A Case of Cutaneous Reaction with Tenofovir Disoproxil Fumarate

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Hypersensitivity reaction to tenofovir consisting of maculopapular rash on the face, extremities and trunk has been reported in HIV patients. We report the first case in a hepatitis B patient. (J CLIN EXP HEPATOL 2013;3:254-255)

Hypersensitivity reaction to tenofovir consisting of maculopapular rash on the face, extremities and trunk has been reported in Human immunodeficiency virus (HIV) patients.¹ We report the first case in a hepatitis B patient who did not have HIV infection.

A 32-year old-male patient presented with constipation and bleeding per rectum for 5 months. On investigation he had a normal hemogram, liver function test, prothrombin time, Hepatitis B, C markers negative and chest X-ray normal. Colonoscopy done showed a friable, ulcerated growth in anal canal involving two-third of circumference. Biopsy from the growth was suggestive of mucinous adenocarcinoma. He underwent abdominoperineal resection with neoadjuvant chemoradiation (oxaliplatin and capecitabine followed by radiotherapy) and was given blood transfusion for anemia. He had jaundice in the course of radiotherapy which was preceded by fever for 2 days. Jaundice was insidious in onset and gradually progressive with no cholestatic features and associated with lower limb swelling and altered sensorium for 1 day. Investigation showed a normal hemoglobin, total leukocyte count, platelet, bilirubin of 5.6 mg/dl with a conjugated fraction of 3.2, AST/ALT of 6160/3270 U/L, serum alkaline phosphatase of 530 U/L, prothrombin time prolonged by 4 s, IgM anti-HBc positive, HBs Ag, IgM anti-HAV, IgM anti-HEV negative. His Carcinoembryonic antigen was normal. Ultrasound abdomen showed hepatomegaly, hypoechoic liver and pericholecystic edema.

A possibility of acute liver failure-hepatitis B related kept. He was managed with antibiotics, lactulose, L-ornithine L-aspartate and showed symptomatic improvement. He was given tenofovir in view of reactivation of hepatitis

B as the IgM anti-HBc ratio of patient to normal was less than 10 and HBV-DNA was of the order 1.7×10^5 U/L.

After taking tenofovir for a month the patient developed pruritis with few wheal-like lesions over trunk, face, upper and lower limbs. The lesions did not subside at their own. In few days the lesions converted to erythematous to violaceous maculopapular lesion (Figure 1a and b) with generalized distribution in the affected area. There was no mucous membrane involvement. The lesions were progressive in nature and slowly covered whole of body surface area including face and sparing mucosa. Tenofovir was stopped and he was switched over to entecavir 0.5 mg once a day. The rashes slowly resolved over the next 10 days (Figure 2a and b).

At follow-up at 2 months he had altered sensorium and bleeding from ileostomy site. His prothrombin time was prolonged. He was started on antihepatic coma regime with packed cell transfusion, vitamin K injection, tranexamic acid and fresh frozen plasma infusion was given. Despite resuscitation, he could not be saved from this terminal episode.

DISCUSSION

Tenofovir is an acyclic nucleotide analog, reverse transcriptase inhibitor. It is active against a broad range of DNA virus, including hepadnaviruses (as HBV) and retrovirus (as

Figure 1 Erythematous to violaceous macular rash over upper limb (a) and lower limb (b).

Keywords: cutaneous rash, tenofovir, hepatitis B

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Abbreviations: HIV: Human immunodeficiency virus; HBV: hepadnaviruses <http://dx.doi.org/10.1016/j.jceh.2013.02.020>

Figure 2 Resolving rashes over hand (a) and lower limb (b).

HIV). Tenofovir is both safe and well tolerated. The most frequent adverse reactions are mild gastrointestinal events such as nausea, diarrhea, vomiting, and flatulence.^{2,3} Others side effects reported are renal insufficiency, pancreatitis, fever, pneumonia, lactic acidosis, bone abnormalities.³

Cutaneous reactions reported in HIV patients are maculopapular rash or vesicular rash, with a mean onset of 15 days (range 24 h to 6 weeks). There has been a case report of lichenoid drug eruption to tenofovir in an HIV/hepatitis B virus co-infected patient.⁴ Facial involvement is a notable feature. Consistency among the patient was observed in

the onset time and initial location of reaction. This patient had a cause and effect relationship. The skin eruptions occurred after 1 month of starting of Tenofovir and started resolving at 10 days after stopping tenofovir.

The optimal management is currently unknown. The rash severity and the presence of concomitant symptoms such as fever, mucosal involvement and angioedema should be taken into consideration while continuing therapy.

An increased awareness of reaction to tenofovir can improve the ability of clinicians to diagnose and manage adverse cutaneous reaction.

CONFLICTS OF INTEREST

All authors have none to declare.

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