Acute hypoxic hepatitis (‘liver shock’): still a frequently overlooked cardiological diagnosis

Caroline Denis, Caroline de Kerguenec, Jacques Berneau, Florence Beauvais, Alain Cohen Solal

Service de Cardiology, Hôpital Beaujon, AP-HP, 100 boulevard du Général Leclerc, 92110, Clichy, France
Service de Hepatology, Hôpital Beaujon, AP-HP, 100 boulevard du Général Leclerc, 92110, Clichy, France

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Abstract

The diagnosis of acute hypoxic hepatitis remains problematic. We describe a series of 14 patients who were initially hospitalized in an hepatic care unit with a diagnosis of fulminant hepatitis, and were subsequently found to have acute hypoxic hepatitis (‘liver shock’) secondary to heart failure. A diagnostic algorithm is proposed.

Keywords: Acute hypoxic hepatitis; Heart failure

1. Introduction

Acute hypoxic hepatitis—sometimes still described as liver shock—is generally defined on the basis of histologic evidence of centrolobular hepatocytic necrosis [1]. It usually results from severe, although sometimes transient, circulatory failure [2]. Controversy remains about the respective roles of acute low hepatic blood flow (‘forward failure’) and venous congestion (‘backward failure’) in its pathophysiology, and about whether or not both mechanisms must be present simultaneously for acute hypoxic hepatitis to occur [3–6].

The diagnosis of acute hypoxic hepatitis is usually based on a combination of severe cardiac clinical signs (signs of congestion and low blood flow) and major hepatic disorders. It is generally confirmed by specialized cardiologic investigations, a favourable response to cardiologic treatment and in some cases, liver biopsy.

Diagnosis is generally considered to be easy, and the topic is generally not addressed in major books of cardiology. This diagnosis, in fact, still remains problematic, as illustrated by the present series of 14 consecutive patients who were admitted to the intensive care unit of the hepatology department of the Beaujon University Hospital over a three-year period for suspected fulminant hepatitis. The final diagnosis was acute hypoxic hepatitis, leading to the transfer of the patients to our cardiac intensive care unit. These patients had signs of acute hepatitis but none of them had cardiogenic shock or pulmonary edema. We propose a diagnostic algorithm that should help to avoid delays in diagnosis and appropriate cardiac treatment of the heart failure of these patients.

2. Study population

The four women and ten men were hospitalized between 1997 and 1999. Their mean age was 56 ± 10 years, and their socioeconomic status was generally poor. Six patients had a known cardiac problem, two were on anti-hypertensive treatment, one was receiving treatment for angina pectoris, and five had no known cardiac history. Only three patients had a previous history of heart failure. Four had taken drugs with known hepatotoxic effects. The hepatology department was often the second or third ward in which the patient had been hospitalized: five patients were referred from another teaching hospital, four from a general hospital, three from a private clinic, and two from a medical emergency room. The interval between initial hospitalization and arrival in our cardiology unit ranged from 1 to 8 days (mean 4 days). The
diagnosis was generally corrected within a few hours in the liver unit. It is noteworthy that two patients had already been examined by a cardiologist—who did not consider the diagnosis of acute hypoxic hepatitis—before their transfer to the liver unit.

3. Clinical manifestations

Gastrointestinal manifestations generally predominated, with nausea, vomiting and right hypochondrial pain in eight cases each; and acute diarrhea in three cases. Six patients had patent jaundice and 11 had markedly altered general status. In the preceding days, six patients had complained of increasing breathlessness and one of chest pain. Eight patients had no cardiac symptoms before their hospitalization.

Physical examination always showed marked hepatomegaly, a sign that is generally absent in fulminant hepatitis (Table 1). The liver was tender in seven patients, and seven patients had jugular turgescence or hepatojugular reflux. Ascites was present in five cases and lower-limb edema in eight cases. Four patients had encephalopathy. All the patients had relatively low blood pressure (mean 100/60 mmHg). Mean heart rate was 100 bpm: in fact, seven had a heart rate >100/min and two had bradycardia (related to hypokalemia and right ventricular infarct). A systolic murmur was noted in five patients. Five patients had hyperkalaemia and right ventricular infarct). A systolic heart rate >100/min and two had bradycardia (related to hypokalemia and right ventricular infarct). A systolic murmur was noted in five patients. Five patients had hyperkalaemia and right ventricular infarct. Marked pulmonary arterial hypertension (mean 65 mmHg for systolic pressure) was found in seven patients. Echocardiography always showed the cause of acute hypoxic hepatitis, namely dilated cardiomyopathy in five cases, ischemic cardiopathy in three cases, hypertrophic cardiomyopathy in three cases, and cardiac tamponade, aortic stenosis and acute myocarditis in one case each.

Right heart catheterization was performed in five cases, and confirmed the very low cardiac index (1.7 l/min/m² on average). Three patients had needle biopsy of the liver, which always showed centrolobular hepatocytic necrosis.

