TENOFOVIR INDUCED FANCONI SYNDROME IN A MIDDLE AGE AFRICAN FEMALE FROM KENYA, EAST AFRICA: CASE REPORT AND BRIEF LITERATURE REVIEW

Fredrick Otieno¹, Nareeba Shallot¹, Grace Mkanjala¹, Ann Wangari¹, and Vashti Nyangau¹
¹Maua Methodist Hospital

September 18, 2023

ABSTRACT
This is a case presentation of a 50-year-old African female who had been on a Tenofovir based regimen for twelve years and developed Fanconi syndrome. She recovered after discontinuation of the Tenofovir Disoproxil Fumarate (TDF).

KEY CLINICAL MESSAGE
This case presentation highlights the need to routinely monitor renal function in patients on Tenofovir Disoproxil Fumarate (TDF) due to its side effect of proximal tubule dysfunction.

INTRODUCTION
Tenofovir Disoproxil Fumarate (TDF) is one of the newest and more tolerable backbone of highly active antiretroviral therapy (HAART) in the class of nucleotide reverse transcriptase inhibitor (NRTI). In 2016, World Health Organization (WHO) published a consolidated guideline that recommended Tenofovir based regimen as the first line for adults and adolescents and henceforward this regimen has been extensively rolled out. References WHO (2018, January 1). Updated recommendations on the first line and second line antiretroviral regimens and post exposure prophylaxis and recommendations on early infant diagnosis of HIV. Despite its excellent safety profile and tolerability TDF is known to cause proximal tubule renal dysfunction. TDF renal tubulopathy can manifest as Fanconi syndrome (FS), Acute kidney injury or chronic kidney disease. References Verhelst D, Monge M, Meynard JL, et al. Fanconi syndrome and renal failure induced by tenofovir: a first case report, Am J Kidney Dis , 2002, vol. 40(pg. 13313). Here, we present the case of a middle age African female on Tenofovir based regimen who developed Fanconi syndrome after 12 years of Tenofovir based HAART.

CASE REPORT
We present a case of a 50-year-old black African female on management of HIV for the last 12 years who presented to our hospital with complaints of longstanding generalized body aches and bone pains for a duration of 2 years. These symptoms got worse 3 weeks prior to admission and were associated with muscle weakness of both the upper and lower limbs. In addition, she had joint pains worsened by activity but not associated with stiffness. A year prior to admission she suffered a trivial fall without a fracture that rendered
her unable to walk. She denied any of history of cough, weight loss, night sweats, back pain or paraesthesia. Moreover, she had normal bladder and bowel control without polydipsia, polyuria or even polyphagia.

Our patient was initiated on HAART in 2011 and has been on drugs with excellent adherence since then. She was on TDF/3TC/EFV, however in 2019 she was transferred to TDF/3TC/DTG as part of a Nationwide optimization program.

She has a history of pulmonary TB treatment 13 years ago but no history of any other opportunistic infection, hypertension or diabetes.

General exams revealed a middle-aged female who was alert and responsive, groaning and moaning in pain. She was wasted with a BMI of 17.8 kg/m² and a weight of 48 Kgs. There was no pallor, jaundice, dehydration, oedema or lymphadenopathy. Her vital signs were within the normal ranges. On musculoskeletal exams she had reduced muscle bulk, reduced muscle power graded at 3/5 and tenderness on palpation of the muscles and along the long bones. Range of motion of the right hip joint was also restricted. The other systemic exams were normal.

Laboratory investigations done at admission revealed reduced GFR at 35.80 ml/min/1.73m² (CKD-EPI) with raised creatinine levels of 152.58 umol/l. Her Calcium and Uric acid levels were low at 1.8 mmol/l and 2.26 mg/dl respectively. She had normal HBA₁c of 4.6% with a normal random blood sugar of 6.7 mmol/L. Abnormal urinalysis findings that included glycosuria of 250mg/dl, proteinuria of 100 mg/dl and urine pH of 7.0. She had normal full hemogram and electrolytes, and a negative Rheumatoid factor.

KUB ultrasound was normal, but the Bone survey x-rays (attached) revealed features of osteoporosis and osteoarthritis of the Hip joints.

A diagnosis of Fanconi syndrome secondary to Tenofovir nephrotoxicity was made based on clinical symptoms of generalized body aches and bone pains and supporting laboratory findings of elevated creatinine levels, proteinuria, glycosuria, hypouricemia, osteoporosis and a urine pH of >5.

Our patient was then switched from TDF based regimen to an Abacavir based one, Abacavir/Lamivudine/Dolutegravir. Serial creatinine levels were done, See table 1.

<table>
<thead>
<tr>
<th>Day</th>
<th>Admission</th>
<th>Day 10</th>
<th>Day 25</th>
<th>Day 81</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine levels</td>
<td>152.58 umol/l</td>
<td>126.2 umol/l</td>
<td>118.7 umol/l</td>
<td>110 umol/l</td>
</tr>
</tbody>
</table>

Table 1: Creatinine trends

She had progressive reduction in the creatinine levels and repeat of urinalysis 11 weeks later revealed clearance of the proteinuria and glycosuria, normal calcium levels of 2.25 mmol/l and Improvement in muscle power and activities of daily living. She was now able to walk with support using a walker.
X-ray 1: Skull
DISCUSSION

The bone pain and generalized body aches are possibly a consequence of osteomalacia, which is a late manifestation of proximal tubulopathy secondary to phosphate wasting and/calcitriol deficiency, since calcitriol is synthesized by the mitochondria in the proximal tubules. Perrot S, Aslangul E, Szwebel T, Caillat-Vigneron N, Le Jeunne C. Bone pain due to fractures revealing osteomalacia related to tenofovir-induced proximal renal tubular dysfunction in a human immunodeficiency virus-infected patient. Journal of Clinical Rheumatology. 2009;15(2):72–74.


The patient symptoms and renal function markedly improved following TDF discontinuation. 6 weeks later, she had no glycosuria, proteinuria, hypocalcemia and had reduced creatinine levels. Alexandre Karras et al. 2020. Tenofovir-related nephrotoxicity in human immunodeficiency virus-infected patients: three cases of renal failure, Fanconi syndrome, and nephrogenic diabetes insipidus. Clin Infect Dis. 2003 Apr 15;36(8):1070-3. doi: 10.1086/368314. Epub 2003 Apr 4. PMID: 12684922. reported that most of laboratory values in TDF tubulopathy returned to normal following its discontinuation.

In conclusion, we would like to emphasize the need for routine monitoring of renal function of patients on TDF based regimen for nephrotoxicity, even years after initiation of drugs. On any occasion TDF tubulopathy signs are recognized, the drug should be stopped to prevent further complications.

Hosted file


Hosted file