Complex Convergence: Unraveling Tenofovir Nephrotoxicity, Osteoporosis and Vertebral Histoplasmosis in an Immunocompetent AIDS Patient

Tasnim R[1], Naher N[2], Liza JB[3], Khan MMR[4], Khan AH[5], Arafat SM[6]

Presenter: Dr. Refaya Tasnim

FCPS Part-2 Trainee

BSMMU

Introduction

- Bangladesh's HIV prevalence in 2021 estimates suggest 14,000 PLHIV (People Living With HIV), only 8,761 are diagnosed, with 5,553 on life-saving antiretroviral Therapy[1].
- Tenofovir Disoproxil Fumarate (TDF) associated nephrotoxicity global rate ranges from 0.5% to 45%[2].
- Histoplasmosis was designated an AIDS-defining illness by WHO in 1987[4].
- AIDS wasting syndrome, hematologic abnormalities like anemia can be used to predict mortality[6].
- Osteopenia, osteoporosis and avascular necrosis has been described in both antiretroviral-treated and untreated AIDS patients[7].

Case summary

- Mrs. X, a 34-year-old HIV positive woman for 5 years, presented with a
  - Low back pain and
  - 7 kg weight loss for 9 months.

- She was compliant with her treatment (Lamivudine, TDF, Efavirenz and Co-trimoxazole) with intact immune response (CD4 count 1001 cells/µl).

- She had a BMI of 16.3 kg/m^2, moderately anemic, bilateral hip joint movements were restricted on all direction and positive FABER test.

