A Woman with Congenital HIV Infection and Medication-Induced Fanconi Syndrome

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INTRODUCTION

The first antiretroviral to be approved to prevent perinatal HIV transmission was zidovudine in the mid-1990’s.¹ Since that time, many different drugs have been developed which have successfully reduced transmission rates dramatically.¹ The use of up to four medications in combination allows for the viral replication cycle to be interrupted at multiple steps.¹ Tenofovir is a nucleotide reverse transcriptase inhibitor which prevents replication of the virus by competing for incorporation into its DNA.² The drug’s synergistic actions with other HIV medications make it perfect for use in a multi-drug regimen. One of the complications of this drug, however, is the development of proximal renal tubular acidosis (usually hypokalemic) with hypophosphatemia, glucosuria, and aminoaciduria (Fanconi syndrome).²

CASE DESCRIPTION

A 19-year-old woman with congenital human immunodeficiency virus infection was admitted to the hospital with nausea, vomiting, diarrhea, and fatigue for one week. Her CD4 count was 27. She had undergone percutaneous endoscopic placement of a gastrostomy tube for feeding 5 months earlier. She had extensive genitalian ulceration due to infection with herpes simplex virus complicated by secondary bacterial infection. Her home medications included tenofovir disoproxil fumarate, sulfamethoxazole and trimethoprim, lamivudine, lopinavir/ritonavir, duloxetine hydrochloride, nystatin, azithromycin, hydromorphone, and lorazepam.

An electrocardiogram 11 months earlier had been normal for sinus tachycardia. In addition to sinus tachycardia, the electrocardiogram recorded at admission showed changes suggestive of severe hypokalemia (Figure 1). Other serum concentrations were sodium 139; chloride 119; and bicarbonate 14. Serum calcium concentration was 7.8 mg/dL, and the creatinine and urea concentrations were 1.9 mg/dL and 6 mg/dL, respectively. The hyperchloremic, hypokalemic, metabolic acidosis was thought to be due to therapy with tenofovir. After five weeks in the hospital, the patient had improved and her electrocardiogram was normal. She was discharged to inpatient hospice care on numerous medications including electrolyte replacement of potassium chloride, 60 mEq three times per day by mouth.

CASE DESCRIPTION - CONTINUED

Six days after discharge the patient was readmitted with confusion and profound weakness. The admission electrocardiogram and interpretation is seen in Figure 2. Serum potassium concentration in mEq/L at this time was 10.5. Other serum concentration were sodium 153, chloride 120, and bicarbonate 12. The serum calcium level was 14.5 mg/dL despite a serum albumin level of only 2.2 g/mL. This was the highest albumin level recorded during either admission. Her serum creatinine and urea nitrogen concentrations were 2.5 mg/dL and 41 mg/dL, respectively. The discharge dosage of her oral potassium from the previous admission in the presence of her renal dysfunction undoubtedly caused the hyperkalemia that occasioned the second admission. Her stay was complicated by multiple nosocomial infections, pressure sores, and worsened debilitation, and she eventually developed gram-negative sepsis and died 6 weeks after admission.

DISCUSSION

Complications of tenofovir therapy include lactic acidosis, Fanconi syndrome, immune reconstitution syndrome, severe acute exacerbation of hepatitis, decreases in bone mineral density, and severe hepatomegaly with steatosis. Fanconi syndrome has occurred in about 1.6% of patients who used the drug and has been characterized by the passage of glucose, amino acids, uric acid, phosphate, and bicarbonate in the urine.³ Because of the low incidence of this side effect, it was not widely recognized until tenofovir was used in large populations.² The nephrotoxicity of tenofovir is due to mitochondrial dysfunction. This causes a significant decrease in the energy for the Na⁺-K⁺ pump in the proximal tubules, which allows for electrolytes and small molecules that would normally be reabsorbed to be lost in the urine.² Not all these abnormalities will be present in every case; many times, the kidneys will compensate and only one or two of these disturbances will be seen.² Risk factors for tenofovir-associated nephrotoxicity include pre-existing kidney disease or elevated creatinine, poorly controlled HIV disease with overall function.

REFERENCES