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Avascular Necrosis of Bilateral Femoral Head in a HIV Patient on Protease Inhibitor in Haart Regimen

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Abstract: *Avascular necrosis is due to ischemic death of bone involving typically the femoral heads. Its incidence rate is higher in HIV infected patients and is multi factorial. Factors like dyslipidemia, alcohol use, steroid use, protease inhibitor in Highly Active Anti Retroviral Therapy regimen and HIV infection itself increases the incidence of avascular necrosis.*
We report a case of bilateral avascular necrosis of femoral heads in a HIV infected patient on protease inhibitor with alcohol abuse. The aim of this case report is to alert the clinicians involved in HIV care regarding avascular necrosis as a subtle yet frequent complication in a HIV infected patient with known predisposing factors when presenting with acute spontaneous non traumatic bilateral hip joint pain.
Keywords: *Avascular necrosis, Femoral head, HAART, HIV, Protease Inhibitor*.

I. Introduction

Avascular necrosis (AVN) or osteo necrosis is a pathological process resulting from ischemic death of bone secondary to loss of blood supply. It typically involves femoral head and can lead to subchondral collapse leading to severe osteoarthritis[1].The incidence of AVN in general population is 0.135%[2] whereas in HIV patients it is 0.45%[3]. The exact aetiology of the increased incidence of AVN in HIV patients compared to general population is unclear but can be due to HIV related complication, HIV associated disease or due to adverse event of highly active antiretroviral therapy(HAART)[4].Some other factors such as hypertriglycerideimia, hypercholesterolemia, alcohol abuse and corticosteroid use may also increase the risk of AVN development in these patients.[5] Protease inhibitors(PIs), one of the drugs used in second line HAART in our country might be an independent risk factor among HIV infected patients for development of AVN as several small studies and case reports have suggested a possible link[6].Metabolic factors such as hyper lipidemia have been strongly associated with the use of protease inhibitors[7]. With advent of the use of anti retroviral therapy the course of HIV and its manifestations have changed but with multitude of side effects including osteonecrosis(AVN) and metabolic abnormalities.

We report a case of a HIV patient presenting with spontaneous non traumatic bilateral hip joint pain who was diagnosed to have bilateral AVN femoral head of hip joint. This case is discussed in context of HIV and other causes of acute hip joint pain.

II. Case Report

Chief Complaints: 45 years old male with HIV infection presented with pain in both hip joints and difficulty in bearing weight on standing and walking for three days duration.

Past Medical History: The individual was detected to have HIV infection in 2007 when being evaluated for chronic cough and was diagnosed to be a case of aspergilloma left upper lobe of lung. He was on regular follow up with our facility from May 2011 and was on ART comprising of AZT/3TC/NVP with cotrimoxazole (septran) prophylaxis and itraconazole. During initial evaluation his adherence to HAART was more than 95%.On subsequent follow ups his adherence to HAART was found to have fallen to less than 95% despite adherence counselling due to persistent alcohol abuse. His follow up CD4 counts were 47 cells/mm3 in May 2011, 64 cells/mm3 in July 2011 and 34 cells/mm3 in September 2011.Thereafter with help of de-addiction measures to alcohol and serial counselling for improving adherence to HAART he started taking medicines regularly under direct medical attendant observation but his follow up CD4 count was still less than 100 cells/mm3.It was found to be 55 cells/mm3 in March 2012 and 30 cells/mm3 in October 2012. His viral load for HIV was 92104 copies /ml and was started on second line HAART with TDF/INDV/RTV/3TC along with itraconazole 200mg once daily, septran prophylaxis and tablet azithromycin 1200 mg weekly. Thereafter his follow up CD4 count in January 2013 was 54 cells/ mm3 and 31 cells/mm3 in October 2013. His adherence was poor due to increased pill counts and pain in flanks. His protease inhibitor of the regimen was changed to Lopinavir/ Ritonavir in place of indinavir, but despite good adherence to the changed regimen his CD4 count in March 2014 was 44 cells/mm3 and 27 cells/mm3 in November2014.His viral load increased to 2,83,458 copies/ml and drug resistance testing showed high level resistance to all NNRTIs with reistance K103N. NRTI

mutation revealed M41L, D67N, V75M, M184V with high resistance to 3TC/FTC/D4T/AZT and possible resistance to TDF. Resistance was also found due to mutations for protease inhibitors like IDV/ATV/TPV/Lopinavir/ RTV. He was started on third line HAART with Tab Darunavir 600 mg twice daily, Tad Ritonavir 100 mg twice daily, Tab Raltegravir 400 mg twice daily, Tab Tenofovir 300 mg once daily, Tab Lamivudine 150 mg twice daily along with Tab itraconazole 200 mg once daily with septran and azithromycin prophylaxis.

Current History: He developed pain in both hip joints with intensity more on left side and progressed within three days. He was unable to bear weights on standing and walking. His pain increased after rest and morning stiffness was less than 30 minutes with no gel phenomenon during day time. There were no history of fever, trauma, skin rash, any other joints involvement, genitourinary or bowel symptoms. He did not give history of steroid use and intravenous drug use but was reformed alcoholic. He has been alcoholic for last ten years and consumed 120 to 160 ml daily but presently abstinent for last two years. On physical examination there was restriction in all passive movements and active movements around both hip joints were painful. There was no obvious swelling and other joints of the body were also normal. Other general and systemic examination including musculoskeletal and neurological examination was essentially normal. Biochemical investigations revealed Serum Calcium-8.0 mg/dl, serum phosphate 80 mg/dl, Alkaline Phosphatase 80 U/L,ESR 20mm 1st hour, CRP 7.6 mg/dl, serum uric acid 4.2 mg/dl, Lipid profile was normal, HBsAg and Anti HCV were nonreactive, VDRL was nonreactive.CPK level was 88 U/l and ANCA/ANA/APLA was not raised. His haematological investigations were normal. Urine routine examination was normal. X-ray pelvis with both hip joints did not reveal any abnormality (Fig1). MRI Both Hip joints including the sacroiliac joints revealed T2 hyperintense geographical lesion with hypointense margins in both bilateral femoral heads (Fig 2) and heterogenous enhancement of neck marrow and synovial enhancement after intravenous contrast. The findings were suggested of bilateral avascular necrosis of the femoral heads.

