Role of Anti-Hbs Titer to Prevent Reactivation of Hepatitis B after Kidney Transplant in a Patient with Resolved Hepatitis B Infection: A Case Report and Review of Literature

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Abstract

Introduction: Hepatitis B infection is associated with significant morbidity and mortality in Kidney Transplant Recipients (KTRs). The reported incidence of reactivation varies from 0%-6.5%. We present a case of resolved hepatitis B infection with hepatitis B surface antibody (anti-HBs) titer of <100 IU/L who had reactivation of hepatitis B, five months after Kidney Transplant (KT).

Case Presentation: A 54 year old male with end stage renal disease who had resolved hepatitis B infection underwent cadaveric renal transplant. Five months after KT, he presented with elevated Liver Function Tests (LFTs). Hepatitis B Virus (HBV) serology revealed active hepatitis B infection with a viral load of 1.5 x 10^6 IU/ml.

Discussion: It was observed in different studies that patients with pre-transplant anti-HBs titer <100 IU/L had reactivation of hepatitis B after KT. Based on these observations, we encourage physicians to raise the anti-HBs titer to >100 IU/L prior to KT and maintaining at that level in post-transplant period.

Introduction

Hepatitis B infection is associated with significant morbidity and mortality in Kidney Transplant Recipients (KTRs). Immunosuppression after kidney transplant affects T and B cell functions; these cells play an important role in maintenance of immunological memory against hepatitis B infection [1,2]. The reported incidence of reactivation varies from 0%-6.5% in KTRs, however the risk of reactivation appears to be increased with a low hepatitis B surface antibody level (anti-HBs) [3]. We present a case of a patient with resolved hepatitis B infection, confirmed with negative Hepatitis B Surface Antigen (HBsAg) and positive total anti-HBs with a titer of<100 IU/L, who developed Hepatitis B reactivation five months after kidney transplant. Despite starting tenofovir, the patient developed septic shock and died.

Case Presentation

A 54 year old male with end stage renal disease due to hypertension maintained on hemodialysis for 7 years, underwent cadaveric renal transplant. The patient was originally from Nigeria and emigrated to the United States approximately 30 years ago. The patient had a history of resolved hepatitis B infection confirmed serologically and biochemically prior to kidney transplant. Perioperative blood work showed negative HBsAg, positive anti-HBs with a titer of 16.4 IU/L, positive hepatitis B core total Antibody (anti-Hbc), negative Hepatitis B E-Antigen (HBeAg) and positive Hepatitis B E-Antibody (anti-HBe) (Table-1).

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBs</th>
<th>Anti-HBc</th>
<th>HBeAg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Positive</td>
<td>Anti-HBs titer (IU/L)</td>
<td>HBVDNA by PCR (UL/ml)</td>
<td>LFTs</td>
</tr>
<tr>
<td>16.4</td>
<td>Not detected</td>
<td>Normal</td>
<td></td>
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</tbody>
</table>

Table 1: Perioperative blood work.

Hepatitis B Virus (HBV) DNA was not detected by qualitative Polymerase Chain Reaction (PCR) technique. Liver Function Tests (LFTs) were normal with Aspartate Aminotransferase (AST) 18 IU/L, Alanine Aminotransferase (ALT) 37 IU/L, Alkaline Phosphatase (ALP) 48 IU/L and Total Bilirubin (TB) 0.4 mg/dl. The donor organ was free of Hepatitis B infection. The patient was started on mycophenolate mofetil and tacrolimus for immunosuppression after transplant. 5 months after the kidney transplant, he was hospitalized for malaise and generalized weakness. Blood work revealed LFTs, which was normal prior to transplant, were found to be elevated: AST 844 IU/L, ALT 1787 IU/L, ALP 206 IU/L, TB 12.2 mg/dl, INR 3 on the day of admission (Table-2).

| AST (IU/L) | ALT (IU/L) | ALP (IU/L) | TB (mg/dl) |
| 844 | 1787 | 206 | 12.2 |
| HBsAg | Anti-HBs | IgM Anti-HBc | Anti-HBc |
| Negative | Positive | Negative | Positive |
| HBeAg | Anti-HBe | HBVDNA by PCR (UL/ml) | INR |
| Negative | Positive | 1.5 x 10^6 | 3 |

Table 2: Blood work five months after kidney transplant.

Hepatitis B serology showed positive HBsAg, negative anti-HBs, negative IgM anti-HBc, positive total anti-HBc, negative HBeAg and positive anti-HBe. HBV DNA was detected by qualitative PCR and viral load was found to be 1.5×10^6 IU/ml or 6.19 Log IU/ml (quantitatively>20 IU/L was accepted as positive). Other workup including CMV, BK virus, Hepatitis A, C and D, and Toxoplasma came back negative. The patient was started on tenofovir; however his LFTs remained elevated and his clinical condition deteriorated. HBV genotype testing showed genotype E. He developed hepatic encephalopathy. He was listed for liver transplant however he developed septic shock, went into ventricular fibrillation and subsequently cardiac arrest. Unfortunately, he died after 11 days of hospitalization and prior to liver transplant.

Discussion

Hepatitis B infection is associated with significant morbidity and mortality in Kidney Transplant Recipients (KTRs). Immunosuppression after kidney transplant affects T and B cell functions; these cells play an important role in keeping Hepatitis B infection under control [1,2]. The reported incidence of reactivation varies from 0%-6.5% in KTRs and these studies also suggested that if reactivation occurs, its consequences are benign [3]. However, the study by Kanan et al., revealed that the patients without anti-HBs titers at transplantation were 26 times more likely to develop reactivation compared to those with anti-HBs titers [4,5]. Moreover the patients who became anti-HBs negative after KT had a pre-transplant antibody titer below 100 IU/L [5]. In comparison, patients with pre-transplant anti-HBs antibody levels>100 IU/L did not experience re-activation. This was also reported by Savas et al., who described 2 cases of reactivation, the titer level of anti-HBs was 12 IU/ml in one case and 33 IU/ml in another [6].

A prospective study evaluating dialysis patients vaccinated against Hepatitis B observed that 92% of patients with anti-HBs≥100 IU/L had protective titers at 12 months, compared to 44% of those who had anti-HBs titer between 10 and 100 IU/L. Based on these observations, the Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend annual anti-HBs titer assessment and booster vaccination if anti-HBs titer falls below 10 IU/L in order to raise the titer to 100 IU/L [7,8]. Others have suggested that booster vaccination should be considered in HBsAg negative KT candidates with an anti-HBs titer<100 IU/L regardless of anti-HBc status and in anti-HBc positive KTRs with an anti-HBs titer<100 IU/L [9].

Conclusion

Our patient had an anti-HBs titer of 16.4 IU/L prior to KT. He did not receive any booster hepatitis B vaccination prior to transplantation. 5 months after KT he showed an evidence of reactivation and his hospital course was complicated by septic shock. He eventually developed ventricular fibrillation and even after prolonged resuscitation he could not be revived. Based on our evaluation of the existing literature, we encourage physicians to consider raising the anti-HBs titer to>100 IU/L prior to KT and maintaining the titer at that level post-transplant.

References