Multiple Organ Failure Caused by Non-exertional Heat Stroke After Bathing in a Hot Spring

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Heat stroke is a life-threatening illness, and the disease spectrum can include the involvement of multiple organs to varying degrees. Rhabdomyolysis with renal function impairment is frequently noted in this disease. However, acute hepatic failure has been rarely reported in non-exertional heat stroke. We report a case of acute hepatic failure combined with disseminated intravascular coagulopathy, acute renal failure, and neurological deficit caused by heat stroke after bathing in a hot spring. Molecular adsorbent recirculating system (MARS) treatment was performed daily on days 10–12 of admission. 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. According to available evidence, MARS and hemodialysis are beneficial in treating exertional heat stroke. However, a limited number of studies have treated non-exertional heat-stroke-related acute hepatic failure. Early cooling to reduce the overwhelming heat-stress-related cytokine storm, and advanced MARS to eliminate circulating toxin might have a role in treating this rare but fatal illness. [*J Chin Med Assoc* 2010;73(4):212–215]

Key Words: hepatic failure, molecular adsorbent recirculating system, multiple organ failure, non-exertional heat stroke

Introduction

Heat stroke is a life-threatening illness that is defined by elevation of core body temperature above 40°C and central nervous system dysfunction such as delirium, convulsions, or coma. The disease spectrum can include the involvement of multiple organs to varying degrees. Rhabdomyolysis, acute renal failure, acute hepatic failure, elevation of serum pancreatic enzymes, myocardial injury, and disseminated intravascular coagulopathy (DIC) have all been reported.[1] The current concept of the pathophysiology of heat stroke favors excessive heat causing a systemic inflammatory response that leads to a syndrome of multiple organ dysfunction. However, the pathophysiology is not fully understood. Heat stroke is traditionally classified into 2 groups by etiology. Classical or non-exertional heat stroke results from excessive environmental heat exposure. Exertional heat stroke (EHS) is caused by heat generation from strenuous exercise. Liver injury that occurs in most cases of EHS is usually asymptomatic, with only mild, reversible elevations in plasma aminotransferase levels.[2] However, acute liver failure is documented in 5% of EHS patients.[2] There are only limited reports of fulminant hepatic failure after classical heat stroke. Hot spring baths are a unique cultural feature of eastern countries. We report a rare case of acute hepatic failure combined with DIC, acute renal failure, and neurological deficits caused by heat stroke while in a hot spring.

Case Report

A 57-year-old man was sent to the emergency department of National Yang-Ming University Hospital for loss of consciousness while bathing in a hot spring. He was found unconscious in the hot spring (water temperature approximately 40°C), and was believed to have been in that state for approximately 20 minutes. His medical history was negative except for a 5-year history of gouty arthritis, and he was taking no medication. On examination, his body temperature was 41°C,

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blood pressure was 113/83 mmHg, and pulse was 151 beats/min. His skin was hot and dry, and a shallow burn was noted over his back. No neck stiffness or localized neurological deficits were found. Laboratory studies (normal range in parentheses) revealed: white blood cell count of 4,590/mm^3 (4,500–11,000); hemoglobin, 15.3 g/dL (14–18); platelet count, 110,000/L (150,000–350,000); alanine aminotransferase, 47 U/L (0–40); total bilirubin (TBil), 0.52 mg/dL (0.2–1.6); prothrombin time international normalized ratio, 1.3 (0.85–1.15); creatine phosphokinase, 272 U/L (27–168); creatine phosphokinase-MB, 13 U/L (< 5 U/L); troponin-I, 0.53 ng/mL (0–0.05); blood urea nitrogen, 25 mg/dL (7–20); creatinine, 2.07 mg/dL (0.5–1.5); C-reactive protein, 0.04 mg/dL (0–0.5); sodium, 141 mmol/L (135–147); and potassium, 3.9 mmol/L (3.4–4.7). Brain computed tomography indicated no intracranial hemorrhage or abnormal mass lesions.

The patient was intubated and admitted to the intensive care unit. As a result of rhabdomyolysis with acute renal failure, aggressive fluid hydration and sodium bicarbonate were administered. There was no hemodynamic change or vasopressor use. On the 3rd day of admission, creatine phosphokinase was elevated to 9,565 U/L and alanine aminotransferase was 3,392 U/L. Abdominal sonography showed negative results. Progressive elevation of TBil up to 20 mg/dL occurred in subsequent days. The patient was transferred to the intensive care unit of Taipei Veterans General Hospital 6 days after admission.

