CASE REPORT

First case of ivermectin-induced severe hepatitis

Olivia Veita,∗, Bernhard Becka, Michael Steuerwaldb, Christoph Hatza

a Swiss Tropical Institute, Medical Department, Socinstrasse 57, 4002 Basle, Switzerland
b University Hospital, Department of Gastroenterology & Hepatology, 4002 Basle, Switzerland

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Loiasis; Loa loa; Ivermectin; Liver disease; Drug-induced hepatitis

Summary Loiasis, caused by the filarial parasite Loa loa, is endemic in West and Central Africa. Ivermectin has been shown to be an effective treatment of loiasis. We report the case of a 20-year-old woman originally from Cameroon who was infected by the L. loa parasite and developed severe hepatitis, identified 1 month after a single dose of ivermectin. Liver biopsy showed intralobular inflammatory infiltrates, confluent necrosis and apoptosis, compatible with drug-induced liver disease. To our knowledge, this is the first case of ivermectin-induced severe liver disease published in the literature.

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1. Case report

In October 2000, a 20-year-old woman was referred to the Swiss Tropical Institute, Basle, Switzerland, for evaluation of a migrating worm in the sclera of her right eye (Figure 1). She reported general body itching over several years, headache and dizziness. She had lived in Cameroon until the age of 15; she had moved to Switzerland 5 years previously and had not visited Africa since then. She had had meningitis with subsequent persistent deafness and a history of hepatitis A and B. Initial physical examination was inconspicuous except for moderate abdominal pain.

The worm that was removed from the patient’s right eye was identified as an adult Loa loa, with a length of 2 cm. Initial L. loa microfilaraemia was 820/ml of whole blood. There was an eosinophilia of 18.5% (absolute count 350/µl), and liver enzymes were normal. The patient was treated with albendazole (600 mg/d) for 21 d. One month after the end of therapy, the microfilaraemia dropped to 250/ml and was still at this level 3 months thereafter (Table 1). Clinical signs and liver enzymes remained normal, and no abdominal pain was reported. A single dose of 15 mg (300 µg/kg) ivermectin, a dosage previously reported as having no major side effects (Kombila et al., 1998), was given to reduce the microfilaraemia further. At a routine follow-up 1 month after administration of ivermectin, the patient reported moderate new diffuse abdominal pain. Physical examination showed a new tenderness in the upper right quadrant; the liver was not enlarged. Laboratory investigation revealed elevated liver enzymes: ALAT 907 IU/l (normal range 7—42), ASAT 279 IU/l (normal range 5—39) and γGT 66 IU/l (normal range 8—78); bilirubin, alkaline phosphatase, C-reactive protein, and red and white blood cell counts were in the normal range. Viral hepatitides were ruled out by means of serology (HAV, HBV, HCV, CMV, EBV). An HIV test was also negative. The patient had no his-
The filarial parasite *Loa loa* is endemic in West and Central Africa, with an estimated 13 million people infected (Toure et al., 1998). Typical manifestations are transocular migration or subcutaneous swelling ('Calabar swelling'), caused by migrating adult nematodes (macrofilariae). Other common symptoms are generalized pruritus, fatigue and arthralgas. Hepatic dysfunction has not been reported. In exceptional cases, complications such as endomyocardial fibrosis and renal complications arise.

Diethylcarbamazine is the standard treatment of loiasis but is associated with an elevated risk of encephalitis in patients with high microfilaraemia (Carme et al., 1991). Ivermectin is used for treatment in many diseases, including loiasis, scabies, onchocerciasis and strongyloidiasis. In the treatment of onchocerciasis with ivermectin, where *L. loa* is endemic, encephalitis has been reported (Boussinesq et al., 1998; Ducorps et al., 1995; Gardon et al., 1997).

### Table 1 Laboratory findings

<table>
<thead>
<tr>
<th>Date</th>
<th>5/10/00</th>
<th>27/12/00</th>
<th>20/02/01</th>
<th>26/03/01</th>
<th>23/04/01</th>
<th>13/07/01</th>
<th>23/07/01</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>11.8</td>
<td>13.6</td>
<td>13.2</td>
<td>12.5</td>
<td>12.4</td>
<td>12.1</td>
<td></td>
</tr>
<tr>
<td>Leucocytes (10 × 3/µl)</td>
<td>12.7</td>
<td>7.0</td>
<td>8.0</td>
<td>10.5</td>
<td>8.7</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>Eosinophilia (%)</td>
<td>18.5</td>
<td>9.5</td>
<td>14.0</td>
<td>6.6</td>
<td>4.5</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>ALAT [7—42 IU/l]</td>
<td>21</td>
<td>35</td>
<td>907</td>
<td>111</td>
<td>54</td>
<td>23</td>
<td>13</td>
</tr>
<tr>
<td>ASAT [5—39 IU/l]</td>
<td>23</td>
<td>23</td>
<td>279</td>
<td>47</td>
<td>27</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>rGT [46—93 IU/l]</td>
<td>22</td>
<td>42</td>
<td>66</td>
<td>27</td>
<td>27</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Alkaline phosphatase [38—126 IU/l]</td>
<td>58</td>
<td>40</td>
<td>61</td>
<td>57</td>
<td>43</td>
<td>46</td>
<td>38</td>
</tr>
<tr>
<td>Bilirubin [2—24 µmol/l]</td>
<td>11</td>
<td>8</td>
<td>22</td>
<td>16</td>
<td>20</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>Microfilaraemia (Loa loa) /ml</td>
<td>820</td>
<td>220</td>
<td>9</td>
<td>9</td>
<td>19</td>
<td>0</td>
<td></td>
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</tbody>
</table>
In our patient the results of the liver biopsy were compatible with drug-induced hepatotoxicity. At the time of the diagnosis of drug-induced liver disease, the patient had received two drugs in the previous 5 months: albendazole and ivermectin. Albendazole, which has good effect against *L. loa* microfilariae, was initially chosen over standard therapy with DEC because of the mentioned elevated risk of encephalitis in patients with high microfilaraemia. Albendazole can produce hepatotoxicity, but in most cases this is associated with the treatment of echinococcosis, in which elevations of enzymes occur as the cysts are destroyed (Horton, 1989). There are a few cases of drug-induced hepatitis reported in this paper.

Conflicts of interest statement

We wish to thank F. Vornmo MD, Department of Ophthalmology, University Hospital Basle, for referring the patient to our department, and S. Krähenbühl MD, Department of Pharmacology, University Hospital Basle, for contributing pharmaceutical aspects.

References


