

Case Report: A man on antiretroviral therapy with painful thighs

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A 54 year old man presented with increasing pain in both thighs for three months during a follow up visit at the antiretroviral therapy (ART) clinic of Queen Elizabeth Central Hospital.

He was first seen at the same clinic three years and eight months before the current presentation, when he started ART with stavudine-lamivudine-nevirapine. He was in WHO clinical stage III, but it was not documented which condition this was based on. No CD4 count had been done at that point. Two months later he had developed a rash that was believed to be caused by hypersensitivity to nevirapine which was then replaced efavirenz. Subsequently he developed pain and numbness in feet and lower legs due to peripheral neuropathy and because of that stavudine was changed to zidovudine one and a half years before presentation. Otherwise he was in good general condition; he had a stable weight and experienced no opportunistic infections. He reported good adherence to ART throughout.

Despite the substitution of stavudine he remained in regular need of symptomatic treatment¹ for pain in his legs such as ibuprofen and amitriptyllin. However over the recent months the character of the pain in the legs had changed: the location was now mostly in the thighs and only occurred when he was standing. The pain worsened when walking, which had become progressively difficult. The numbness and pain in the feet in the lower legs and feet was still present, but it was overshadowed by the thigh pain. The patient had not used corticosteroids in the past and did not consume excessive amounts of alcohol. There had been no preceding trauma. He had never been treated for tuberculosis. Inspection of his legs showed no abnormalities. Passive movement of the knees and hips was not remarkably abnormal and hardly painful.

Which conditions would you consider as the cause of his painful thighs and which investigations are needed?

The complaints raised a strong suspicion of osteonecrosis of the femoral heads. We also considered osteoarthritis of the hips and malignant bone disease, such as multiple myeloma and bone metastases. We ordered an X-ray of the pelvis. This showed characteristic abnormalities of advanced, bilateral osteonecrosis of the femoral heads, with sclerosis and cystic bone changes, bone collapse, joint space narrowing and secondary degenerative changes (figure 1).

Fig 1



The patient was referred to an orthopaedic surgeon for further management and underwent bilateral hip replacement (figure 2 below) in two stages.



Discussion

Osteonecrosis is also known as avascular-, aseptic- or ischaemic necrosis and is believed to be caused by ischaemic damage to the bone at sites vulnerable to vascular compromise. The femoral heads are affected in 85% of the cases and bilateral involvement is present in around half¹. It affects males eight times more frequently than females and occurs mostly in younger adults. Osteonecrosis is an uncommon condition in the general population, but it has been suggested that it is more often seen in HIV infected patients. Several important risk factors that have been identified for this condition are common in patients with HIV infection: previous use of corticosteroids, hypertriglyceridemia (often caused by antiretroviral drugs), alcohol, and hyper-coagulability. In addition, it has become clear that HIV may cause vasculitis or vasculopathy and that HIV and probably also ART can lead to premature atherosclerosis. It is likely that all these factors contribute to the increased risk of osteonecrosis in HIV infected patients.

For making the diagnosis correctly, it is important that clinicians are aware of this condition, since symptoms and signs are non-specific. The diagnosis is made by imaging. MRI and to a lesser degree CT scanning are more sensitive than plain X-rays, although the latter is generally diagnostic

in more advanced cases. Initial investigation of AP and lateral X-rays of the affected hip is therefore a reasonable first step, reserving MRI scanning for those with equivocal radiological findings where such resources exist. If available, bone scintigraphy can be used to screen whether other bones are also affected if osteonecrosis is diagnosed in one location¹.

Osteonecrosis will usually be diagnosed in Malawi at an advanced stage due to the lack of sensitive diagnostic methods (mainly MRI scanning) and because it is easy to overlook the diagnosis in the earlier stages, especially in very busy ART clinics within the National ART programme. Conservative measures, such as reducing weight bearing and modification of risk factors, for instance stopping smoking, will therefore rarely be sufficiently effective at the time of diagnosis and surgical treatment is usually indicated. For early disease surgical core decompression may be of value, but for more advanced cases the only effective intervention is joint arthroplasty.

In Malawi there is limited but increasing experience with joint prosthesis surgery. A national joint registry was established in 2005. Data from this registry indicate that osteonecrosis was the most common indication for joint prosthesis surgery, in particular for hip replacement. Of those with osteonecrosis undergoing hip replacement 52% (11 out of 21 patients) were HIV positive². Patients with HIV infection may have an increased chance of infected prosthesis, and patients who undergo hip replacement for osteonecrosis have a higher chance of aseptic loosening of the prosthesis, whether HIV infected or not.³ Experience in Malawi with joint replacement for osteonecrosis is not yet large enough to determine whether HIV is associated with complications in our setting.

Apart from osteonecrosis, HIV and ART also increase the risk of osteopenia and osteoporosis, which are progressively degrees of metabolic bone disease. The prevalence of

these conditions increases at higher ages and osteoporosis is expected to become a relevant public health concern as the population of ageing patients on ART expands⁴. It is possible that the incidence of osteonecrosis will also increase in Malawi.

Health care workers involved with ART in Malawi will be confronted with many patients who complain about painful legs. If the nature of the pain is of gradual onset but differs from the characteristic pattern of peripheral neuropathy and especially if it is located in the thighs or hips, there should be a high index of suspicion of osteonecrosis of the femoral heads.

References

1. G.T. Allison, M. P. Bostrom, M.J. Glesby. Osteonecrosis in HIV disease: epidemiology, etiologies, and clinical management. *AIDS* 2003, 17:1-9
2. N. Lubega, N.C. Mkandawire, G.C. Sibande, A.R. Norrish, W.J. Harrison. Joint replacement in Malawi. Establishment of a national joint registry. *J Bone Joint Surg [Br]* 2009, 91:341-3.
3. W.J. Harrison. HIV/AIDS in trauma and orthopaedic surgery. *J Bone Joint Surg [Br]* 2005, 87:1178-81.
4. M. Borderi, D. Gibellini, F. Vescini, E. De Crignis, L. Cimatti, C. Biagetti, L. Tampellini, M.C.Re. Metabolic bone disease in HIV infection. *AIDS* 2009, 23:1297-1310