CASE REPORT

TENOFOVIR INDUCED SEVERE LACTIC ACIDOSIS AND HEPATITIS

Chirag M Chhatwani, Jinesh B Purohit, Ankit P Vakil, Sanjay L Khunt

Author's Affiliations: Resident, Dept. of Internal Medicine, SMIMER, Surat, Gujarat
Correspondence: Dr Chirag M Chhatwani Email: chirag7166@gmail.com

ABSTRACT

Tenofovir induced hepatitis and severe lactic acidosis is rare. We report a rare case of tenofovir causing hepatitis in severe lactic acidosis in a seropositive patient with none of the identifiable risk factor. A 50 years old seropositive male on ZLN (Zidovudine, Lamivudine, Nevirapine) regimen since 3 years admitted under medicine care with complaints of weakness, fatigability and giddiness since 1 month. All investigations were normal apart from hemoglobin which was 4.5 gm/dL. ART regimen was changed to TLE (Tenofovir, Lamivudine, Efavirenz). After 3 days, patient had nausea, vomiting, upper abdominal pain and breathlessness. Investigations showed aspartate transaminase was 2400 IU/L, alanine transaminase 2706 IU/L, serum bilirubin 0.6 mg/dL, alkaline phosphatase 108 IU/L, PT 14 sec, INR 1.4, serum urea 16 mg/dL and serum creatinine 0.8 mg/dL. Arterial blood gas evaluation showed pH 6.96, PaO 2 116, PaCO2 12, HCO3 1.6. Serum lactate levels were 42 mg/dl. Viral markers were negative. Diagnosis of tenofovir induced hepatitis and lactic acidosis was made. Patient improved after stopping Tenofovir.

Keywords: HIV, Anti retroviral therapy, Tenofovir, Severe Lactic Acidosis, Hepatitis

INTRODUCTION

Introduction of Anti retroviral therapy for management of HIV seropositive patients has brought drastic improvement in their life span and their quality of life. Because of the long term use of ART, recognizing their side effects and toxicity is keystone in management. Stavudine and Didanosine are known to be associated with increased risk of hyperlactemia. Zidovudine and Tenofovir are less likely to cause the same[1]. Tenofovir induced hepatitis and severe lactic acidosis is rare. The reported incidence of NRTI induced severe lactic acidosis is 1-2%[1]. Identified risk factors of tenfovir induced severe lactic acidosis are female gender, obesity, pregnancy, and liver injury[2].

Here, we report a rare case of tenofovir causing hepatitis in severe lactic acidosis in a seropositive patient with none of the identifiable risk factor.

CASE REPORT

A 50 years old seropositive male on ZLN regimen (Zidovudine, Lamivudine, Nevirapine) since 3 years admitted under medicine care with complaints of weakness, fatigability and giddiness since 1 month. On general examination, vital parameters were normal, severe pallor was present. On systemic examination no significant abnormality was found. Investigations showed severe anemia with hemoglobin 4.5 gm/dL, total leucocyte count 5000 cells/dL, platelet count of 2.12 lakh/dL. In liver function test, aspartate transaminase was 18 IU/L, alanine transaminase 30 IU/L and total bilirubin 0.5 mg/dL. In renal function test, serum urea was 15 mg/dL and serum creatinine 0.5 mg/dL. Patient was suspected to have Zidovudine induced anemia, thus ART regime was changed to TLE (Tenofovir, Lamivudine, Efavirenz).

After the third day of starting TLE, patient complained of nausea, vomiting, right upper abdominal pain and breathlessness. On general examination, patient was conscious, orientated to time, place and person; pulse 124/min, blood pressure 96/60 mm Hg in right upper arm in supine position, respiratory rate 36/min; severe pallor was noted and dehydration was present. There were no signs of liver cell failure. Systemic examination was unremarkable except right upper quadrant tenderness. Hematological investigations revealed aspartate transaminase was 2400 IU/L, alanine transaminase 2706 IU/L, serum bilirubin 0.6 mg/dL, alkaline phosphatase 108 IU/L, PT 14 sec, INR 1.4, serum urea 16 mg/dL and serum creatinine 0.8 mg/dL. Arterial blood gas evaluation showed pH 6.96, PaO_2 116, $PaCO_2$ 12, HCO_3 1.6 and oxygen saturation was 94% on room air. Serum lactate levels were 42 mg/dl. Viral markers were negative for Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis E. Diagnosis of Tenofovir induced hepatitis and lactic acidosis was made.

Tenofovir was stopped immediately and patient was kept under close observation. The liver function test and arterial pH normalized within next 2 days after stopping TLE regime and supportive treatment.

DISCUSSION

The mechanism postulated behind NRTI causing lactic acidosis is inhibition of mitochondrial DNA polymerase gamma. Mitochondrial toxicity can lead to a variety of manifestations such as lactic acidosis, hepatic steatosis, myopathy, nephrotoxixcity, pancreatitis and peripheral neuropathy[3,4]. The relative potential of inhibition of mitochondrial DNA polymerase gamma in cell cultures have been postulated as zalcitabine > didanosine > stavudine > lamivudine > zidovudine > abacavir[4]. Still, there are reported cases of lamivudine causing severe lactic acidosis inspite of the lower potency to cause mitochondrial toxicity. In all the reported cases patients had some or the other underlying factor or some risk factor predisposing to mithochondrial toxicity[5,6]. In the case reported by Murphy et al, the predisposing factor was preexisting renal insufficiency, co-administration of Didanosine which has high affinity for mitochondrial DNA polymerase and use of diuretics. In another case reported by Hashim el al, there was underlying HCV infection, E.coli bacteremia and hypotensive episodes. Contrary to this in the present case, none of the identifiable risk factors were present and patient's baseline investigations were all normal.

To conclude, though rare tenofovir can cause severe lactic acidosis and hepatitis in a patient with all normal parameters. Clinicians should keep these identified adverse effects in mind and look for the warning signs in patient on ART, especially while switching over to another ART regimen.

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