Successful treatment of a case with acute hepatic failure following hot bath immersion

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Heat stroke is often complicated by hepatic dysfunction as a manifestation of multiple organ dysfunctions, but acute hepatic failure rarely progresses to become the major morbid condition of heat stroke. We encountered a case who survived life-threatening classic heat stroke; the patient developed this condition, subsequently associated with acute hepatic failure, while bathing at home.

A 73-year-old man was found in the bath in his home with unconsiousness, and was transferred to a nearby hospital. At the time he was in a coma, but no remarkable abnormalities were detected on blood examination. Rubor of his entire body beneath the cervical region was recognized. Under the diagnosis of a burn with consciousness disturbance, he was referred and transferred to our hospital. He was comatose and his axillaly body temperature was 39.7°C. His consciousness improved after admission, but blood examination revealed rhabdomyolysis, DIC and hepato-renal dysfunction. Subsequent blood examination findings showed rapid exacerbation. On the 2_{nd} hospital day, PT% was 12, INR was 4.8. On the 3_{ed} hospital day, serum ALT was elevated to 3,873 U/L, and the patient had hyperammonemia. On the 13_{th} hospital day, serum total bilirubin was elevated to 33 mg/dl. Thereafter, additional conservative treatment produced gradual recovery of hepatic function.

Keywords: hot bath, immersion, heat stroke, hepatic failure, DIC

ABBREVIATION AND NORMAL VALUE

DIC: disseminated intravascular coagulation, PT%: prothrombin time% (>79%), INR: international normalized ratio (0.80-1.20), ALT: alanine aminotransferase (<35U/L), GCS: Glasgow Coma Scale, CT: computerized tomography, ECG: electrocardiography, WBC: white blood cell (4,000-8,000/ul), RBC: red blood cell ($410-530\times10^4$/ul), Hb: hemoglobin (13.5-17.5 g/dl), Ht: hematocrit (40.0-48.0%), Plt: platelet ($14.0-40.0\ 10^4$/ul), Cr: creatinine (0.5-1.1mg/dl), BUN: blood urea nitrogen (8-20mg/dl), AST: aspartate aminotransferase (<30U/L), γ-GTP: γ-glutamyl transpeptidase (<80 U/L), LDH: lactate dehydrogenase (110-219U/L), CK: creatine kinase (40-190U/L), T-Bil: total bilirubin (0.2-1.1mg/dl), CRP: C-reactive protein (<0.3mg/dl), NH_3: ammonia nitrogen (<90ug/dl), APTT: activated partial hromboplastin time (23-36sec), PT: prothrombin time (10.7-14.0sec), PT%: PT percent (>69), CTR: cardiothoracic ratio, MRI: magnetic resonance imagination, EEG: lectroencephalogram, ICU: intensive care unit, D-dimmer: D-peptide dimmer (<0.5ug/ml), FDP: fibrin degradation product (<10), AT-III: antithrombin III (71-121%), D-Bil: direct bilirubin (0.0-0.3mg/dl), ChE: cholinesterase (180-430U/L), HA-IgM: hepatitis A-immunoglobulin M, HBs: hepatitis Bs, HCV: hepatitis C virus, CMV: cytomegalovirus, EB: Epstein-Barr, VCA: viral capsid antigen, EBNA: EB nuclear antigen.

INTRODUCTION

Heat stroke is a life-threatening state characterized by an elevated core body temperature that rises above 40°C and central nervous system abnormalities[1,2,3]. It has been classified as classic or exertional. Classic (or non-exertional) heat stroke frequently occurs in the elderly develops in high-temperature environments and exertional heat stroke occurs during work or exercise[1,2,3,4]. Although the pathophysiology of heat stroke remains unclear, its elucidation at the cellular and molecular levels has been progressing in recent years. Thus, the following definition is being advocated: "it is a form hyperthermia associated with a systemic inflammatory response leading to a syndrome of multiorgan dysfunction in which encephalopathy predominate."[1]. Heat stroke is often complicated by hepatic dysfunction as a manifestation of multiple organ dysfunction, but it is rare for acute hepatic failure to progress to become the major morbid condition[5,6,7]. Severe acute hepatic failure associated with heat stroke is almost always due to exertional heat stroke, and cases due to classic heat stroke are even rare.

We encountered a case who survived life-threatening classic heat stroke; the patient developed this condition, subsequently associated with acute hepatic failure, while bathing at home. The clinical course is described herein.

