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A Case Report on Multiple Fragility Fractures in an HIV Infected 42 Year Old Female

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Abstract **Introduction:** Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fractures. Osteopenia and osteoporosis are newly recognized problems in HIV-infected patients and a number of studies have reported a lower bone mineral density (BMD) in HIV-infected men and women as compared to age, race, and gender matched controls. **Aim:** The case study seeks to present and highlight a typical presentation of multiple fragility fractures as reported in a relatively young HIV patient and to underscore a potential role HIV infection status and some antiretroviral therapy might play in reducing the bone mineral density. **Case Presentation:** We report a case of fragility fractures in a 42 year old female who presented to a university teaching hospital with general body weakness and bone pain with no history of trauma or a fall. She was not on any other drugs apart from the antiretroviral therapy and had no family history of osteoporosis. She was not menopausal either. Patient is a known HIV infected patient who has been on antiretroviral therapy for 11 years by time of presentation. Diagnosis was based on the atraumatic fractures and osteoporotic bone picture on x-ray as well as history taken from the patient. The ideal definitive diagnosis of osteoporosis in this population is by assessment of bone loss by dual energy X-ray absorptiometry (DEXA) scan testing. **Conclusion:** Multiple fragility fractures arising from decreased bone density occur in the HIV infected patients and may be under-reported and receive sub-optimal management. Study findings add to the body of knowledge suggesting a potential role of HIV infection and/or ART towards reducing the bone mineral density and the need for further research.

Keywords Fragility fractures, Low bone mineral density, HIV, Osteoporosis, Osteopenia, Premenopausal

1. Introduction

Osteopenia and osteoporosis are newly recognized problems in HIV-infected patients. Several studies report lower bone mineral density (BMD) in HIV-infected men and women as compared to age, race, and gender matched controls [1,2,3]. Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fractures (consensus). Because osteoporosis is asymptomatic until the development of a bone fracture, the diagnosis can be based on a history of fragility fracture (a fracture resulting from trauma equivalent or less than a fall from a standing position) [4].

Low bone mineral density (BMD) is a recognized metabolic complication of HIV infection and its treatment [5]. It has been reported in cross-sectional studies involving both young [6] and old [2] HIV-infected individuals. Anastos et al (2004) reported that the prevalence of osteoporosis was 3 times higher among HIV-infected patients than among HIV-negative control subjects, especially among those receiving antiretroviral therapy (ART) [3]. Duvivier, et al. (2009) in their study reported that the BMD was impaired in 34% of patients before starting any ART, suggesting either a direct or an indirect role of HIV. They further suggest that after 1 year on combined antiretroviral treatment, the decrease was more pronounced with PI-containing regimens compared with non-PI regimens consisting of an NNRTI and two NRTIs [7].

The causes of low BMD in HIV appear to be multifactorial and likely represent a complex interaction between HIV infection, traditional osteoporosis risk factors exacerbated by consequences of chronic HIV infection (e.g. poor nutrition and low weight), high rates of tobacco and alcohol use, low vitamin D levels, and ART-related factors. A study has shown that tenofovir (TDF) was associated with decrease in BMD while abacavir was associated with increased BMD [8].

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TDF may affect bone indirectly through proximal tubule toxicity, resulting in phosphate wasting and increased bone turnover.

In HIV-infected individuals, low BMD has been linked most frequently to low body weight [9] but has also been linked to testosterone or estrogen deficiency, glucocorticoids, malabsorption, tobacco use, alcohol and opiate abuse, nadir CD4+ cell count, duration of HIV infection, lipodystrophy, insulin resistance, and hyperlactatemia. Secondary causes of osteoporosis have to be ruled out in every patient as well as risk factor assessment done.

Appropriate investigations include vitamin D levels, calcium and phosphate levels, PTH levels, thyroid function tests, hormonal profile, serum lactate and alkaline phosphatase.

In their study, McComsey et al (2010), found that calcium supplementation was the most commonly prescribed therapy, either alone, with vitamin D supplementation, or with alendronate for majority of the patients in their study. However bisphosphonates are considered as the first line therapy. They act by binding to the bone matrix and inhibiting osteoclast-mediated bone resorption [10].

We report an uncommon presentation of multiple fragility fractures in a non-menopausal middle aged female patient who was HIV positive with no prior history of trauma or metabolic bone disease. Patient was diagnosed and initiated on HAART 11 years prior presentation. She was referred from a military hospital to Ndola Teaching Hospital (NTH) for further management. The aim of this case report write-up is to share on a typical presentation of multiple fragility fractures as reported in a relatively young HIV patient and to underscore a potential role HIV infection status and some antiretroviral therapy may play in reducing the bone mineral density.