5. Treatment and outcome

Medical treatment of heart failure (diuretics in 12 patients, positive inotropes in 12 patients and vasodilators in four patients) was started on admission to the cardiac intensive care unit. One patient was treated by pericardial puncture, two by temporary cardiac stimulation, and one patient had an emergency aortic valve replacement. Cardiac signs resolved in every case, after a mean of 5 days. Transaminase activity returned to normal after 7 to 10 days. Two patients died suddenly, one due to severe, uncontrolled heart failure and one due to secondary septicemia.

6. Discussion

Despite regular review articles on the diagnosis of acute hypoxic hepatitis (‘liver shock’) (mainly in non-cardiological journals) and proposed measures to limit diagnostic errors [4,8], this syndrome remains a major pitfall. Previous studies have mainly involved intensive care units patients with a variety of clinical manifestations. For example, respiratory distress was the most frequent sign in Fuchs’ study [5], while the study published by Henrion et al. [9] involved intensive care units patients with low cardiac output. Hemodynamic signs of circulatory failure rarely predominated in our study, making the diagnosis even less obvious, especially in those patients who had no previous cardiac history [4]. A transient event such as arrhythmia or
Table 1
Clinical and laboratory findings in 14 patients with AHH admitted to an hepatic care unit

<table>
<thead>
<tr>
<th>N</th>
<th>Age</th>
<th>Cardiac history</th>
<th>Functional signs</th>
<th>Hepatomegaly</th>
<th>Jugular venous turgescence or reflux</th>
<th>Ascites, Edema</th>
<th>Encephalopathy</th>
<th>Arterial pressure</th>
<th>Heart rate</th>
<th>Congestive (ASAT/ALAT)</th>
<th>Bilirubin</th>
<th>Alkaline Phosphatases</th>
<th>Prothrombin time</th>
<th>Factor V</th>
<th>Plasma creatinine</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>Hypertension, ascites, asthenia</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>0</td>
<td></td>
<td>90/60</td>
<td>130</td>
<td>+</td>
<td>860/680</td>
<td>21</td>
<td>110</td>
<td>14%</td>
<td>35%</td>
<td>160 Death</td>
</tr>
<tr>
<td>2</td>
<td>72</td>
<td>Atrial fibrillation, left ventricular hypertrophy</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td></td>
<td>80/40</td>
<td>37</td>
<td>+</td>
<td>600/400</td>
<td>40</td>
<td>102</td>
<td>60</td>
<td>–</td>
<td>449 Death</td>
</tr>
<tr>
<td>3</td>
<td>73</td>
<td>Left ventricular dysfunction, dyspnea, ascites</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td></td>
<td>120/70</td>
<td>100</td>
<td>+</td>
<td>2000/2000</td>
<td>46</td>
<td>46</td>
<td>54</td>
<td>42</td>
<td>143 Favourable</td>
</tr>
<tr>
<td>4</td>
<td>53</td>
<td>Dilated cardiomyopathy, dyspnea, asthenia, vomiting</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td></td>
<td>110/60</td>
<td>108</td>
<td>+</td>
<td>3100/1860</td>
<td>127</td>
<td>300</td>
<td>15</td>
<td>16</td>
<td>78 Favourable</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>Mitral regurgitation, dyspnea, asthenia, vomiting</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>0</td>
<td></td>
<td>100/80</td>
<td>80</td>
<td>+</td>
<td>841/877</td>
<td>72</td>
<td>106</td>
<td>30</td>
<td>32</td>
<td>136 Favourable</td>
</tr>
<tr>
<td>6</td>
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<td>Dilated cardiomyopathy, dyspnea, vomiting</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td></td>
<td>100/70</td>
<td>100</td>
<td>+</td>
<td>940/1240</td>
<td>55</td>
<td>116</td>
<td>30</td>
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</tr>
<tr>
<td>7</td>
<td>45</td>
<td>Hypertension, dyspnea, vomiting</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td></td>
<td>140/80</td>
<td>90</td>
<td>–</td>
<td>8176/4278</td>
<td>66</td>
<td>95</td>
<td>26</td>
<td>27</td>
<td>306 Favourable</td>
</tr>
<tr>
<td>8</td>
<td>77</td>
<td>Angina pectoris</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>+ (stage I)</td>
<td></td>
<td>100/60</td>
<td>88</td>
<td>+</td>
<td>760/1000</td>
<td>52</td>
<td>95</td>
<td>23</td>
<td>29</td>
<td>Favourable</td>
</tr>
<tr>
<td>9</td>
<td>48</td>
<td>Dyspnea, vomiting</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+ (stage II)</td>
<td></td>
<td>120/60</td>
<td>150</td>
<td>(Atrial fibrillation) +</td>
<td>8730/3330</td>
<td>171</td>
<td>242</td>
<td>19</td>
<td>32</td>
<td>87 Favourable</td>
</tr>
<tr>
<td>10</td>
<td>64</td>
<td>Dyspnea</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+ (stage II)</td>
<td></td>
<td>110/70</td>
<td>77</td>
<td>+</td>
<td>12555/5465</td>
<td>97</td>
<td>158</td>
<td>14</td>
<td>21</td>
<td>236 Favourable</td>
</tr>
<tr>
<td>11</td>
<td>53</td>
<td>Asthenia</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>0</td>
<td></td>
<td>100/60</td>
<td>90</td>
<td>–</td>
<td>925/1506</td>
<td>46</td>
<td>233</td>
<td>33</td>
<td>17</td>
<td>136 Favourable</td>
</tr>
<tr>
<td>12</td>
<td>45</td>
<td>Dyspnea</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>0</td>
<td></td>
<td>110/80</td>
<td>110</td>
<td>+</td>
<td>3279/2348</td>
<td>61</td>
<td>189</td>
<td>32</td>
<td>27</td>
<td>117 Favourable</td>
</tr>
<tr>
<td>13</td>
<td>70</td>
<td>Vomiting</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>0</td>
<td></td>
<td>120/70</td>
<td>56</td>
<td>–</td>
<td>3690/4520</td>
<td>28</td>
<td>66</td>
<td>27</td>
<td>21</td>
<td>380 Favourable</td>
</tr>
<tr>
<td>14</td>
<td>43</td>
<td>Asthenia</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td></td>
<td>90/50</td>
<td>100</td>
<td>–</td>
<td>1220/2320</td>
<td>29</td>
<td>247</td>
<td>30</td>
<td>48</td>
<td>100 Favourable</td>
</tr>
</tbody>
</table>
major hypotension can sometimes cause acute hypoxic hepatitis, hindering retrospective diagnosis [3,10]. The diagnostic delay was particularly striking in our study, especially as all 14 patients were initially hospitalized in highly competent medical services. Most of the patients had a known history of heart disease, but cardiac signs were totally absent in approximately 50% of cases; when present, these signs were sometimes overlooked, possibly owing to the severity of the hepatic signs. In most cases the diagnosis of fulminant hepatitis was probably considered on the basis of marked hepatic cytolysis, even though signs of heart failure had been noted in some patients. While prior intake of hepatotoxic drugs was always taken into account, the patient interview obviously neglected the cardiac history. The diagnosis was usually corrected within hours of admission to the intensive care unit of our hepatology department, thanks mainly to our past experience of such diagnostic errors.

