Tenofovir induced Fanconi syndrome: A rare cause of hypokalemic paralysis

E. P. Venkatesan, M. B. Pranesh, G. Gnanashanmugam, J. Balasubramaniam[1]

Department of Neurology, PSG Institute of Medical Science and Research, Coimbatore, [1]Department of Nephrology, Kidney Care Centre, Thirunelveli, Tamil Nadu, India

ABSTRACT

We report a 55-year-old female who presented to the emergency department with acute onset quadriparesis. She was diagnosed to have acquired immunodeficiency syndrome 7 years ago and was on tenofovir based anti-retroviral therapy for past 10 months. As the patient also had hypophosphatemia, glucosuria and proteinuria Fanconi syndrome (FS) was suspected. She improved dramatically over next 12 h to regain normal power and also her renal functions improved over next few days. Tenofovir induced FS presenting as hypokalemic paralysis is very rare complication and is the first case reported from India.

Key words: Anti-retroviral therapy, Fanconi syndrome, tenofovir

Introduction

Tenofovir disoproxil fumarate (TDF), an oral prodrug of tenofovir, was the first nucleotide analogue reverse transcriptase inhibitor to be approved for the treatment of human immunodeficiency virus (HIV) infection.TDF is extensively excreted by glomerular filtration with 20-30% actively transported into renal proximal tubule cells by organic anion transporter-1.[1,2] Acute renal failure, Fanconi's syndrome (FS), dysregulation of divalent ion metabolism and diabetes insipidus have been reported with its use. Tubular dysfunction is reversible if detected early and TDF is stopped.[3,4] Here, we describe an uncommon complication of TDF induced FS presenting as hypokalemic periodic paralysis. Although there are few reports of FS presenting as renal failure, dyselectrolytemia and osteomalacia there is no report of periodic paralysis.

Address for correspondence:
Dr. E. Prasanna Venkatesan, 3, Vijayarahavachari Road, Gandhi Road, Salem - 636 007, Tamil Nadu, India.
E-mail: eprasanna2k1@gmail.com

Access this article online	
Quick Response Code:	Website: www.indianjnephrol.org
	DOI: 10.4103/0971-4065.127898

Case Report

A 55-year-old female presented with acute onset weakness of all four limbs of one day duration. She also noted increased fatigue and polyuria over the past three days. There was no past history of diarrhea or upper respiratory infection in the recent past or any past history of neurological or renal disorders. She was diagnosed to have HIV infection 7 years back and was started on tenofovir, emtricitabine and atazanavir 10 months ago. Physical examination revealed cachexia and muscle power of 2/5 in all four limbs. Deep tendon reflexes were sluggish and pin prick sensation was normal. There was no respiratory distress and her vital parameters were also normal.

In the emergency room her potassium was 1.66 meq/l, serum glucose 112 mg/dl, serum sodium 140 meq/l, serum chloride 118 meq/l, serum bicarbonate 9.4 meq/l, serum phosphorus 2.2 mg/dl and calcium 8.4 mg/dl. Patient had normal anion gap metabolic acidosis and hence renal tubular acidosis was suspected. Urine anion gap was positive (15). Her serum creatinine was 2.2 mg/dl, urea 41 mg/dl, urine analysis showed 2 + albuminuria, 3 + glucosuria, 2 + myoglobinuria, pH 5.5, spot potassium 32 meq/l, spot sodium 75 meq/l and spot chloride 92 meq/l. Arterial blood gas values were pH 7.194, pCO_2 23.4, pO_2 107, bicarbonate 8.8, lactate 2.5. Complete blood count showed high erythrocyte sedimentation rate of 62 and creatinine phosphokinase was 616, rest were within normal limit.

FS leading to hypokalemic paralysis was suspected given the presence of a hyperchloremic metabolic acidosis, hypokalemia, hypophosphatemia, glucosuria and proteinuria. The patient was aggressively rehydrated with intravenous fluids. She required replacement with intravenous potassium chloride for 2 days to keep potassium above 3 meq/l. Patients muscle power dramatically improved within 12 h of hospital admission with potassium correction. Other renal parameters, also improved slowly with treatment. Tenofovir was stopped as we suspected it to be the cause for FS.

