Transmission of Hepatitis B Virus From an Orthopedic Surgeon With a High Viral Load

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(See the Editorial Commentary by Henderson, on pages 225–7.)

Background. During the evaluation of a needle-stick injury, an orthopedic surgeon was found to be unknowingly infected with hepatitis B virus (HBV) (viral load >17.9 million IU/mL). He had previously completed two 3-dose series of hepatitis B vaccine without achieving a protective level of surface antibody. We investigated whether any surgical patients had acquired HBV infection while under his care.

Methods. A retrospective cohort study of all patients who underwent surgery by the surgeon was conducted. Patients were notified of their potential exposure and need for testing, and samples with positive HBV loads underwent DNA sequencing. Characteristics of the surgical procedures for the cohort were evaluated.

Results. A total of 232 (70.7%) of potentially exposed patients consented to testing; 2 were found to have acute infection and 6 had possible transmission (evidence of past exposure without risk factors). Genome sequence analysis of HBV DNA from the infected surgeon and patients with acute infection revealed genetically related virus (>99.9% nucleotide identity). Only age was found to be statistically different between those with confirmed or possible HBV transmission and those who remained susceptible to HBV.

Conclusions. We documented HBV transmission during orthopedic surgery to 2 patients from a surgeon with HBV. This investigation highlights the importance of evaluating individuals who do not respond to 2 series of HBV vaccination, the increased risk of HBV transmission from providers with high viral loads, and the need to evaluate the clinical practice of providers with HBV and implement appropriate procedure-based practice restrictions.

Keywords. hepatitis B virus; reverse exposure; transmission.
We identified a surgeon with HBV infection and a high viral load (HBeAg positive) during evaluation of a needle-stick injury. Herein we report the results of an investigation of patients who had undergone operative procedures by the surgeon to evaluate potential provider-to-patient HBV transmission.

**MATERIALS AND METHODS**

In 2009, a surgeon was identified as being unknowingly and asymptptomatically infected with HBV following baseline evaluation during an exposure workup. Laboratory results included a positive hepatitis B surface antigen (HBsAg), positive HBeAg, negative immunoglobulin M (IgM) anti–hepatitis B core antibody (anti-HBc), and normal liver enzymes. The source patient of the exposure had negative HBV serology (HBsAg and anti-HBc) results. The surgeon was removed from performing operative procedures after testing revealed a viral load of >17.9 million IU/mL (Versant HBV bDNA 3.0 assay, Siemens Healthcare Diagnostics, Tarrytown, New York) while an investigation of potentially exposed patients was conducted. The surgeon had immigrated to the United States and completed orthopedic residency training before being employed by Facility A. Having previously completed 2 hepatitis B vaccination series, the surgeon indicated no prior HBV exposure. However, at the time of this initial review.

One patient hospitalized with active hepatitis B was found at one of the source patient’s facilities. A telephone hotline was established to answer patient questions and provide counseling. Follow-up letters and telephone calls conducted by Facility A were carried out to contact patients who did not respond to the initial communication. Patients consenting to testing had blood drawn and serum samples tested for HBsAg, anti-HBs, and anti-HBc. An additional sample was collected and held at Facility A to enable sera from HBsAg-positive patients to undergo serotyping and genetic analysis by the Division of Viral Hepatitis at the Centers for Disease Control and Prevention (CDC). The results of the tests were shared with seropositive patients by phone in order to determine possible risk factors for potential conversion through confidential structured interviews and to recommend additional testing if necessary. Seronegative and immune patients were informed of test results by letter.

**Review of Infection Control Practices**

Interviews were conducted with the surgeon, operating room personnel, and surgical colleagues in order to identify potential lapses in surgical technique or infection control practices. Individuals were interviewed privately to ensure anonymity using a semi-structured interview process. All individuals were asked about (1) surgical technique, (2) compliance with double gloving and sterile technique, (3) recollection of prior glove breaches, and (4) regloving practices of the surgeon. Additional discussions pursued with some interviewees included review of events surrounding the index case and impressions of the surgeon’s nontechnical skills, acumen, and professionalism. A total of 13 interviews were conducted.

