Brief communication

Schistosomal liver fibrosis and hepatocellular carcinoma – case series of patients submitted to liver transplantation

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Abstract

Schistosomiasis affects approximately 207 million people in 76 countries. The association between hepatocellular carcinoma and Schistosoma mansoni infection has been investigated. Studies using animal models suggest that the parasite may accelerate the oncogenic process when combined with other factors, such as hepatitis C virus infection or exposure to a carcinogen. Herein, we report a case series of six hepatocellular carcinoma patients from Northeast Brazil, with negative serology for both hepatitis B and C virus, submitted to liver transplantation, whose explant showed evidence of schistosomal liver fibrosis. Since all patients enrolled in this study were submitted to liver transplantation, we were able to access the whole explanted liver and perform histopathological analysis, which is often not possible in other situations. Although 50% of them showed signs of liver failure, no cirrhosis or any liver disease other than schistosomal fibrosis had been detected. These uncommon findings suggest that Schistosoma mansoni infection might predispose to hepatocellular carcinoma development, regardless of the absence of other risk factors.

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Table 1 – Demographic, clinical, laboratory and histopathological data of six patients with HCC and SLF submitted to liver transplantation in Recife – Brazil.

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
<th>Patient 6</th>
</tr>
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<tbody>
<tr>
<td>Sex</td>
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<td>Female</td>
<td>Male</td>
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<tr>
<td>Age (years)</td>
<td>53</td>
<td>45</td>
<td>46</td>
<td>34</td>
<td>70</td>
<td>57</td>
</tr>
<tr>
<td>UGB</td>
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<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Splenectomy</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
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<td>Ascites</td>
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<td>No</td>
<td>Ascites</td>
<td>Ascites + jaundice</td>
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</tr>
<tr>
<td>MELD</td>
<td>12</td>
<td>7</td>
<td>7</td>
<td>10</td>
<td>15</td>
<td>8</td>
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<tr>
<td>Comorbidities</td>
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<td>DM, AC</td>
<td>None</td>
<td>None</td>
<td>DM, AC</td>
<td>DM</td>
</tr>
<tr>
<td>Liver/body weight (%)</td>
<td>1.61</td>
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<td>2.22</td>
<td>2.14</td>
<td>1.34</td>
<td>1.60</td>
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<tr>
<td>Liver parenchyma</td>
<td>SLF + SG</td>
<td>SLF + SG</td>
<td>SLF</td>
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<td>SLF + SG</td>
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<tr>
<td>Milan criteria</td>
<td>In</td>
<td>Out</td>
<td>Out</td>
<td>In</td>
<td>In</td>
<td>Out</td>
</tr>
</tbody>
</table>

HCC, hepatocellular carcinoma; SLF, schistosomal liver fibrosis; UGB, upper gastrointestinal bleeding; LFS, liver failure signs; MELD, model for end-stage liver disease; DM, diabetes mellitus; AC, alcohol consumption; SG, schistosomal granuloma.

**Table 1**

**Fig. 1** – Explant showing a hepatocellular carcinoma in the left lobe of a liver with schistosomal fibrosis and absence of nodular transformation (A). Microscopic slides showing stellate portal fibrosis with vascular proliferation (B – Masson’s trichrome, 40×) and a schistosomal granuloma (C, arrow, hematoxylin–eosine, 100×).
such as diabetes and alcohol consumption, the histopathological analysis of their explants did not show any cirrhosis, steatosis, or other liver diseases. No complete portal vein thrombosis was found in any case; only one patient had partial occlusion of this vessel.

It is speculated that parasitic infections may play a role in carcinogenesis due to changes of the host inflammatory response. The association between Schistosoma haematobium and squamous cell carcinoma of the bladder is already well established. The association between SMI and HCC has been studied since the 1970s. Studies with experimental animals showed a higher frequency of liver dysplasia and HCC in the group exposed concomitantly to carcinogens and SMI. It is speculated that parasitic infections may play a role in carcinogenesis due to changes of the host inflammatory response. The association between Schistosoma haematobium and squamous cell carcinoma of the bladder is already well established.

In a case–control study with 75 patients with HCC and HCV divided according to the presence of SMI, El-Tonsy et al. observed that the co-infected patients were younger and had a higher proportion of larger and multifocal tumors. Sabry et al. found serologic evidence of SMI in 20 of 60 HCC cases in Egypt, of whom only four were co-infected with HCV. Another Brazilian cases series described seven HCC patients with schistosomiasis; however, some of these patients had portal thrombosis or previous hepatitis B. It is important to highlight that none of these studies performed histopathological analysis of the liver to exclude other predisposing diseases or some degree of liver cirrhosis.

It is important to note that, in this study, half of the patients had clinical signs of liver failure, with no histological evidence of cirrhosis, and they were precisely those who had a history of UGB. Due to portal obstruction, schistosomiasis patients present hepatic sinusoidal arterialization. Consequently, they are more vulnerable to sudden falls in blood pressure due to UGB episodes, developing focal areas of hepatic necrosis.

In summary, by studying HCC patients from a schistosomiasis endemic region who had undergone liver transplantation, we were able to perform histopathologic analyses of the explanted liver, which is not commonly available in non-transplanted HCC patients due to biopsing-related risks. Therefore, the present case series is the first to describe an association between HCC and SLF based on the whole analysis of the liver, which permits the exclusion of other associated hepatic diseases. Although this case series brings clinical evidence about the possible association between SMI and HCC, it does not establish a causal relation, thus, further investigations are required to better understand the current observations.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES