CASE REPORT

Avascular necrosis: a growing concern for the HIV population

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SUMMARY

A 33-year-old woman with history of HIV presented with 4 months of gradually progressing right hip pain and was found to have avascular necrosis (AVN) of both femoral heads. She had no other risk factors for AVN including sickle cell disease, systemic lupus erythematosus, prolonged steroid use or trauma. She initially failed conservative management and ultimately had bilateral hip core decompressions. After decompression therapy, the left femoral head collapsed and patient underwent a left total hip arthroplasty. Her postsurgical course was complicated by the left sciatic nerve neuropathy for which she is currently being managed with duloxetine. She has yet to follow-up with her orthopaedic surgeon for further evaluation.

2 AVN. Follow-up MRI revealed moderate effusion, reactive marrow oedema and mild flattening of the articular surface consistent with stage 3 disease ([figure 1](#)). She failed medical management including anti-inflammatories, narcotics, walker and physical therapy. She subsequently underwent bilateral hip core decompressions; however, follow-up imaging showed that the left femoral head ultimately collapsed, and the right hip had evidence of partial collapse. She ultimately underwent left total hip arthroplasty with the use of cemented prosthesis. No record of preoperative or postoperative hip score was documented. Nonetheless, significant improvement in her symptoms was noted after surgery and physical rehabilitation.

BACKGROUND

The importance of our case is to highlight the correlation between HIV as a lone risk factor for development of avascular necrosis (AVN) especially in polyarticular cases.

CASE PRESENTATION

A 33-year-old woman with history of HIV presented with 4 months of gradually progressing bilateral hip pain. Pain was sharp in nature, exacerbated with movement, present at rest and at night. She endorsed worsening hip pain and decreased range of motion further requiring crutches to ambulate. She denied fevers, cough, night sweats, weight loss, alcohol use, prolonged exogenous glucocorticoid use, hormonal therapy and trauma. Bilateral inguinal tenderness and a positive flexion, abduction and external rotation test were elicited in both hips on physical examination.

At the time of evaluation, her absolute CD4 count was 335 cells/ μ L (normal range: 490–1740 cells/ μ L) or stage 2 (chronic, asymptomatic) HIV infection. HIV viral load was 4690 copies/mL. HIV regimen included lamivudine-zidovudine, dolutegravir and darunavir boosted with ritonavir. Virological failure was attributed to poor medication adherence. Complete blood count and basic metabolic panel were unremarkable. Serum lipid panel had no evidence of hypertriglyceridaemia or hypercholesterolaemia. Purified protein derivative test for tuberculosis was negative. C-reactive protein was 26.9 mg/L and erythrocyte sedimentation rate was 67 mm/hour. X-ray of the hips revealed linear sclerosis within both femoral heads, consistent with grade

INVESTIGATIONS

- X-ray hip.
- MRI hip.

TREATMENT

- Bilateral hip core decompressions.
- Left hip total arthroplasty.

OUTCOME AND FOLLOW-UP

After our patient underwent left total hip arthroplasty, ambulation improved with physical therapy as an outpatient. However, after discharge, she developed left sciatic neuropathy which was managed with duloxetine after failing therapy with gabapentin.

DISCUSSION

AVN symptoms are non-specific, with mild to moderate periarticular pain elicited by weight bearing or by moving the affected limb towards the extreme outer ranges of its motion, as in the case of our patient. In recent years, AVN of the femoral head has emerged as a significant culprit of morbidity in the HIV population. Risk factors for AVN found in the HIV population include smoking, alcohol, megestrol acetate, antiphospholipid antibodies, use of glucocorticoids, hypercholesterolaemia and hypertriglyceridaemia.^{1–5} Our patient had none of the aforementioned risk factors. Moreno-Cuerda *et al* reported five cases of AVN in patients with HIV infection. In this case series, the most important isolated risk factors for AVN were: hyperlipidaemia, steroid use and alcohol consumption.³ Chokotho *et al* reviewed 26 consecutive cases of AVN of the

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Figure 1 Bilateral osteonecrosis of the femoral heads. The right hip exhibits a moderate effusion, reactive marrow oedema and mild flattening of the articular surface, consistent with stage 3 disease.

