Acute liver failure due to non-exertional heatstroke after sauna

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ABSTRACT

Acute liver failure is defined as rapid loss of liver function that patients without previously recognized liver disease sustain a liver damage. Acute liver failure due to non-exertional heatstroke has rarely been reported. We reported here an unusual case of heat stroke induced acute liver failure (ALF) after sauna. A 63 year old man without previously recognized liver and other systemic disease was admitted for loss of consciousness and impaired liver function after sauna. Despite intensive supportive care, ALF developed. Liver transplantation was planned but the patient died on the sixth day of hospitalization. Non-exertional heatstroke induced ALF is a rare and serious condition. ALF caused by non-exertional heatstroke which requires liver transplantation for definitive solution should be kept in mind in early period.


INTRODUCTION

Acute liver failure is defined as rapid loss of liver function, the onset of hepatic encephalopathy within 8 weeks becoming jaundiced in a patient.1,2 It is a syndrome of different etiology, in which patients without previously recognized liver disease sustain a liver damage.3 Although the survival of acute liver failure (ALF) has improved over time, the prognosis of ALF remains poor, with 33% mortality and a 25% liver transplant rate in the United States.4 ALF usually requires emergency liver transplantation.5

Heatstroke is characterized by an increased core body temperature over 40 °C and predominant central nervous system dysfunction resulting in delirium, convulsion or coma which can result from exposure to a high environmental temperature (classic, non-exercise-induced) or from exhausting exercise (exercise-induced).6 Mild or moderate hepatic injury is common feature of exertional heatstroke7,8 but some patients experience fatal hepatocellular damage.9-11 The prognosis of heat stroke depends on how early it is diagnosed and the timing of treatment with appropriate measures including cooling methods and correction of water and electrolyte balance.12

CASE REPORT

A 63-year-old man was admitted to the Emergency Department of our hospital for loss of consciousness after sauna. Our patient had stayed in the sauna almost 1 h and had already gone to sauna a few times before the last event. Sauna’s temperature was 85-95 centigrade. The patient did not have any other medical condition and was on no other medication or natural product. There was no history of alcohol abuse or intravenous drug use. His physical examination revealed a core temperature of 40 °C, blood pressure of 76/43 mmHg, pulse rate of 124/min and respiratory rate 39/min and no other pathological finding on admission. He was unconscious but there was no focalization in neurological examination. He was severely dehydrated on admission, so intensively crystalloid liquid (5 to 6 liters per 24 h) had been infused intravenously. Despite further decreasing the body temperature to 38.5 °C via external cooling and infusion of fluids, the semicomatous mentality was not changed and so endotracheal intubation and mechanical ventilation were started and he was transferred to Intensive Care Unit.

Laboratory tests on admission were depicted in table 1. His arterial blood gas analysis showed pH: 7.42, pO2: 47.2 mmHg, pCO2: 28 mmHg, and HCO3:

Table 1. Laboratory data on arrival at the emergency room and in Intensive Care Unit.

