Case Report

Hypokalemic paralysis secondary to tenofovir induced fanconi syndrome

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Abstract

Tenofovir induced fanconi syndrome (FS) presenting as hypokalemic paralysis is an extremely rare complication in patients on anti-retroviral therapy. We report a 50-year-old male with acquired immunodeficiency syndrome on tenofovir-based anti-retroviral therapy who presented with acute onset quadriparesis. On evaluation, he was found to have hypokalemia with hypophosphatemia, glucosuria and proteinuria suggesting FS. He regained normal power in limbs over next 12 h following correction of hypokalemia. Ours would be the second reported case in India.

Key words: Fanconi syndrome, hypokalemic paralysis, tenofovir

INTRODUCTION

Tenofovir disoproxil fumarate (TDF), an oral prodrug of tenofovir, is a nucleotide analogue reverse transcriptase inhibitor (NRTI) approved for the treatment of human immunodeficiency virus (HIV) and hepatitis B infection. Approximately 20–30% of the TDF is excreted unchanged in the urine via active secretion by the proximal tubular cells where the free drug is actively taken up by the organic anion transporter-1 receptor located at the basolateral surface of the tubular cells and concentrated in the cytosol which can lead to tubular dysfunction.[1] Tubular dysfunction causing acute renal failure, fanconi's syndrome and diabetes insipidus have been reported which is reversible if detected early, and TDF is stopped. Here, we describe an uncommon complication of TDF induced fanconi syndrome (FS) presenting as hypokalemic paralysis.

CASE REPORT

A 50-year-old male presented with acute onset weakness of all four limbs of one day duration to the infectious department services. He also noted increased fatigue and polyuria over the past 5 days. There was no history of diarrhea, upper respiratory infection, vaccinations, or similar complaints in the recent past. He did not have any previous neurological and renal ailments. He was diagnosed to have HIV infection 3 years back and was started on tenofovir based antiretroviral therapy 6 months ago. Physical examination revealed mild dehydration but stable vitals with no respiratory distress. Higher functions and cranial nerve examination was normal with no signs of meningeal irritation. Muscle power was 2/5 in all 4 limbs with hypotonia and sluggish deep tendon reflexes.

His potassium on admission was 1.66 mEq/l, and diagnosis of hypokalemic paralysis was suspected, and nephrology consult was sought for the management of hypokalemia. Other investigations

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were-serum sodium 140 mEq/l, serum chloride 118 mEq/l, serum bicarbonate 11.4 mEq/l, serum phosphorus 1.6 mg/dl, calcium 8.4 mg/dl, and serum glucose 112 mg/dl. Patient had normal anion gap metabolic acidosis and hence renal tubular acidosis was suspected. His serum creatinine was 3.2 mg/dl and blood urea nitrogen 72 mg/dl. Urine analysis showed pH 5.5, with a specific gravity of 1.010, 2 + albuminuria, 3 + glucosuria with no red blood cells. Transtubular potassium gradient was 11.4, and urine anion gap was positive – 14. Urine protein creatinine ratio was 2.1 mg/mg. Electrocardiogram showed prolonged P-R interval with ST/T segment depression and U waves. Complete blood count and liver function test were within normal limit.

Fanconi syndrome leading to hypokalemic paralysis was suspected given the presence of a hyperchloremic metabolic acidosis, hypokalemia, hypophosphatemia, glucosuria, and proteinuria. The patient was rehydrated with intravenous fluids. Patient was given intravenous potassium chloride via central venous catheter and oral supplementation of 150 mEq on day 1 with cardiac monitoring.

Outcome

Pateints muscle power dramatically improved within 12 h of potassium correction to 3 meq/l. He was kept on a high phosphate diet (dairy products) and oral phosphate supplementation oral phosphate supplementation of approximately 1400 mg/day. His tenofovir was stopped and with adequate hydration his creatinine declined to normal. Patient was discharged on oral potassium and phosphate supplements with normal muscle power.

