

# Tenofovir Induced Bilateral Femoral Neck Stress Fracture

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**Abstract:- Case:** A 47 year old male, came with history of bilateral hip pain ,insidious in onset gradually progressive, with difficulty in walking unassisted since 2 years. No history of fall/ trauma. Patient is known case of retroviral disease and on ART (TLE regimen ) since 2 years. Relevant radiographs were done and was diagnosed with bilateral neck of femur stress fracture (Tenofovir induced) associated with hypophosphatemia. ART regimen was changed to (Abacavir ,Lamivudine , Dolutegravir) . Patient on regular follow up every 2 months with serial radiographs. . On 6 months follow up patient is symptomatically improved with healing bilateral neck of femur stress fracture.

**Keywords:-** Tenofovir, Stress Fracture , ART.

## I. INTRODUCTION

The global pandemic sickness known as the human immunodeficiency virus. HIV-related osteoporosis has a complex pathogenesis. Main processes are believed to involve HIV-associated variables like systemic inflammation, viral impact, and antiretroviral regimen side effects<sup>[7]</sup>. Osteoclast activation may result from persistent systemic inflammation and increased levels of pro-inflammatory cytokines like interleukin-1 and interleukin-6<sup>[8]</sup>. The functions of osteoblastic cells may be disrupted not only by systemic inflammation but also by the direct harmful effects of some viral proteins.<sup>[1]</sup> Tenofovir disoproxil fumarate (TDF) is regarded as a first-line medication for the treatment of HIV infections in humans.TDF, an acyclic nucleotide derivative of adenosine monophosphate, has shown promise as an antiretroviral medication. HIV-positive persons have been shown to experience faster bone loss as well as increased incidences of osteopenia and osteoporosis<sup>[2,3]</sup>. It has also been demonstrated that HIV-positive patients had greater rates of osteoporotic fractures than age-matched controls<sup>[4,5]</sup>. Compared to other antiretroviral medications, tenofovir has

been observed to be linked to a higher decrease in bone mineral density (BMD)<sup>[6]</sup>

## II. CASE

The orthopedic outpatient department received a complaint from a 47-year-old male patient who appeared normal two years prior. The patient complained of bilateral hip pain that started off as a dull aching pain, gradually progressed, non radiating type, got worse with prolonged walking, and got slightly better with rest. The patient found it difficult to walk on his own. An x-ray of the pelvis during the radiological examination revealed a compression fracture of the medial and lateral cortex of the femoral neck. It also displayed osteoporotic signs. After undergoing magnetic resonance imaging of pelvis, the patient's bilateral neck of femur was found to have a linear, undisplaced fracture.

The patient was subsequently sent to the endocrinology team for a follow-up assessment of the bilateral neck stress fracture of the femur. The patient had pulmonary tuberculosis in the past.

And received a full course of treatment with category 2 anti-TB drugs. The patient has been receiving antiretroviral medication (a combination of Tenofovir, Lamivudine, and Efavirenz) with high adherence since receiving their HIV diagnosis years ago. He was suspected of having stress fractures in both of his neck of femur and osteoporosis brought on by tenofovir. Serum phosphorus was 1.61 (2.7–4.5 mg/dl), serum calcium was 8.49 mg/dl, and alkaline phosphatase was high at 616 IU (40–129 IU/L) on routine tests. There was 56.48 ng/ml of 25-hydroxy vitamin D (20-47 ng/ml). The range of the serum creatinine was 0.7–1.3 mg/dl. Phosphorous urine: 343 mg/24 hours (400–1300 mg/24 hours). 851.4 mg/24 hours of urine creatinine (1040–2350 mg/24 hours). A diagnosis of persistent hypophosphatemia was made for the patient.



