CASE REPORT

Tenofovir Alafenamide (TAF) Induced Liver Failure

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Abstract

Tenofovir alafenamide induced liver failure: The objective of our case report is to present a rare case of tenofovir alafenamide (TAF) induced liver failure. TAF has been widely used for hepatitis B infection since its release in 2016. Our patient is a 56 year old male with chronic hepatitis B cirrhosis who was switched from tenofovir disoproxil fumarate TDF to TAF for its higher safety profile. In less than a week, he was jaundiced with markedly elevated transaminases. Liver biopsy was consistent with drug induced liver injury. His liver chemistries remarkably improved upon the withdrawal of the medication. Four weeks later, he had rapid deterioration in his liver chemistries requiring liver transplantation.

Keywords: Tenofovir disoproxil fumarate, Tenofovir alafenamide, Acute liver failure, Vemlidy, Viread.

Introduction

Tenofovir is an acyclic nucleotide analogue of adenosine and is used as one of the first line drugs for treatment of chronic hepatitis B virus (CHB) infection. Tenofovir requires a prodrug since it is poorly absorbed in the intestine. Currently, the two prodrugs of tenofovir are Viread (Tenofovir disoproxil fumarate (TDF)) which was FDA approved in 2008 at 300 mg dosage and Vemlidy (Tenofovir alafenamide (TAF)) which was approved in 2016 at 25 mg dosage [1,2,3]

TAF has antiviral efficacy similar to TDF but at 10% of the dose and with fewer bone marrow and renal side effects. This is due to higher plasma stability and more adequate delivery of TAF to hepatocytes compared to TDF [2].

There are a few case reports of liver failure when tenofovir has been combined with other medications [4, 5], but no definitive reports of acute, clinically apparent liver injury related to use of tenofovir alone. Thus, to our knowledge, this is the first case of TAF induced liver failure.

Case Report

The patient is a 56 year old male with advanced stage (cirrhotic) chronic hepatitis B infection that was previously treated with TDF for 5 years with undetectable viral load. The patient’s antiviral therapy had recently been changed to TAF one week prior to his current presentation. Three days after beginning TAF, his family noticed that he became jaundiced with scleral icterus prompting him to stop the medication and seek medical attention. Outpatient laboratory studies were significant for total bilirubin of 32 mg/dL, AST 2200 U/L, ALT 1800 U/L and INR 2.0. The patient was promptly sent to the emergency department by his gastroenterologist for further evaluation. His mental status remained intact. Inpatient laboratory studies revealed consistent elevation in his liver tests, as well as HBV viral load of 44,000 IU/ml with equivocal HBV anti-core IgM. Due to concern for drug induced liver injury and HBV reactivation, liver biopsy was performed and the specimen showed active cholestatic hepatitis with extensive interface and lobular hepatitis in a background of advanced stage (cirrhotic) liver disease (Figure 1).

Trichome and reticulin stains confirmed the advanced stage of disease (not shown). Canalicular cholestasis was prominent (Figure 2) indicating a cholestatic hepatitis in keeping with the clinical findings. Immunostaining for Hepatitis B surface antigen confirmed the chronic hepatitis B infection (Figure 2). In the absence of autoantibodies indicative of new, concomitant autoimmune hepatitis and with a low HBV viral load making reactivation of HBV unlikely, the patient was believed to have acute cholestatic hepatitis secondary to recently initiated Vemlidy therapy. With sustained discontinuation of the medication, the patient’s serum aminotransferase levels improved to AST 686 U/L, ALT 787 U/L respectively upon...
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discharge. He was discharged on entecavir for continued treatment of chronic HBV infection. At his 4 weeks outpatient follow-up visit, his creatinine increased to 3.7 mg/dL from baseline of 0.7 mg/dL in addition to worsening liver chemistries. Calculated MELD (Model for End Stage Liver Disease) score was 40. The patient was admitted for expedited liver transplant evaluation and two days later, he received an orthotopic liver transplant.

Discussion

Since 2008, tenofovir is one of the first line treatment for HBV as per practice guideline. Serious side effects have been reported when tenofovir is used in combination with other medications. Rivas et al. reported a case of liver failure in an HIV/HCV co-infected patient on didanosine, stavudine and tenofovir who developed severe lactic acidosis and died within 36 hours of admission. It was believed that lactic acidosis was either a direct effect from tenofovir or drug-drug interaction as tenofovir can increase the dose of didanosine by 60% [6,7].

Another reported case of tenofovir induced liver failure when combined with efavirenz/emtricitabine (Atripla) as HIV therapy, that patient was found to have elevated liver tests of AST and ALT greater than 1000 U/L. Upon withdrawal of the medications, these elevations improved and the patient recovered [5].

With respect to our patient, there was a debate regarding whether HBV reactivation was the cause of his liver failure. However, we felt that because jaundice preceded the cessation of Vemlidy, hepatitis B anti-core serum IgM was equivocal, and the patient had a relatively low HBV viral load, reactivation was unlikely to be the prime driver of acute cholestatic hepatitis. The low level HBV viral load probably reflect that the viral load was measured 4 days after stopping the medication. Drug associated injury is further supported by the patient’s aminotransferase improvement following discontinuation of TAF.

Upon literature review, tenofovir (alafenamide or disoproxil fumarate) appears to have scant or no direct hepatotoxicity. Although minimal elevation of liver chemistries has been reported upon the initiation of treatment for chronic hepatitis B patients and that slight ALT elevation is usually short term and does not prompt to stop the treatment [6]. Our case is the first reported case of acute liver failure induced by tenofovir alafenamide.

Conflict of interest

None

References

3. https://www.jwatch.org/na42940/2016/12/02/tenofovir-alafenamide-treatment-hepatitis-b-virus


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