Is there any evidence implying the use of a different criterion for protective anti-HBs titer after HBV vaccination in immunosuppressed patients?

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Dear Editor,

In the last decade, it has been well established that hepatitis B virus (HBV) reactivation is one of the important complications of immunosuppression depending on the risk category of the immunosuppressive agent. This reactivation which poses a serious threat for clinicians can occur in a wide range of clinical spectra including organ transplantation, chemotherapy for solid organ malignancies and treatment with biological agents.

In patients exposed to HBV, it is possible to prevent reactivation with different approaches according to the risk category of the immunosuppressive agent. On the contrary, vaccination remains an important but neglected approach for protecting patients who are seronegative (Hepatitis B surface antigen (HBsAg) negative and anti-hepatitis B core total antibody (anti-HBc) total negative) for HBV. In daily practice, immunosuppressive patients are evaluated in detail in terms of HBV reactivation risk, but vaccination of a seronegative patient may be overlooked.

The consensus report regarding immunosuppressive therapy and the risk of hepatitis B reactivation by Aygen et al. (1) was published in this journal in May 2018. This valuable and enlightening consensus report provides comprehensive and concise information to clinicians regarding the follow-up of immunosuppressive patients for hepatitis B reactivation. However, in the report, there is a controversial point concerning postvaccination protective anti-HBs titer. The recommendation in the algorithm presented in the report is as follows: "If anti-HBs is negative, double-dose HBV vaccination (40 µg) at months 0, 1, and 6; if it is >10 to <100 IU, double-dose HBV vaccination one time" (1). However, there are no data on the protective titer of postvaccination anti-HBs concentration in the articles which Aygen et al. (1) referred for this recommendation. They refer to four articles for their algorithm. However, none of these, including the Review of American Gastroenterological Association Institute, have conclusions regarding the evaluation of a vaccine response in patients who are negative for HBsAg, anti-HBc, and anti-HBs (2-5). It should be noted that protective anti-HBs titer response of a seronegative individual is fundamentally different from that of an individual who has been exposed to HBV and hence is carrying a reactivation risk. A technical review of the American Gastroenterological Association Institute on prevention and treatment of hepatitis B reactivation during immunosuppressive drug therapy states that anti-HBs titers >100 IU may provide protection against HBV reactivation in patients receiving B-cell depleting drugs (6). However, this vague presumption is based on only a few studies with a limited number of patients and only covers patients who have a reactivation risk due to previous HBV exposure.

Many factors including the type, dosage, and schedule of vaccination used as well as age, gender, genetic factors, co-morbidity, and the status of the immune system of the patient are shown to affect the antibody response to the hepatitis B vaccine (7). It is clear that a reduced humoral immune response due to immunosuppressive treatment can impair the response to the HBV vaccine. Consequently, the double-dose hepatitis B vaccination approach in immunosuppressed patients has been clarified in recent years (8); however, there is no change regarding protective anti-HBs titer. Although the decrease in vaccine response provides the basis for high-dose vaccine administration, it does not mean that the protective antibody titers should be higher. A postvaccination an-

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ti-HBs concentration of ≥10 mIU/mL is protective when measured one to two months after having received a complete immunization schedule regardless of the immunity status of the patient. The latest position paper of the World Health Organization and the Morbidity and Mortality Weekly Report of the CDC regarding recommendations of the Advisory Committee on Immunization Practices state this antibody titer as ≥10 mIU/mL (7, 8). IDSA clinical practice guidelines for vaccination of an immunocompromised host recommends a second 3-dose series of HBV vaccine if a postvaccination anti-HBs concentration of ≥10 mIU/mL is not attained in immunosuppressed patient groups such as hematopoietic stem cell transplant recipients, solid organ transplant recipients, and patients with human immunodeficiency virus (HIV) infection (9).

In conclusion, there is no evidence for the use of a different criterion for protective antibody titer after HBV vaccination in immunosuppressed patients.

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