Reply to comments on “What can be revealed by extending the sensitivity of HBsAg detection to below the present limit?”

To the Editor:

We appreciate the interest and comments from Dr. Shi-Ying Xuan and colleagues and Dr. Huang Ching-I and colleagues regarding our paper [1]. The issues they have raised are highly relevant. Although the sensitivity of commercial HBsAg assays needs to be improved, the clinical relevance of positivity for low HBsAg has not been clarified. Our study demonstrated that infection with HBV, including occult HBV, is far more prevalent than previously thought, as a result of increasing the sensitivity of HBsAg detection to below the present limit [1].

Occult HBV infection has been considered to be transmitted via blood transfusion and tissue or organ transplantation [2]. However, as details of the infection routes and involvement of occult HBV in liver diseases have been obscure, establishment of a convenient screening method for occult HBV infection will inevitably be required. Although occult HBV infection may be clinically inoffensive in itself, when other important causes of liver damage co-exist, the minimal lesions produced by the immune response to the occult virus might contribute to exacerbating the course of the liver disease over time [2]. If this is indeed the case, then the low-level HBV viraemia we have demonstrated could be clinically relevant. We believe that radical immunoassay measurement for HBsAg is one convenient option for the screening of occult HBV infection. The radical immunoassay should make it possible to perform scientifically valid epidemiological surveys of occult HBV infection status and its pathologic role in areas where HBV infection is endemic should be performed scientifically. Science based investigations never cause unnecessary unease in the community.

We consider it unrealistic to detect HBV DNA in the liver tissues along the lines suggested by Dr. Xuan and colleagues from the viewpoint of invasiveness and specificity. It might be better to reconfirm false negativity for anti-HBc using more sensitive anti-HBc measurements as Dr. Huang and colleagues suggested; however anti-HBc measurements are not superior because of their presumed non-specificity. In addition to being highly sensitive, the radical immunoassay method has both satisfactory within-run and run-to-run reproducibility is satisfactory, as we have reported previously [3]. We consider that radical immunoassay method for the measurement of HBsAg is a practically useful analytical procedure in view of its low cost, rapidity, and simplicity.

Radical immunoassay method for the detection of low HBsAg in combination with real-time PCR detection of HBV DNA is a promising new approach for screening occult HBV carriers among healthy subjects and patients with various liver diseases. As Dr. Xuan and colleagues and Dr. Huang and colleagues point out, an important issue is how to deal with individuals who have low HBsAg positivity without HBV DNA. Of course, we cannot diagnose HBV carriers based solely on low HBsAg positivity using the radical immunoassay method. We speculate that the presence of some cases showing low HBsAg but negativity for HBV DNA might reflect the process of natural clearance of HBsAg or integration of the surface gene into hepatocytes without the core gene. To further clarify these issues, we are planning two projects. Firstly, we intend to follow up the changes in low HBsAg concentration and the appearance of HBV DNA in cancer patients who have a low HBsAg concentration and HBV DNA negativity after anti-cancer chemotherapy. Secondly, we intend to survey the status of occult HBV infection in a country where HBV infection is more endemic than in Japan. We are grateful to Dr. Xuan and colleagues and Dr. Huang and colleagues for their thoughtful comments.

References


Hitoshi Togashi *
Sumio Kawata
Yamagata University Health Administration Center,
Department of Gastroenterology, Course of Internal Medicine and Therapeutics, Yamagata University Faculty of Medicine, 1-4-12 Kojirakawa-machi, Yamagata 990-8560, Japan
*Tel.: +81 236284154; fax: +81 236284157.
E-mail address: htogashi@med.id.yamagata-u.ac.jp