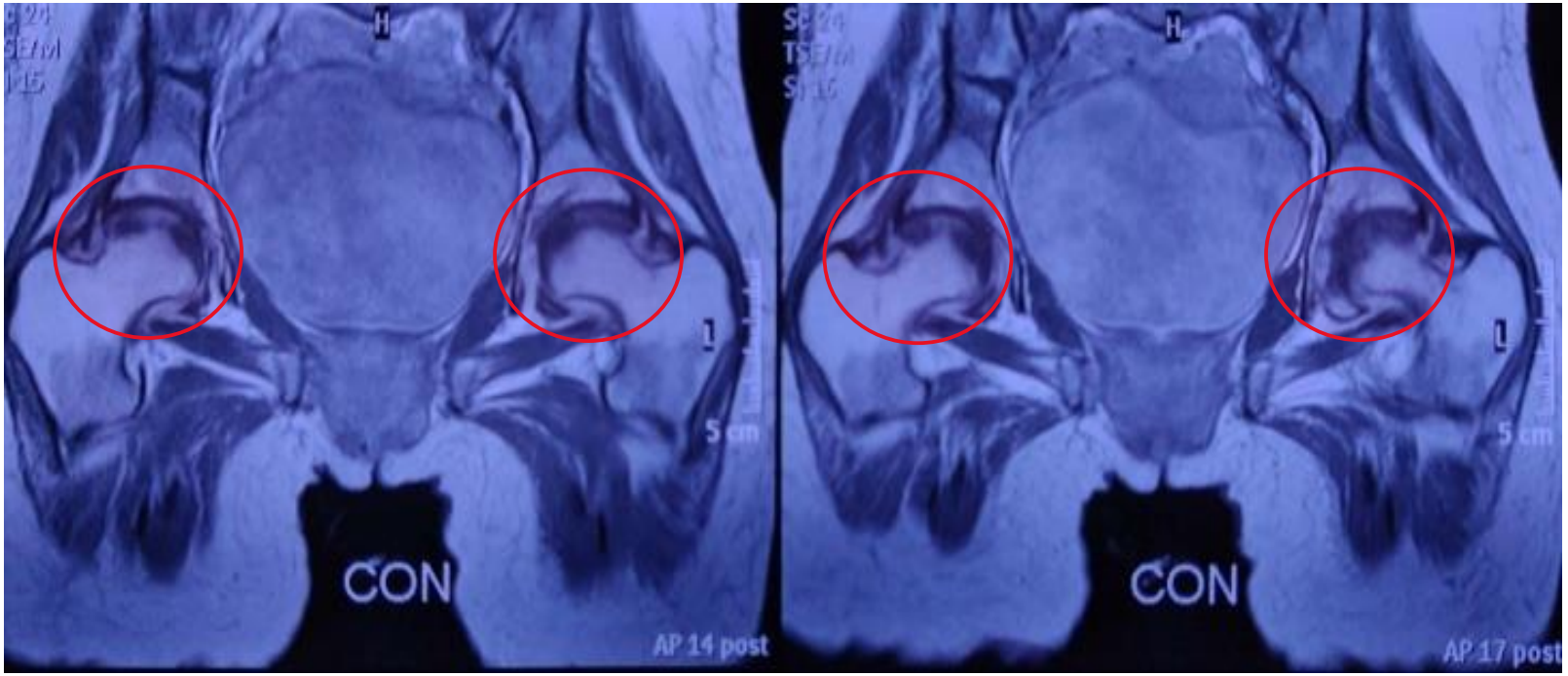
Case summary

- The laboratory abnormalities revealed, hemoglobin 7.7g/dL, Serum folate level <20 ng/mL. Serum creatinine was 1.60mg/dL with eGFR 36.9mL/min/1.73m^2. Urine routine analysis showed gross glycosuria and proteinuria. 24-hour UTP was 1.02g/day. Arterial blood gas analysis and serum electrolyte revealed normal anion gap metabolic acidosis with hypokalemia and hyperchloremia. Ultrasonography of whole abdomen showed increased cortical echogenicity of both kidneys with ill-defined cortico-medullary differentiation.

- Her bone profile showed hypocalcemia, hypophosphatemia, low vitamin D level. Bone mineral density showed severe osteoporosis.

Case summary

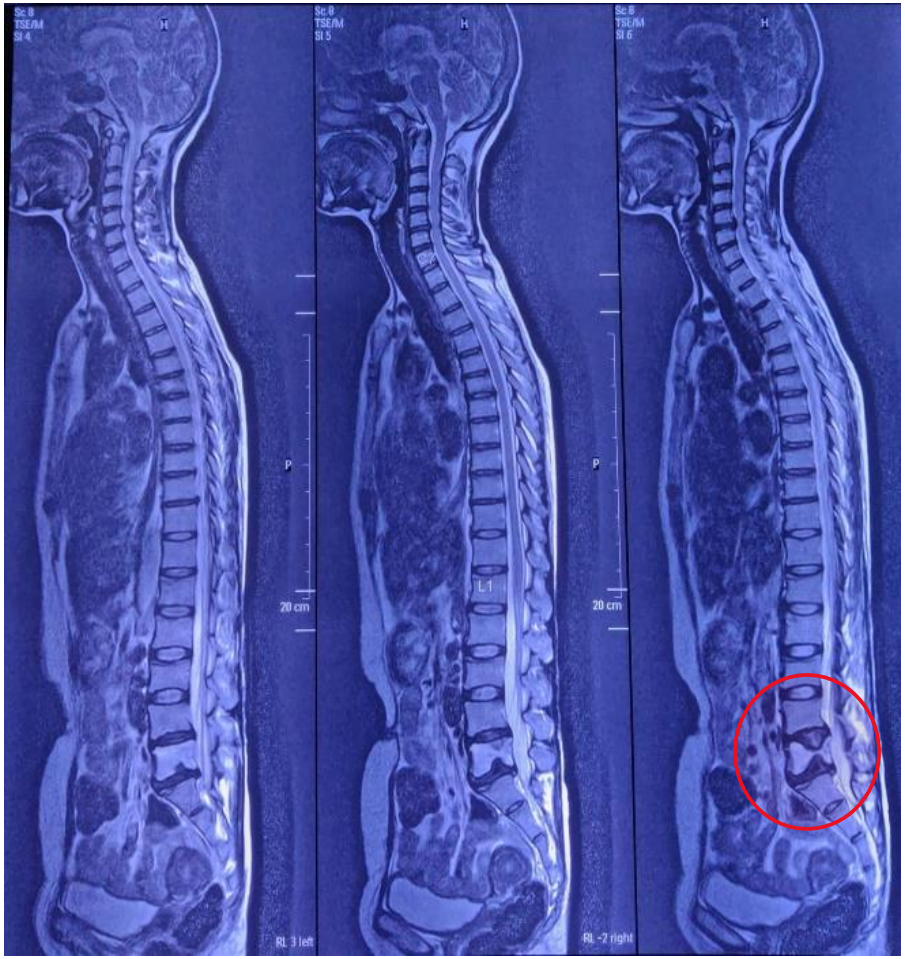
- MRI of both Hip joints suggestive of avascular necrosis of both femoral heads.



Case summary

MRI of L/S spine showed collapse of L5 vertebral body, Intervertebral disc bulging and thecal sac indentation and neural foraminal narrowing L5-S1, and C5-C6 canal stenosis.

