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Case Report

Idiopathic Bilateral HIV-Associated Osteonecrosis of the Femoral Heads: A Case Report

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Abstract

Background: Avascular necrosis (osteonecrosis) is an increasingly recognized complication in patients living with HIV, particularly when weight-bearing joints such as the hip are involved. Although previously attributed primarily to antiretroviral therapy, HIV infection itself may be an independent risk factor.

Case Report: A 33-year-old woman with HIV infection diagnosed three years earlier presented with an eight-month history of progressively worsening bilateral hip pain, eventually resulting in an inability to ambulate without assistance. Clinical examination was suggestive of avascular necrosis, which was confirmed by bilateral hip radiographs and magnetic resonance imaging, demonstrating Steinberg Stage IV disease. There was no history of other recognized causes of osteonecrosis. She was compliant with highly active antiretroviral therapy (HAART) consisting of tenofovir, emtricitabine, and efavirenz. The advanced disease at presentation suggests that osteonecrosis may have developed substantially earlier than expected in the course of her HIV infection.

Conclusion: Although HAART may be associated with avascular necrosis, HIV infection itself may represent an independent risk factor. This case highlights that severe osteonecrosis may develop early in the course of HIV infection, emphasizing the importance of early recognition of musculoskeletal symptoms in these patients.

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Introduction

Osteonecrosis is increasingly recognized as a debilitating complication among patients with HIV infection. Individuals with HIV are reported to have a 45- to 100-fold greater risk of developing osteonecrosis than the general population.^{3,4} In addition to the conventional risk factors observed in the general population, other factors associated with osteonecrosis in HIV-infected patients include intravenous drug use, corticosteroid therapy (typically prescribed for concomitant medical conditions), multiple sexual partners, excessive alcohol consumption, and highly active antiretroviral therapy (HAART). The use of protease inhibitors (PIs) has, over the years, been associated with several bone-related complications, particularly osteoporosis and drug-induced fractures.⁵ However, these complications generally occur only after prolonged adherence to HAART. Even if HIV infection

itself is considered an independent risk factor for avascular necrosis, as suggested by several authors^{4,6,7}, clinical manifestations typically develop several years after the initial diagnosis of HIV infection.

Our case is unique because, based on the Steinberg classification^{2,8}, osteonecrosis appears to have developed much earlier than anticipated, despite the absence of the conventional risk factors commonly associated with its development in HIV-infected individuals.

Case Report

We report the case of a 33-year-old woman with a three-year history of HIV infection. She had been receiving a daily regimen of tenofovir 300 mg, emtricitabine 200 mg, and efavirenz 600 mg with good treatment adherence. She denied any history of illicit drug use, multiple sexual

partners, corticosteroid use, alcohol consumption, or smoking. Approximately 2.5 years after her HIV diagnosis, she developed progressively worsening bilateral hip pain over an eight-month period, which eventually rendered her unable to ambulate without assistance

She had no history of opportunistic infections, including *Pneumocystis carinii* pneumonia, and had never received treatment for any opportunistic infection. There was no history of preceding trauma, and she was employed as a production line factory worker. Her family and psychosocial histories were otherwise unremarkable.

On examination, the patient was a lean woman with an estimated body mass index (BMI) of 18.6 kg/m². There were no clinical signs suggestive of underlying opportunistic infection. Both hip joints were tender on palpation, with a reduced range of motion, particularly during internal rotation and adduction. Neurological examination of both lower limbs was unremarkable.

Plain radiographs of the pelvis demonstrated sclerosis and flattening of both femoral heads, consistent with at least Steinberg Stage IV osteonecrosis (Figure 1). These findings were confirmed by magnetic resonance imaging (MRI), which also demonstrated narrowing of both hip joint spaces and mild bilateral hip joint effusions, consistent with bilateral femoral head osteonecrosis (Figure 2).

