Bone metabolic disorders in HIV positive patients: a case report

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Summary. Fractures in patients affected by HIV are more frequent than what is reported in patients with no retroviral diseases. Chronic infection with HIV likely contributes to increased systemic inflammation, which has been associated with increased rates of fracture. We report a case of a 56-year-old male (HIV + in treatment with Atripla) heavy worker, at the beginning affected by intra-articular proximal humerus fracture treated with endoprosthesis replacement and later by periprosthetic fracture treated with plate, screws and cerclages. Follow up was performed with clinical evaluation (ROM, VAS, Quick Dash, ASES, Simple shoulder test, UCLA Score, Constant score) and shoulder radiographs. Bone metabolism disorders in HIV patients lead to low BMD values, changes in bone turnover markers, and histomorphometric abnormalities, especially when HIV is present along with HCV or other hepatopathies. Additional therapy with bisphosphonate and Vitamin D should always be carried out when possible to prevent such types of orthopaedic complications. (www.actabiomedica.it)

Keywords: HIV +; HCV +; periprosthetic fracture; Proximal humerus fracture; Bone disorders;

Introduction

Fractures in patients affected by HIV, whether spontaneous, after trauma, or after orthopedic procedures are higher than what is reported in patients with no retroviral diseases (1). In Literature, some authors have already shown how the use of antiretroviral drugs might affect bone mineral density (BMD) thus leading to a higher risk of fractures (2).

So far it has been demonstrated how co-infection of HCV and HIV brings on a significant decrease in BMD, worse than when HCV or HIV are singularly present as infectious disease. Moreover it has been prospected that the longer the diagnosis of HIV, the higher the percentage of risk fracture, setting as a turning point 7 years after the diagnosis, according to what Mondy(3) proposed; still, the majority of case reports and studies published report their experiences with regard to lower limbs and spine fractures, with few experiences reported with regard to upper limb or periprosthetic fractures.

Case Report

Our case report is on a 56-year-old man involved in heavy-lifting work activities. This man had been diagnosed with HIV infection 6 years earlier: for this reason, he was undergoing medical therapy with antiretroviral drugs (Atripla, 1 tablet per day). In June 2011 he experienced a traumatic fracture of the proximal humerus with significant dislocation of bone fragments (Fig. 1). He was then admitted to our Orthopaedic Department, where he was surgically treated with endoprosthesis replacement. At the time of admission his blood exams did not show significant
alterations (AST 64 U/L, ALT 58 U/L, LDH 724 U/L, PCR 0.60 mg/dl, WBC 8.51 × 10³ /μL, HCV and HBV negative). At follow-ups clinical and radiological exams showed satisfactory results in terms of functional recovery and osteointegration of the prosthesis. Fourteen months after surgery, while swimming, the patient started experiencing shoulder pain: admitted to our ER Department he underwent an X-Ray which showed a periprosthetic fracture (Fig. 2). For this reason, he underwent a revision of the fracture with a long-stem cuff tear arthropathy (CTA) endoprosthesis and the use of a plate with screws and metallic cerclages (Fig. 3). After revision of the fracture, his antiretroviral treatment was modified in order to avoid a potential decrease of BMD. Atripla was substituted with a new drug which did not contain Tenofovir, since it was thought to be responsible for a potential important alteration of bone mineral metabolism. In addition, he was given a therapy for further prevention of osteoporosis with alendronates and cholecalciferol.
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Fig. 2 Periprosthetic fracture;

Fig. 3 Osteosynthesis of the fracture with plate, screws and cerclages.

At this time (84-month follow-up), patient reported satisfaction with regard to his functional activity, being able to perform normal daily living and working activities; he had stopped performing heavy-lifting activity since he was made aware of potential negative consequences arising from a re-refracture. Physical examination showed a forward flexion of 80°, an internal rotation of 60° and an external rotation of 30°. Patient was evaluated at the final follow up with the following rating scales: VAS 2 Quick Dash 4.8 ASES 81.6 SST 66.7 UCLA Score 24 Constant score 42; no signs of infection or further periprosthetic bone density decrease have been shown on X-Rays, despite his continued use of retroviral therapy.

