Reactivation of Hepatitis B Infection following Allogeneic Bone Marrow Transplantation in a Hepatitis B–Immune Patient: Case Report and Review of the Literature

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Background. Reactivation of hepatitis B virus (HBV) infection following allogeneic bone marrow transplantation is a rare phenomenon.

Methods. Reverse seroconversion, defined as the clearance of antibody to hepatitis B surface antigen (HBsAb) and the appearance of hepatitis B surface antigen (HBsAg) in a patient with resolved HBV infection (i.e., a HBsAg-negative, HBsAb-positive, hepatitis B core antibody–positive patient) following receipt of a bone marrow transplant is described. A review of related cases in the literature was undertaken to identify clinical features associated with this phenomenon.

Results. We present a case of reactivation of HBV infection in a 47-year-old man after receipt of an allogeneic bone marrow transplant for acute myelogenous leukemia. Before undergoing bone marrow transplantation, the presence of HBsAb and hepatitis B core antibody and the absence of HBsAg indicated clearance of natural HBV infection. The donor was HBsAg and HBsAb negative. Twenty-nine months after bone marrow transplantation, the patient developed transaminitis and evidence of active HBV infection (the patient had test results positive for HBsAg, negative for HBsAb, and positive for HBV DNA). A total of 28 other cases of reverse seroconversion have been described in the literature, 11 of which provided adequate information to be summarized in detail together with the present case. Reactivation of HBV infection following bone marrow transplantation appears to occur almost exclusively in patients who have received marrow from an HBsAb-negative donor and have experienced graft-versus-host disease, the onset of which is associated with tapering of immunosuppressive therapy.

Conclusions. Although HBV reverse seroconversion is an uncommon event, understanding the clinical features associated with the development of HBV reverse seroconversion may provide insight into how such a potentially fatal complication may be avoided.

Immunosuppression, including that which occurs following bone marrow transplantation (BMT), potentially results in the reactivation of infections that are otherwise latent or controlled by effective immune surveillance. Although development of surface and core antibodies and loss of surface antigen following acute hepatitis B virus (HBV) infection is thought to represent clearance of the virus (i.e., clinical cure), evidence exists to support the possibility that the virus may remain latent within the liver [1, 2]. If this is the case, significant immune suppression may then potentially lead to reactivation of HBV infection.

We describe a case of reactivation of HBV infection (or reverse seroconversion) in a patient with prior infection and apparent clearance of HBV (i.e., test results positive for antibody to hepatitis B surface antigen [HBsAb], positive for hepatitis B core antibody [HbcAb], and negative for hepatitis B surface antigen [HBsAg]) who developed active HBV infection (i.e., became HBsAg positive and HBsAb negative and tested positive for HBV DNA) after bone marrow transplantation. A small number of similar cases have been reported in the literature. We review these cases and discuss the implications for future management of patients.
who have recovered from earlier HBV infection and are undergoing bone marrow transplantation.

CASE REPORT

In January 1998, a 47-year-old man received an allogeneic BMT for acute myelogenous leukemia. Conditioning prior to transplantation included receipt of busulfan daily for 4 days and cyclophosphamide daily for 2 days. Results of serological testing conducted in October of 1997 were consistent with prior natural HBV infection and immunity without evidence of active HBV infection (table 1).

Serological testing of the patient’s sister (the bone marrow donor) showed her to be HBsAg negative and HBsAb negative, indicating no evidence of either prior infection with HBV or prior vaccination for hepatitis B. The patient had a history of heavy alcohol use, yet denied intravenous drug use or sexual contacts other than his wife of 29 years. Two units of packed RBC from an HBsAg-negative donor were administered 7 days before BMT.

The patient received graft-versus-host disease (GVHD) prophylaxis, which included cyclosporine A and methotrexate on days 1, 3, 6, and 11 following BMT. He continued to receive cyclosporine therapy (700 mg administered daily), which began to be tapered on day 90 following BMT and was discontinued on 19 May 1998. On 9 June 1998, 6 months after BMT, the patient developed oral and dermatological manifestations of chronic GVHD. The patient was treated with prednisone therapy (80 mg administered daily) for 2 months, which was tapered over the subsequent 2 months. The patient received trimethoprim-sulfamethoxazole for pneumocystis carinii pneumonia prophylaxis following BMT until after resolution of GVHD. He also received ganciclovir to treat concurrent cytomegalovirus infection.

