Generalized lymphadenopathy as a marker of ongoing inflammation in prolonged cholestatic hepatitis A
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Extrahepatic manifestations of hepatitis A are very unusual. We describe a case of prolonged cholestatic hepatitis A in a patient with generalized lymphadenopathy. With normalization of transaminases, there was an accompanying reduction in size of these lymph nodes. Lymphadenopathy reflects ongoing hepatic inflammation in prolonged cholestatic hepatitis A. Eur J Gastroenterol Hepatol 14:877–878 © 2002 Lippincott Williams & Wilkins


Keywords: hepatitis A, adult, lymphadenopathy

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Received 1 August 2001
Accepted 26 March 2002

Introduction
Extrahepatic manifestations of hepatitis A are very rare. The described manifestations include transient arthralgias and rashes, neurological complications such as polyradiculopathy, meningoencephalitis and Guillain–Barré syndrome, and haematological complications such as aplastic anaemia [1–5]. Hepatitis A is a rare cause of pancreatitis in children [6].

Lymph node enlargement at the hepatic hilum, pancreas and omentum has been described as ultrasound features of acute hepatitis A in children [7]. We describe a case of prolonged cholestatic hepatitis A in an adult patient with generalized lymphadenopathy. The reduction in size of the nodes paralleled the gradual decrease in transaminase levels.

Case report
A 25-year-old engineer noticed yellowing of his eyes and urine for 2 months, but he had not noticed any prodromal symptoms. He had no abdominal pain, fever, clay-coloured stools, weight loss or anorexia. There was no history of melaena, abdominal distension or pedal oedema.

On physical examination, the patient was minimally icteric. There were no stigmata of chronic liver disease. He had bilaterally palpable cervical and axillary nodes. Abdominal examination revealed a just palpable, non-tender liver. The spleen was not palpable. No free fluid was detected. Cardiac and respiratory system examinations were normal.

The patient’s relevant initial and subsequent investigations are listed in Table 1. Initial investigations for jaundice showed a positive IgM for hepatitis A. Serology for hepatitis B, C and E were negative. Ceruloplasmin was normal (106 U/l) and antinuclear antibody test was also reported negative. He was seronegative for HIV infection.

Initial ultrasound showed mild hepatomegaly and mild splenomegaly. Nodes were noted in the periporal, peripancreatic and para-aortic regions. At follow-up visits, there was a gradual reduction and ultimately disappearance of these nodes. This correlated with the reduction in the transaminases, as shown in Table 1.

Bone marrow trephine and aspiration were reported

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Table 1  Relevant investigations carried out in our patient

<table>
<thead>
<tr>
<th>Investigation</th>
<th>2nd month of illness</th>
<th>3rd month of illness</th>
<th>4th month of illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g %)</td>
<td>15</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>AST (IU/l)</td>
<td>497</td>
<td>362</td>
<td>61</td>
</tr>
<tr>
<td>ALT (IU/l)</td>
<td>551</td>
<td>805</td>
<td>78</td>
</tr>
<tr>
<td>Total bilirubin (mg %)</td>
<td>3.1</td>
<td>2.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Direct bilirubin (mg %)</td>
<td>2.2</td>
<td>1.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>450</td>
<td>420</td>
<td>156</td>
</tr>
<tr>
<td>Peripheral nodes detected</td>
<td>Cervical, axillary and abdominal nodes</td>
<td>Abdominal nodes</td>
<td>No nodes</td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; AST, aspartate aminotransferase.
normal. Axillary lymph node biopsy showed nonspecific reactive hyperplasia. Liver biopsy showed primarily lobular inflammation with no evidence of fibrosis or cirrhosis.

Discussion

Lymphadenopathy is a common manifestation of a number of viral infections, including Epstein–Barr virus, rubella, adenovirus, HIV and measles [8]. However, it is an unusual finding in hepatitis A. The possible mechanism for lymphadenopathy is immune hyperplasia in response to the viral infection [8].

Local perihepatic lymphadenopathy has been reported in cases of chronic hepatitis C and hepatitis B [9,10]. It has been postulated that the nodal enlargement in the hepatoduodenal ligament may reflect the inflammatory activity in the liver. In hepatitis C, perihepatic lymphadenopathy correlated with severe histological inflammation [10]. In chronic hepatitis B, lymph node volume showed a significant correlation with serum aspartate transaminase, alanine transaminase, G-glutamyl transpeptidase, histological activity index, and necroinflammatory score, but not fibrosis score or serum hepatitis B viraemia [9]. It is therefore logical to infer that lymphadenopathy is due to the quantum of host response and not the viral load in hepatitis B.

Prolonged cholestatic hepatitis A is similar to chronic hepatitis B and C, as there is an unusual persistence of the hepatitis A virus. This may reflect an aberration in the immune clearance mechanisms. The lymphadenopathy seen in our patient may have been due to a nonspecific lymphoid hyperplasia as a result of continuing viral infection and inflammation. The reduction of the transaminases paralleled the reduction in size and disappearance of the lymph nodes, further strengthening this concept.

References