Title:
Fulminant hepatitis due to spontaneous reactivation of virus B in an immunocompetent patient

Authors:
Ana Suárez-Saro Fernández, Carolina Muñoz Codoceo, Raquel Muñoz Gómez, Inmaculada Fernández Vázquez

DOI: 10.17235/reed.2023.9707/2023
Link: PubMed (Epub ahead of print)

Please cite this article as:

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
Fulminant hepatitis due to spontaneous reactivation of virus B in an immunocompetent patient

Ana Suárez-Saro Fernández, Carolina Muñoz Codoceo, Raquel Muñoz Gómez, Inmaculada Fernández Vázquez

Digestive Diseases Service. Hospital Universitario 12 de Octubre. Madrid, Spain

Correspondence: Ana Suárez-Saro Fernández
e-mail: ana.suarezsaro@salud.madrid.org

Conflict of interest: the authors declare no conflict of interest.

Keywords: Reactivation. Hepatitis B virus. Liver transplant.

Dear Editor,

We present the case of a 52-year-old female with a history of HBeAg-negative chronic hepatitis B virus (HBV) infection, viral load (VL) Z+ < 20,000 UI/ml with no evidence of liver fibrosis, who therefore was untreated. She presented to the Emergency Department with jaundice, epigastric pain, nausea and vomiting. On admission, blood analysis revealed alanine aminotransferase (ALT) 3,982 U/l, aspartate aminotransferase (AST) 3,221 U/l, gamma-glutamyl transferase 80 U/l, alkaline phosphatase 252 U/l, lactate dehydrogenase (LDH) 960 U/l, bilirubin 12.5 mg/dl, with no elevation of acute phase reactants, 141,000 platelets and coagulopathy with a prothrombin activity of 29 %. Abdominal ultrasound showed no relevant findings. The serological profile revealed AgHBs+, anti-HBe+ and anti-HBc IgM+ and VL VHB > 100 mills. Ul/ml, the remaining serology was negative and other causes of liver disease were ruled out. With the diagnosis of severe acute hepatitis (SAH) due to HBV reactivation (HBVR), treatment with entecavir was initiated.
Given the analytical evolution (Table 1) and the appearance of encephalopathy grade I-II/IV, an urgent liver transplant was performed. The histological result of the explant was conclusive with intense interphase and lobular hepatitis with extensive areas of massive necrosis in both lobes, without hepatic fibrosis compatible with fulminant hepatitis (FH).

**Discussion**

HBVR is defined as an increase in viral replication (VR) in patients with detectable VL or HBV-DNA positivity in patients with undetectable VL or resolved infection (1). HBVR is caused by alterations in the balance between host immune status and VR; the most common cause is immunosuppression due to drugs or immunosuppressive disease (1). The severity of the injury is variable, ranging from asymptomatic increases in transaminases to SAH o acute liver failure (1,2). Therefore, the latest HBV guidelines recommend initiating prophylactic antiviral treatment two weeks before the onset of immunosupression in HBsAg+ patients at moderate or high risk of reactivation and in HBsAg- y anti-HBc+ patients at high risk (2,3).

The presence of HBVR without immunosuppressive factors is rare, with only one case reported of FH in a patient with chronic VHB HBeAg infection (4,5). This case demonstrates the feasibility of HBVR under stable conditions and raises awareness of potential triggers for VR that are still poorly understood.

**References**

1. Shi Y, Zheng M. Hepatitis B virus persistence and reactivation. BMJ 2020;370:m2200. DOI: 10.1136/bmj.m2200


Table 1. Analytical data evolution prior to liver transplantation

<table>
<thead>
<tr>
<th>Day</th>
<th>Day 0</th>
<th>Day +1</th>
<th>Day +2</th>
<th>Day +3</th>
<th>Day +4</th>
<th>Day +5</th>
<th>Day +6</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (U/l)</td>
<td>3,195</td>
<td>2,182</td>
<td>1,298</td>
<td>1,015</td>
<td>896</td>
<td>584</td>
<td>559</td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td>3,737</td>
<td>2,851</td>
<td>2,135</td>
<td>1,662</td>
<td>1,422</td>
<td>815</td>
<td>608</td>
</tr>
<tr>
<td>GGT (U/l)</td>
<td>75</td>
<td>62</td>
<td>60</td>
<td>52</td>
<td>50</td>
<td>44</td>
<td>34</td>
</tr>
<tr>
<td>AF (U/l)</td>
<td>265</td>
<td>228</td>
<td>265</td>
<td>251</td>
<td>285</td>
<td>230</td>
<td>193</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>15.4</td>
<td>14.1</td>
<td>20.8</td>
<td>20.4</td>
<td>23.5</td>
<td>19.7</td>
<td>14.3</td>
</tr>
<tr>
<td>PT (Sec)</td>
<td>38.9</td>
<td>40.8</td>
<td>54.8</td>
<td>54.2</td>
<td>60.7</td>
<td>37.1</td>
<td>39</td>
</tr>
<tr>
<td>PT Ac (%)</td>
<td>18</td>
<td>23</td>
<td>17</td>
<td>17</td>
<td>15</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>INR</td>
<td>3.26</td>
<td>3.42</td>
<td>4.55</td>
<td>4.5</td>
<td>5.02</td>
<td>3.11</td>
<td>3.27</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>263</td>
<td>267</td>
<td>159</td>
<td>157</td>
<td>130</td>
<td>107</td>
<td>105</td>
</tr>
</tbody>
</table>

GPT: alanine aminotransferase; GOT: aspartate aminotransferase; GGT: gamma-glutamyl transferase; FA: alkaline phosphatase; PT: prothrombin time; INR: international normalized ratio.