In June 2000, the patient presented to the Ottawa General Hospital (Ontario, Canada) with fever and vague abdominal pain. Laboratory results revealed transaminitis (aspartate transaminase level, 183 U/L; alanine transaminase level, 64 U/L) (table 1) but normal international normalized ratio, albumin level, and total bilirubin level. The patient was discharged with a diagnosis of alcoholic hepatitis. Viral serological testing conducted at the time of admission but reported after the patient was discharged from the hospital revealed hepatitis B serological test results indicative of active hepatitis B infection (results were HBsAg positive, hepatitis B envelope antigen [HBeAg] positive, and HBsAb negative) (table 1).

At his clinic visit in October of 2000, the patient felt physically well. At examination, he was afebrile with a soft, nontender abdomen, no splenomegaly, no ascites, and a liver edge palpable 2–3 cm below the costal margin. Laboratory investigations revealed continued elevation of liver function test values and unchanged HBV serological test results (table 1). Viral tests revealed the presence of HBV DNA (HBV DNA level, >2000 pg/mL).

An abdominal ultrasound in November 2000 revealed no abnormal findings except for a slightly enlarged right lobe of the liver. An ultrasound-guided core needle liver biopsy was

<table>
<thead>
<tr>
<th>Date</th>
<th>Treatment with lamivudine</th>
<th>AST level, U/L</th>
<th>ALT level, U/L</th>
<th>Serological test result</th>
<th>HBV DNA level, pg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dec 1997 *</td>
<td>No</td>
<td>36</td>
<td>11</td>
<td>– + + NA NA</td>
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<tr>
<td>Jan 1998 b</td>
<td>No</td>
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<td>15</td>
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<tr>
<td>June 2000</td>
<td>No</td>
<td>183</td>
<td>64</td>
<td>+ – + + –</td>
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<tr>
<td>Sept 2000</td>
<td>No</td>
<td>166</td>
<td>54</td>
<td>+ … + + –</td>
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<tr>
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<td>No</td>
<td>159</td>
<td>47</td>
<td>+ – + + –</td>
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<tr>
<td>Nov 2000</td>
<td>No</td>
<td>430</td>
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<tr>
<td>Dec 2000</td>
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<td>…</td>
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<tr>
<td>2 Jan 2001</td>
<td>Yes</td>
<td>239</td>
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<td>31 Jan 2001</td>
<td>Yes</td>
<td>91</td>
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<td>Yes</td>
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<td>40</td>
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<td>No</td>
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<td>92</td>
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<tr>
<td>March 2004</td>
<td>No</td>
<td>598</td>
<td>124</td>
<td>… … … … …</td>
<td>…</td>
</tr>
</tbody>
</table>

NOTE. HBcAb, hepatitis B core antibody; HBsAb, antibody to hepatitis B surface antigen; HBeAg, hepatitis B envelope antigen; HBsAb, antibody to hepatitis B surface antigen; NA, not available; +, positive; –, negative.

a Before transplantation.
b Time of transplantation.
performed at the time and revealed changes consistent with chronic HBV infection with moderate disease activity and moderate-to-severe fibrosis (septal and early bridging), moderate large-droplet fatty change, and mild hepatocytic and Kupffer cell iron overload. There were no changes in serological test results for HBV, and transaminase levels remained elevated. In December 2000, the patient began to receive lamivudine (Hep토바이; GlaxoSmithKline) at a dosage of 100 mg daily, which he continued to receive until June 2001. The results of serological tests remained unchanged as of February 2001. Viral tests performed on 2 January 2001, while he was receiving lamivudine, revealed suppression of HBV DNA to an undetectable level; however, in July 2001, after stopping lamivudine therapy, the HBV DNA level was elevated at 1370 pg/mL. HBV DNA level has not been measured since that time. Transaminase levels have remained elevated since July 2001. In the management of the patient’s chronic hepatitis, additional anti–hepatitis B therapy has been considered, but because of the patient’s persistent, excessive use of alcohol and lack of interest in initiating long-term therapy, no medication is currently being used.

**REVIEW OF PUBLISHED CASES**

We have summarized a case of reverse seroconversion from apparent immunity to HBV infection (HBsAg-negative, HBsAb-positive status) to active HBV infection (HBsAg-positive status). Eleven other cases of reactivation of HBV infection following allogeneic bone marrow transplantation have been reported in detail and are summarized in table 2 [3–10].

