
TENOFOVIR ASSOCIATED ANAPHYLAXIS- A RARE PHENOMENON

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ABSTRACT

Case report: We present a forty five year old male of chronic hepatitis in active phase and was started on antiviral treatment with Tenofovir 300 mg daily once. Patient when first time took the tablet then within fifteen minutes, felt some uneasiness and mild itching which progressed to severe allergic reaction all over body within two hours. He was symptomatically treated with anti-allergic by local private practitioner and within two three hours settled. After few days, he again tried tablet tenofovir and same kind of episode of allergic reaction occurred and was treated in same way. Next day, he reported to our department. We had treated more than 1500 patients with tenofovir in last few years but never has seen such type of allergic reaction. For exact confirmation of symptoms, we in our own presence in hospital with all emergency drugs by corner, gave a tablet of tenofovir 300 mg of different and fresh batch. He within fifteen minutes complained about abnormal vague sensation near oral cavity. Hence for reconfirmation, he was sent for dermatological consultation in the same institute. But due to overcrowding of patients in dermatology department, there was delay in consultation of this patient of around one hour. In this duration, patient developed severe anaphylactic reaction, as evidenced by severe itching and rash all over the body, hypotension, vomiting, dizziness and tachypnoea. The itching was so intense, that he was just trying to peel of his skin with nails. He was immediately admitted to our indoor ward and treated with anti-allergic, intravenous steroid and other supportive therapy. He responded to treatment within two hours and became totally asymptomatic. He was labeled as allergic to tenofovir in his medical records and was discharged after one day observation. He was called on follow up for starting on another group of antiviral treatment but due to fear of allergic reaction has not reported till date.

Conclusion: Tenofovir associated severe allergic reaction and anaphylaxis are rare but do occur, hence merit a careful vigil for the same. If overlooked then can lead to life threatening condition. We also for confirming the same, did a drug challenge test but in hospital surrounding with all emergency measures backup.

Keywords: Hepatitis B virus, Tenofovir, Allergic reaction, Anaphylaxis, HBV DNA Quantitative.

INTRODUCTION

Hepatitis B virus (HBV) infection, a pan global health problem has already effected one-third of the world population. Around 2 billion people have been infected worldwide and out of them, 350 million suffer from chronic HBV infection. In patients of HBV infection, 15–40% of patients will develop cirrhosis, liver failure and hepatocellular carcinoma (1-4). The prevalence of Hepatitis B surface antigen (HBsAg) is used to classify geographical areas as high (where > 8% of the population is HBsAg positive), intermediate (2–7%) or low (< 2%) HBV endemicity (5). India harbours around 40 million HBV carriers, thus accounting for 10–15% share of total pool of HBV carriers of the world. Every year over 100,000 Indians die due to illnesses related to HBV infection (6,7) and HBsAg positivity ranges between 2–4.7% (8-9). The routine assessment of HbsAg-positive persons is needed to guide HBV management and indicate the need for treatment. This generally includes assessment of measuring aminotransferase levels to help determine liver inflammation and stage of liver fibrosis by non-invasive tests (NITs) such as aspartate aminotransferase (AST) to-platelet ratio index (APRI). Serum HBV DNA levels/viral load quantified by real-time polymerase chain reaction (PCR) correlate with disease progression and are used for decisions to treat and subsequent monitoring. Antiviral agents active against HBV are available, and have been shown to suppress HBV replication, prevent progression to cirrhosis, and reduce the risk of HCC and liver-related deaths. However, currently available treatments fail to eradicate the virus in most of those treated, necessitating potentially lifelong treatment.

CASE REPORT

We present a forty five year old male of chronic hepatitis B whose general and systemic examination including Cardiovascular, Chest, Per abdomen, Dermatological and Neurological was normal. The complete haemogram revealed hemoglobin of 12.6 g/dL, white blood cell count 8,300/L, normocytic normochromic anemia with no malaria parasite. The liver function test (LFT) revealed serum bilirubin of 1.3 gm% with conjugated and unconjugated being 0.8 gm% and 0.5 gm% respectively. The transaminases were elevated i.e. AST & ALT were 90 and 102 I.U. respectively. The International normalized ratio (INR) was normal i.e. 1. The HbsAg, and HbeAg were positive and HBe Ab and IgM anti Hbc were negative with HBV DNA quantitative load of 2.1×10^6 I.U. per ml. The ultrasound abdomen was normal and Fibroscan score was 8.5 Kpa suggestive of F2 fibrosis. The renal function test, blood sugar, serum electrolytes, urine complete examination, thyroid & lipid profile, anti HCV, anti HIV antibody, IgM HAV antibody, IgM HEV antibody, autoimmune profile level were all normal. The electrocardiogram and chest x-ray were normal. As patient was in active phase and hence was started on antiviral treatment with Tenofovir 300 mg daily once. Patient when first time took the tablet then within fifteen minutes, felt some uneasiness and mild itching which progressed to severe allergic reaction all over body within two hours. He was symptomatically treated with anti-allergic by local private practitioner and within two three hours settled. After few days, he again tried tablet tenofovir and same kind of episode of allergic reaction occurred and was treated in same way. Next day, he reported to our department. We had treated more than 1500 patients with