Fig 1: MRI of Pelvis Showing Bilateral Femoral Stress Fracture

As tenofovir was the causative agent for the bilateral femoral stress fracture, tenofovir was stopped due to its potential role as an inciting agent for the patient's condition. The new antiretroviral regimen consists of Abacavir, Lamivudine, and Efavirenz. The patient is receiving calcium, cholecalciferol (vitamin D), and phosphorus supplements to support bone health. The patient's symptoms have improved, allowing them to walk independently without a walker. This indicates functional improvement and likely reduction in pain. Calcium, phosphorus, and alkaline phosphatase levels have improved over follow-up visits. This suggests better

bone metabolism and healing. Serial repeat X-rays have shown healing of stress fractures. There is also noted cortical thickening and endosteal sclerosis of both femoral necks, indicating ongoing repair and strengthening of bone structure.

Overall, the combination of medication change, appropriate supplementation, and regular follow-up has contributed to clinical and radiological improvement in the patient's condition. Regular monitoring and continued management will be crucial to ensure sustained progress and bone health.

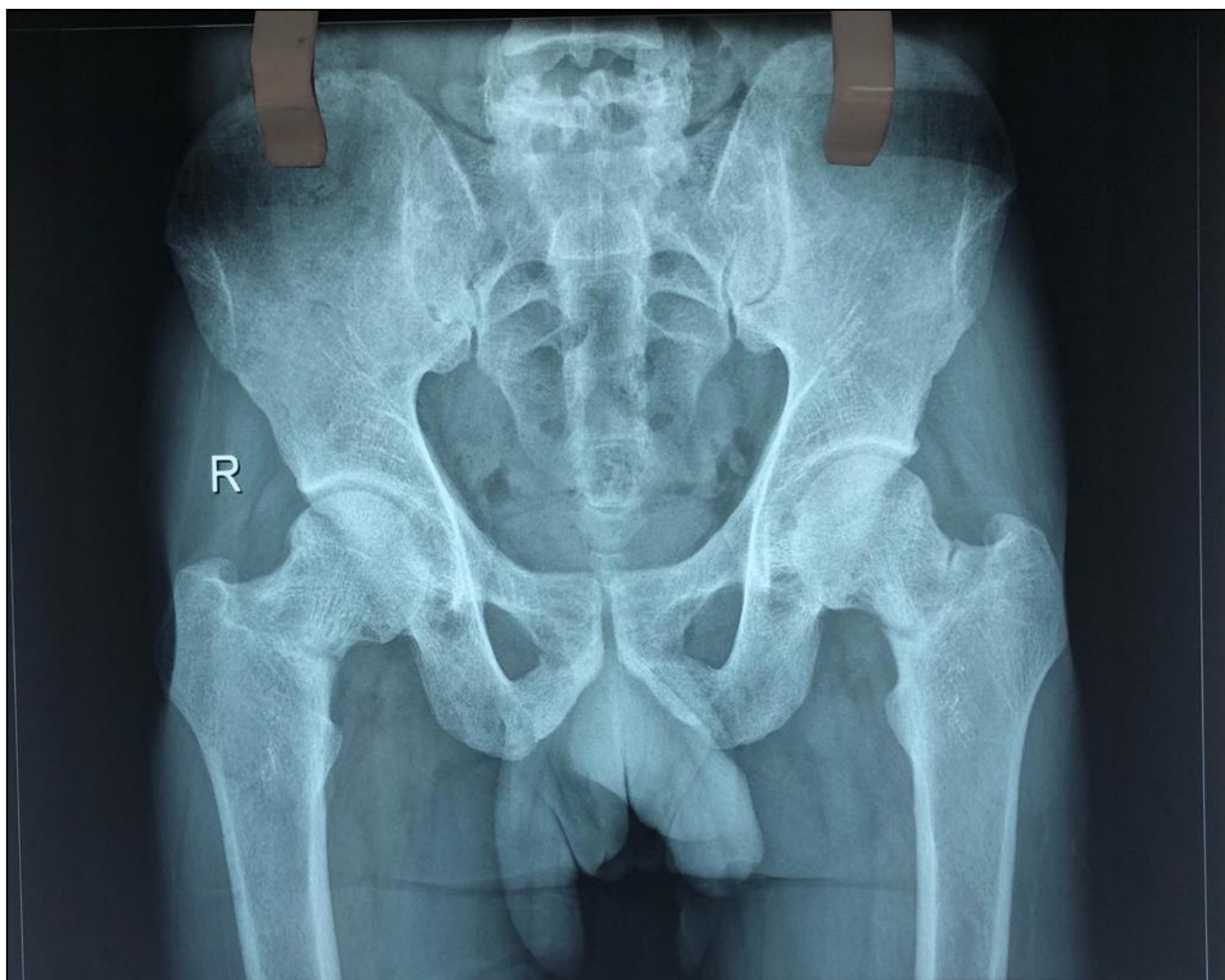


Fig 2: Xray Pelvis with Both Hip AP with Cortical Break in Neck of Femur

### III. DISCUSSION

Stress fractures of the femoral neck in young individuals are indeed rare but can occur, especially in certain conditions such as in HIV-infected patients on antiretroviral therapy (ART). Studies have shown a higher prevalence of osteopenia (reduced bone density) in HIV-infected individuals, which may be exacerbated by factors including the virus itself, ART medications, and lifestyle factors. The exact mechanism is not fully understood but is believed to involve a combination of direct effects of ART on bone metabolism, immune system dysregulation, chronic inflammation, and other factors. This can lead to bone demineralization and increased risk of fractures. Stress fractures in young people often result from repetitive mechanical stress on normal bone architecture, causing microdamage. In the case of femoral neck stress fractures, this can lead to weakened bone structure and microfractures, which, if not diagnosed and managed promptly, may progress to complete fractures. Stress fractures can be challenging to diagnose early due to their often subtle symptoms and lack of a history of significant trauma. Incomplete stress fractures of the femoral neck can be particularly difficult to detect on plain X-rays. This

delayed diagnosis is compounded by their rarity and low suspicion by healthcare providers.