Further evidence of reactivation of HBV infection following BMT can be found in the literature. Seth et al. [11] has reported reactivation in 6 of 42 patients with evidence of prior HBV infection and recovery before receipt of a transplant (HBsAg-negative, HBeAb-positive status). Similarly, Dhedin et al. [12] has reported reverse seroconversion in 4 of 37 patients with test results positive for HBeAb and HBsAb and negative for HBsAg before BMT. In addition, Onozawa et al. [13] described reverse seroconversion in 7 of 14 patients with serological evidence of resolved hepatitis B before hematopoietic stem cell transplantation [13]. In an additional 5 of these 14 patients, HBsAb levels decreased to <10.0 mIU/mL following hematopoietic stem cell transplantation, but HBsAg did not appear. With the cases described by Seth et al. [11], Dhedin et al. [12], and Onozawa et al. [13], a total of 28 cases of hepatitis B reverse seroconversion have been reported; however, these 3 studies did not provide sufficient clinical detail to be included in table 2.

Of the 12 patients whose cases are summarized in table 2 (including our own case patient), 8 were male, and 4 were female; the mean age was 38 years (range, 14–55 years) at the time of BMT. Reasons for transplantation included leukemia (8 patients), β-thalassemia (2), myelodysplastic syndrome (1), and anaplastic anemia (1).

Reported serological test results indicated that all patients were HBsAb positive before BMT, and all patients were explicitly reported as being HBsAg negative. In 3 cases, HBV DNA test results were negative before BMT [3, 6, 7]; in 2 cases, test results were HBV DNA positive [3]; in the other 7 cases, HBV DNA test results were not reported. In 11 cases, BMT donors were reported to have had no serological evidence of past or current HBV infection; one report indicated that the donor “was not infected nor immunized against HBV” [7, p. 58]. Specific serological testing of samples from BMT donors was reported in only 6 cases (including ours); all 6 donors were HBsAg negative and HBsAb negative. The serological status of transplant donors in the study by Seth et al. [11] was not specified. In the study by Dhedin et al. [12], all patients who experienced reverse seroconversion received transplants from HBsAg-negative, HBsAb-negative donors; none of the 7 patients in that study who received transplants from HBsAb-positive donors experienced seroconversion. In the study reported by Onozawa et al. [13], 4 of 7 patients who experienced reactivation of HBV infection had received transplants from HBsAg-negative, HBsAb-negative donors; donor HBsAb status was not reported for the remaining 3 patients.

The mean time to appearance of HBsAg after BMT was 23 months (range, 12–51 months); however, HBsAg was not tested for at regular intervals after transplantation. With the exception of 5 cases in which such testing was routine [3, 10] and 1 case in which serological testing was only performed after the onset of HBV infection in the patient’s wife [9], monitoring for HBsAg was likely only conducted as indicated by clinical criteria, including elevated transaminase levels with or without the appearance of clinical symptoms. Eight patients were reported to have test results positive for HBV DNA, and 1 patient was reported to have undetectable HBV DNA levels. HBV DNA test results were not reported for 3 patients. Nine patients developed HBeAg positivity; in the remaining cases, 1 patient had an HBeAg-negative HBV mutant variant, and 2 patients were HBeAg negative.

In the clinical evaluation of cases, all but 3 patients developed clinical hepatitis and evidence of liver dysfunction. Only 4 cases were reported to involve specific treatment for clinical hepatitis; in each of these 4 cases, the treatment included lamivudine. Of the 12 patients whose data is included in table 2, 1 patient died of hepatic failure [5], and 1 patient died of relapsed leukemia [3]. Of the 10 remaining patients, 3 experienced resolution of HBV infection (i.e., became HBsAg negative), and 7 had chronic active HBV infection or became HBsAg-positive carriers.

Eleven of the 12 patients developed GVHD following BMT; in 2 cases, the disease was defined as acute GVHD; in 5 cases, as chronic GVHD; in 3 cases, as both acute and chronic GVHD; and in 1 case, the type of GVHD was unspecified. In cases that
Table 2. Demographic and clinical characteristics of individuals with hepatitis B virus (HBV) reverse seroconversion following allogeneic bone marrow transplantation (BMT).

