Reactivation of Hepatitis B Virus After Steroid Treatment in Rheumatic Diseases

To the Editor:

Hepatitis B virus (HBV) infection is a global problem and is particularly endemic in some regions of the world. More than one-third of the world’s population has been infected with the HBV and there are 350 million people with chronic infection; 75% of them live in Southeast Asia and the Western Pacific regions.1–2 There is a chance of reactivation of a previous HBV infection in patients undergoing chemotherapy or immunosuppressive therapy for rheumatology, malignancies, autoimmune hepatitis, and systemic lupus erythematosus (SLE); this reactivation is a major cause of morbidity and mortality.3 Reactivation of HBV was first described by Wands, et al, who in 1975 reported the condition in 20 patients with lymphoproliferative and myeloproliferative disorders.4–5 Induced immunosuppression allows a rapid increase in viral replication and antigen expression. Restoration of immune function causes rapid, T cell–mediated destruction of HBV-infected hepatocytes that manifests clinically as asymptomatic self-limiting anicteric hepatitis to severe hepatitis, potentially fatal progressive decompensated hepatitis, and even death.6

In routine clinical practice, it is common to come across patients with rheumatic diseases who have HBsAg-positive serology (“overt” carriers). It is estimated that 21%–67% are affected (mean 50%), with a mean mortality rate of 20%.6–7 However, clinical events can also develop in “occult” carriers, i.e., patients who are HBsAg-negative but positive for other markers of prior exposure to the virus, including HBeAb alone or in combination with HBsAb. Further, about 12% of anti-core-positive subjects (HBsAg-negative) experience reemergence of HBsAg (seroreversion).8–9 Several risk factors have been proposed for reactivation of hepatitis B such as hematological malignancies, younger age, male sex, and high pretherapy HBV-DNA levels. Glucocorticoid is often reported to be associated with reactivation hepatitis. Serum levels of aminotransferases, bilirubin, and HBV-DNA are important for diagnosing hepatitis reactivation.10–11

Hepatitis attributable to HBV reactivation is defined as HBsAg seroreversion or an absolute level of HBV-DNA that exceeds 10^5 copies/ml in the absence of clinical or laboratory features of acute infection with hepatitis A virus, hepatitis C virus, or other systemic infections.2 Recent development of the prophylactic use of antiviral agents against HBV has made screening and monitoring of HBV status essential in patients with rheumatic diseases who are starting glucocorticoids, to ensure adequate prophylaxis and/or preemptive therapy for reactivation.12–13 We describe the cases of 2 patients taking glucocorticoids for rheumatic diseases without timely prophylactic treatment of nucleoside analog against HBV reactivation.

The first case was a 32-year-old man with autoimmune hepatitis treated by prednisone (60 mg/day, oral administration for 7 days; 40 mg/day, oral administration for 7 days; then 30 mg/day, oral administration for maintenance treatment) from May 2009. Family history of hepatitis B and history of alcohol abuse were not observed. Pretreatment screening for HBV serology displayed the following pattern: HBsAg-positive, hepatitis C virus, and other systemic infections. Recent development of the prophylactic use of antiviral agents against HBV has made screening and monitoring of HBV status essential in patients with rheumatic diseases who are starting glucocorticoids, to ensure adequate prophylaxis and/or preemptive therapy for reactivation.12–13 We describe the cases of 2 patients taking glucocorticoids for rheumatic diseases without timely prophylactic treatment of nucleoside analog against HBV reactivation.

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Patients who are HBsAg-negative, anti-HBc positive (with or without anti-HBs positive), and who have past HBV infection, should have periodic observation (every 1–3 months) of liver function, HBV serology, and HBV-DNA at the time of immunosuppressive treatment.

Once regular surveillance of HBV reactivation (detection of serum HBsAg in the reverse conversion in time) has begun, the patient should be offered antiviral treatment in time to avoid liver damage, or even liver failure, even though such cases are relatively rare.

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