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CASE REPORT

Present illness

A 73-year-old man, who was previously healthy, took a bath at home. Thirty minutes later a family found him in a state in which his body, beneath the cervical region, was immersed in the bath. He was unconscious. He was taken to a nearby hospital by ambulance.

On transfer to the hospital, his consciousness level was GCS 3, respiratory rate 30/min, pulse rate 156/min, blood pressure 69/42 mmHg, and body (axillary) temperature 37.1°C. Rubor was recognized on the body surface beneath the cervical region.

Radiological examinations revealed no abnormal findings. Electrocardiogram (ECG) revealed sinus tachycardia, and wall motion was normal on echocardiography. Under the diagnosis of a burn of 80% of the body surface, the patient underwent rapid infusion of 2,500 ml of normal saline solution. His blood pressure improved to 150/70 mmHg, but consciousness was unchanged. Approximately 5 hours after he was found unconscious in the bath, he was transferred to our hospital. During this 5-hour period, he underwent burn cooling therapy with ice water.

Findings on initial medical examination at our hospital

On transfer to our hospital his consciousness level was GCS 3, respiratory rate 24/min, pulse rate 111/min, blood pressure 190/120 mmHg, and body (axillary) temperature 39.7°C. On physical examination, rubor was recognized on the body surface beneath the cervical region, and coarse crackles were audible in both lung fields. Heart sounds were normal. The abdomen was soft and flat. The pupil was 3.5 mm in each, and light reflex was prompt. There were no abnormalities of deep tendon reflexes. Neither morbid reflexes nor nuchal rigidity was recognized. Red urine was recognized. He was immediately intubated because of the serious consciousness disturbance.

He had no remarkable past medical history, family history or allergies, and did not take any commonly used drugs. His history of alcohol use was moderate social drinking.

Laboratory findings on the initial examination

Blood findings on initial examination at our hospital were: WBC 8,900/μl, RBC 474×10^4/μl, Hb 15.5 g/dl, Ht 43.2%, Plt 15.6×10^4/μl, Cr 1.3 mg/dl, BUN 18 mg/dl, AST 143 U/l, ALT 90 U/l, γ-GTP 71 U/l, LDH 564 U/l, CK 561 U/l, T-Bil 0.5 mg/dl, Na 143 mEq/l, K 3.3 mEq/l, Cl 111 mEq/l, CRP 3.7 mg/dl, NH_3 41 μg/dl, myocardial troponin I 2.89 ng/ml, serum myoglobin 2,240 ng/ml, and serum lactate 36 mg/dl. Blood coagulation test results were APTT 34 seconds, PT 16.2 seconds, PT% 61% and PT-INR 1.36. The arterial blood gas analysis with a mask, delivering 10 L of oxygen per minute, results were: pH 7.43, $PaCO_2$ 20.3 torr, PaO_2 62.8 torr, base excess- 8.8 mmol/l, and HCO_3^-13.2 mEq/l, showing hypoxemia and respiratory compensation of metabolic acidosis. The patient was positive for urinary occult blood and urinary myoglobin, and his urinary myoglobin level was 12,000 ng/ml. All qualitative screening parameters for drugs in urine were negative, and the blood concentration of alcohol was lower than 1 mg/dl.

Chest X-ray revealed a CTR of 61% and infiltrative shadow in bilateral lung. No findings of cholecystitis or obstruction of the hepatic artery, vein, or portal vein was noted on abdominal CT. Head CT and MRI showed no hemorrhage, infarction or space-occupying lesions. ECG revealed atrial flutter and a pulse of 158/min. There were no spike waves on the electroencephalogram (EEG).

The aforementioned findings indicated a burn with consciousness disturbance and rhabdomyolysis, and the patient was brought to our ICU 4.5 hours after arriving at our hospital. During the time from the treatment at the first hospital until admission to our hospital, the total infusion amount was 4,200 ml of lactated Ringer's solution and his urine volume was 800 ml. The patient's entire body was cooled with a blanket at 20°C because of hyperthermia.

