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Case Report

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Vaccination and transient hepatitis B surface antigenemia

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Abstract
Hepatitis B vaccination is mandatory for all hepatitis B surface antigen (HBsAg)-negative hemodialysis (HD) patients with low hepatitis B surface antibody titers. We report a case of transient hepatitis B surface antigenemia, detected incidentally, in an HD patient after the second dose of Hepatitis B vaccine. The patient had to be isolated on a separate HD machine, in a separate room, until further investigations ruled out a true hepatitis B virus infection. This led to further unnecessary testing and generated great concern and anxiety for the patient. We present this case to emphasize that HD units should be aware of this phenomenon and that HBsAg testing be deferred until 4 weeks after vaccination to avoid HBsAg false positivity.

Keywords: hemodialysis; hepatitis B surface antigen; hepatitis B vaccine; vaccine-induced-positive hepatitis B surface antigen

Introduction

Infection with hepatitis B virus (HBV) is a well-known and an important cause of liver disease in patients on hemodialysis (HD). Recombinant hepatitis B vaccines are commonly utilized in HD patients for prophylaxis against HBV infections. The presently available vaccines contain purified recombinant hepatitis B surface antigen (HBsAg) obtained by culturing genetically engineered *Saccharomyces cerevisae*, which carry the surface antigen gene of HBV.

Case history

An 83-year-old Iranian woman was commenced on HD in March 2010 for chronic kidney disease Stage 5 secondary to hypertensive nephrosclerosis via a temporary right internal jugular catheter.

Viral serologies (HIV ag/ab, HBsAg, hepatitis C virus ab) done prior to initiation of dialysis were negative. In accordance with our unit protocol, where viral screening is done every 3 months, serological tests were repeated on 1 June 2010. HBsAg was weakly positive and the same repeated after 3 days was again reported as positive. A separate HD machine, in a separate room, was allocated for her dialysis. She had not received any blood transfusions in the recent past. Liver function tests were normal. Hepatitis B surface antibody (HBsAb), HBeAg and HBV DNA were all negative. In further discussion with the patient's relatives, it was determined that she had received her second dose of Engerix B vaccination (40 μg intramuscular) 5 days prior to serological testing (27 May 2010). The first dose of the vaccine had been administered on 4 April 2010. On 16 June 2010, 3 weeks after the second hepatitis B vaccination, HBsAg was repeated and was negative. Liver function test was normal. Hepatitis B core (HBc) IgM antibody was negative, ruling out recent HBV infection. Hence, it is most likely that the HBsAg was falsely positive in the wake of recent HBV vaccination.

Discussion

The practice of extensive infection control measures, the decrease in the need for blood transfusions after the introduction of erythropoietin, the development of an effective HBV vaccine and segregation of HBsAg-positive patients during HD have significantly contributed to the progressive reduction of HBV prevalence among HD patients [1, 2].

HBsAg is the most common serological marker used to identify acute or chronic HBV infections. HD patients with HBsAg positivity are considered to have HBV and are segregated to limit transmission. Hepatitis B vaccination is administered to HBsAg-negative patients who lack or have low levels of anti-HBsAb ($<$10 U/L), which is the protective antibody against HBV.

It was initially thought that hepatitis B surface antigenemia did not occur after hepatitis B vaccination; however, the study used only the plasma-derived HBV vaccine [3]. There have been several reports of detectable hepatitis B surface antigenemia after vaccination, especially in neonates, children and blood donors [4–6].

Transient hepatitis B antigenemia in HD patients following HBV vaccination was reported as early as 1996 [2, 7]. The duration of hepatitis B surface antigenemia after vaccination is brief, usually 1–7 days, however, this may be prolonged up to 20 days in patients on HD [2]. Ly *et al.* [8] performed a prospective study of de novo HBV infection in $>$2400 HD patients who were screened monthly for HBsAg. They concluded that HBV immunization was the

most common cause of detectable HBsAg in HD patients. In their opinion, HD patients should not be screened for HBV within a week of immunization and caution should be exercised when interpreting HBsAg seropositivity within 4 weeks of HBV immunization.

The transient HBsAg positivity may result from early, slow, variable and non-reproducible absorption of vaccine from the muscle. This phenomenon, though surprising, is plausible. In our laboratory, blood samples are tested for HBsAg by a third-generation microparticle enzyme immunoassay (AXSYM®; Abbott laboratories, Chicago, IL, USA). The amount of vaccine injected (40 μg) and the sensitivity of the AXSYM® monoclonal assay (0.1–0.6 ng/mL) calculates to a Vd (volume of distribution) of 70–400 L. Therefore, if the injected vaccine is distributed in total body water (~42 L) or if the antigen is circulating in a smaller space, i.e. extracellular fluid (~12 L) or plasma volume (~3 L), this would account for the vaccine antigen being detectable [2].

In such circumstances, the surface antigenemia is caused by a passive transfer of antigen by vaccination and not by viral replication; hence, there is no risk for vaccination-induced infection. An important implication of this phenomenon is that the results of HBsAg assays should be interpreted according to the time elapsed since the last administration of a vaccine against hepatitis B [9].

The period of incidental HBsAg (false) positivity, albeit brief, generated significant concern and anxiety among the patients' family and our dialysis unit staff. The patient had to be isolated on a separate HD machine, in a separate room, until further HBV- and HBsAg-negativity reports were obtained.

Although, the CDC guidelines with regard to hepatitis B screening, published in April 2001, recommend that susceptible new HD patients (those with Anti-HBsAb < 10 U/L) be screened every month for HBsAg until their anti-HbsAb is >100 U/L, most HD centers carry out Hepatitis B screening with testing of HBsAg once in 3 months [10, 11]. In either case, we recommend that HBsAg testing be done only after 4 weeks of having administered a vaccine dose, to avoid false positivity, as noticed in our patient. This would mean new HD patients who are being vaccinated have an individualized HBsAg testing schedule, so as to maintain a gap of 4 weeks between the vaccination dose and HBsAg testing.

In conclusion, based on our experience with this patient and review of existing literature, we reemphasize previous recommendations that HBsAg screening should not be carried out until 4 weeks after HBV immunization. This applies, all the more, in HD units where hepatitis B screening is carried out routinely throughout the year and hepatitis B vaccines are frequently administered. A history of recent hepatitis B vaccination should be meticulously elicited when a previously negative patient is detected as 'HBsAg positive'. Hepatitis B vaccines are clearly noninfectious and do not pose a risk of transfusion-transmitted disease. The occurrence of transient post-vaccination HBsAg positivity needs to be fully acknowledged to prevent misdiagnosis, anxiety and confusion.

Conflict of interest statement. None declared.

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