**HBV DNA Sequencing and Phylogenetic Analysis**

Blood specimens from the infected surgeon and patients found to have active HBV infection (HBsAg positive, HBeAg positive, positive HBV load) were sent to the Division of Viral Hepatitis Laboratory at the CDC for serotyping and HBV molecular testing. To determine the genetic relatedness of HBsAg-positive samples, partial HBV genomes were amplified by nested polymerase chain reaction (PCR), sequenced, and compared using the Kimura 2-parameter model of nucleotide substitution, as previously described [9].

**Case Definitions**

Confirmed surgeon-to-patient transmission was defined as a patient from the cohort who had active HBV infection with a virus genetically related (≥99.9% nucleotide identity) to the surgeon. Possible surgeon-to-patient transmission was defined as a patient from the cohort with evidence of past HBV infection (HBsAg negative, anti-HBs positive, anti-HBc positive) who was either previously documented to be HBV seronegative or who had no lifetime HBV infection risk factors (identified by patient interview and review of the medical chart). Those patients with evidence of past HBV infection (HBsAg negative, anti-HBs positive, anti-HBc positive) but who had lifetime risk factors for HBV exposure and no prior HBV testing were defined as indeterminate. Patients who had a positive anti-HBs,
negative anti-HBc, and negative HBsAg were considered to be immune due to vaccination. The remaining patients were deemed to be nonimmune and susceptible to HBV infection (HBsAg negative, anti-HBs negative, anti-HBc negative).

Cohort Analysis
We compared features of patients with confirmed and possible transmission with those patients susceptible to infection at the time of testing. All analyses were conducted using SPSS software, version 18.0 (SPSS Inc, Chicago, IL). Comparisons of categorical variables were made using the $\chi^2$ test, and comparisons of continuous variables were made using Student $t$ test for normally distributed variables and the Mann-Whitney $U$ test for nonparametric variables.

RESULTS

Identification of Cases
We identified 328 patients who underwent 350 procedures by the surgeon. Five patients were identified to have died prior to the notification (none with recognized hepatitis). Two hundred one patients (61.3%) responded to the initial letter and an additional 25 (7.6%) responded to the second letter. The remaining 97 patients were contacted by phone; of these, 7 (2.1%) responded to phone calls, while 90 either refused or did not return phone calls.

A total of 232 (70.7%) patients consented to testing (Figure 1). Two hundred eight (89.7%) patients were susceptible to HBV infection, and 14 (6.0%) patients were immune owing to vaccination. Two (0.9%) patients were identified with active HBV infection, and 8 (3.4%) had evidence of past HBV infection. Six (2.6%) patients with past infection reported having no lifetime risks for HBV exposure and were therefore considered to have possible surgeon-to-patient HBV transmission; one was previously documented to be HBV seronegative prior to surgery. The remaining 2 patients reported lifetime risk factors for HBV infection and were classified as having an indeterminate risk for transmission: one, who had renal failure requiring hemodialysis, had evidence of HBV seroconversion prior to surgery, whereas the second had previously been told of being exposed to HBV while serving as a medic in the Vietnam War.

Of the 2 patients with active disease (both with elevated IgM anti-HBc titers), one was admitted for symptomatic hepatitis with an alanine aminotransferase level of 2880 U/L and HBV DNA level of 120 000 IU/mL to Facility A. The patient started tenofovir 21 weeks after transmission, and antiviral therapy was discontinued 5 months later, once he developed anti-HBs and cleared HBeAg and HBV viremia. The other patient had asymptomatic disease with mildly elevated hepatic enzymes and a high HBV load (>17.9 million IU/mL). He was placed on tenofovir 11 months after transmission, having not demonstrated evidence of serologic conversion. More than 2 years later, he remains on tenofovir with positive HBsAg and HBeAg, negative anti-HBe, and low positive HBV DNA level of <100 IU/mL.

HBV Phylogenetic Analysis
HBV from both patient samples was found to be genetically identical to HBV from the surgeon. Partial HBV genomes

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Figure 1. Overview of study. Of 328 identified patients, a total of 232 were evaluated. Two individuals had active hepatitis B virus (HBV) (hepatitis B surface antigen [HBsAg] positive, hepatitis B e antigen positive, positive HBV load), and 6 individuals had evidence of past infection (anti-HBsAb positive, anti–hepatitis B core antibody positive) and no lifetime risk factors. Ninety patients refused testing and 5 patients had died prior to contact.
(1790 nucleotides) in the region comprising the complete HBsAg-coding gene as well as significant parts of the core and polymerase genes were obtained from 7 HBV PCR-positive serum specimens (6 from the patients and 1 from the surgeon). All 7 sequences were closely related genetically (shared 99.9%–100% nucleotide identity), belonged to HBV genotype D2 subtype ayw3 (Figure 2), and formed a patient-surgeon HBV sequences cluster, suggesting a common source of infection.