Course on admission

Six hours and 30 minutes after the patient arrived at our hospital (approximately 12 hours after being found in the bath), his consciousness level had improved to GCS 3-T-4, with respiratory rate 28/min, pulse rate 120/min, blood pressure 140/85 mmHg, and rectal temperature 38.8°C. Blood examination results were: Cr 1.3 mg/dl, BUN 18 mg/dl, AST 425 U/l, ALT 294 U/l, LDH 943 U/l, T-Bil 1.3 mg/dl, CK 2,566 U/l, lactate 57 mg/dl, PT% 36%, PT-INR 1.98, D-dimer 127.3 μg/ml, FDP 179.0 μg/ml, fibrinogen 352 mg/dl, AT-III activity 63%, rapid elevations of liver enzyme and CK, prolonged PT-INR, high D-dimer and FDP levels, and elevation of serum lactic acid. The arterial blood gas analysis results were: FiO_2 0.7, pH 7.44, $PaCO_2$ 25.5 torr, PaO_2 173 torr, base excess- 4.6 mmol/l, and HCO_3^-17.3 mEq/l. Based on his course and clinical findings, the patient was diagnosed with disseminated intravascular coagulation (DIC), rhabdomyolysis, hepato-renal dysfunction. Changes in blood examination results after he arrived in our hospital are shown in Figures 1a, 1b, 1c, 1d, 1e, 1f and 1g.

Second hospital day

His consciousness level was GCS 3-T-4, pulse rate 110/min, blood pressure 120/70 mmHg, and rectal temperature 37.2°C. Blood examination results were: Plt 4.2×10^4/μl, Cr 1.1 mg/dl, BUN 15 mg/dl, AST 2,333 U/l, ALT 1,798 U/l, LDH 3,273 U/l, T-Bil 3.2 mg/dl, CK 5,711 U/l, PT% 12%, PT-INR 4.80, D-dimer 171.8 μg/ml, FDP 263 μg/ml, fibrinogen 263 mg/dl, and AT-III activity 51%, showing rapid elevations of liver enzyme and CK, prolongation of PT-INR, decline of PT%, exacerbation of high D-dimer and FDP elevations, and elevated serum T-Bil. Echocardiography revealed favorable (regional) wall motion, and there were no sinus rhythm abnormalities on ECG. Continuous intravenous injection of heparin sodium at a daily dose of 10,000 U and administration of fresh frozen plasma were started for treatment of DIC.

