To the Editor:

We read with interest the study by Zacharakis et al. [1] regarding the role of serial measurement of HBV DNA levels in Greek patients with chronic HBeAg(−) hepatitis B infection. We agree that serial HBV DNA level assessment may be crucial in the prediction of the natural history of HBeAg(−) patients, indeed, HBV carriers who are negative for HBeAg may replicate HBV to low levels and reactivation of HBV may occur spontaneously or as a result of immunosuppression. Similarly, HBsAg negative patients with occult HBV infections may reactivate in several contexts and such HBsAg negative patients were also shown to be associated with high risk of severe liver disease including cirrhosis or hepatocellular carcinoma. We collected data concerning occult HBV infections studying a group of 26 patients (15 men, mean age 48) suffering from cryptogenetic hepatitis. Patients remained negative at the time of diagnosis for HBsAg by three different immunoassays (AgHBs plus, Bio-rad, HBsAg Ultra, bioMerieux, HBsAg Enzy-
A total of 274 serum samples were tested showing elevation of ALT, GGT or both in 80% of the cases (Fig. 1A). A high dynamic in viral loads was observed and may reach $10^6$ or $10^7$ HBV genome per ml as detected by light cycler PCR as shown on Fig. 1B and C [2].

Since molecular biology tools are improving it appears that monitoring of HBV chronic infection may include HBV DNA levels. It has recently become evident that HBV may also persist in the form of serologically silent infections, leading to the concept of occult infection. Such infection may represent a non-negligible part of cryptogenetic hepatitis cases whose diagnosis and clinical spectrum remain unclear. In a recent statement, occult HBV infection has been defined as the presence of viral DNA in the liver in the absence of HBsAg but with low titer or even absence of HBV DNA in serum [3]. Our study as well as the study by Zacharakis et al., underline the importance of sequential testing of patients for HBV DNA level, which is a key for assessing liver disease activity and predicting the risk of cirrhosis or hepatocellular carcinoma. It is also the clue to decide on the possibility of adapted antiviral treatment in order to prevent HBV reactivations or transmission of HBV in the transplantation context.

References


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