**Characteristics of Surgical Procedures**

The median age of patients susceptible to HBV was statistically older (median, 64 years [interquartile range (IQR), 19 years]) compared to those with HBV (median, 55 years [IQR, 26 years]). When the analysis was restricted to only confirmed cases of HBV transmission, the median age (73 years) was statistically older than that of susceptible patients ($P = .001$).

Among cases of confirmed or possible transmission, there were 5 (50%) knee replacements and 5 (50%) hip
replacements. Among the HBV-susceptible patients, there were 102 (49.05%) knee replacements and 99 (47.68%) hip replacements. The remainder of patients in the susceptible group had nonjoint replacement procedures. No significant difference between the 2 patients groups by surgical procedure or total operative time was observed (Table 1). This remained true when the analysis was restricted to only patients with confirmed transmission.

**Table 1. Clinical Characteristics of Patients With Confirmed or Possible Hepatitis B Virus (HBV) Transmission Compared With HBV-Susceptible Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HBV Transmission (n = 8)</th>
<th>HBV Susceptible (n = 208)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (IQR)</td>
<td>55 (29–84)</td>
<td>64 (45–83)</td>
<td>.037</td>
</tr>
<tr>
<td>Total operative time, h, median (IQR)</td>
<td>3.25 (1.65–4.85)</td>
<td>2.63 (1.47–3.78)</td>
<td>.125</td>
</tr>
<tr>
<td>Total joint arthroplasty</td>
<td>8 (100%)</td>
<td>201 (92.6%)</td>
<td>.713</td>
</tr>
</tbody>
</table>

Abbreviations: HBV, hepatitis B virus; IQR, interquartile range.

* Confirmed and possible HBV infection.

the cohort of patients at risk was possible only through the self-report of a needle stick injury by the surgeon. This underscores the importance of healthcare facilities implementing robust systems of reporting and evaluating occupational blood and body fluid exposures.

The CDC and the Society for Healthcare Epidemiology of America (SHEA) urge all providers who perform invasive procedures to know their status for blood-borne transmissible diseases [2, 11–13]. This report highlights the importance of these recommendations. Guidelines for hepatitis B vaccination for healthcare workers also recommend evaluating for a response after completion of the hepatitis B vaccine series, completing a second vaccine series for individuals who do not respond to the first series, and determining the HBV infection status for individuals who fail to have a serologic response after completion of 2 vaccine series [13]. Until recently [12], however, the recommendation to determine the infection status of a provider who fails 2 HBV vaccine series may have been overlooked, as it only appeared in the appendix of the guideline [13]. In this case, the surgeon was documented to have completed the hepatitis B vaccine series on 2 occasions but did not mount a protective serologic response. In addition, the surgeon met criteria for evaluation of chronic HBV infection, because he had emigrated from a country of high HBV endemicity [10]. The guidelines extend to US-born individuals whose parents emigrated from a region with high HBV endemicity [10]. These findings emphasize the importance of HBsAg for healthcare workers who do not respond appropriately to 2 series of HBV vaccination [13] and for HBsAg testing for foreign-born persons from regions of the world with HBV prevalence of ≥2%, regardless of vaccination status, to aid the identification of persons with chronic HBV infection and ensure appropriate clinical and public health management [10].

Our findings also reinforce the increased risk for HBV transmission from providers with high viral loads who perform exposure-prone procedures, which are defined as procedures with an increased risk of injury that may lead to a patient exposure to worker blood or tissues. The decision to remove the surgeon from operative duties while this investigation took place is in accordance with recommendations to restrict the practice of infected physicians based on their viral load [2]. Although presence of HBeAg has previously been used to assess infectivity of a provider, this is no longer recommended as providers can be HBeAg negative yet still have

**DISCUSSION**

There is no systematic surveillance system for reporting of healthcare provider-to-patient HBV transmission; therefore, each identified episode provides an important opportunity to further define risk factors for these infrequently reported incidents. Among a cohort of 232 patients undergoing surgical procedures performed by an HBV-infected, HBeAg-positive orthopedic surgeon during a 7-month time period, we identified confirmed provider-to-patient HBV transmission in 2 (0.9%) patients and possible provider-to-patient HBV transmission in an additional 6 (2.6%) patients, resulting in a total confirmed and possible HBV transmission rate as high as 3.4%. Identification of provider-to-patient transmission and the cohort of patients at risk was possible only through the self-report of a needle stick injury by the surgeon. This underscores the importance of healthcare facilities implementing robust systems of reporting and evaluating occupational blood and body fluid exposures.