DISCUSSION

Tenofovir, an NRTI is a widely used drug approved by US Food and Drug Administration in 2001 for the treatment of HIV in combination with other antiretrovirals. Tenofovir nephrotoxicity is rare and not well-investigated and ranges from 1% to 6%.[2-5] Although the exact mechanism of TDF induced nephrotoxicity remains unclear, it is proposed that TDF inhibits mitochondrial DNA γ-polymerase and thereby exerts its mitochondrial toxicity and leads to caspase-mediated proximal tubular cell injury. The long-term consequence of the damage to the proximal tubular cells leads to FS, diabetes insipidus, acute, and chronic renal failure.

Fanconi syndrome results from generalised dysfunction of the proximal renal tubule leading to impaired absorption of aminoacids, glucose, urate, bicarbonate, and phosphate; and their consequent increased excretion into the urine. The classic clinical features of FS include polyuria, dehydration, hypokalemia, hypophosphatemia, normal anion gap metabolic acidosis. Long standing FS may manifest as rickets in children or osteomalacia in adults. Wilson's disease, cystinosis, galactosemia, tyrosinemia, Lowe syndrome, and hereditary fructose intolerance cause heritable FS presenting in childhood. Acquired causes include multiple myeloma, light-chain deposition disease and tubulotoxic drugs such as aminoglycosides, ifosfamide, cisplatin, streptozocin, mercaptopurine, tetracycline, and NRTIs.

Tenofovir induced FS was reported first in 2002 and has been reported infrequently over the years. Recently reported Indian data of 274 patients on tenofovir showed 2.5% with FS.[5-7] Most of these patients had long-standing HIV infection for years with features of classical FS usually developing after 6–12 months of tenofovir therapy. Though they had osteomalacia and related muscular weakness due to FS, hypokalemic paralysis responding to the correction of hypokalemia and withdrawal of tenofovir has not been reported except for a recent case report.[8]

CONCLUSION

Hypokalemic paralysis due to FS is an uncommon complication of tenofovir therapy, and we report the second case from India. With increasing use of tenofovir as first-line ART and for management of hepatitis B, clinicians must regularly follow-up these patients with urine analysis, creatinine, and potassium for early diagnosis as the nephrotoxicity is reversible with withdrawal of the drug.

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Conflicts of interest

There are no conflicts of interest.

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MYCOPLASMA GENITALIUM

Mycoplasma genitalium was first identified in the early 1980s and has been recognized as a cause of male urethritis. M. genitalium are common commensals of the human urogenital tract and are transmitted efficiently by sexual contact. M. genitalium is responsible for approximately 15%–25% of nongonococcal urethritis (NGU) cases in United States. In most settings, it is more common than N. gonorrhoeae but less common than C. trachomatis. While M. genitalium is often the sole pathogen detected, coinfection with C. trachomatis is not uncommon in selected areas.

Although strong and consistent evidence has linked M. genitalium to urethritis in men, it remains unknown whether this infection can cause male infertility or other male anogenital tract disease syndromes.

The pathogenic role of M. genitalium is less definitive in women than it is in men. M. genitalium infections in women are commonly asymptomatic. M. genitalium can cause PID, endometritis, cervicitis, impaired fertility and possibly preterm birth in women. There is strong association between M. genitalium and HIV infection.

Possible infuence of M. pneumoniae infection

M. pneumoniae and M. genitalium are genomically distinct but they share various antigens that induce some serological cross-reactivity. Therefore, it is plausible that resistance to genital tract infection with M. genitalium might occur as a consequence of antibody induced by a previous respiratory infection with M. pneumoniae, particularly as the latter infection occurs at an early age and is therefore likely to be experienced first. However, such a respiratory infection does not provide any immunity against avaginal infection with M. genitalium, suggesting that infection of the human respiratory tract by M. pneumoniae is unlikely to protect against infection of the genital tract by M. genitalium.

Laboratory Diagnosis

M. genitalium is a slow-growing organism and can be cultured on Pleuro Pneumonia Like Organisms Broth containing arginine (PPLO). The colonies show a "fried egg appearance".

M. genitalium is diagnosed by NAAT testing of urine or semen in men, urethral swabs, high vaginal or cervical swabs and purulent aspirate from salpinges (in non-bacterial salpingitis cases) in women using in-house DNA-based PCR assay or research-only transcription-mediated amplification (TMA) assays (Gen-Probe Incorporated).

Serological tests for mycoplasmas are not standardized.

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