<table>
<thead>
<tr>
<th>Study</th>
<th>Age in years, sex</th>
<th>Reason for BMT</th>
<th>Serological status before BMT</th>
<th>GVHD onset and treatment&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Time between BMT and reactivation of HBV infection, months</th>
<th>Course of immunosuppressive therapy for GVHD and status at reactivation</th>
<th>Serological status and HBV DNA level at reactivation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present report</td>
<td>47, M</td>
<td>AML</td>
<td>HBsAg−; HBsAb+; HBcAb+</td>
<td>Chronic oral and dermatological GVHD, onset 6 months after BMT, treated with prednisone for 2 months</td>
<td>30</td>
<td>Immunosuppressive therapy for GVHD tapered over 2 months, then not received for 20 months before reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb+; HBV DNA−; HBeAg−; HBeAb+; HBeAb−</td>
</tr>
<tr>
<td>Knoll et al. [3]</td>
<td>41, M</td>
<td>ALL</td>
<td>HBsAg−; HBsAb+; HBcAb+; HBeAg+; HBeAb−; HBV DNA−</td>
<td>Unspecified chronic GVHD, onset at unknown time; treatment unspecified</td>
<td>14</td>
<td>Not receiving immunosuppressive therapy for 3 months at time of reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA−; HBeAg−; HBeAb+</td>
</tr>
<tr>
<td>Knoll et al. [3]</td>
<td>55, M</td>
<td>CML</td>
<td>HBsAg−; HBsAb+; HBcAb+; HBeAb+; HBV DNA−</td>
<td>Unspecified acute and chronic GVHD, onset at unknown time; treatment unspecified</td>
<td>22</td>
<td>Receiving cyclosporine A and mycophenolate mofetil at time of reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA+; HBeAg−; HBeAb+</td>
</tr>
<tr>
<td>Knoll et al. [3]</td>
<td>51, M</td>
<td>CML</td>
<td>HBsAg−; HBsAb+; HBcAb+; HBeAb+; HBV DNA−</td>
<td>Unspecified acute and chronic GVHD, onset at unknown time; treatment unspecified</td>
<td>12</td>
<td>Receiving mycophenolate mofetil at time of reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA+; HBeAg−; HBeAb+</td>
</tr>
<tr>
<td>Hashino et al. [4]</td>
<td>35, F</td>
<td>CML</td>
<td>HBsAg−; HBsAb+; HBcAb+; HBV DNA−</td>
<td>Acute hepatic and chronic oral and dermatological GVHD, onset 68 days after BMT, treated with prednisone and tacrolimus until HBV reactivation</td>
<td>51</td>
<td>Not receiving immunosuppressive therapy for 40 months prior to reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA+; HBeAg−; HBeAb+</td>
</tr>
<tr>
<td>Iwai et al. [5]</td>
<td>50, M</td>
<td>CML</td>
<td>HBsAg−; HBsAb−</td>
<td>Acute dermatological GVHD, onset 68 days after BMT, treated with prednisone and tacrolimus until HBV reactivation</td>
<td>22</td>
<td>Receiving low-dose tacrolimus and prednisone at time of reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA+; HBeAg−; HBeAb+</td>
</tr>
<tr>
<td>Nordbo et al. [6]</td>
<td>42, M</td>
<td>Myelodyplastic syndrome</td>
<td>HBsAg−; HBsAb+; HBcAb−; HBV DNA−</td>
<td>Acute GVHD, onset at unspecified time; treated with steroids and antithymocyte globulin for an unspecified period</td>
<td>17</td>
<td>Receiving cyclosporine A at time of reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA+; HBeAg−; HBeAb+</td>
</tr>
<tr>
<td>Li Viti et al. [7]</td>
<td>26, M</td>
<td>Homozygous β-thalassemia</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA−</td>
<td>No report of GVHD received unspecified GVHD prophylaxis and methylprednisolone for 3 weeks for rubella infection</td>
<td>24</td>
<td>Not receiving immunosuppressive therapy for 13 months before reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA+; HBeAg−; HBeAb+</td>
</tr>
<tr>
<td>Kostaridou et al.[8]</td>
<td>14, F</td>
<td>β-thalassemia major</td>
<td>HBsAg−; HBsAb+; HBcAb−</td>
<td>Chronic pulmonary and dermatologic GVHD, onset at unspecified time after BMT; treated with methylprednisolone and cyclosporine A until reactivation</td>
<td>16</td>
<td>Receiving high-dose methylprednisolone and cyclosporine A at time of reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA+; HBeAg−; HBeAb+</td>
</tr>
<tr>
<td>Martin et al. [9]</td>
<td>44, M</td>
<td>AML</td>
<td>HBsAg−; HBsAb+; HBcAb−</td>
<td>Acute hepatic GVHD, onset 30 days after BMT; chronic dermatologic GVHD, onset at unspecified time; chronic hepatic GVHD, onset 21 months after BMT; treated with prednisone and cyclopin for 200 days and prednisone for 260 days; also receiving IVIG for 18 months</td>
<td>27</td>
<td>Not receiving immunosuppressive therapy for 16 months at time of reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBV DNA+; HBeAg−; HBeAb+</td>
</tr>
<tr>
<td>Chen et al. [10]</td>
<td>20, F</td>
<td>Severe anaplastic anemia</td>
<td>HBsAg−; HBsAb+; HBcAb−; HBeAg−</td>
<td>Chronic oral and dermatological GVHD, onset 7 months after BMT, treated with azathioprine and prednisone until reactivation</td>
<td>15</td>
<td>Tapered prednisone and azathioprine over 5 months; receiving low-dose immunosuppressive therapy at time of reactivation</td>
<td>HBsAg+; HBsAb−; HBcAb−; HBeAg−; HBeAb−</td>
</tr>
<tr>
<td>Chen et al. [10]</td>
<td>28, F</td>
<td>AML</td>
<td>HBsAg−; HBsAb+; HBcAb−; HBeAb+</td>
<td>Acute dermatological GVHD, onset at day 25 after BMT; chronic dermatological GVHD, onset at day 214 after BMT; treated with azathioprine and prednisone until reactivation</td>
<td>21</td>
<td>Tapered prednisone and azathioprine over 13 months; receiving low-dose immunosuppressive therapy at time of reactivation</td>
<td>HBsAg−; HBsAb−; HBcAb−; HBeAg−; HBeAb−</td>
</tr>
</tbody>
</table>

