and Ca levels were within appreciative limits. All secondary causes of osteoporosis were rule out and further evaluation suggested that osteoporosis could be secondary to HIV medication, and his Atripla was then changed to abacavir, dolutegravir, and lamivudine(Triumeq), along with Fosfomax, Vitamin D, and calcium supplements. After a brief period, he stopped taking medication due to fear of osteonecrosis, following which DEXA showed stable osteoporosis

without improvement. Later, the patient was switched to Forteo for another year and was restarted on Fosamax weekly doses with Vitamin D and Ca supplements. Recently updated DEXA showed significant improvement in BMD in the spine and the hip and has been compliant with once-weekly dosing and monitoring with a DEXA scan every 24 months.

DISCUSSION

Nucleoside reverse transcriptase inhibitors (NRTIs) represent the foundation of highly active antiretroviral therapy (HAART). Tenofovir is a nucleotide analog and was granted approval in 2001 for HIV treatment and, more recently, for chronic hepatitis B infection as well[1]. Despite its success, there have been clinical reports of tenofovir-associated side effects such as bone loss.

Data implicating TDF exposure in bone pathology are limited [4]. Some prior research indicates simultaneous inhibition of osteoblast and stimulation of osteoclast activity, leading to bone loss and osteoporosis. It can additionally cause proximal renal tubular dysfunction leading to hypophosphatemia due to phosphate wasting [3], and calcium abnormalities that can disrupt bone mineralization and contribute to osteoporosis as well as secondary hyperparathyroidism, further exacerbating bone loss[7]. Tenofovir has been associated with mitochondrial toxicity, which can impair cellular function, including in bone cells, interfering with normal bone metabolism, and contributing to osteoporosis[2].

Tarantal et al. proposed that persistent prenatal and postnatal tenofovir can affect bone metabolism in some animals[6]. Other studies (McComsey et al., 2011; Stellbrink et al., 2010; Haskelberg et al., 2012) suggested osteopenia and osteoporosis are more detected with TDF regimens than abacavir/lamivudine. Fractures mainly involved the femoral neck, in comparison to protease inhibitors (PIs), which involved lumbar spine (Duvivier et al., 2009)[5]. The BMD loss caused by TDF is mostly reversible, as demonstrated in several switch studies[9]. Tenofovir alafenamide (TAF), another improved tenofovir formulation, is associated with less side effects related to bone and kidneys than TDF. Transitioning from TDF-containing regimens to TAF-containing regimens has been found to improve bone mineral density without compromising viral suppression.[8]

Our case emphasizes the importance of physicians anticipating and appropriately managing the adverse effects of TDF on bone, which involves calcium and vitamin D supplements, regular monitoring of BMD, lifestyle modifications, and consideration of alternative antiretrovirals with a more favorable bone safety profile. Vitamin D and calcium supplements have been shown to increase BMD by 1.73% at the total hip and 0.78% at the lumbar spine in HIV patients on ART [11]. For patients with an increased risk of fractures, bisphosphonates have been found to increase BMD at the lumbar spine by 2.84% and total hip by 2.12% after using for 48 weeks.[12]

CONCLUSION

Healthcare practitioners prescribing regimens that include tenofovir should remain vigilant for indications of bone demineralization and osteoporosis. We intend to encourage a proactive approach by employing preventative measures and therapeutic interventions to mitigate the heightened risk of fractures within this susceptible

demographic. Moreover, additional research is required to elucidate optimal management strategies and ascertain long-term skeletal outcomes in individuals exposed to tenofovir therapy.

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