The development of dry eye disease during tenofovir and entecavir therapy in a patient with chronic hepatitis B

To the Editor,

A 32-year-old lady was seen for the complaint of fatigue. The family history was remarkable for chronic hepatitis B (CHB) in her mother. Physical examination was normal. Laboratory results were significant for AST (39 U/L), ALT (43 U/L), and GGT (43 U/L); other parameters were normal. Viral serologic tests indicated that she was positive for HBsAg and Anti-HBe antibody and negative for Anti-HBc IgM, Anti-HCV, and Anti-HDV antibodies. Serum HBV DNA was found to be more than 107 U/mL. An upper abdominal ultrasound was normal.

At 3 and 6 months follow-up visits, her transaminase levels continued to increase and a liver biopsy was performed. The histological features were consistent with CHB with grade 2 and stage 2 (Ishak's scoring system), and tenofovir therapy was started. At 3 months of treatment, the patient suffered from dryness, redness, and itching of her eyes. Following a full ophthalmic evaluation, including slit-lamp examination and Schirmer testing, she was accordingly diagnosed as having dry eye disease (DED). Additional laboratory evaluations, including thyroid function tests, anti-SS-A/Ro, anti-SS-B/La, ANA, anti-ds-DNA, AMA, ASMA, anti-LKM 1, c-ANCA, and p-ANCA, were all negative. Despite appropriate topical therapies, the patient's symptoms continued unabated, and worsened.

Since the patient's symptoms emerged after tenofovir treatment, she was switched to entecavir at 9 months of treatment, and her symptoms completely resolved within 3 weeks. However, the symptoms of DED started again following entecavir treatment and continued to worsen. She discontinued entecavir during a travel abroad (for 3-month language course) and started to use tenofovir again. Following a partial relief, she presented the same symptoms again within 2 weeks of tenofovir.

When she was seen in outpatient clinic (after returning), tenofovir treatment was switched to telbivudine therapy. The patient immediately experienced dramatic relief of symptoms, and she currently is in symptomatic remission without using any ophthalmic therapy at 15 months of telbivudine treatment with HBV DNA negativity.

Although the hepatitis B virus can be detected in tear and aqueous humor samples of HBsAg-positive patients (1,2), CHB infection has not been directly associated with ophthalmic disease (3). The development of DED due to the treatment with tenofovir or entecavir has not been mentioned so far in the literature. We report this case to alert clinicians of the possibility that tenofovir and entecavir may cause severe DED unresponsive to ophthalmic therapies during the treatment of CHB infection. In this instance, telbivudine may be a reasonable option that can provide complete resolution of dry eye symptoms.

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