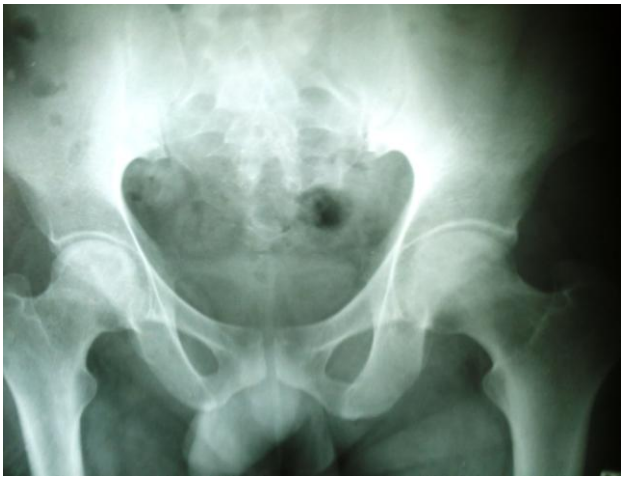

Fig1: X- Ray Pelvis with Bilateral Hip Joint.

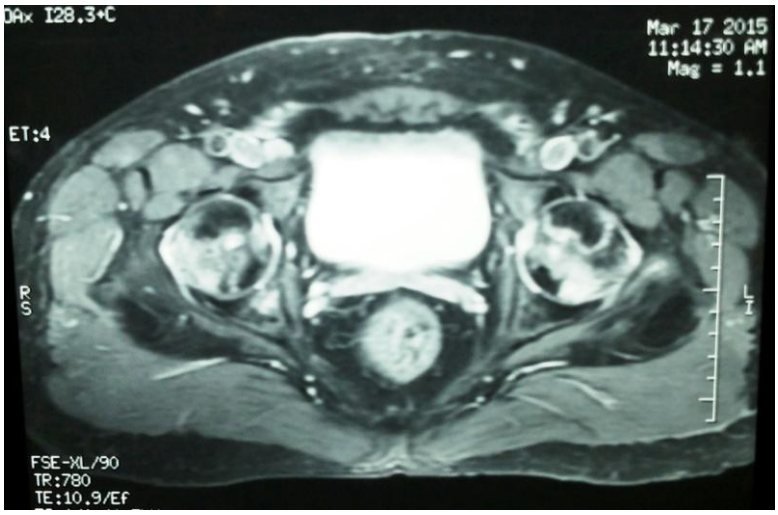

Fig2: T2 weighted MRI scan of the pelvis.

III. Discussion

In HIV positive patients development of avascular necrosis is more frequent [8] and it may be caused due to increased prevalence of predisposing factors in this population like hyperlipidemia, corticosteroid use, alcohol use and protease inhibitor containing HAART regimen [9]. AVN mostly involves femoral head and hip though multiple sites may be affected [10].

In our case the HIV infected individual was a known alcoholic for more than ten years and was consuming about 120 to 160 ml daily. He was on protease inhibitor containing regimen since last two years four months and presented with acute spontaneous non traumatic pain in bilateral hip joint for the first time during this presentation. The possible differential diagnosis of gout, pseudogout, septic arthritis, osteopenia/ osteoporosis and osteonecrosis(AVN) was thought of as HIV has been linked to these variety of rheumatologic and orthopaedic conditions[11]. With the help of biochemical and radiological investigations diagnosis of avascular necrosis was made after excluding other conditions mentioned in the differential diagnosis of acute pain of hip joints. The possible etiological factors in our case may be multifactorial as the patient had prolonged alcohol use (more than ten years), use of protease inhibitor in the HAART regimen (more than two years) and HIV infection (for eight years) with poor immunological recovery on HAART as evident by persistent CD4 count less than 100 cells/mm3 and high HIV viral load.

However there was no evidence of dyslipidemia during any point of evaluation and follow up of the patient. Also there was no evidence of osteoporosis radiologically or biochemically in the patient though bone scan was not done because of resource limited setting.

Thus the accepted explanation of protease inhibitors and alcohol causing AVN due to altered cholesterol and triglyceride metabolism[12] was not found in our case but these predisposing factors might have been contributory to the HIV infection perse to cause AVN in the patient as he was infected for eight years and HIV infection facilitate cytokine mediated bone resorption[13] particularly with the help of pro inflammatory cytokines IL-6 and TNF α [13].Even though our patient had poor immunological recovery on HAART, low CD4 count has no correlation with increased incidence of AVN as studies have suggested that AVN can occur at any level of immunosuppression[14,15].

IV. Conclusion

AVN in HIV patient is multifactorial.HIV infection itself along with predisposing factors like dyslipidemia, alcohol use, corticosteroid use and protease inhibitor containing HAART regimen increases the incidence of avascular necrosis in the HIV infected patient. This case report of AVN tried to discuss its causative factors associated with HIV infection so that clinicians involved in HIV care can be alert to the subtle yet frequent complication of AVN in HIV infected patient on protease inhibitor based HAART regimen and concomitant alcohol use.

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