In our intensive care unit, his consciousness level was E4 VT M6. A series of laboratory studies revealed evidence of acute hepatic failure and DIC (normal range in parentheses): international normalized ratio, 1.81; activated partial thromboplastin time, 40.6 seconds (23.9–35.5); alanine aminotransferase, 2,638 U/L; aspartate aminotransferase, 204 U/L; alkaline phosphatase, 83 U/L (10–100 U/L); γ-glutamyltransferase, 52 U/L (8–60); TBil, 30.50 mg/dL; direct bilirubin, 18.54 mg/dL (0–0.3 mg/dL); C-reactive protein, 0.56 mg/dL; amylase, 613 U/L (0–190 U/L); lipase, 1,333 U/L (< 190 U/L); blood ammonia, 186 μg/dL (5–69); serum lactate, 64 mg/dL (5–15 mg/dL); and creatinine, 1.30 mg/dL. Tests for possible causes of acute hepatic failure including hepatitis B surface antigen, anti-hepatitis C virus, anti-hepatitis A virus IgM, ceruloplasmin, serum copper, autoimmune antibodies (antinuclear antibody, dsDNA, antineutrophil cytoplasmic antibody, antimitochondrial antibody and antismooth muscle antibody) were all within normal limits. Tests for other infectious causes including herpes simplex virus, cytomegalovirus, human immunodeficiency virus, Epstein–Barr virus, varicella–zoster virus, and leptospirosis were also negative. There was no history of hepatotoxic medication or toxins. Urine drug screening also showed negative results. Doppler sonography revealed no obvious thrombosis or embolus formation. Abdominal computed tomography disclosed no evidence of liver cirrhosis. Additional laboratory data revealed fibrinogen degradation products, 8.65 μg/mL (< 5 μg/mL); D-dimer, 4.40 μg/mL (< 2.09 μg/mL); and fibrinogen, 132 mg/dL (200–400 mg/dL). These results were consistent with DIC.

Molecular adsorbent recirculating system (MARS) treatment was performed daily on days 10–12, and TBil decreased from 27 to 18.7 mg/dL and remained at approximately 20 mg/dL (Figure 1). After extubation, the patient was found to be irritable, with impaired cognitive ability. No focal neurological signs were identified. On day 26 of admission, oliguric acute renal failure occurred. As a result of progressive azotemia with blood urea nitrogen of 126 mg/dL and creatinine

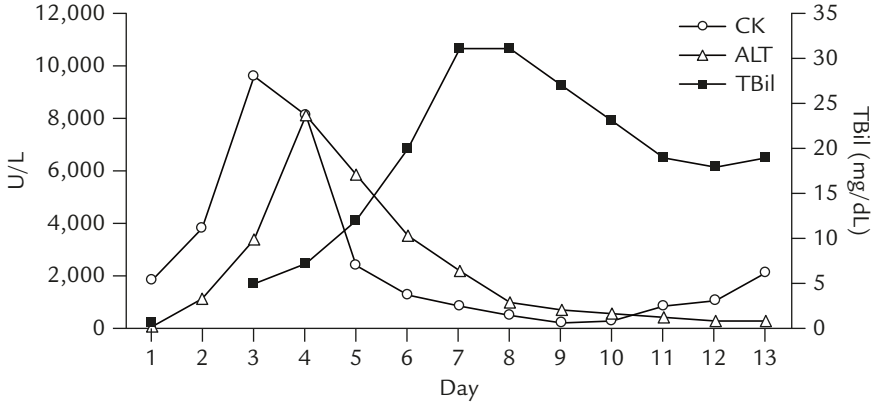

Figure 1. Serum alanine aminotransferase (ALT) and creatine phosphokinase (CK) increased in the initial days after thermal injury, and then declined. The total bilirubin (TBil) level followed after the peak of ALT and CK. We performed molecular adsorbent recirculating system treatment on days 10–12. The TBil level initially declined, but then remained at approximately 20 mg/dL.

of 9.07 mg/dL, hemodialysis was performed. On day 65 of admission, the patient died as a result of septic shock and multiple organ failure.

Discussion

We report a rare case of multiple organ dysfunction caused by classical heat stroke following a hot spring bath, which initially presented predominantly as acute hepatic failure. Heat stroke is defined as marked elevation of core body temperature, with central nervous system dysfunction. The exact mechanism of heat-stroke-related multiple organ dysfunction has not been elucidated; however, it is thought that direct thermal injury to cellular architecture, reactive cytokine storm, and endotoxemia play central roles in its pathogenesis.[1] All of these factors can contribute to further tissue damage and functional impairment of organs. Similar histopathological findings in hepatocytes and endothelial lining cells are found in heat stroke as in shock, ischemia, hypoxia, anaphylaxis, and certain immune-mediated injuries.[3] Heat shock occurs at a temperature of 41.6–42°C, over a time period of 40 minutes to 8 hours. Some authors have suggested that this variance is caused by genetic polymorphisms in heat shock protein; adaptive proteins that are produced in response to temperature elevation.[1]