The results of the patient's laboratory investigations are summarized in Table 1. Notably, she had a subnormal CD4 cell count with an undetectable HIV viral load. Renal and liver function tests were within normal limits. Screening for antiphospholipid antibodies is not routinely performed at our institution and was therefore not undertaken.

The patient was treated conservatively with oral tramadol for pain control and was referred for physiotherapy. Her HAART regimen was subsequently changed to Combivir (lamivudine/zidovudine) and efavirenz. She remains under close clinical surveillance for further deterioration of her hip disease, and surgical intervention is being planned. At the time of writing, her condition remains stable, and she continues to receive conservative management consisting of physiotherapy and oral analgesia.

Discussion

Osteonecrosis of the hip can have devastating consequences, frequently resulting in the need for surgical intervention, with its associated risks and long-term functional implications. It is a well-recognized complication of various traumatic injuries to the hip, including femoral neck and femoral head fractures, hip dislocations, and acetabular fractures. However, osteonecrosis may also develop insidiously in association with numerous atraumatic conditions, one of which appears to be HIV infection.

The majority of osteonecrosis cases reported in patients

with HIV are associated with one or more recognized risk factors. Several studies have demonstrated this association through long-term follow-up of HIV-infected patients presenting with hip pain. Whitlock et al. reviewed 15 HIV-infected patients with osteonecrosis and compared them with 15 unmatched controls, reporting that 80% of affected patients had at least one established risk factor similar to those observed in the general population, including dyslipidaemia, corticosteroid use, smoking, and alcohol consumption.⁹ Comparable findings were reported by Borges et al., who additionally identified previous osteonecrosis or fractures and HIV-defining illnesses as independent risk factors.⁴ Across published studies, the most frequently reported risk factors for osteonecrosis include smoking, excessive alcohol consumption, and corticosteroid use.^{3,4,7,10}

Interestingly, several authors have also described patients who developed osteonecrosis without any identifiable predisposing risk factors, a condition referred to as primary HIV-associated osteonecrosis.¹¹ In a review of 22 HIV-infected patients with osteonecrosis, Mehta et al. found that no predisposing factors could be identified in 9% of cases.⁶ Similarly, Whitlock et al. reported that 20% of their patients had no discernible risk factors.⁹ These observations have led some investigators to propose that HIV infection itself may represent an independent risk factor for osteonecrosis.^{6,7}

Our patient closely resembles this subgroup. She reported having only a single sexual partner and denied smoking, alcohol consumption, illicit drug use, corticosteroid exposure, and other lifestyle factors known to predispose to osteonecrosis. Throughout the course of her HIV infection, there had also been no indication for corticosteroid therapy or treatment of opportunistic infections that might have contributed to the development of osteonecrosis.

Since her HIV diagnosis, the patient had been treated exclusively with nucleoside and nucleotide reverse transcriptase inhibitors together with a non-nucleoside reverse transcriptase inhibitor. Although tenofovir has been suggested to be associated with osteonecrosis in some reports, this relationship has not been consistently demonstrated after adjustment for other confounding factors.^{4,10,12} Furthermore, osteonecrosis is not listed as a recognized adverse effect in the manufacturer's prescribing information or in the HIV treatment guidelines reviewed.^{13–15} The principal skeletal adverse effects associated with tenofovir are reduced bone mineral density, osteoporotic fractures, and disturbances of calcium metabolism secondary to proximal renal tubular dysfunction and Fanconi syndrome. None of these complications were evident clinically or biochemically in our patient. Likewise, emtricitabine and efavirenz have not been implicated as causes of osteonecrosis.^{14,15} In contrast, protease inhibitors have been more consistently associated with osteonecrosis, possibly through the development

of dyslipidaemia resulting from altered triglyceride and cholesterol metabolism.^{5,7} Importantly, protease inhibitors were not included in our patient's antiretroviral regimen.

Another noteworthy aspect of this case is the unusually early onset of osteonecrosis. At presentation, radiographic and MRI findings demonstrated at least Steinberg Stage IV disease following only eight months of progressively

individuals.

