Acute renal failure and Fanconi's syndrome in an HIV patient treated with tenofovir

Shkendie Velia [1],Irida Hasalla [2], Tauseef Sarguroh [3], Muhammad Umer Aslam [4], Padmini Muthyala [5]

[1, 2, 3, 4, 5] Internal Medicine, Saint Barnabas Hospital Bronx NY, United States

Corresponding Author: Shkendie Velia MD, Internal Medicine, Saint Barnabas Hospital Bronx NY. E-mail: shkendie.velia@yahoo.com

ABSTRACT

Fanconi's syndrome (FS) is a disease of proximal renal tubule with inherited or acquired etiology. Nucleotide reverse transcriptase inhibitors (NtRTIs) are well known causes of this entity. Tenofovir is one of the safest drug in this group, successfully used in HIV and Hep B infected patients. Case reports have shown FS occurring at the initiation of therapy and recommend renal function and electrolyte monitoring up until 18 months[1]. We present a case of Fanconi's Syndrome in an HIV patient occurring more than 6 years after starting Tenofovir therapy.

Keywords: renal tubular acidosis, nephrotoxicity, Fanconi's syndrome, Tenofovir

CASE DESCRIPTION

A 46 year old female with past medical history: Human Immunodeficiency Virus (HIV) infection diagnosed more than 6 years ago, CD4 count 371, Hodgkin lymphoma treated 5 years ago in complete remission, right hip fracture repair seven months ago, multiple rib fractures found on an XR, Osteoporosis- started on alendronate 3 weeks back, presented with severe epigastric pain and multiple episodes of nonbloody, nonbilous vomiting for one day, complaining of nausea since she started alendronate, compliant with treatment and HIV clinic appointments. On physical exam, vital signs were normal. Patient was found to have dry mucous membranes and epigastric tenderness. The rest of the physical exam was normal. Initial laboratory findings: Serum- sodium 138 mEq/L, potassium 3.0 mEq/L chloride 112 mEq/L,

bicarbonates 14 mEq/L, glucose 81 mg/dL, creatinine 1.9 mg/dL, blood urea nitrogen 22 mg/dL, albumin 2.7 gr/dL , phosphorus 1.6 mg/dL , Serum anion gap12, calculated serum osmolality 282, Arterial blood gas: pH 7.228, PaCO2 25.2 mmHg, PaO2 122 mmHg, O2Sat. 97.2 %, HCO3 12.2 mEq/L. Urine- sodium 71 mEq/L, potassium 19.7 mEq/L, blood urea nitrogen 72 mg/dL, creatinine 18.6, Urine anion gap19.5, fraction excretion of sodium 0.67 %, urinalysis- urine pH 5,0, protein 30 mg/dL, glucose 1000 mg/dL and Wright's stain negative. Serum protein electrophoresis was normal ruling out multiple myeloma- the most common cause of Fanconi's Syndrome in adults, alkaline phosphatase- bone fraction was increased,

Patient was transferred to intensive care unit with the impression of hypercloremic nonanion gap metaboloc acidosis and acute gastritis. Fanconi's Syndrome was on the differential diagnosis, supported by the presence of hypophosphatemia, hypokalemia, proteinuria and glycosuria in a non- diabetic patient. Tenofovir was suspected as the culprit and was discontinued. Generous intravenous fluids, potassium, phosphate and bicarbonate replacement were the mainstay of therapy. Patient improved gradually and was discharged home with potassium and phosphate. Her serum creatinine on discharge was 1.0 mg/dL, bicarbonates of 16 mEq/L, potassium 3.2 mEq/, urine pH 7. Three weeks later bicarbonates were 20mEq/L and normal electrolytes.

Reviewing patient's records, she was started on tenofovir more than six years ago. During these years patient had a slow decrease in glomerular filtration rate, increase of creatinine but within normal range, chronic hypophosphatemia, increasing proteinuria and glycosuria culminating on this admission.

DISSCUSSION

Fanconi's Syndrome is a disease of proximal renal tubule in which glucose, amino acids, uric acid, phosphates, potassium, sodium and bicarbonates are not reabsorbed. It is presented with hypercloremic nonanion gap metabolic acidosis, deranged electrolytes, glycosuria, proteinuria, and variable urine pH, complicated with acute or chronic kidney injury, rickets in children and osteomalacia in adults.

Fanconi's Syndrome is a well-known complication of NtRTIs and a well-known preceding syndrome of acute and chronic kidney injury. Among these medications tenofovir is considered the safest[2]. It has a wide use in HIV infected patients, in combination with other retroviral medications. Tenofovir inhibits mitochondrial DNA polymerase resulting in depletion of mtDNA, causing structural mitochondrial abnormalities and mitochondria depletion. ATP depletion, as a result of this, leads to dysfunction of proximal renal tubule cells, co-transporters and Na-K-pump[3] , resulting in Tenofovir accumulation, starting a vicious circle of proximal renal tubule damage. Despite early clinical trials supporting renal safety, proximal renal tubule dysfunction and Fanconi's Syndrome, are increasingly reported with time and the increase use of this medication. With recent data coming up, showing renal dysfunction occurring years after starting therapy, monitoring renal function for life, every three months initially and then every 6 months is crucial in preventing disabling disease such as CKD, AKI and osteomalacia. Our case of Fanconi's syndrome, occurring more than 6 years of starting tenofovir supports this.