In terms of the general management of heat-stress-related illness, rapid cooling and advanced medical support are crucial to the outcome. A previous study has suggested that reducing the core body temperature to <38.9°C within 30 minutes improves survival.[4] Aggressive intravenous fluid hydration, cold saline irrigation via a nasogastric tube, and cold saline enema are all management options. Cold hemodialysis using cold dialysate and endovascular cooling to combat hyperthermia have been reported as useful for patients who are refractory to other hyperthermic management.[5,6]

The treatment for EHS-related acute hepatic failure includes conservative treatment or liver transplantation. Hadad et al have compared conservative treatment with aggressive liver transplantation.[2] In the conservatively managed group, 8 patients (61.5%) recovered spontaneously and 5 died (38.5%). However, all of the 3 patients who received liver transplantation died during the follow-up period. Recently, the first long-term follow-up of liver transplantation for hepatic failure caused by EHS has been reported.[7] This has indicated that EHS with multiple organ involvement, DIC and renal function impairment can increase the liver transplantation failure rate. Some authors believe that more aggressive liver–kidney transplantation might improve the outcome.[8] However, no conclusions have been drawn because of the limited experience available.

MARS treatment has also been utilized for the acute stage of EHS-related hepatic failure, and the results are encouraging.[9,10] However, hepatic failure that results from classical heat stroke has been rarely reported. Dematte et al reported 58 cases of classical heat stroke with nearly fatal outcomes during the 1995 heat wave in Chicago.[11] Multiple organ dysfunction with neurological impairment was seen in all cases, moderate to severe renal insufficiency in 53%, DIC in 45%, and acute respiratory distress syndrome in 10%. None of the 58 patients developed fulminant hepatic failure. A heat wave in France also resulted in the death of 83 individuals, but there were only 2 cases (2.4%) of documented hepatic dysfunction.[12] Therefore, classical heat stroke is a fatal illness but rarely causes hepatic failure. Kim et al reported a case of multiple organ failure caused by heat stroke following a warm bath.[13] The patient developed fulminant hepatic failure with profound jaundice on day 8 after admission. MARS treatment was not applied, and TBil rose to 60 mg/dL. The patient died as a result of septic peritonitis secondary to complications of hepatic failure on day 25 after admission. Weigand et al reported another case that developed heat stroke with fulminant hepatitis and acute renal failure after working outdoors on a hot day.[14] The patient recovered after supportive treatment and dialysis. In that case, the maximum TBil was only 2.0 mg/dL.

In our case, the patient had taken a non-strenuous hike during the day and a hot spring bath at night. He had consumed a little alcohol at dinner. He was then found unconscious in the hot spring pool. At the emergency department, elevated core body temperature and central nervous system dysfunction were consistent with the diagnosis of heat stroke. Multiple organ impairment and DIC were also compatible with this condition. We surveyed other possible causes of acute hepatic failure and the results were negative. It seems unlikely that shock-induced hepatic failure occurred because no hemodynamic change developed. However, previously healthy and young adults seldom develop classical heat stroke unless they are under heat wave conditions at a temperature of more than 32.2°C on 3 or more consecutive days.[1] We believe that the development of the overwhelming illness in our case was a result of a special feature of oriental culture, namely, the hot spring bath. The temperature of hot springs is always >40°C, which causes rapid elevation of core body temperature. Excessive vasodilatation in the lower extremities can lead to brain hypoperfusion and change in consciousness. The high humidity in a hot spring room also impairs sweating. These features all cause

excessive heat load and impair thermoregulation. Although our patient did not have a history of chronic renal disease, poor renal function, especially anuria, is also a poor prognostic factor in heat stroke patients.[12]

After admission, aggressive saline infusion, ice pillow application, and antipyretic administration were used for reducing body temperature. However, persistent suboptimal body temperature control was still noted. Poor response to early aggressive cooling could have been an indicator of grave prognosis.

Previous case reports have suggested that early MARS treatment in EHS when TBil is mildly elevated can improve outcome.[10] In spite of 3 sessions of MARS therapy in our patient, TBil improved only slightly, and liver function did not recover. Early clearance of endotoxin and cytokines can facilitate breakdown of the vicious cycle of the cytokine storm. The patient finally developed irreversible multiple organ failure and died of ventilator-associated pneumonia with septic shock on day 65.

In conclusion, non-EHS can be diagnosed by clinical history and findings. Although multiple organ failure is described in this disease entity, our case report demonstrated predominantly fulminant hepatic failure, which has been rarely reported. When the diagnosis is made, the aim is to achieve rapid lowering of the core body temperature by any means. We believe that supportive therapy, including mechanical ventilation, hemodialysis, and MARS, can lead to improved outcomes.

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