Despite extensive clinical evaluation, we were unable to identify a definitive aetiology for the development of osteonecrosis in this patient. Consequently, this case is most consistent with idiopathic primary HIV-associated osteonecrosis, as previously described by Green et al.¹¹

Table 1. Table of blood investigations upon admission

Investigation	Value
CD4	323 cells/mm ³
Viral load	Undetected
Haemoglobin	12.6g/dL
Total white cell count	5.9 x 10 ⁹ /L
Platelet count	230 x 10 ³ /μL
Urea/ Sodium/Potassium/Chloride	2.2/139/3.9/56 mmol/L
Calcium/Phosphate/Magnesium	2.14/1.08/0.59 mmol/L
International Normalized Ratio	1.03
Total protein/Albumin/Globulin	69/33/36 g/L
ALP/ALT/AST/Bilirubin	74/7.7/23 U/L /6.0 μmol/L

Conclusion

In conclusion, this patient represents a case of primary HIV-associated osteonecrosis as described by Green et al.¹¹ The absence of conventional predisposing factors makes early recognition particularly challenging. Furthermore, the unusually early onset and advanced stage of disease at presentation suggest that osteonecrosis may develop much earlier in the course of HIV infection than has traditionally been recognized. This case highlights the importance of maintaining a high index of suspicion for osteonecrosis in HIV-infected patients presenting with persistent hip pain, even in the absence of established risk factors. It also serves as a reminder that HIV infection should be considered as a potential underlying diagnosis in patients presenting with apparently idiopathic osteonecrosis, particularly when surgical intervention is being contemplated.

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CONFLICT OF INTEREST

No conflict of interest is reported.

INFORMED CONSENT

Informed consent from the patient was obtained for case report publication.

ETHICAL APPROVAL

Approval for case report applied and approved by hospital



Figure 1: Pelvic AP radiograph showing bilateral femoral head sclerosis and flattening of both femoral heads. Findings are similarly seen on MRI examination which additionally shows reduced joint space in both hips.

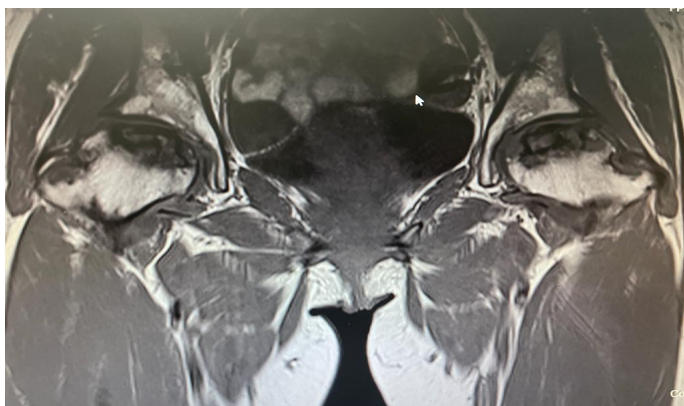


Figure 2: T2 image of both hips showing evidence of avascular necrosis bilaterally showing reduction in both hip joint spaces with mild bilateral hip joint effusions.

worsening bilateral hip pain. It is therefore reasonable to infer that the osteonecrotic process had begun approximately two to two-and-a-half years after the diagnosis of HIV infection. This timeline is considerably shorter than that reported in the literature. Mehta et al. reported a median interval of approximately 13.5 years between HIV diagnosis and the development of clinically apparent osteonecrosis, irrespective of the presence of predisposing risk factors.⁶ Similarly, Lawson-Ayayi et al. reported a mean interval of 10.4 years in the French Aquitaine cohort.¹⁰ Our patient's presentation therefore suggests that osteonecrosis may occasionally develop much earlier than is generally anticipated in HIV-infected

committee

AUTHORS CONTRIBUTION

TM – concept, data acquisition

Z-N ZF – literature review, manuscript writing

Organization;

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