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Rhabdomyolysis with Acute Kidney Injury Successfully Treated with External Cooling

Hye In Jung, M.D., Yong Sik Kwon, M.D., Jae Cheul Pi, M.D., Jae Seok Park, M.D., Sun Hyo Park, M.D., Jin Young Kim[1], M.D., Won Il Choi, M.D.

Department of Internal Medicine, Radiology[1], Keimyung University School of Medicine, Daegu, Korea

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Corresponding Author: Won Il Choi, M.D.,
Department of Anesthesiology,
Keimyung University School of Medicine,
56 Dalseong-ro, Jung-gu, Daegu 41931, Korea
Tel: +82-53-250-7572
E-mail: wichoi@dsmc.or.kr

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Hyperthermia can cause severe complications such as rhabdomyolysis, which can induce acute kidney injury. Normal thermoregulation can be disturbed by high fever, and maintenance of a normal body temperature by external cooling can reduce oxygen consumption, and increase vascular tone. Several studies have been conducted to determine the effectiveness of external cooling in treat rhabdomyolysis or renal failure. We report a case of rhabdomyolysis leading to multiple organ dysfunction, including renal failure. The use of an external cooling device achieved fever control and successfully treated rhabdomyolysis and renal failure.

Keywords: Acute kidney injury, Body temperature, Rhabdomyolysis

Introduction

Fever is a physiological response to infectious or aseptic stimuli, and it is regulated by thermoregulatory centers located throughout the brainstem and spinal cord [1]. Fever arises from a normal thermoregulatory mechanism and reaches a specific set point, while hyperthermia results from abnormal temperature regulation [2]. Hyperthermia can cause severe complications such as rhabdomyolysis if normal thermoregulation cannot be maintained. Rhabdomyolysis has several potential causes: traumatic causes such as muscle compression; non-traumatic non-exertional causes such as drugs, toxins, infections, or electrolyte disorders; and non-traumatic exertional causes such as exercise by untrained individuals and hyperthermia [3,4]. Severe rhabdomyolysis, regardless of the cause, induces acute kidney injury when water is sequestered in injured muscles. The prognosis is substantially worse if renal failure develops [4]. Therefore, treatment of rhabdomyolysis could prevent acute renal failure

and reduce mortality. Fever control can be achieved through various methods such as external cooling using an alcohol sponge, cold saline, antipyretics, or an external cooling device. The most effective method for achieving fever control is the use of an external cooling device [5]. We report a case in which normothermia was achieved using an external cooling device, which prevented muscle enzyme elevation and rhabdomyolysis-associated kidney injury without renal replacement therapy. The patient recovered from multiple organ failure.

Case Report

A 37-year-old man had no history of cardiac problems. He drank over three bottles of 20% alcoholic beverage daily and smoked one pack of cigarettes daily for 10 years. He was found collapsed on the floor of a bathroom. The emergency physician found the patient to be drowsy and appearing acutely ill. The initial blood pressure was 160/100 mmHg, heart rate was 67 beats per minute, respiratory rate was 20 breaths per minute, and body temperature was 37.9℃. The initial electrocardiogram showed sinus tachycardia. The patient subsequently developed respiratory insufficiency and circulatory failure. He was immediately intubated and cardiac massage was performed for 1 minute before the heart returned to sinus rhythm. The patient remained hypotensive, requiring immediate use of catecholamines (epinephrine and vasopressin). Laboratory findings included white blood cell count of 6,260/L and hemoglobin value of 10.2 g/dL. Blood urea nitrogen level was 19 mg/dL, serum creatinine level was increased to 2.78 mg/dL and C-reactive protein was 6.6 mg/dL. Other laboratory findings at emergency department were summarized in Table 1. Although there was no demonstrable abnormal pulmonary infiltration visible on an initial chest X-ray, right lower lung haziness was found after intubation. A slightly increased cardio-thoracic ratio was noted, probably due to incomplete inspiration (Fig. 1). The patient was subsequently diagnosed with alcoholic ketoacidosis (positive for serum and urine ketone), aspiration pneumonia, and rhabdomyolysis, and was admitted to the Intensive Care Unit (ICU). The patient had no evidence of ischemic heart disease. Antibiotics were administered, and re-hydration therapy was performed. He underwent re-hydration, and was given catecholamines (norepinephrine and vasopressin). Upon arrival at ICU, the patient's temperature was 40.0℃ as measured by tympanic thermometry. Temperature control methods, including the use of external cooling device, were applied for 48 hours, this led to a significant decrease in core body temperature of 37℃ in 90 minutes, which was then maintained with a margin of error of 0.1℃. The target temperature of 37℃, as measured using an esophageal catheter, was reached using an Arctic Sun® 5000 Temperature Management System (Bard Medical, GA, USA).