Discussion

Tenofovir is a nucleotide reverse transcriptase inhibitor approved for the treatment of HIV in combination with other antiretrovirals. It was US Food and Drug Administration approved in 2001. It is closely related to adefovir, which is mainly used for hepatitis B treatment. Tenofovir is one of the widely used anti-retroviraltherapy (ART) as its nephrotoxicity is less compared with adefovir and cidofovir.

FS results from generalized dysfunction of the proximal renal tubule leading to impaired reabsorption of aminoacids, glucose, urate, bicarbonate and phosphate and increased excretion of these solutes into the urine. The classic clinical features of FS include polyuria, dehydration, hypokalemia, hypophosphatemia, metabolicacidosis and rickets in children or osteomalacia in adults. FS may be heritable or acquired. Cystinosis, galactosemia, Wilson's disease, tyrosinemia, Lowe syndrome and hereditary fructose intolerance may all cause heritable FS usually in childhood. Acquired causes include multiple myeloma, light-chain deposition disease, renal transplantation and medications such as aminoglycosides, ifosfamide, cisplatin, streptozocin, mercaptopurine, tetracycline and adefovir.[5,6]

The first case of tenofovir induced FS was reported in 2002. Later Karras *et al*., Peyrière *et al*., and Earle *et al*., reported similar cases. Most of these patients had HIV infection for several years and they developed gradually progressive weakness of limbs, bone pain and fractures due to osteomalacia. Renal dysfunction with classical signs of FS developed usually 6-12 months after starting tenofovir just like in our patient. However, in contrast, our patient presented with acute onset of hypokalemic periodic paralysis, which rapidly improved with treatment and after stopping tenofovir.[3,7,8]

Conclusion

FS is an uncommon complication of tenofovir therapy. FS presenting as hypokalemic periodic paralysis is extremely rare. We report the first case from India. With increasing use of tenofovir as first-line ART clinicians must be aware of this complication. We suggest regular follow-up of these patients with urine analysis, creatinine and potassium for the first 12 months so as to detect it earlier. This case highlights the importance of early diagnosis as it is completely reversible.

References

1. Gallant JE, DeJesus E, Arribas JR, Pozniak AL, Gazzard B, Campo RE, *et al*. Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. N Engl J Med 2006;354:251-60.
2. Zimmermann AE, Pizzoferrato T, Bedford J, Morris A, Hoffman R, Braden G. Tenofovir-associated acute and chronic kidney disease: A case of multiple drug interactions. Clin Infect Dis 2006;42:283-90.
3. Karras A, Lafaurie M, Furco A, Bourgarit A, Droz D, Sereni D, *et al*. Tenofovir-related nephrotoxicity in human immunodeficiency virus-infected patients: Three cases of renal failure, Fanconi syndrome, and nephrogenic diabetes insipidus. Clin Infect Dis 2003;36:1070-3.
4. Szczech LA. Renal dysfunction and tenofovir toxicity in HIV-infected patients. Top HIV Med 2008;16:122-6.
5. Lacy MQ, Gertz MA. Acquired Fanconi's syndrome associated with monoclonal gammopathies. Hematol Oncol Clin North Am 1999;13:1273-80.
6. Melnick JZ, Baum M, Thompson JR. Aminoglycoside-induced Fanconi's syndrome. Am J Kidney Dis 1994;23:118-22.
7. Peyrière H, Reynes J, Rouanet I, Daniel N, de Boever CM, Mauboussin JM, *et al*. Renal tubular dysfunction associated with tenofovir therapy: Report of 7 cases. J Acquir Immune Defic Syndr 2004;35:269-73.
8. Earle KE, Seneviratne T, Shaker J, Shoback D. Fanconi's syndrome in HIV+ adults: Report of three cases and literature review. J Bone Miner Res 2004;19:714-21.

How to cite this article: Venkatesan EP, Pranesh MB, Gnanashanmugam G, Balasubramaniam J. Tenofovir induced Fanconi syndrome: A rare cause of hypokalemic paralysis. Indian J Nephrol 2014;24:108-9.

Source of Support: Nil, **Conflict of Interest:** None declared.