**Note:** ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; CML, chronic myelogenous leukemia; GVHD, graft-versus-host disease; HBcAb, hepatitis B core antibody; HBeAb, antibody to hepatitis B envelope antigen; HBeAg, hepatitis B envelope antigen; HBsAb, antibody to hepatitis B surface antigen; HBsAg, hepatitis B surface antigen; IVIG, intravenous immunoglobulin G.

<sup>a</sup> Acute GVHD was defined as developing within the first 3 months after transplantation; chronic GVHD was defined as developing or persisting beyond 3 months after transplantation.
reported when the GVHD began, the mean onset of GVHD was 3.4 months after BMT (range, 25 days to <1 year) and 19.6 months before reactivation of HBV infection (range, 8–26 months). GVHD was treated with increased regimens of immunosuppressive drugs, which included prednisone (in 1 case); tacrolimus (1); tacrolimus and prednisone (1); steroids and antithymocyte globulin (1); methylprednisolone, azathioprine, and cyclosporine A (1); cyclosporine A and prednisone (1); azathioprine and prednisone (2); and unspecified immunosuppression (3). The patient who did not develop GVHD had received GVHD prophylaxis (unspecified) along with methylprednisolone for rubella infection. Five of 6 patients who experienced reverse seroconversion in the study by Seth et al. [11] had been treated for GVHD. Although it was stated that there was no hepatic GVHD in the 4 patients who had reverse seroconversion following BMT in the study by Dhdin et al. [12], presence or absence of extrahepatic GVHD was not reported. All of the patients in the study by Onozawa et al. [13] who experienced reverse seroconversion developed chronic GVHD. The use of immunosuppressive therapy to treat GVHD in patients with reverse seroconversion was not specifically stated in the Onozawa study [13].

In five of 12 cases described in table 2, including the present case, immunosuppressive therapy for GVHD had been discontinued before the detection of HBsAg and clinical reactivation of hepatitis. Patients had been receiving immunosuppressive therapy for a median duration of 10 months (range, 4–11 months), and it was discontinued at a median of 16.5 months before reactivation of HBV infection (range, 3–40 months). In the remaining 7 cases, patients were still receiving immunosuppressive therapy at the time of reactivation and had been receiving it for a median duration of 12 months (range, 8–20 months). In 2 of these 7 cases, it was explicitly stated that immunosuppressive therapy was being tapered at the time of detection of HBsAg. Of the other 5 cases, 1 involved a patient who was still receiving low-dose tacrolimus and prednisone; in another case, the patient was still receiving cyclosporine A; and in a third case, unspecified corticosteroids were still being administered at the time of clinical detection of reactivation. Two patients in the study by Knoll et al. [3] were receiving immunosuppressive therapy (mycophenolate mofetil with or without cyclosporine A) at the time of reactivation; however, it was not explicitly stated whether the regimen was being tapered. In all cases reported by Seth et al. [11], clinical evidence of HBV reactivation occurred during the tapering or withdrawal of immunosuppressive therapy. Similarly, reactivation occurred a median of 2–9 months after the cessation of immunosuppressive therapy in all cases reported by Dhdin et al. [12]. The use of immunosuppressive therapy in the study by Onozawa et al. [13] was not specified.