<table>
<thead>
<tr>
<th>Laboratory data</th>
<th>Reference values</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>Hemoglobin (g/dL)</td>
<td>12.2 - 18.1</td>
<td>15.4</td>
<td>15.1</td>
<td>13</td>
<td>13</td>
<td>13.2</td>
<td>10.6</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>37.7 - 53.7</td>
<td>46.3</td>
<td>45.2</td>
<td>37.7</td>
<td>37.4</td>
<td>39</td>
<td>31.5</td>
</tr>
<tr>
<td>PLT (K/uL)</td>
<td>142 - 424</td>
<td>229</td>
<td>55</td>
<td>25</td>
<td>41</td>
<td>45</td>
<td>28</td>
</tr>
<tr>
<td>WBC (K/uL)</td>
<td>4.60 - 10.2</td>
<td>14.4</td>
<td>10.6</td>
<td>11.7</td>
<td>15.7</td>
<td>10.7</td>
<td>4.10</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>70 - 115</td>
<td>135</td>
<td>209</td>
<td>145</td>
<td>190</td>
<td>177</td>
<td>67</td>
</tr>
<tr>
<td>Urea (mg/dL)</td>
<td>10 - 50</td>
<td>38</td>
<td>66</td>
<td>122</td>
<td>116</td>
<td>105</td>
<td>108</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.5 - 1.5</td>
<td>16</td>
<td>2</td>
<td>3.77</td>
<td>6.2</td>
<td>6.6</td>
<td>7.7</td>
</tr>
<tr>
<td>Bilirubin, total (mg/dL)</td>
<td>0.2 - 1.2</td>
<td>1.4</td>
<td>2</td>
<td>4.3</td>
<td>4.7</td>
<td>5.5</td>
<td>7.8</td>
</tr>
<tr>
<td>Bilirubin, direct (mg/dL)</td>
<td>0 - 0.3</td>
<td>0.2</td>
<td>0.8</td>
<td>1.4</td>
<td>2.8</td>
<td>4</td>
<td>5.7</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>5 - 40</td>
<td>142</td>
<td>824</td>
<td>1,568</td>
<td>2,351</td>
<td>3,450</td>
<td>560</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>5 - 40</td>
<td>89</td>
<td>775</td>
<td>1,495</td>
<td>2,134</td>
<td>2,600</td>
<td>1,420</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>80 - 280</td>
<td>267</td>
<td>256</td>
<td>279</td>
<td>264</td>
<td>230</td>
<td>217</td>
</tr>
<tr>
<td>GGT (IU/L)</td>
<td>10 - 50</td>
<td>97</td>
<td>112</td>
<td>76</td>
<td>45</td>
<td>54</td>
<td>48</td>
</tr>
<tr>
<td>LDH (IU/L)</td>
<td>207 - 480</td>
<td>380</td>
<td>780</td>
<td>850</td>
<td>1,100</td>
<td>1,234</td>
<td>930</td>
</tr>
<tr>
<td>CPK (IU/L)</td>
<td>35 - 232</td>
<td>929</td>
<td>1,743</td>
<td>-</td>
<td>2,485</td>
<td>2,494</td>
<td>-</td>
</tr>
<tr>
<td>Total protein (g/dL)</td>
<td>6.3 - 8.4</td>
<td>-</td>
<td>5.3</td>
<td>4.39</td>
<td>-</td>
<td>3.08</td>
<td>-</td>
</tr>
<tr>
<td>Albumine (g/dL)</td>
<td>3.8 - 5.1</td>
<td>-</td>
<td>2.8</td>
<td>2.61</td>
<td>-</td>
<td>2.16</td>
<td>-</td>
</tr>
<tr>
<td>INR (INR)</td>
<td>0.9 - 1.14</td>
<td>1.5</td>
<td>2.3</td>
<td>4.7</td>
<td>4.3</td>
<td>5.01</td>
<td>9.48</td>
</tr>
<tr>
<td>PT (sec)</td>
<td>0.4 - 13.4</td>
<td>16.1</td>
<td>24.1</td>
<td>36.6</td>
<td>52.2</td>
<td>60.4</td>
<td>91.8</td>
</tr>
<tr>
<td>D-dimer (ng/mL)</td>
<td>125 - 342</td>
<td>-</td>
<td>-</td>
<td>1,840</td>
<td>1,902</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>


18 mmol/L. Computed tomography of the brain revealed no pathological finding. On day 2, AST/ALT increased to 824/775 IU/L, total bilirubin increased to 2 mg/dL, albumine of decreased to 2.8 g/dL and platelet count decreased to 55 K/uL. CPK levels on admission were consistent with rhabdomyolysis (Table 1). Abdominal ultrasound and portal vein Doppler ultrasound examination was normal. Other possible causes of ALF including viral hepatitis A, B, C, D and fulminant Wilson’s disease were ruled out by the patient’s history and the appropriate laboratory tests. Testing of blood for antibodies to cytomegalovirus, herpes simplex virus, human immunodeficiency virus, Epstein-Barr virus, and autoimmune antibody panel (ANA, ANCA, SMA, LKM, mitochondrial antibodies) were also negative. Serum levels for ceruloplasmin (serum), alpha-1-antitrypsin and copper (serum and 24-h urine), iron, transferrin and ferritin were within the normal range. A toxic screening was negative. The laboratory findings were considered to represent acute hepatic failure combined with acute renal failure (ARF) and disseminated intravascular coagulation (DIC) following heat stroke (Table 1).

On the 4th day, INR increased to 4.3 and the PT prolonged 52 sec. Transaminase levels had peak level on the 5th day, and started to decline on the 6th day. Moreover, serum total bilirubin level increased to 7.8 mg/dL and INR level increased to 9.48 on day 6th (Table 1). In spite of intensive supportive treatment, ALF, ARF and DIC progressed. Therefore liver transplantation was planned. However, he died on the sixth day of hospitalization.

**DISCUSSION**

In the present case, we report a very unusual case with severe heat stroke after sauna, which was complicated by ALF. Classical heatstroke occurs due to sustained environmental heat and humidity especially when the humidity is high; the most susceptible, the victims are infants and elderly persons suffering with comorbid diseases such as diabetes, congestive heart failure, malnutrition or dehydration. When the ambient temperature is higher than the basic body temperature, sweating with evaporation accounts for almost all of heat loss, but when the humidity exceeds 75%, sweating becomes inefficient. The ALF, defined as the abrupt loss of liver function, characterized by hepatic encephalopathy and coagulopathy, within 26 weeks of the onset of symptoms (classically jaundice) in a patient without previous liver disease is very uncommon in...
heatstroke. The mechanism underlying liver failure in classical heatstroke patients is not totally understood, but direct thermal injury to the endothelium and the hepatocytes, tissue ischemia and/or activation of the inflammatory and coagulatory pathways, endotoxemia and cytokines have been suggested. An earlier study reported that systemic or intrahepatic circulatory disturbance as seen in DIC may be the cause. In one case, a portal vein thrombosis was found, which could result in liver and other organ failure. In our case, the portal vein Doppler ultrasound examination was normal, although he developed DIC.