When core body temperature reached at 37℃, extremities felt coldness without cyanosis. Alcoholic ketoacidosis, multiple organ dysfunction, and rhabdomyolysis led to increased levels of myoglobin and creatinine kinase (CK), which gradually improved. After re-hydration, a continuous infusion of catecholamines, and the use of cooling device, the patient's renal function was improved, urine output increased, blood pressure was elevated, and creatinine levels gradually returned to normal. A urinary excretion rate of >70-100 mL/h led to a fluid turnover of up to 2,000 mL/24 hours. We might succeeded in treating the patient without using extracorporeal hemofiltration. The patient's body temperature, blood pressure, urine output, myoglobin, CK, blood urea nitrogen (BUN), creatinine, anion gap, and daily catecholamine requirement are summarized in Table 2. The patient's respiratory rate was stable throughout his hospital stay, and he was safely extubated at 11th

Table 1. Laboratory data at emergency department

Variable	Reference range, adults	Emergency department
White-cell count (10^3/μL)	5,200-12,400	6,260
Hemoglobin (g/dL)	12-18	10.2
Hematocrit (%)	37.0-52.0	30.0
Prothrombin time (sec)	10.0 -14.0	14.5
Activated partial thromboplastin time (sec)	20.0-38.0	31.0
Serum creatinine (mg/dL)	0.7-1.3	2.78
Blood urea nitrogen (mg/dL)	9.0-23.0	19
C-reactive protein (mg/dL)	0.0–0.5	6.6
Creatine kinase (U/L)	32.0-294.0	161

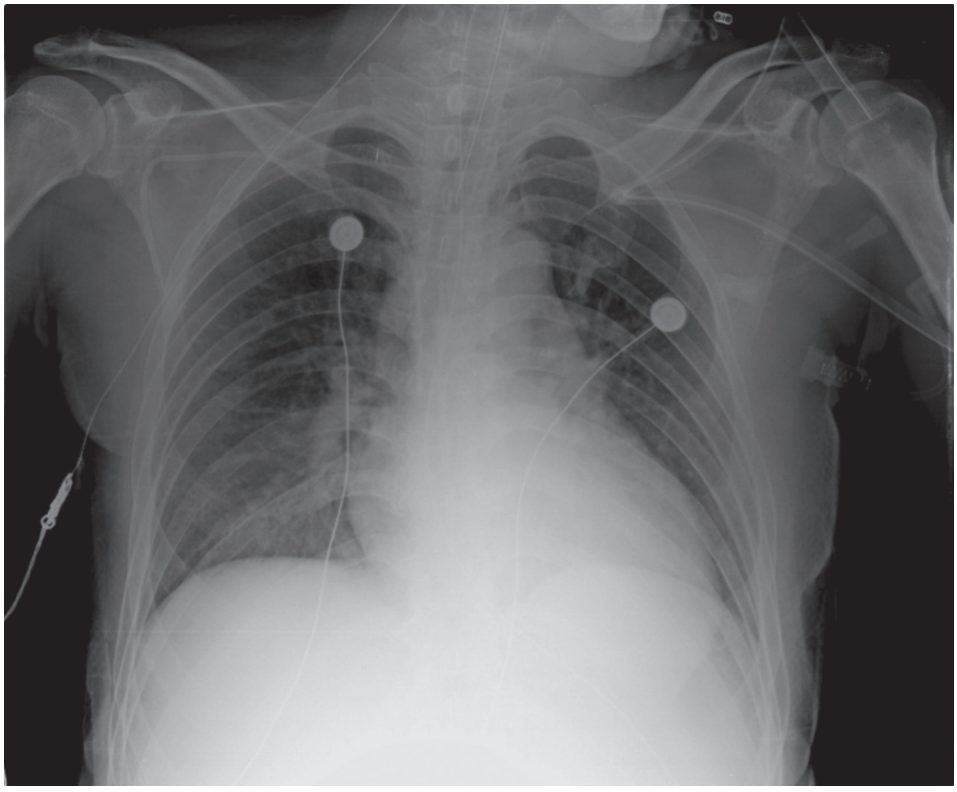

Fig. 1. The chest radiograph after intubation shows abnormal pulmonary infiltrations in the right lower lung field. A slightly increased cardio-thoracic ratio is noted, probably due to incomplete inspiration.

