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False-Positive Hepatitis B Antigenemia After Vaccination in a Patient With CKD

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INTRODUCTION

Iatrogenic blood-borne virus transmission in dialysis units has been recognized as a concern since the early days of hemodialysis.[1] The prevalence of hepatitis B infection has steadily declined over the years, however, due to infection control measures, including physical isolation, environmental disinfection, and dedicated dialysis equipment for seropositive patients. Blood product screening and reduced transfusion requirements due to erythropoietin use have reduced viral transmission from infected blood products. Patient and staff vaccination against hepatitis B have also helped to reduce iatrogenic transmission.[1]

In patients with advanced chronic kidney disease (CKD) and in patients supported with long-term hemodialysis, hepatitis B vaccination is routine. However, advanced CKD has been associated with reduced immunogenicity, and only 50% to 70% of hemodialysis patients develop a protective antibody response after hepatitis B vaccination.[2,3] Strategies that have been used to improve the seroconversion rate include doubling the vaccine dose, increasing the number of vaccine doses, and starting vaccination at an earlier stage of CKD.[4]

National guidelines have recommended the screening of hepatitis B serology for dialysis patients as part of infection control recommendations. While hepatitis B screening every 6 months is commonly reported, there is no consensus on the frequency of hepatitis B screening, with some guidelines advocating monthly screening for nonimmune patients.[5]

The development of new-onset hepatitis B antigenemia in a hemodialysis patient is significant and requires a rapid review. Iatrogenic transmission of hepatitis B is the most worrisome diagnosis, necessitating contact tracing and review of infection control measures to detect any lapses. However, a more benign cause is that of postvaccination transient hepatitis B antigenemia, which has been reported sporadically in dialysis patients since the 1990s.[6–8] This creates a conundrum for physicians, in particular medical directors of dialysis units, because hepatitis B antigenemia could represent either of the 2 possibilities.

In this report, we discuss our case series of 5 patients with CKD who developed transient false-positive hepatitis B antigenemia closely related to vaccination.

CASE PRESENTATIONS

During a 5-year period from 2016 to 2020, 5 patients were identified with transient hepatitis B surface antigen positivity closely related to hepatitis B vaccination. These results were noted in various clinical settings, for instance, as part of routine investigations ordered before an outpatient clinic visit, during regular blood investigations for an affiliated dialysis center, as well as during a hospital admission where the previous hepatitis B serology results had lapsed in validity. These patients had recently received an intramuscular hepatitis B vaccination by a primary health care provider. Hepatitis B surface antigen was tested according to standard laboratory practice across 3 different accredited laboratories.

At the point of diagnosis, 3 of the 5 patients were supported with long-term in-center hemodialysis, and 2 patients had non–dialysis-dependent stage 5 CKD. Their baseline characteristics are summarized in Table 1.

Hepatitis B surface antigen was positive in all 5 patients at a median of 4 days (interquartile range, 3–6 days) after vaccination, and a repeat hepatitis B surface antigen test result was negative at a median of 13 days (interquartile range, 12.5–54 days) after vaccination.

Table 1. Baseline characteristics

Index patient	Patient information (age, sex, weight, ESRD vintage)	Comorbidities	Hepatitis B vaccine and dose	Days after hepatitis B vaccination	
				HbsAg antigenemia detected	HbsAg antigenemia cleared
1	81, male, 57 kg, ESRD 39 mo	Diabetes mellitus, gout, hypertension, pancreatic neuroendocrine tumor, hard palate carcinoma	Engerix, dose unknown (1st dose)	3	17
2	63, female, 50 kg, CKD-ND	Diabetes mellitus, hypertension, hyperlipidemia, previous tuberculosis, previous hysterectomy for complex ovarian cyst	Unknown	8	91
3	54, female, 61 kg, ESRD 4 mo	Diabetes mellitus, hypertension, hyperlipidemia, previous tuberculosis	Engerix, 40 μg (2nd dose)	4	13
4	44, male, 125 kg, ESRD 4 mo	Ischemic heart disease	Engerix, 40 μg (2nd dose)	4	12
5	72, male, 63kg, CKD-ND	Diabetes mellitus, hypertension, benign prostatic hyperplasia, gout, stroke	Engerix, 20 μg (1st dose)	3	13

CKD-ND, chronic kidney disease–nondialysis dependent; ESRD, end-stage renal disease; HbsAg, hepatitis B surface antigen.

The wide range was mainly due to patient 2, who had yet to be initiated on dialysis at the point of vaccination and who received a clinical diagnosis of vaccine-induced transient hepatitis B antigenemia when the antigenemia was initially investigated. Results of hepatitis B DNA amplification by polymerase chain reaction were negative for all patients.