Hyperpyrexia per se is believed to represent the major pathogenic factor for liver injury in heatstroke. In addition, vasodilatation due to heat of skin blood vessels and re-distribution of blood from the splanchnic area into the skin may be lead to liver ischemia, increased extrahepatic tissue oxygen requirement secondary to hyperpyrexia may cause relative liver hypoxia, and DIC may further contribute to liver damage. In a rat model, similar liver changes were observed. Histological and/or ultrastructural changes, which included centrilobular necrosis, vacuolization and diminution of hepatocellular microvilli, and loss of sinusoidal endothelium were observed. Liver dysfunction and increased serum levels of liver enzymes are commonly observed in heatstroke, whereas ALF is a rare event and carries a poor prognosis. De matte, et al. reviewed 58 cases of nearly fatal heat stroke that occurred during the 1995 heat wave in Chicago and they suggested that multisystem organ dysfunction such as acute renal failure and DIC was also common in classical heat stroke, which is similar to that reported for exertional heat stroke. However, none of the 58 patients developed fulminant liver failure. Argaud, et al. reported 83 patients in France during a heat wave, with 2 cases with liver dysfunction. Kim, et al. reported an unusual case of heat stroke due to a warm bath, presenting as fulminant liver failure combined with ARF and DIC and later by infection. Correlatively, our patient generated the typical features of ALF with progressive increases in transaminases, bilirubin and PT and his later clinical course was complicated with ARF and DIC.

Elevated serum aminotransferases are the principle liver chemistry test abnormality in liver damage due to heatstroke which peaks between days 3-5. The present case had peak level of AST, ALT and LDH by day 5, similarly. Typical laboratory progress of our case was depicted in table 1. Liver damage in most cases of exertional-heatstroke (EHS) is usually asymptomatic and exhibits only mild reversible elevation in plasma aminotransferase levels and ALF is documented in 5% of EHS patients. However, ARF is a common finding in exertional heatstroke. Varghese, et al. demonstrated that 21 of 28 patients with heat stroke developed organ dysfunctions. In their study they found that acute respiratory distress syndrome is the frequently encountered complication, while liver dysfunction has not been reported.

Liver transplantation is the only possible treatment for fatal liver injury. Takahashi, et al. reported a 16-year-old male with exertional heat stroke induced ALF. This patient was the first long term survivor (> 1 year) after liver transplantation for exertional heat stroke. Lee, et al. reported a case of acute hepatic failure caused by heat stroke after bathing in a hot spring. Molecular adsorbent recirculating system (MARS) treatment was performed, as a result of progressive azotemia, hemodialysis was performed. Unfortunately, after a long course of intensive care, the patient died from septic shock and multiple organ failure. Biais, et al. reported a similar case who was referred for liver transplantation and benefited of MARS therapy. According to available evidence, MARS and hemodialysis can be beneficial in treating exertional heat stroke. Liver transplantation was also planned in our case. However, he died on the 6th day.

In cases of severe heat stroke, presenting with multiple organ dysfunction and elevation of cytokines and chemokines, which are resistant to conventional antipyretic treatment, endovascular cooling may contribute significantly to the reduction of body temperature and possibly avoid a fatal result. In patients presenting classic heat stroke with multiple organ dysfunction and hypercoagulable state resistant to conventional whole body cooling and antipyretic therapy, the use of hyperbaric oxygen therapy (HBOT) may rescue them from death. Niu, et al. indicated that hyperbaric oxygen therapy may resuscitate rats that had a heatstroke by decreasing multiple organ dysfunction and brain oxidative stress. In a similar study, combined activated protein C and hyperbaric oxygen therapy heightens benefit in combating heatstroke reactions in rat models. Liu, et al. compared the effectiveness of different small volume resuscitation in a rat model of heatstroke. Anesthetized rats, immediately after the onset of heatstroke, were randomly divided into 5 groups and given the following:
• Nothing.
• 0.9% NaCl.
• Hydroxyethyl starch (HAES).
• 7.2% NaCl.
• Hyper-HAES (6% HAES plus 7.2% NaCl).

Their results suggest that hyper-HAES is superior to 7.2% NaCl or HAES alone in resuscitation of heatstroke. They explain the benefit of hyper-HAES during heatstroke by its relation to restoration of normal multiorgan function.42

Although heatstroke is a widespread condition, ALF due to non-exertional heatstroke is rare. We reported herein an unusual case of heat stroke-induced fatal ALF after sauna. In those cases, liver transplantation should be kept in mind in early period.

CONFLICT OF INTEREST

The authors disclose no conflicts of interest.

REFERENCES