tenofovir in last few years but never has seen such type of allergic reaction. For exact confirmation of symptoms, we in our own presence in hospital with all emergency drugs by corner, gave a tablet of tenofovir 300 mg of different and fresh batch. He within fifteen minutes complained about abnormal vague sensation near oral cavity, hence for reconfirmation, dermatology consultation was sought in the same institute. But due to overcrowding of patients in dermatology department, there was delay in consultation of this patient of around one hour. In this duration, patient developed severe anaphylaxis, as evidenced by severe itching and rash all over the body, hypotension, tachypnoea, dizziness and vomiting. The itching was so intense, that he was just trying to peel of his skin with nails. He was immediately admitted to our indoor ward and treated with anti-allergic, intravenous steroid and other supportive therapy. He responded to treatment within two hours and became totally asymptomatic. He was labeled as allergic to tenofovir in his medical records

and was discharged after one day observation. He was called on follow up for starting on another group of antiviral treatment but due to fear of allergic reaction has not reported till date.

DISCUSSION

Tenofovir is an antiviral pro-drug acyclic nucleotide diester analog of adenosine monophosphate; the active drug is tenofovir-diphosphate.⁴ It belongs to the class of Nucleotide Reverse Transcriptase Inhibitors. For HIV-1 treatment, TDF is currently recommended as a component of backbone combination in first-line ART (10). Reverse transcriptase is a part of HIV required to infect cells and make more virus. Tenofovir prevents reverse transcriptase from working properly, thus lowering the amount of HIV in the blood. Tenofovir does not cure AIDS, but it may help to slow down the progression of the disease. Tenofovir is also used to treat chronic hepatitis B. It prevents the enzymes needed for the hepatitis B virus replication.



PICTURE 1: Showing Anaphylactic Reaction Changes on Abdominal Skin



PICTURE 2: Showing Anaphylactic Reaction Changes on Upper Limb Skin

Tenofovir may help lower the amount of hepatitis B virus in the body by decreasing the ability of the virus to multiply and infect new liver cells. Tenofovir does not prevent HIV or hepatitis B from being spread to others through sexual contact or blood contamination. There are many side effects reported in literature with Tenofovir like abdominal pain, vomiting, diarrhea, dizziness, flatulence, headache, loss of appetite, muscle pain, muscle weakness, nausea, bone pain, liver and renal problems but severe allergic reaction like hives, shortness of breath and swelling of the face or throat are very rare. In another study, the most commonly identified adverse drug reactions noted with tenofovir were nausea and vomiting in 54 (30.3%) cases, headache and fatigue in 30 (16.85%) cases, heartburn and diarrhea in 17(9.5%) cases, lab abnormalities like dyslipidemia in 12(6.74%), hyperphosphatemia in 10 (5.6%), hypocalcaemia in 5(2.85%) and

renal problems in 2.24% (11). In another study by our group, tenofovir has minimal side effects like dyspepsia, allergic rash, anxiety, generalized weakness and constipation that too only in 4% of patients and none of patients had any significant renal or bony side effects due to deranged renal function tests and serum calcium levels (12). In an another study by our group, thirty two pregnant patients on tenofovir were followed during whole pregnancy, delivery period and till new born achieved one year of age. None of the newborn had any congenital formation during pregnancy as evidenced by ultra sonogram of pregnant mothers and follow up by neonatologist for period of one year. It was concluded that tenofovir is safe in pregnancy for both mother and newborn as none of the thirty two infants develop any kind of congenital malformation (13).

CONCLUSION

Tenofovir associated severe allergic reaction and anaphylaxis are rare but do occur, hence merit a careful vigil for the same. If overlooked then can lead to life threatening condition. We also for confirming the same, did a drug challenge test but in hospital surrounding with all emergency measures backup.

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