Table 2. Daily changes in septic condition parameters with normothermic therapy

	Before NT (at ER)	NT start (Day 1)	NT continue (Day 2)	NT continue (Day 3)	NT continue (Day 4)	NT stop (Day 5)	NT stop (Day 6)
Body temperature (℃)	38.0	38.3	38.1	37.2	37.3	38.6	37.6
SBP	128	126	123	102	105	145	137
DBP	60	57	74	68	74	94	93
Total fluid intake (mL)	3,060	5,937	3,176	3,363.5	3,694	3,796	3,297
UO (mL)	0	7,000	3,320	2,130	2,375	2,725	2,100
Nor-epine-phrine (ug/day)	1,200	1,200	600	600	600	480	240
Vasopressin (U/day)	3	3	2.4	2.4	2.4	2.4	2.2
Na/K/Cl (mEq/L)	131/5.2/89	124/3.2/84	126/3.3/85	123/3.7/83	121/3.5/83	121/2.9/84	122/3.2/88
CK (U/L)	161	2795.2	4,154.9	3,324.3	1,797.1	1,404.8	712.3
Myo-globulin (ng/mL)		693	1619	340	94	128	89
BUN (mg/dL)	19	21	23	17	24	23	17
Creatine (mg/dL)	2.78	3.36	1.38	0.66	0.53	0.53	0.57
Lactic acid (mmol/L)	17	16	3.2	3.0	2.9	2.2	1.4
pH	7.184	6.92	7.431	7.453	7.534	7.57	7.534
Anion gap	37.8	22.8	20.1	15.7	12	9.4	9.6
SAPS 3	69						
APACHE II	32						

NT: normothermic therapy, SBP: systolic blood pressure, DBP: diastolic blood pressure, UO: urine output, ER: emergency room, CK: creatine kinase, BUN: blood urea nitrogen, SAPS 3: simplified acute physiology score 3, APACH II: acute physiology and chronic health evaluation II score.

day of admission. After transport to a general medical ward, the patient recovered from alcoholic ketoacidosis, rhabdomyolysis, and multiple organ dysfunction, and he was discharged from the hospital after a total of 24 days.

Discussion

We present a case in which rhabdomyolysis-associated multiple organ failure was treated using an external cooling device, thus preventing renal injury. The patient's blood pressure recovered immediately after restoring normothermia.

In cases of severe sepsis, reducing the body temperature with antipyretic drugs may decrease cardiac output and oxygen consumption and increase vascular tone and serum lactate clearance [6], on the other hand, an external cooling device may not cause significant side effects.

In a multicenter randomized controlled trial, the use of external cooling to reduce fever significantly decreased required vasopressor doses within 12 hours of treatment. Patients who received external cooling treatment had a significantly lower 14-day mortality compared with those who did not receive external cooling treatment [5]. Normothermic therapy can induce vasoconstriction and can lead to moderate impairment of peripheral circulation, evident in an increased core-peripheral temperature gradient. Consequently, re-warming reduces the peripheral circulation impairment [7]. Fortunately, the current patient did not experience symptoms of impaired peripheral circulation, such as skin necrosis.

In this case, CK was significantly decreased after normothermic therapy. The current treatment for rhabdomyolysis is to identify the specific causes and employ appropriate countermeasures to the triggering events. Prevention of acute kidney injury requires early, aggressive fluid resuscitation. The use of bicarbonate, loop diuretics, mannitol, or dialysis to prevent renal injury has not been demonstrated to be effective, despite their potential benefits to rhabdomyolysis [8-10]. Rhabdomyolysis was associated with fever in the current patient. Accordingly, fever control can prevent CK elevation. In this case, we managed to control the fever using an external cooling device and muscle enzyme levels returned to a normal range. Antipyretic treatment for reducing body temperature in cases of sepsis may increase mortality [11]. The use of alcohol or cold saline massage has only transient effects on temperature, making it difficult to maintain a consistent core temperature reduction. In contrast, an external cooling device can quickly achieve sustainable normothermia and it is expected to be widely used for treatments in the future.

Previous studies using small-animal experimental models such as cats have shown that mild to moderate decreases in brain temperature can significantly reduce cerebral intracellular acidosis, both during ischemia and recirculation [12]. In patients with cerebral ischemia, mild to moderate decreases in brain temperature are neuroprotective, whereas mild brain temperature elevations increase brain injury [13]. In the current case, the patient developed respiratory insufficiency and cardiovascular failure, was immediately intubated, and cardiac massage was performed for 1 minute. The patient was expected to have brain injury. However, the patient fully recovered.

In this case, an external cooling device was able to improve the patient's renal function and recovery from rhabdomyolysis and decrease brain injury despite of hypertheramia in the ICU. Several studies have been performed to reveal the effectiveness of an external cooling device in treating rhabdomyolysis. Nevertheless, further studies are needed to investigate the benefits of normothermia for improving rhabdomyolysis and decreasing renal failure.

In this case, external cooling device may help

improving the patient's renal function and recovery from rhabdomyolysis, and decreased brain injury despite of hypertheramia in the ICU.

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