2. Case Presentation

History and examination

Presenting a female patient aged 42, who came in with complaints of generalized body weakness and pain for five years and localized left forearm and right arm pain for six months. Patient was last well 5 years prior when she first experienced pain in the right lower limb. She was then admitted to the University Teaching hospital and managed as a case of deep vein thrombosis under the general surgery department. She was discharged after two weeks and was able to ambulate. In 2019 patient developed pain in the right arm and left forearm generalized body weakness which was followed by pain in the left forearm and the right arm. She went to the military hospital and was referred to NTH for further management. There was history of dizziness, palpitations, loss of appetite, and weight loss. The patient reported no joint pains or swelling, muscle aches, rashes, hypopigmentation and/or desquamation of the skin. There was no history of trauma or history of a fall. No history of fever or night sweats.

Review of Systems

Gastrointestinal system: The patient's appetite was not altered. She had no history of painful oral ulcers, difficulties/pain on swallowing, abdominal pain and nausea. There was history of vomiting once, vomitus was yellow in color and non-bloody. The patient was passing stool which was soft and non-bloody.

Respiratory system: She had no history of running nose, cough, and difficulties in breathing and/or chest pain. Patient had never expectorated bloody sputum before.

Genital urinary system: Patient was able to pass urine without difficulty or experiencing pain. No abnormal vaginal discharge was reported and her menstrual cycles and flow were normal.

Past Medical History: patient has never had any past surgeries. The patient was not diabetic, nor epileptic and reported no epileptiform seizures in the past. She was non-asthmatic, had no known TB exposure and her HIV status was positive and had taken antiretro-viral therapy for about 11 years. Last CD4 count was 120 cells and viral load was high (she could not recall the figure).

Reproductive History: Gravida 4 Para 4, and reported normal menstrual flow.

Drug History: Patient was on Atripla (combination of tenofovir, lamivudine and efavirenz), no history of corticosteroids, and no other drugs. She had no known allergies or history of herbal medications.

Social History: patient was married with four children, she did not smoke or drink alcohol.

Family History: No history of chronic illnesses and no family history of osteoporosis.

Examination

On general examination patient was stable and not in any obvious respiratory distress. She appeared ill and wasted, was oriented to time, place and person. Patient was afebrile to touch with no finger clubbing. Pulse was regular and rapid, there was no lymphadenopathy. She was moderately pale but had no jaundice or cyanosis. Oral cavity was clear and mucous membranes were moist. Blood pressure was 118/77 mmHg, pulse rate was 92 bpm, and temperature was 36.9℃.

Musculoskeletal Exam

On examination of the lower limbs, no deformities were noted, there were no scars or rashes either. There was generalized decrease in muscle bulk noted. On palpation, there was tenderness noted in the lower back after extension at the hip from her flexed position and in the right ankle. No deformities were palpated, there was tenderness around hip area on extension of right leg. Reflexes and test for clonus was not done because she was in pain. Tone was normal and sensation was intact.

On examination of the upper limbs, deformity was noted in distal 3rd of left arm, tenderness was noted on distal 3rd of arm close to the wrist and middle 3rd of right forearm sensation was intact.

Respiratory Exam

On inspection chest was moving with respiration, there were no scars, visible masses or deformities noted. On palpation chest expansion was symmetrical, no areas of tenderness, no palpable masses or deformities palpable. On percussion, the note was resonant. On auscultation vesicular breath sounds were heard with bilateral equal air entry, there were no abnormal findings.

Cardiovascular System

On inspection there was normal precordial activity. Palpation revealed a normal apex beat in the 5^{th} intercostal space midclavicular line, no heaves or thrills were palpated. Auscultation revealed normal heart sounds, they were tachycardic. No abnormal or added heart sounds were heard.

Per Abdomen

Abdomen was moving with respiration, not visibly distended, no scars were noted. Palpation revealed no tenderness or organomegaly, no palpable masses were felt. Percussion note was tympanic. Bowel sounds were heard on auscultation.