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high circulating viral loads and infect their patients [14]. Rather, measurement of quantitative HBV DNA levels is considered to be a better indicator of infectivity [2, 8]. However, defining a threshold viral load level that predicts surgeon-to-patient transmission of HBV remains problematic. Clinical studies suggest that the lowest level of serum HBV DNA that has occurred in a case of provider-to-patient transmission is 40 000 genome equivalents (GE)/mL (approximately 8000 IU/mL) [15]. These data are used as supporting evidence for the CDC and SHEA guidelines to restrict providers with HBV loads of \( \geq 5000 \text{ GE/mL} \) (1000 IU/mL) or \( \geq 10 000 \text{ GE/mL} \) (2000 IU/mL), respectively, from performing exposure-prone procedures [2, 8].

The method of transmission in the cases reported here is not clear. No incidents of percutaneous exposure, glove perforation, or other breaches in surgical technique were identified during the investigation. He was known by his peers and supervising surgeons to have excellent surgical technique and reported double gloving for 100% of surgical procedures, standard practice for all orthopedic procedures at Facility A. As has been speculated for prior examples of surgeon-to-patient transmission of HBV without documented breach of infection control practices [5], we hypothesize that unknown or microperforation of the glove might have occurred. Glove microperforation has been shown to occur with a high frequency [16, 17]. Bacterial transmission through microperforations has been estimated to occur at a rate of 5% [17]; however, the rate of viral transmission is unknown. In addition to microperforation, glove laceration during arthroscopic shoulder surgery occurs in 51% of outer gloves and 17% of inner gloves [18]. The recognition of perforations ranged from 14% [19] to 85% [17], an uncomfortably large range. Despite this, there is limited evidence to support measures beyond double gloving at this time [16].

There are several limitations to this study. Like previous reports, this study is limited by its retrospective nature. We were unable to obtain samples from all potentially exposed patients in the cohort due to patient refusal, loss of follow-up, and patient death unrelated to surgical issues or liver disease, and this creates the potential for responder bias. Similarly, recall bias is introduced owing to a retrospective review of the surgeon’s practice. Given the uniformity of the responses from surgeons and nurses, we hope recall bias is minimal; however, this was not systematically evaluated. In addition, the small number of confirmed cases makes firm conclusions regarding operative risk factors for HBV transmission difficult. While inclusion of cases of possible HBV transmission may help define the upper limit of HBV provider-to-patient transmission in this incident, whether some or all cases were truly due to operative HBV exposure is not known. Moreover, patient self-reports of HBV risk factors are limited by potential inaccuracies and recall biases.

One noteworthy aspect of this report is that the investigation was initiated and led by Facility A. The CDC provided requested technical support, including phylogenetic analysis of the HBV isolates. This model of investigation can be applied to other facilities. In response to this event, Facility A reviewed all of its policies regarding infected healthcare workers. This review led to the formation of a standing infected healthcare workers oversight panel, which had previously only existed ad hoc. Consistent with CDC and SHEA recommendations, this panel is charged with reviewing the virologic status and scope of clinical practice for practitioners at Facility A chronically infected with blood-borne pathogens, so that their risk of transmission can be assessed and appropriate guidance can be provided [2, 8].

On the basis of all available evidence, surgeon-to-patient transmission of HBV appears to be a rare event. However, our understanding of the epidemiology is limited owing to the lack of a systematic surveillance and reporting systems. Therefore, healthcare facilities should assess their employee vaccination, blood and body fluid exposure, and infected provider oversight programs to ensure that they are sufficiently robust to identify healthcare workers with chronic HBV infection and that HBV-infected healthcare workers are evaluated and monitored appropriately. These measures are crucial to minimize the risk of HBV transmission to patients and help prevent the serious sequelae of chronic liver disease.

Notes

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Potential conflicts of interest. All authors: No reported conflicts.

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