For patients on hemodialysis, the dialysis machine the patient was dialyzing on was isolated until the repeat hepatitis B results returned negative, confirming a transient vaccination response. In all patients, the hepatitis B surface antigen remained negative during the duration of follow-up up to 2 years after the initial vaccination.

Serial measurements of alanine aminotransferase that were performed as part of regular dialysis monitoring did not reveal any transaminitis. IgM hepatitis B core antibody was performed for patients 3 and 4, and the result was negative.

DISCUSSION

Our experience highlights that transient hepatitis B antigenemia after vaccination is not uncommon and occurs most frequently in the first 2 weeks after vaccination.[6–8] One study observed this in 31% of unselected hemodialysis patients after vaccination.[7] In our study, we have observed the same phenomenon also occurring in nondialysis patients with CKD. We postulate that this transient antigenemia occurs after vaccination in some patients regardless of CKD status, given previous reports in healthy blood donors.[9] This often goes undetected in the non-CKD population given the rapid clearance of the antigenemia and infrequent testing. However, in patients with CKD or on hemodialysis, hepatitis B surface antigen testing is more frequent, hence the likelihood of detection is increased.

For an individual patient, the possibility of acquiring a new hepatitis B infection is likely to be a stressful event, because the patient may have to consider the future health implications of a chronic, incurable disease. Furthermore, patients may face intrusive questioning into their personal life and behaviors, with serious implications for relationships with partners and families. Additional nucleic acid testing and repeat hepatitis B surface antigen testing entails greater anxiety and cost.

For staff working in a hemodialysis unit, misinterpretation of the hepatitis B results as a new hepatitis B infection could lead to the patient being inadvertently dialyzed using designated hepatitis B equipment and thus potential exposure to true infection. In addition, any suspicion of iatrogenic transmission of hepatitis B would lead to a review of infection control practices, notification to local health authorities, screening, and surveillance potentially lasting for months after the event. The positive result for hepatitis B surface antigen would, in effect, trigger processes that are manpower- and cost-intensive, not to mention the disruption and stress to staff and patients.

In our health care system, as with others, multiple providers may care for the same patient, with imperfect information transfer between health care providers. In our context, hepatitis B vaccination was provided by the primary health care team, whereas blood tests for hepatitis B surface antigen were ordered by the dialysis centers or tertiary hospital. Improving communication between stakeholders, patient education, use of vaccine passports, regular review of the vaccination record, and education of dialysis staff so that patients are asked about recent vaccination before blood is drawn for serology may help prevent such occurrences. Also, it would be ideal if a specified minimum interval between vaccination and testing for hepatitis B can be incorporated into hemodialysis infection control guidelines. Vaccinating patients for hepatitis B is encouraged early on in the course of CKD because it elicits a better and sustained immune response than when they are vaccinated in end-stage kidney disease.[1,5]

Table 2. Teaching points

1. All nephrologists and staff working in hemodialysis units should be aware that hepatitis B antigenemia may occur after vaccination. This should not be assumed or treated as iatrogenic transmission of hepatitis B without confirmatory testing. The patient should not be dialyzed using a designated hepatitis B machine pending confirmatory testing.
2. Hepatitis B surface antigen should not be tested for at least 14 to 28 days after vaccination to prevent interpretation issues.
3. Patient and dialysis staff education on the appropriate timing of hepatitis B surface antigen testing would help to reduce misinterpretation, particularly in health care settings where vaccination and dialysis are administered by different providers. Hepatitis B vaccine passports may help in this regard.
4. Should a patient on dialysis develop a positive hepatitis B surface antigen, vaccination history should be sought, and investigations including a repeat hepatitis B surface antigen and viral load should be performed expeditiously to rule out hepatitis B infection while the patient's dialysis machine is isolated.

Transient hepatitis B antigenemia occurs fairly commonly in the population with CKD, and while benign, has downstream effects, as described above. This may affect individual patients, hemodialysis staff and centers, as well as the broader health care system as a whole. We suggest that deferring testing for hepatitis B surface antigen for at least 14 and ideally 28 days after vaccination would avoid this diagnostic conundrum and its negative downstream effects (Table 2).

CONCLUSION

Transient hepatitis B surface antigenemia in patients with CKD may occur after vaccination, particularly in the first week. The development of a positive hepatitis B surface antigen test result in a hemodialysis patient leads to challenges in interpretation and requires additional investigations to distinguish between iatrogenic hepatitis B transmission and a transient vaccination response. Hepatitis B surface antigen should thus not be tested within 14 to 28 days after vaccination, and this is best achieved through education and increasing awareness of this phenomenon among patients, dialysis staff, and nephrologists.

DISCLOSURES

All the authors declared no competing interests.

PATIENT CONSENT

The authors declare that they have obtained consent from the patients discussed in the report.

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