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Letter to the Editor

Fanconi-like syndrome and rhabdomyolysis in a person with HIV infection on highly active anti-retroviral treatment including tenofovir

The nucleotide analogue, tenofovir disoproxil fumarate (DF), a drug effective against HIV and hepatitis B, is considered to have a favourable toxicity profile.¹ In short-term clinical trials, tenofovir DF did not exhibit more frequent nephrotoxicity compared to placebo. Recently, however, case reports of acute renal failure and Fanconi syndrome have been described.²⁻⁵ We report a patient who developed a Fanconi syndrome and rhabdomyolysis two months after the initiation of tenofovir DF.

A 47-year-old Caucasian HIV seropositive woman developed acute generalised muscle pain and weakness. After two days, she complained of muscle cramps and spasms, especially in both hands. One month before the onset of symptoms, she reported polydipsia and polyuria. She had been treated with antiretroviral therapy since 1996. Antiretroviral drugs were often switched for reasons of resistance and/or side effects. Her current treatment consisted of lopinavir/ritonavir (400/100 mg BID), saquinavir soft gel capsules (600 mg BID), abacavir (300 mg BID), efavirtide (90 mg BID subcutaneously) and tenofovir DF (300 mg QD). Concomitant therapy consisted of paracetamol, lormetazepam, phenytoin and trimethoprim-sulfamethoxazole.

Four months before the start of tenofovir DF, a low serum level of potassium (2.8 mmol/l, normal range: 3.6-5.0) was noted, probably due to vomiting. When tenofovir DF was started, the serum potassium level was 3.5 mmol/l and renal function tests were normal. At the time of onset of her symptoms, laboratory tests showed the following results: creatinine 2.3 mg/dl (normal range: 0.70-1.2), ureum 43 mg/dl (normal range: 15-37), potassium 2.3 mmol/l (normal range: 3.6-5.0), phosphorus 1.7 mg/dl (normal range: 2.6-4.6), uric acid 2.9 mg/dl (normal range: 2.5-7.5), lactate 2.2 mmol/l (normal range: 0.5-2.0), CK 1399 U/L (normal range: 30-135). Serum cortisol level was

within normal range. Her CD4 + lymphocyte count was $0.277 \times 10^9/l$ and her viral load 489 HIV RNA copies/ml. A urine sample showed marked glucosuria (27 mg/dl) with normoglycemia, proteinuria (133 mg/dl), presence of lysine, cyctine and myoglobinuria (11,998.5 ng/ml). A 24 h urine collection revealed a proteinuria of 1109 mg/d. The potassium concentration in the urine was 14 mmol/l.

She received 54 mEq of potassium orally and 80 mEq intravenously, with two litres of normal saline solution every 24 h. Tenofovir DF was discontinued. Within one month after discontinuation of the tenofovir DF, CK and potassium levels normalized and the glucosuria disappeared. The creatinine level remained slightly elevated, 1.82 mg/dl (normal range: 0.7-1.2), and a slight proteinuria, 0.79 g/l (normal value <0.20), persisted.

Our case report is the first describing a coinciding Fanconi syndrome and symptomatic rhabdomyolysis associated with the use of tenofovir DF. An asymptomatic elevation of serum CK during tenofovir DF treatment has been described previously.⁶ More recently in a French study of 74 patients on tenofovir DF, 3 (46%) of them developed a Fanconi syndrome.⁴ Two of them reported myalgias. The rhabdomyolysis in our patient may have been caused through a direct toxic effect of the tenofovir DF to the muscle cell and indirectly through a Fanconi syndrome, resulting in hypokalemia and hypophosphoremia, both known causes of rhabdomyolysis.^{7,8}

HIV seropositive persons on a tenofovir DF containing HAART regimen should have a stringent laboratory follow-up including electrolytes, CK, renal function tests and urine analysis to detect glucosuria and proteinuria.

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Steven Callens^{a,b}, Ann De Roo^a,
Robert Colebunders^{a,b,*}

^aDepartment of Clinical Sciences, Institute of
Tropical Medicine, University Hospital Antwerp,
Nationalestraat 155,
Antwerp B-20000, Belgium

^bTropical Diseases Unit,
University Hospital Antwerp, Antwerp, Belgium
E-mail address: bcoleb@itg.be

*Corresponding author. Address: Department of Clinical Sciences, Institute of Tropical Medicine, University Hospital Antwerp, Nationalestraat 155, Antwerp B-20000, Belgium. Tel.: +32-3-247-64-26; fax: +32-3-247-64-32.