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Editorial

Antiviral Prophylaxis Against Hepatitis B Virus in Patients Treated with Anti-Tumor Necrosis Factor α Agents for Inflammatory Bowel Disease

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See "Clinical Course of Hepatitis B Viral Infection in Patients Undergoing Anti-Tumor Necrosis Factor α Therapy for Inflammatory Bowel Disease" by Ji Min Lee, et al. on page 396, Vol. 16, No. 3, 2022

Hepatitis B virus (HBV) infection is common in East Asia including Korea and Taiwan. Korea is an intermediate endemic country for HBV infection.[1] For this reason, HBV vaccination is recommended as a mandatory vaccination for infants in Korea. Liver cirrhosis and hepatocellular carcinoma (HCC) can develop from chronic HBV infection. HCC is the sixth most common cancer and second leading cause of cancer mortality in Korea.[2] Approximately 70% of HCC is associated with chronic HBV infection.[3] Chronic HBV infection is defined as the positive result of HBV surface antigen. Inactive HBV carrier state is defined as hepatitis B envelope antigen-negative state, low levels of HBV DNA, and normal liver function. Resolved HBV infection is defined as a seroconverted state with anti-hepatitis B core antigen-positive. HBV can be reactivated when immunosuppressed in inactive HBV carriers or in those with resolved hepatitis. Chemotherapy or use of immunomodulators, anti-tumor necrosis factor α (anti-TNF-α) agents, or corticosteroids are known to be related to reactivation of HBV. Therefore, a preemptive use of antiviral agents in case of anti-TNF-α therapy is recommended.

As the prevalence of inflammatory bowel disease (IBD) increases in Korea, the rate of anti-TNF-α therapy in patients with IBD is also increasing.[4-6] Prophylactic antiviral therapy is recommended for patients with IBD and chronic HBV infection treated with anti-TNF-α therapy in the guidelines.[7-9] However, the level of evidence of recommendation of antiviral prophylaxis of HBV is relatively low. There have been insufficient studies on whether HBV prophylaxis should be implemented in patients with IBD and particularly in those with chronic HBV infection receiving anti-TNF therapy.

Regarding the last issue, Lee *et al.*[10] reported the clinical courses of HBV infection in patients with IBD who had anti-TNF-α treatment. The authors aimed to investigate the risk of HBV reactivation in IBD patients receiving anti-TNF-α therapy. Patients with IBD with either chronic or resolved HBV infection and underwent anti-TNF-α therapy were included. Given results of the liver function test of the study population, enrolled patients were considered inactive carriers or at the stage of immune tolerance. A total of 191 patients with IBD were included. Of them, 87 patients (46%) were diagnosed as having chronic HBV infection. Fifty-four of the 87 patients (28.3%) were treated with a prophylactic antiviral agent. Fifty-two of the 54 patients (96%) had chronic HBV infection. This retrospective multinational study showed that 7.3% of patients (14/191) had liver dysfunction due to HBV reactivation during anti-TNF therapy. Most of the patients who experienced HBV reactivation were chronic HBV-infected state and had no prophylactic antiviral agents (non-prophylaxis group [26%] vs prophylaxis group [8%], p=0.02). Antiviral prophylaxis significantly reduced the risk of liver dysfunction due to HBV reactivation in chronic HBV-infected patients (odds ratio, 0.16; 95% confidence interval, 0.04 to 0.66; p=0.01). However, there was no significant prophylactic effect of antiviral therapy in the group with resolved infection. There was no further increased risk of reactivation of HBV when anti-TNF-α therapy was combined with immunomodulatory agents. Moreover, antiviral prophylaxis did not affect

the clinical course of IBD including cumulative disease flare, hospitalization, or surgery rates.

HBV reactivation in patients with chronic HBV infection can be fatal in cases of liver failure. Liver dysfunction due to HBV reactivation leads to discontinuation of anti-TNF-α therapy, which may affect the disease courses of IBD. Antiviral prophylaxis suggested by the existing guidelines is justified. However, it is not helpful for patients with resolved HBV infection. There were several limitations in this study in terms of the nature of the retrospective study and the small sample size. Data of preferred biologics, duration of treatment, and follow-up plans were also lacking. More research is needed on how to effectively prevent and manage chronic HBV infection in endemic countries including Korea and Taiwan. Studies on the relationship between the risk of hepatitis A or C and anti-TNF-α therapy are also needed. Randomized controlled trials are usually difficult to conduct because several studies have already shown beneficial effects of antiviral prophylaxis. Furthermore, studies are needed to investigate the effects of antiviral prophylaxis in patients with both IBD and chronic HBV infection undergoing other biologics and small molecules, such as ustekinumab, vedolizumab, or tofacitinib.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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