Diagnostic focus and assessment

The following investigations were done for the patient and results obtained were as follows:

a) Kidney Function tests
   Urea 3.30mmol/l
   Creatinine 99.5 µmol/l
b) Electrolytes
   Ca+2 levels 7.8mg/dL (Normal 8.5-10.5mg/dl)
c) Full blood count
   White Cell Count 12.90 x 10^9/l
   Red cell count 2.99 x 10^6/l
   Hemoglobin 10g/dl
   Mean cell volume 108.4 fl
   Mean cell Hemoglobin 30.9g/dl

X-Ray Report

The different x-rays done showed generalized osteoporosis with no osteolytic lesion shown in the long bones. Skull X-ray showed no lytic lesions. Left forearm fractures: distal radius transverse minimally displaced with angulation. Ulnar showed a distal ulnar non-union fracture.

Other investigations that were planned for were PTH, serum Vitamin D, Phosphate levels and hormonal profile (estrogen and progesterone levels).

Therapeutic focus and assessment

Therapies administered included Calcium 500mg PO OD, Vitamin D supplementation and analgesia for the pain. Patient was counselled on importance of adherence to anti-retroviral therapy and importance of consuming food high in calcium and vitamin D.

3. Discussion

Patient presented with general body weakness and pain. She did have symptoms of anemia but denied any history of trauma or a fall or any bone disease in the past or anyone in the family. Deformities and tenderness were noted on examination of the musculoskeletal system as well as pallor and wasting on the general examination. There was no positive history of steroid use, tobacco use, chronic alcohol intake, or opiate use in this patient. Among the tests done for the patient was serum calcium levels which were relatively low. Her full blood count showed moderate anemia. The patient was put on calcium and vitamin D supplements and pain management therapy. She improved gradually and was later on discharged for follow up. Low BMD is a recognized complication of chronic infection with the HIV virus and its treatment. Various studies have documented this in spite of lack of definitive etiology being described. In one study, it has been revealed that a few available antiretroviral therapies are also linked with osteoporosis, particularly those involving tenofovir disoproxil fumarate (TDF) and that HIV and hepatitis C coinfection is associated with a greater risk of osteoporosis and fracture than HIV monoinfection [11]. Most of the fracture events described in literature are traumatic [4]. In other studies special considerations have been suggested for women living with HIV and their bone health. For instance, Ahmed et al. demonstrated that women with HIV are likely to experience early menopause, and this may make them more prone to developing osteoporosis [12,13]. Similarly some studies have shown that even in newly diagnosed, therapy naïve HIV infected patients, without any known secondary causes of osteoporosis, low BMD and high bone resorption are significantly prevalent [14]. In this case, the increased risk of osteopenia/ osteoporosis in HIV+ patients is not only due to ART, but there are ART-related, HIV-related, and even not-HIV not ART-related risk factors for bone loss [15,16]. In a study by Grana E, D et al (2019) a direct correlation between the HIV viremia and the number and severity of fractures and, on the other hand, an inverse correlation between CD4+ cell count and the number of fractures was found. The data confirmed an increased fracture rate in individuals with worse indices of infection [17].

Definitive diagnosis of osteoporosis is by assessment of bone loss by dual energy X-ray absorptiometry (DEXA) scan testing [11]. Supportive investigations include bone-related laboratory investigations such as calcium, phosphorus, alkaline phosphatase, thyroid-stimulating hormone (TSH), 25-hydroxy-vitamin D, lactate, parathyroid hormone (PTH), and follicular stimulating hormone (FSH) levels. These help in ruling out secondary causes of osteoporosis, however not all were done due to limited resources which was one of the diagnostic challenges. Laboratory abnormalities include low calcium and phosphorus levels, low 25 hydroxyvitamin D (25[OH] D) levels, and elevated alkaline phosphatase and parathyroid hormone (PTH) levels.

4. Conclusions

Multiple fragility fractures arising from decreased bone

density occur in the HIV infected patients and may be under-reported and receive sub-optimal management. Findings from this case study add to the body of knowledge suggesting a potential role of HIV infection and/or ART towards reducing the bone mineral density. HIV infected patients may have a significant prevalence of fragility fractures independent of age, gender, and virologic control. The exact rates of atraumatic fractures in the HIV-infected population can only be determined by controlled prospective trials. In other populations, such fractures are associated with significant morbidity, recurrent fractures, and mortality. Therefore, fracture risk assessment and optimal treatment of osteoporosis should be instituted in all HIV-infected patients with fragility fractures.

Study Limitation: This was a case report based on evaluations of one study subject. Therefore, findings from the case study may lack generalizability and may not present as much evidence as would be expected to be drawn from controlled clinical trials.

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Consent

Informed Consent to assess, case write-up and publication was obtained from the patient.

Conflict of Interest: The authors declare that there was no conflict of interest regarding the publication of the manuscript.

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