Third hospital day

The consciousness level was GCS 3-T-6, pulse rate

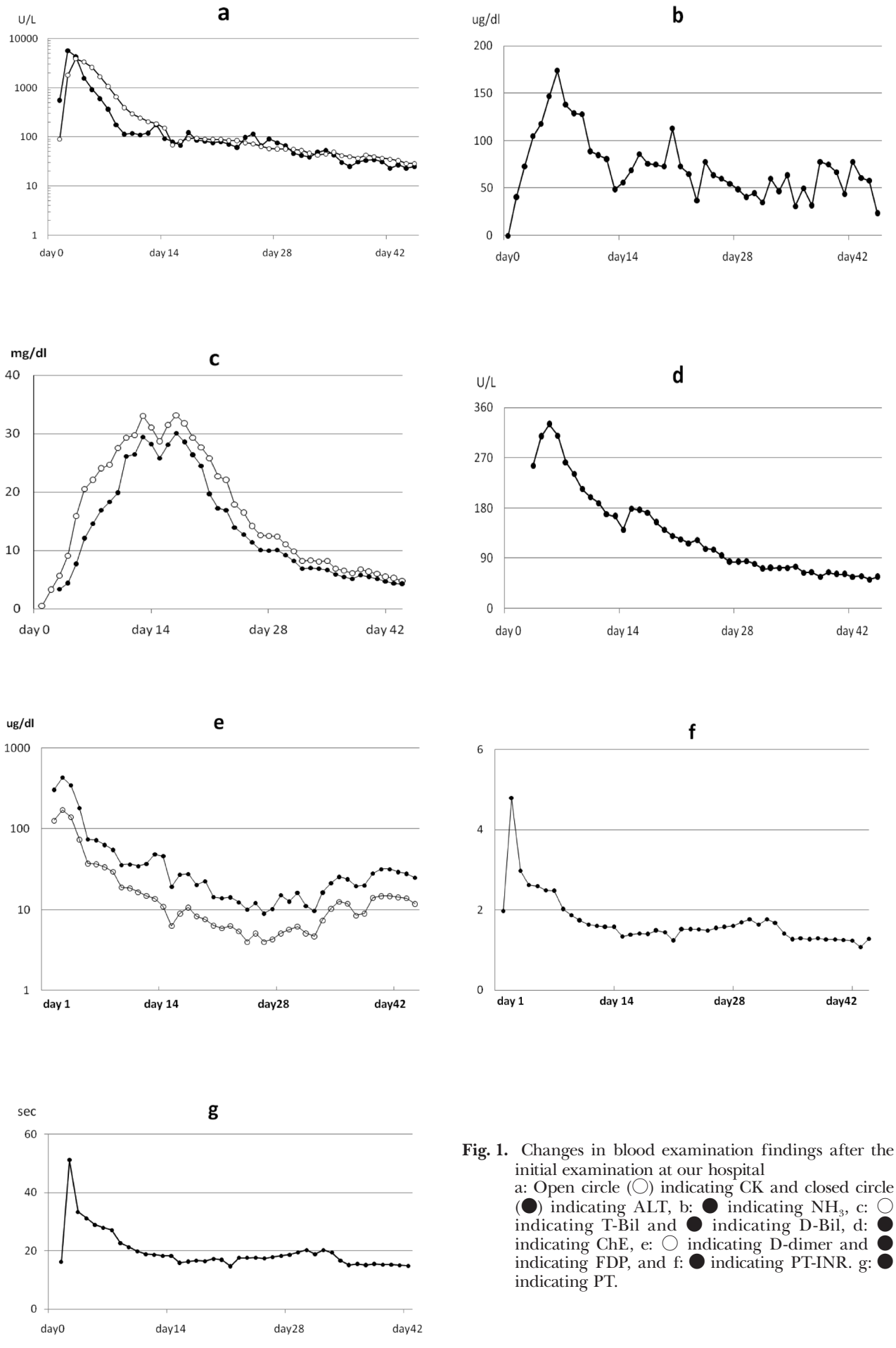

Fig. 1. Changes in blood examination findings after the initial examination at our hospital
a: Open circle (○) indicating CK and closed circle (●) indicating ALT, b: ● indicating NH_3, c: ○ indicating T-Bil and ● indicating D-Bil, d: ● indicating ChE, e: ○ indicating D-dimer and ● indicating FDP, and f: ● indicating PT-INR. g: ● indicating PT.

100/min, blood pressure 140/80 mmHg, and rectal temperature 36.8°C. The blood examination results were: Plt 5.6 x 10^4/μl, AST 4,897 U/l, ALT 3,873 U/l, LDH 5,020 IU/l, T-Bil 15.7 mg/dl, D-Bil 3.4 mg/dl, ChE 256 U/l, NH^3 105 μg/dl, CK 4,299 U/l, PT% 21%, PT-INR 2.98, D-dimer 131.6 μg/ml, FDP 209 μg/ml, and AT-III activity 69%. Although CK and PT-INR tended to decrease, PT% tended to increase, further elevation of liver enzyme, elevation of bilirubin (direct bilirubin predominated), and hyperammonemia were recognized. He was thus diagnosed as having had hepatic failure, and lactulose administration was started. Serum levels of γ -GTP and ALP normalized. He was negative for HA-IgM antibody, HBs antigen, HCV antibody, CMV-IgM antibody, EB anti-VCA-IgA antibody, and EB anti-EBNA antibody. He was also negative for antinuclear, anti-sm, anti-mitochondrial and anti-smooth muscle antibodies.

From these clinical findings, the pathological condition was diagnosed as heat stroke, due to hot bath immersion, associated with DIC, rhabdomyolysis and acute hepatic failure.

Course from the 4th hospital day onward

AST, ALT, CK, and PT-INR tended to decrease, PT% tended to increase, most markedly on the second to third hospital days. However, the T-Bil and NH_3 elevations persisted. NH_3 peaked at 174 μg/dl on the 6_{th} hospital day. Since it tended to decrease thereafter, nasal feeding was gradually started. On the 13_{th} morbid day, plasma exchange was performed, but since T-Bil tended to decrease after its peak of 33.1 mg/dl, plasma exchange was not performed after that day.

During this period, mild consciousness disturbance persisted. Since pneumonia also began to develop on the 7_{th} hospital day, respiratory management was conducted under intubation. Thereafter, the patient showed remission of the pneumonia and his consciousness became clear on the 18_{th} hospital day. The mechanical ventilation was withdrawn with extubation. Head CT on the 35_{th} hospital day revealed no remarkable abnormal findings.

ChE remained low for the long term, with a nadir of 55 U/l on the 44_{th} hospital day, followed by a tendency to rise. On the 62_{nd} hospital day it was elevated to 70 U/l. On the same day, he was referred to another hospital for rehabilitation.

