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LETTERS TO THE EDITOR

"Anti-HBc alone" in human immunodeficiency virus-positive and immuno-suppressed lymphoma patients

Yu Xuan Koo, Daniel SW Tan, Iain BH Tan, Richard Quek, Miriam Tao, Soon Thye Lim

Yu Xuan Koo, Yong Loo Lin School of Medicine, National University of Singapore, 10 Medical Drive, Singapore 117597, Singapore
Daniel SW Tan, Iain BH Tan, Richard Quek, Miriam Tao, Soon Thye Lim, Department of Medical Oncology, National Cancer Centre Singapore, 11 Hospital Drive, Singapore 169610, Singapore
Author contributions: Koo YX, Tan DSW, Tan IBH, Quek R, Tao M and Lim ST designed the research and were involved in writing the final manuscript.
Correspondence to: Dr. Soon Thye Lim, MBBS, MRCP, Department of Medical Oncology, National Cancer Centre Singapore, 11 Hospital Drive, Singapore 169610, Singapore. dmolst@nccs.com.sg
Telephone: +65-64368000 Fax: +65-62256283
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Abstract

Hepatitis B virus (HBV) infection is endemic in various parts of the world. A proportion of patients have resolved prior exposure to HBV, as evidenced by the clearance of circulating hepatitis B surface antigen and the appearance of antibody to hepatitis B core antigen (anti-HBc), which could produce protective antibody to hepatitis B surface antigen (anti-HBs). With time, anti-HBs in some patients may become negative. Such patients are described as having occult HBV infection or "anti-HBc alone". In the context of immunodeficient patients, such as HIV patients or lymphoma patients undergoing immunosuppressive immunotherapy, the lack of protective anti-HBs may increase the risk of hepatitis B reactivation. Serum HBV DNA testing may be necessary in "anti-HBc alone" patients, to detect patients at a high risk of developing HBV infection allowing appropriate prophylactic management.

Key words: Hepatitis B virus; Human immunodeficiency virus; Antibody to hepatitis B core antigen; Hepatitis B virus DNA; Viral hepatitis

Peer reviewer: Dariusz M Lebensztejn, Associate Professor, 3rd Department of Pediatrics, Medical University of Bialystok, 17 Waszyngtona Str, Bialystok 15-274, Poland

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TO THE EDITOR

Patients with negative hepatitis B surface antigen (HBsAg) and positive antibody to hepatitis B core antigen (anti-HBc) but no antibody to hepatitis B surface antigen (anti-HBs) have traditionally been described as having occult hepatitis B virus (HBV) infection[1]. The recent article by Pérez-Rodríguez *et al*[2] in the issue of the *World J Gastroenterol* (March 14, 2009) described these patients as "anti-HBc alone", none of them was positive for serum HBV DNA. Of note, 10 of the 30 patients tested were taking lamivudine or tenofovir when the tests were performed. Furthermore, "anti-HBc alone" was associated with factors such as young age and HCV infection. They concluded that HBV DNA determination should not be performed in every "anti-HBc alone" patient, but only in those with unexplained clinical or analytical signs of liver injury.

Patients with prior exposure to HBV may subsequently clear their serum HBsAg, and become anti-HBc positive. Anti-HBs may be positive or negative, as anti-HBs may fall over time. Some authors considered patients with anti-HBc but no anti-HBs as having occult HBV infection[1,3-6]. Consequently, in a portion of these patients, HBV DNA may be detected. Biologically, it would be difficult to explain why this should not be the case in HIV patients as reported by Pérez-Rodríguez and colleagues[2]. It is uncertain what the authors meant when they considered that patients with defective immune response (anti-HBc) would have undetectable HBV DNA. On the contrary, if one considers that these HIV patients may have defective immune response (i.e. immunodeficiency), one might expect a higher HBV DNA level. We performed a similar study in lymphoma patients, who were HBsAg negative, anti-HBc positive, and tested for anti-HBs and HBV DNA at diagnosis (n = 89). Among the 27 "anti-HBc alone" patients, who were anti-HBs negative as defined by the authors, 2 (7.4%) had a detectable HBV DNA level,

as compared to the negative results by Pérez-Rodríguez *et al*[2]. Although our results were observed in lymphoma patients, it is difficult to explain why this should be different in HIV patients. Interestingly, even among the 63 lymphoma patients with positive anti-HBs, 2 (3.2%) had detectable HBV DNA.

The negative HBV DNA results reported by Pérez-Rodríguez *et al*[2] could be confounded by the fact that 10 patients were on anti-viral agents, suppressing HBV DNA levels. It is also uncertain whether administration of anti-viral agents could have an impact on HBV DNA load, thus it will be important to re-examine the HBV profile of patients with HIV at diagnosis, prior to the usage of anti-viral agents, particularly lamivudine (which suppresses HBV) to confirm the results reported by the authors.

Furthermore, HBV DNA tests were not conducted for all "anti-HBc alone" patients due to non-medical reasons as reported by Pérez-Rodríguez *et al*[2]. Due to the relatively small number of patients tested (n = 30), more patients need to be followed up.

It has also been reported that "anti-HBc alone" is associated with young age, which is consistent with the earlier findings[7]. However, this paper did not provide a biological explanation for the higher prevalence of the defective immune pattern observed in younger patients. Notably, the median age of our 27 patients was 69.3 (range 17.6-83.6) years whereas the mean age of the 59 lymphoma patients with negative HBsAg, positive anti-HBc and anti-HBs was 63.9 (range 24.2-86.5) years. Contrary to the results reported by Pérez-Rodríguez *et al*[2], we observed a higher median age in lymphoma patients with the "anti-HBc alone" pattern.

In conclusion, it is important to verify the author's observations in a proportion of newly diagnosed HIV patients, prior to the usage of anti-viral agents, particularly lamivudine (which could suppress HBV DNA levels) to confirm the results reported by the authors. Testing of HBV DNA in "anti-HBc alone" patients may be necessary.

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