The pathophysiology of acute hypoxic hepatitis remains unclear: nine of our patients did not have clinical signs of raised right venous pressure at least at clinical evaluation and hepatic echography did not reveal dilatation of the supra-hepatic veins of or the inferior vena cava in the two out of the seven patients in whom it was performed. Conversely, seven of the patients had at arrival a systolic arterial pressure greater that 100 mmHg. A systematic hemodynamic evaluation should be performed in these patients to better understand the pathophysiology of the syndrome, knowing, however, that an acute, transient, severe decrease in hepatic blood flow (for example during previous unrecognized arrhythmia) may be overlooked.

In acute hypoxic hepatitis, transaminases can increase to more than 100 times the normal values, in relation with the importance of centro-lobular hepatic necrosis, peaking at 12–24 h and normalizing within 10 days with treatment. Alkaline phosphates and bilirubin increase less. Decreased prothrombin time has an important prognostic value. Other coagulation factors may decrease with the importance of hepatic failure. Thrombopenia, when present, occurs simultaneously with the decrease of the prothrombin time. Importantly, renal failure is found in nearly every case of acute hypoxic hepatitis whereas it occurs in only approximately 30% of the patients with fulminant hepatitis, in association with encephalopathy. Prognosis in our study was better than in the literature (50% mortality) probably because we excluded patients in obvious pulmonary edema or cardiogenic shock and because previous studies enrolled patients from general intensive care units with other co-morbidities.

7. Conclusion

Acute hypoxic hepatitis (‘liver shock’) is still a major diagnostic pitfall. One should remember that a major (even more than 100-fold) elevation of transaminases may not only be due to acute viral or toxic hepatitis, but also to acute hypoxic hepatitis. This latter diagnosis should be seriously considered in patients with (1) past or present cardiac disease (even minimal); (2) electrocardiographic abnormalities (an ECG must be done systematically: our findings suggest that a normal ECG virtually eliminates the diagnosis of acute hypoxic hepatitis); (3) radiographic pulmonary abnormalities (found in about half of all patients with acute hypoxic hepatitis); (4) classical hepatic biochemical abnormalities (marked increase in transaminase activity, contrast-
ing with less severe signs of cholestasis and liver failure; and (5) initial renal impairment, rare in other causes of hepatitis.

In the vast majority of such cases, two examinations rapidly provide the correct diagnosis:

a. abdominal echography is virtually pathognomonic when it shows dilation of the inferior vena cava and suprhepatic veins; and

b. Doppler echocardiography yields the diagnosis.

These examinations should, therefore be undertaken routinely in every patient in whom a diagnosis of fulminant hepatitis is suspected, in particular before liver biopsy.

References