DISCUSSION

Although heat stroke is a state with a core body temperature of at least 40°C[1,2,3,4], the patient's body temperature is not necessarily taken into consideration when making the diagnosis of heat stroke[3,6]. There are some cases in which the initial temperature is taken in the axilla and in which core body temperature is lower than 40°C because of cooling before arrival at the hospital. We consider our present patient to have been immersed in a hot bath for a long time. When he was transferred to our hospital, axillary temperature was 39.7°C and consciousness disturbance was evident. After admission, the patient developed rhabdomyolysis, DIC, and acute hepatocellular hepatic failure. On the other hand, the patient had no particular past history, and was negative on examinations for various types of viruses, drug screening tests at the initial examination, and the blood concentration of alcohol. From these results, his condition was diagnosed as heat stroke, which occurred because of hot water immersion during bathing.

Heat stroke is often complicated by rhabdomyolysis, acute renal failure, acute respiratory failure, shock and multiple organ dysfunction[1,2,3,4]. Although mild or moderate hepatic dysfunction is frequently associated with heat stroke, there have been only a small number of the reports discussing severe acute hepatic failure[7]. Kew et al. recognized mild or moderate hepatic dysfunction in all 39 miners in their study with exertional heat stroke, but only 3 (9%) had acute hepatic failure and 2 of these 3 died[5]. Another report showed 1 (2%) of 50 police officers, who simultaneously developed heat stroke during training, to have acute hepatic failure, and this patient died despite liver transplantation[8]. From these reports, the incidence of acute hepatic failure in exertional heat stroke is considered to be 2–9% and the mortality rate associated with the condition of acute hepatic failure is high[6]. Immediately after the occurrence of exertional heat stroke, patients often present central nervous system abnormalities, shock, respiratory failure, rhabdomyolysis, DIC and acute renal failure. Serum liver enzyme levels peak a few days after the occurrence, and then hepatic failure manifests[2,5,6,12,16]. Histopathological findings of the injured livers are complex, and centrilobular vacuolar degeneration is often recognized[5,6,9,10,11,14]. The mechanism underlying the occurrence of hepatic failure due to heat stroke is not fully understood, however direct cytotoxic effects of heat, ischemia and DIC are considered to be involved[5,6,7,10].

Severe hepatic failure accompanying classic heat stroke is more unusual than that accompanying exertional heat stroke. In 1995, 58 persons with classic heat stroke due to a heat wave in Chicago were hospitalized, but none were described as having acute hepatic failure[12]. According to our literature search, only three cases have been reported to date[4,6]. Kim et al. reported a patient with classic heat stroke, who was found with consciousness disturbance while bathing in hot water and died from acute hepatic failure and multiple organ failure on the 25_{th} hospital day[13]. Deutsch et al. reported a case of a healthy young refugee, who developed severe acute hepatic failure consequently classic heat stroke during his transportation to Greece in a closed container on a ship under unusually high temperatures[14]. Weigand et al. reported 2 patients with acute hepatic failure due to heat stroke. According to these investigators, the death was attributable to classic heat stroke in 1 of the 2 patients[15]. Our present patient developed heat stroke while bathing, and thus resembled the case reported by Kim et al.

Whether or not liver transplantation should be performed becomes an issue, because the mortality rate associated with acute hepatic failure accompanying heat stroke is high. However, in heat stroke cases, no definite indications for liver transplantation have been established[16,17]. There have even been 4 patients with exertional heat stroke, who underwent liver transplantation[7,11,18,19]. Only 1 survived for at least 1 year[18], while many reports have shown remission of heat stroke with

conservative treatment[14,16,17]. In our present patient, the maximum serum ALT level was 3,873 IU/l, INR was 4.8, the blood ammonia level was 174 μg/dl and serum T-Bil was 33 mg/dl, the minimum PT% level was 12%. Thus, the patient's condition was serious, but showed remission with conservative treatment.

In Japan, bathing of the entire body has long been a routine habit, and the most popular temperature for bathing water is 42°C. High temperature baths and prolonged bathing are thought to entail a risk of heat stroke. When the patient's body temperature has already improved by the time the patient arrives at the hospital, classic heat stroke may not be recognized.

When treating consciousness disorders after bathing, we think it is necessary to consider classic heat stroke and the subsequent development of acute hepatic failure, and to monitor the patient's hepatic function.

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