femoral head treated surgically at Beit Cure International Hospital in Malawi from 1999 to 2008. Twelve of these 26 cases were HIV seropositive and more than half of these had a diagnosis of AVN when the clinical stage of HIV/AIDS was advanced. Two out of 12 participants had no other risk factor apart from HIV infection itself.¹ Excessive alcohol consumption was found to be the most common risk factor for AVN in this case series. Protease inhibitor (PI) therapy effect on bone metabolism is controversial as some authors have found that these agents may lead to osteonecrosis by inducing osteopenia and osteoporosis and by causing hyperlipidaemia, which is in turn associated with higher risk of thrombosis of the bone vasculature.^{1–6} In contrast, others presume that these drugs can improve bone remodelling by normalising the level of cytokines involved in this process.⁵ Our patient was taking darunavir-ritonavir at the time of diagnosis; however, it is unlikely that PI therapy alone is an increased risk factor for AVN since case reports began to appear in the literature before the advent of these agents.^{1 5} Almeida-Matos *et al*'s meta-analysis using data from 1995 to 2005 supported the hypothesis that PIs play a role in the development of osteonecrosis via a tendency to cause hyperlipidaemia.⁵ Parperis *et al* conducted a retrospective chart review using data from a tertiary care centre in Arizona, USA, during years 2010–2016 in an attempt to calculate the proportion of rheumatic diseases in patients with HIV who were receiving antiretroviral therapy and to identify association of HIV drugs with the development of rheumatological conditions. They reported that 113 patients out of 2997 (3.8%) were found to have a rheumatic disease, and the most frequent musculoskeletal condition was AVN (1.3%). Furthermore, they reported that those who received integrase inhibitors were actually three times more likely to develop rheumatological manifestations (63.3%) than those who never received this type of therapy (21.6%). These authors also reported that CD4 count and viral load levels were not directly associated with the risk of

rheumatic diseases. In our case, it is unclear if the PI or the integrase inhibitor precipitated or somehow contributed to her AVN given her reported non-adherence to highly active antiretroviral therapy with evidence of virological failure.⁷

As a group of patients appear to have no known predisposing factor for AVN apart from HIV infection, including our case, it has been suggested that HIV infection itself may be a risk factor for osteonecrosis.^{1 5 6} Primary HIV-associated AVN could be due to HIV facilitating cytokine-mediated bone reabsorption, as it has been demonstrated in animal studies. Furthermore, bone tissue homeostasis is regulated by cytokines, specially interleukin-6 and tumour necrosis factor, which are also involved in HIV pathogenesis. Research suggests that HIV infection increases expression of receptor activator of nuclear factor kappa-B ligand (RANKL), a pro-osteoclast protein, and decreases the expression of osteoprotegerin, a known inactivator of RANKL. These complex biochemical associations may explain the effects of HIV infection on bone metabolism.^{5 6} The diagnostic method of choice for AVN is the MRI, as it has a diagnostic sensitivity superior to 90%.^{3 4} Core decompression surgery is the standard of care in patients with early AVN. In this surgical procedure, the necrotic femoral head and neck are drilled to decompress the elevated intraosseous pressure, allowing for improved femoral perfusion. In contrast, total hip replacement is the definitive treatment for patients with advanced AVN. Per Chokotho *et al*'s early response to arthroplasty surgery in AVN of the femoral head is equally good irrespective of the HIV serostatus of the patients.¹ Our patient was ultimately treated with left hip arthroplasty, with a positive outcome. Prevention of AVN focuses on correcting its risk factors, by reducing the amount of alcohol consumption, restricting steroid use and monitoring hyperlipidaemia treatment.^{3 4} This clinical case supports the hypothesis that HIV infection itself is an independent risk factor for AVN. Although multiple osteonecrotic risk factors exist in the HIV population, isolated cases have been well described in the literature. Thus, unexplained cases of osteonecrosis especially those with multifocal involvement should prompt testing for HIV. Although the underlying mechanism may be multifactorial, further research is necessary to elucidate the link between HIV infection and AVN.

Learning points

- ▶ Avascular necrosis (AVN) is a source of significant morbidity in the HIV population.
- ▶ HIV may be a risk factor for the development of AVN.
- ▶ Unexplained cases of osteonecrosis especially those with polyarticular involvement should prompt testing for HIV.

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