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LETTERS TO THE EDITOR

Controversies about occult hepatitis B virus infection

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Abstract

We read with great interest the paper written by Shi *et al*, reviewing the molecular characteristics and stages of chronic hepatitis B virus (HBV) infection. We think that some points in the definition of occult HBV infection (OBI) and their conclusion about the management of OBI may need further considerations.

Key words: Occult hepatitis B; Definition; Reactivation; Management

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TO THE EDITOR

We read with great interest the paper written by Shi *et al*[1], reviewing the molecular characteristics and stages of chronic hepatitis B virus (HBV) infection. We think that some points in the definition of occult HBV infection (OBI) and their conclusion about the management of OBI may need further considerations.

First, they defined OBI as the existence of HBV DNA in serum, at a level < 20000 IU/mL. However, a recent meeting report[2], clarified the confusion about the definition of OBI, describing it as the presence of HBV DNA in the liver (with detectable or undetectable HBV DNA in serum) of individuals with negative HbsAg, and introduced a cutoff value for serum HBV DNA (< 200 IU/mL). So, cases whose serum HBV DNA levels are comparable to those in the different phases of serologically evident (overt) HBV infection are generally due to infection with escape mutants and should be labeled as "false" OBI[2].

Second, Shi *et al*[1] stated that OBI is a common and long-term consequence of acute hepatitis B resolution and termed it as secondary occult infection (SOI). Actually, SOI is the major clinical form of OBI that represents the tails of acute or chronic HBV infection[2]. Cross-sectional studies across the spectrum of HBV infection have revealed a marked increase in OBI prevalence towards cirrhosis or hepatocellular carcinoma (HCC)[3,4]. So, the majority of OBI cases are secondary to overt HBV infection and represent a residual low viremia level suppressed by strong immune response together with histological derangements occured during acute or chronic HBV infection. Moreover, immune response to hepatocytes sustaining a low HBV replication level may contribute to chronic liver damage in the setting of OBI. Berasain *et al*[5] showed that approximately 50% of patients with persistent hypertransaminasaemia of unknown etiology have chronic hepatitis or cirrhosis due to occult HBV or hepatitis C virus (HCV) infection.

Third, the authors concluded that no reports are available on the treatment of OBI. However, therapy should be considered during reactivation and cirrhosis settings. The reactivation of OBI in hemato-oncological malignancies (< 5%), although at a lower rate than that of HBsAg positive cases, carries a significant risk of mortality and morbidity[6], which is much higher in the setting of stem cell transplantation[7]. Many fatalities especially due to rituximab containing regimens have also been reported[8-11]. Although a definitive conclusion cannot be reached at the moment, targeted therapy *via* HBV DNA monitoring or even routine pre-emptive nucleoside analogue prophylaxis was offered to all HBsAg negative/anti-HBc positive patients in recent consensus reports[12,13]. Moreover, recent guidelines offer therapy for cirrhotic patients with a detectable HBV DNA level[14].

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