HBV reactivation and immunosuppressive therapy

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There are already 270 million people worldwide chronically infected by hepatitis B virus (HBV). Although most of these people are inactive carriers, HBV reactivation (HBVr) induced by immunosuppressive or cytotoxic chemotherapy is not uncommon and is potentially life-threatening in the carriers. HBVr results in a variety of outcomes ranging from asymptomatic to severe hepatitis with fatal consequences. HBVr is typically confirmed by an increase in serum HBV DNA levels with active viral replication that may be accompanied by reappearance of hepatitis B e antigen (HBeAg). Usually, HBV viral loads increase when receiving immunosuppressant or cytotoxic chemotherapy. Host immune rebound and then hepatitis flare develop after withdrawal of such treatments.

In general, the HBVr rate in cancer patients receiving cytotoxic chemotherapy is around 26%, and is more than 50% in HBsAg-positive patients undergoing organ transplantation. HBVr not only occurs in hepatitis B surface antigen (HBsAg)-positive patients, but also in patients with resolved hepatitis B (HBsAg-negative/hepatitis B core antibody-positive). In a randomized controlled trial, there were ~10% of lymphoma patients with resolved hepatitis B developed HBsAg reverse seroconversion after chemotherapy with rituximab (anti-CD20)-based regimen.

The risk of HBVr in patients with autoimmune diseases is also high when rituximab or anti-tumor necrotic factor (TNF)-alpha agents were administered in HBsAg-positive carriers. According to the reported literatures, the risk of anti-TNF-alpha induced HBVr ranged from 10% to as high as 62.5% in patients with rheumatoid arthritis (RA) and HBV carriers. However, the risk of HBVr in RA patients was rarely reported.

Screen HBV markers including HBsAg, anti-HBc and anti-HBs is necessary for rheumatologic patients prior to performing immunosuppressive treatment. Antiviral prophylaxis should be applied to patients with high-risk of HBVr before and during immunosuppressive treatment. Closely HBV viral load monitoring with pre-emptive antiviral treatment is also required for those with intermediate-risk group to decrease the risk of the catastrophic event from HBVr.