Patients may not present with acute pain or a clear history of injury, which can delay diagnosis. In HIV-infected individuals, symptoms might be attributed to other causes related to their condition or treatment. Once diagnosed, management typically involves rest, modification of activities, and possibly surgical intervention depending on the severity of the fracture. In the context of HIV, optimizing antiretroviral therapy and managing comorbidities are also crucial aspects of treatment to support bone health.

Stress fractures of the femoral neck are rare in young individuals but can occur, particularly in conditions like HIV infection where bone health may be compromised. It's crucial to maintain vigilance in clinical assessment and consider atypical presentations for timely diagnosis and effective management. Various coexisting conditions such as metastatic disease, metabolic disorders, and infections like hepatitis B and C, severe renal impairment, inflammatory arthritis, adrenal insufficiency, corticosteroid excess, alcohol abuse, and vitamin D deficiency can contribute to weakened bones and predispose to stress fractures. However, in the

presented case, these conditions were ruled out through laboratory investigations and patient assessment. Stress fractures can also occur in osteoporotic bones, which are typically associated with conditions like postmenopausal or senile osteoporosis. While osteoporosis is more common in the elderly due to decreased bone mass, recent evidence suggests that HIV infection and certain ART medications, such as Tenofovir and protease inhibitors, can contribute to osteopenia, osteoporosis, and occasionally osteonecrosis of the femoral head in younger individuals. Diagnosing osteopenia and osteoporosis in HIV-infected patients often involves radiographic assessment with tools like Singh's Index. Ideally, bone mineral density measurements and tools like FRAX (Fracture Risk Assessment Tool) would provide more comprehensive evaluation and risk assessment.

In summary, understanding the etiopathophysiology of HIV/ART-induced secondary osteoporosis is critical in managing bone health in these patients. Continued research and clinical vigilance are essential to improve diagnostic accuracy and therapeutic outcomes in cases of femoral neck stress fractures associated with HIV infection or ART.

#### IV. CONCLUSION

This case highlights the long term treatment of tenofovir intake with secondary changes in the renal parameters leading to the osteopenia. Early identification and proper clinical history and examination will help us to diagnose the disease and early withdrawal of the tenofovir will prevent the fragility fractures and channelizes us to the proper treatment strategy.

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