INTRODUCTION

Hepatitis B virus produces several protein antigens such as HBsAg and HBeAg. HBcAg is produced by hepatitis B virus and is detected in liver tissue.\textsuperscript{1,2} Antibodies to each of these antigens can be measured in blood.\textsuperscript{1,4} 3-4 weeks after the appearance of HBsAg, anti-HBc can be detected and persists for many years.\textsuperscript{5,8}

In the Iranian Blood Transfusion Organization a sample from each donation is tested for HBsAg, Anti-HIV, anti-HCV and a serologic test for syphilis like RPR. All positive donation units are excluded and discarded. The positive results are confirmed, then donors are notified and they are followed-up by the Iranian Blood Transfusion Organization hepatitis clinic.

CASE REPORT

The first-time blood donor was a man. He was 30 years old, born and living in Tehran. At his first donation on June 2001 he was positive for HBsAg and negative for anti-HIV, anti-HCV and RPR so this unit was discarded. Four blood samples were obtained during nearly 24 months. The results obtained from the HBV serological markers included HBsAg, anti-HBc, HBeAg, HBeAb that are shown in detail in Table I. The results remained stable throughout the follow-up.

HBV DNA was analyzed using polymerase chain reaction (PCR). HBV DNA was positive by PCR method and detected by gel electrophoresis (Fig 1). The HBV DNA viral load was $3.4 \times 10^6$ copies per mL. In the immunohistochemical study on the needle liver biopsy, the hepatocytes were positive for HBeAg and HBsAg.

For this immunological situation, the most probable hypothesis is an immunotolerance to HBV due to an in utero HBV infection. This situation does not impose a risk of HBV transmission by blood transfusion, because HBsAg positive donations are excluded and discarded by HBsAg screening tests.


Keywords: Anti-HBc, Hepatitis B Virus (HBV), Tolerance, Immunity.
HBV Infection with Long-Term Anti-HBc Negativity

Fig 1. Detection of HBV DNA by PCR followed by gel electrophoresis.

Anti-HBc negativity in HBsAg positive carrier children and blood donors has been reported in a few studies. In one study in China the absence of anti-HBc occurred in four children who were infected perinatally. They were HBsAg and HBV DNA positive but anti-HBc never appeared. Two blood donors in France exhibited such a profile.

Hepatitis B infection and failure to produce anti-HBc after several months has been described in three different circumstances. First, unresponsiveness to viral infection and antigens like HBV infection and HBcAg are encountered in immunocompromised patients. Second, some partial deletions in the core gene have been detected in HBV infection. These deletions cause the reduction of HBsAg, HBeAg and anti-HBe and their antibodies or absence of anti-HBc and other antibodies. Third, anti-HBc has been found to be negative in some infants who were HBsAg positive and were borne to HBeAg positive carrier mothers. It is suggested that HBeAg can cross the placenta and establish T helper cell tolerance in utero for HBcAg. These results support immune incompetency of the hepatitis B virus antigens in neonates, so HBsAg carrier infants with serum anti-HBc negativity may result from immunologic tolerance in the uterus.

In this case the first hypothesis was excluded because the patient did not have hypogammaglobulinemia and produced antibodies against other viruses like CMV. HBsAg and HBeAg were produced and detected in liver tissue and in long-term follow-up HBV antigens were detected in blood (Table I), so the second hypothesis was unlikely. The third hypothesis seems to be the probable explanation for this immunologic and clinical situation. Serological markers and results of HBV DNA viral load indicated active viral replication but no significant pathologic changes were observed in liver biopsy. These findings were in agreement with possibility with an immune incompetence to HBV infection in this subject. Long term follow-up of the patient in the future was recommended because a delayed immune response could not be definitively excluded.

This situation does not impose a risk of HBV transmission by blood transfusion because HBsAg positive donations are excluded and discarded by an HBsAg screening test.

DISCUSSION

The patient's mother was evaluated for HBV infection and she was positive for HBcAb.

exhibited antibodies to cytomegalovirus (6.8 IU/mL, Reference Value: Immunity>1.1 IU/ml).

Table I. Hepatitis B Virus (HBV) serological markers through-out the follow-up

<table>
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<tr>
<th>Date of bleed/Marker</th>
<th>April 6, 2001</th>
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<th>June 8, 2002</th>
<th>May 6, 2003</th>
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<td>HBsAg</td>
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<td>Positive</td>
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</tr>
<tr>
<td>Anti-HBc</td>
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<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>HBeAg</td>
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<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Fig 2. Hepatocytes expressed nuclear staining for HBeAg.

Fig 3. Hepatocytes expressed cytoplasmic staining for HBsAg.

REFERENCES