DISCUSSION

It can be hypothesized that the increase in immunosuppressive therapy used to prevent or treat GVHD could have resulted in the loss of immunologic control of HBV infection, resulting in reactivation of HBV infection and the associated presence of HBsAg and HBV DNA. The withdrawal of immunosuppression might be expected to allow for an effective HBV-specific immune response, resulting in recovery from viral reactivation. Alternatively, this restoration of HBV-specific immune function with withdrawal of immunosuppression might result in an exaggerated response that targets HBV-infected hepatocytes, possibly leading to liver inflammation and clinical hepatitis. The majority of cases presented indicate that the tapering or withdrawal of immunosuppression occurred before reverse seroconversion; however, because a number of individuals were still receiving immunosuppressive therapy at the time of reverse seroconversion, it is difficult to conclude that the reduction or cessation of immunosuppression is a necessary trigger for clinical reactivation.

It should be noted that 2 patients who experienced reverse seroconversion in the study by Knoll et al. [3] had HBV DNA present before undergoing transplantation. None of the other patients described had evidence of detectable HBV DNA before transplantation; however, in only 3 cases was it explicitly noted that the patient’s test results were negative for HBV DNA. The presence of HBV DNA in the plasma in the absence of HBsAg indicates a situation of occult hepatitis B infection [14], and suggests that HBV DNA testing before transplantation is likely to be prudent. In such a situation, with presumably low-level viral replication, reactivation of HBV infection after BMT should probably not be surprising and may warrant preemptive treatment with anti-HBV–specific therapy.

It is important to note that reverse seroconversion in HBsAb-positive recipients of bone marrow from HBsAb-positive donors has not been described. In the 12 cases presented in table 2, no donors were reported to be HBsAb positive; 7 cases specifically stated that HBsAb levels were negative, whereas 5 cases were explicitly reported to have involved patients who had no past or current HBV infection. This supports the observation that reactivation occurs exclusively when the donor is HBsAb negative. Dhdin et al. [12] reported reactivation of HBV infection in 4 of 30 patients with seronegative donors and no reactivation of infection among 7 patients with HBsAb-positive donors. There have also been reports of clearance of HBsAg in recipients after transplantation of bone marrow from HBsAg-negative, HBsAb-positive donors [15–18], suggesting that the passive transfer of specific antibodies—or possibly the transfer of HBV-specific cells of the immune system—may play a role in containing HBV infection.

The risk of reactivation of HBV infection is important when
considering BMT and the associated immunosuppression, particularly in patients with GVHD. The potential for poor outcomes (including chronic active hepatitis and fulminant hepatitis) following reactivation of HBV infection should be noted. The apparent absence of reactivation of HBV infection in individuals receiving allogeneic BMT from HBsAb-positive donors suggests that vaccination of HBsAb negative donors prior to transplantation may be beneficial [12, 15]. Preemptive treatment with hepatitis B–specific antiviral therapy may potentially have a role, but this remains to be studied. In addition, monitoring of hepatitis B serological test results and/or HBV DNA levels, as well as clinical evidence of reactivation, may allow for the early detection (and therefore treatment) of this potentially very serious complication. Finally, it should be noted that we have only reviewed cases of reactivation occurring after allogeneic BMT. Senecal et al. [19] and Webster et al. [20] have reported reverse seroconversion in HBsAg-negative and HBsAb-positive patients who have undergone autologous BMT; similar cases of HBV reverse seroconversion after liver, kidney, and peripheral blood stem cell transplantations have been reported [21–24]. It may not be appropriate to generalize our observation to all patients who receive transplants; however, the potential for hepatitis B reactivation should be appreciated in all cases involving immunosuppressive therapy after transplantation, particularly because this may be a preventable complication of the associated significant immunosuppression.

Acknowledgments

We thank Dr. M. Sabloff for his insightful review of the manuscript.

Potential conflicts of interest. All authors: no conflicts.

References