Discussion

Initiation of anti-retroviral treatment (ART) is frequently associated with bone loss of 2–6% in the hip and spine over the first 1–2 years of treatment, with bone mass stabilizing or increasing thereafter (4,5). Available data on the role for antiretroviral drugs in bone loss in HIV patients are conflicting. Some studies suggest a role for antiretroviral drugs, mostly protease inhibitors, whereas other studies do not (6,7,8). It is a matter of debate whether these drugs may influence BMD (9,10): indeed, while antiretroviral drugs may induce bone toxicity, they also improve general health, allowing patients to gain weight and to be physically
active. The exact reason for the increased risk of fracture among HIV patients is unknown, although it is likely multifactorial. Patients with HIV may have higher rates of known risk factors for osteoporosis, such as smoking or hepatitis C co-infection (11,12,13).

Chronic infection with HIV likely contributes to increased systemic inflammation, which has been associated with increased rates of fracture (14,15,16); in addition, the virus may alter bone regulatory mechanisms leading to further decreases in bone density (17).

Low BMD and fracture were increasingly associated with HIV/HCV coinfection compared to HIV monoinfected and HIV/HCV uninfected or seronegative individuals, suggesting that HCV contributes more of a burden than HIV infection alone. In a large retrospective cohort study, a significant increase in the risk of hip fracture was demonstrated in HCV/HIV co-infected subjects when compared between HCV mono-infected and HIV mono-infected or noninfected individuals (18).

A significantly higher risk of osteoporotic fracture, such as vertebral or hip fracture, in HCV/HIV co-infected versus HIV mono-infected individuals was reported by Maalouf et al. (19).

Dual treatment for HIV/hepatitis B co-infection has also been shown to be associated with a higher risk of hip fracture compared to ART treatment in HIV mono-infected and noninfected individuals (20).

In 2006, HIV-infected men and women from the USA with osteoporosis (defined as a BMD T-score ≤2.5) were associated as having a significantly increased incidence of fracture (21).

So far authors have basically focused their attention on the coinfection of HIV and HCV thus showing an additional role of hepatitis C (and its correspondent hepatopathy and drug treatment) in determining a decrease in BMD. This factor has been proved to be significant in regard to hip and spine fractures.

In this case we reported the onset of a significant worsening in BMD in a patient with HIV monoinfectious disease; moreover, bone complications occurred in an upper limb bone, with no typical weight-bearing characteristics as with typical bone fracture complications in HIV patients. What’s more, re-fracture of the operated humerus occurred in an atraumatic way, thus suggesting the severe osteoporosis localized in that bone. Despite what has largely been reported by other authors’ experiences, in this case report we describe the onset of a fracture (and most of all of an atraumatic re-fracture) in a patient with HIV monoinfection whose upper limb was twice subjected to a bone fracture. Thus far, risks of atraumatic bone fractures have usually been reported in patients with HIV and HCV coinfection, in particular with regard to the lower limb and spine, probably because of their mechanical characteristics. In this case, the prolonged antiretroviral therapy with Tenofovir (the active ingredient of the Atripla treatment he was treated with) has probably exposed the patient to an excessive decrease of BMD.

**Conclusion**

Bone metabolism disorders in HIV patients lead to low BMD values, changes in bone turnover markers, and histomorphometric abnormalities, especially when HIV is present along with HCV or other hepatopathies. In this case report we show a case of an HIV monoinfected patient who experienced a significant bone mineral density loss in an upper limb bone, this suggesting that the risk of fractures is not just typical of patients with HIV/HCV coinfection, and it is not just typical of weight-bearing bones, such as femur or vertebra. Additional therapy with bisphosphonate and Vitamin D should always be carried out when possible to prevent such types of orthopaedic complications.

**Patient declaration statement:** The authors certify that they have obtained all appropriate patient consent form. In the form the patient has given her consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initial will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.
Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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