Histopathological study of L5 vertebral body showed vertebral osteomyelitis due to histoplasmosis.



Case summary

- She had been diagnosed as a case of AIDS with L5 vertebral osteomyelitis due to histoplasmosis, TDF-nephrotoxicity (renal impairment with Fanconi syndrome), bilateral AVN of hip joints, osteoporosis, hypovitaminosis D, AIDS wasting syndrome and folate deficient anemia.

- Abacavir, Lamivudine, Dolutegravir reversed nephrotoxicity. Denosumab and Vitamin D improved bone pain. Co-trimoxazole, Itraconazole, Folate were also used.

Discussion

- **Tenofovir disoproxil fumarate (TDF):** [2,8]
  - Generally effective and safe but exhibits nephrotoxic potential.
  - Causes proximal tubular cell injury leading to acute kidney injury, chronic kidney disease, or Fanconi syndrome.
  - Higher risk in older PLHIV, particularly in Asian countries with longer ART durations.
  - TDF withdrawal is main treatment; Tenofovir alafenamide (TAF) is a safer alternative.

Discussion

- **Histoplasmosis:** [3]
  - Prevalent in immunocompromised HIV/AIDS patients in endemic areas.
  - Uncommon occurrence with CD4 count >200 cells/µL and vertebral body involvement.
  - Typical lab findings: anemia, leukopenia, thrombocytopenia, elevated bilirubin and hepatic enzymes, elevated lactate dehydrogenase and ferritin.
  - Treatment includes itraconazole for non-life-threatening cases and liposomal amphotericin B for severe cases.

Discussion

- **Osteopenia, osteoporosis, and avascular necrosis:** [7]
  - Risk factors include longer HIV duration, high viral load, protease inhibitor use, low bicarbonate, elevated lactate and alkaline phosphatase levels, and low body weight.

- **HIV-related malnutrition:** [6]
  - Multifactorial causes including inadequate food intake, malabsorption, metabolic changes, anorexia, dysgeusia, dysphagia, depression, or lack of food access, ART.

- **Anemia in HIV:** [6]
  - Anemia worsens HIV progression and increases mortality.
  - Management involves blood transfusion and regular folate supplementation.

Conclusion

For patients with HIV/AIDS, immunocompetency does not work as a safeguard always.

References

1. https://asp.portal.gov.bd/sites/default/files/files/asp.portal.gov.bd/page/d8838185_351f_49a5_bb9c_4979b8c32a42/2021-12-02-04-41-b16c52f625812a8d5527fe90f1029b17.pdf
2. Asirvatham ES, Ranjan V, Garg C, Sarman CJ, Periasamy M, Yeldandi V, Upadhyaya S, Rao B. A review of Tenofovir Disoproxil Fumarate associated nephrotoxicity among People Living with HIV: Burden, risk factors and solutions. Clinical Epidemiology and Global Health. 2023 Nov 18:101462. https://doi.org/10.1016/j.cegh.2023.101462
3. Myint T, Leedy N, Villacorta Cari E, Wheat LJ. HIV-associated histoplasmosis: current perspectives. HIV/AIDS-Research and Palliative Care. 2020 Mar 19:113-25. https://doi.org/10.2147/HIV.S185631
4. Cernat RC. HIV-Associated Histoplasmosis. Infectious Disease. 2023. http://dx.doi.org/10.5772/intechopen.111389
5. Pinto Peñaranda LF. Histoplasmosis: musculoskeletal manifestations. Infections and the Rheumatic Diseases. 2019:221-33. https://doi.org/10.1007/978-3-030-23311-2_21
6. Alo C, Ogbonnaya LU, Azuogu BN. Effects of nutrition counseling and monitoring on the weight and hemoglobin of patients receiving antiretroviral therapy in Ebonyi State, Southeast Nigeria. HIV/AIDS-Research and Palliative Care. 2014 May 20:91-7. https://doi.org/10.2147/HIV.S60429
7. Thomas J, Doherty SM. HIV infection—a risk factor for osteoporosis. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2003 Jul 1;33(3):281-91. https://journals.lww.com/jaids/Abstract/2003/07010/HIV_Infection_A_Risk_Factor_for_Osteoporosis_.1.aspx
8. Nishijima T, Gatanaga H, Oka S. Tenofovir nephrotoxicity among Asians living with HIV: Review of the literature. Global Health & Medicine. 2019 Dec 31;1(2):88-94. https://doi.org/10.35772/ghm.2019.01021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