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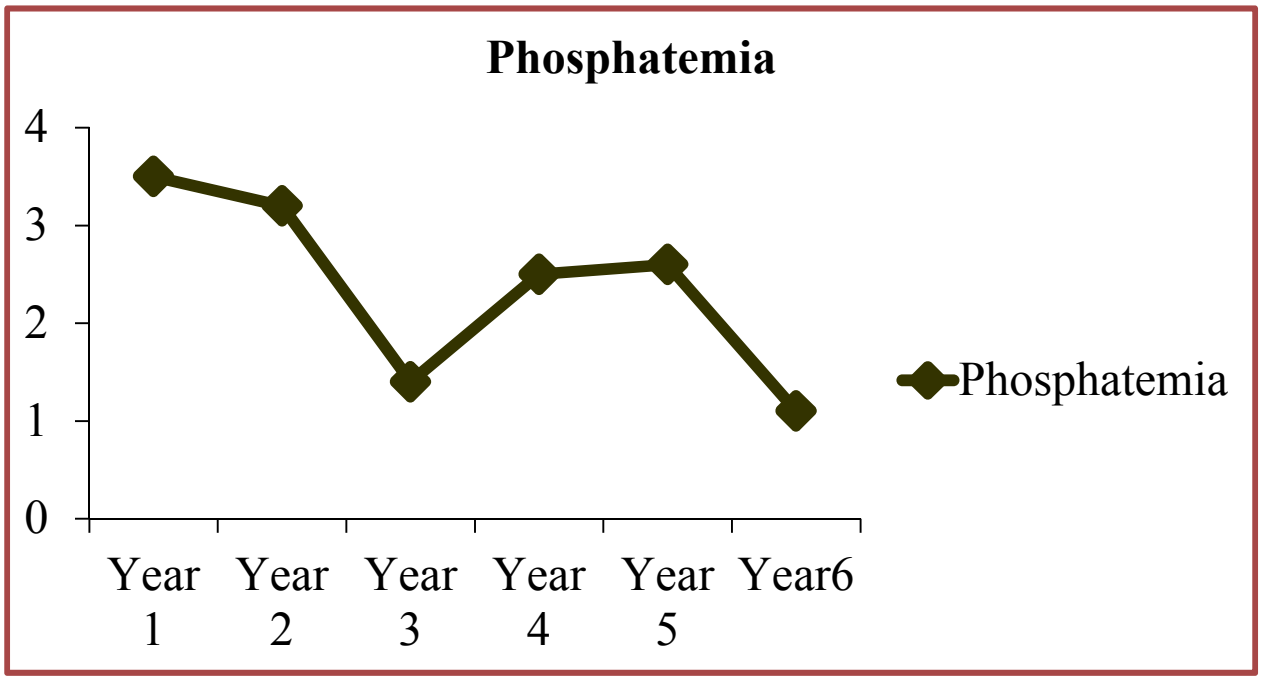
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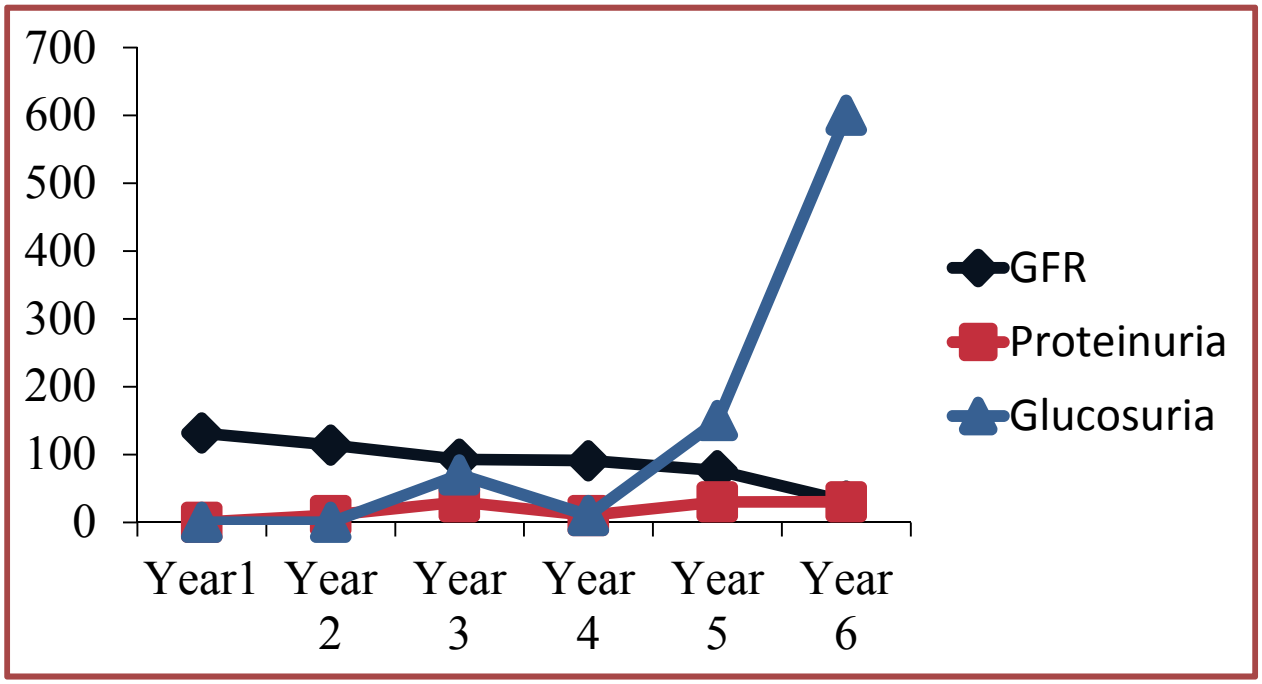
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GFR
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