PULMONARY EDEMA COMPlicATING EXERTIONAL HEAT STROKE: A CASE SERIES

Chi-Hao Liu, Chih-Chiang Wang, Ho-Cheng Lin, Lin, I-Hung Chen, Ming-Kai Tsai, Jeng-Chuan Shiang

Abstract

Introduction: Heat stroke (HS) is an emergent illness characterized by high body temperature and disturbed consciousness. Fluid resuscitation with rapid cooling is the mainstay of HS treatment. However, pulmonary edema (PE) can often complicate the clinical course of HS patients.

Case Series: We reviewed all cases of HS admitted to our hospital from January 2006 to January 2013; of these 20 cases, 5 (25%) were complicated with PE. Multi-organ dysfunction was developed in all cases. We have summarized here the possible reasons that lead to PE in HS patients, including fluid overload, endothelial injury with leakage, acute kidney injury, and transient cardiac dysfunction.

Discussion and Conclusion: In the emergency department, intravenous infusion of approximately 1000-1200 mL saline may be adequate for early resuscitation. Further fluid administration should be based on the patient’s mean arterial pressure, fluid input, and fluid output. Inappropriate fluid supplementation may lead to PE and respiratory impairment. In patients with persistent hypotension despite fluid resuscitation and cooling, central venous pressure is a useful indicator for guiding further fluid supplementation. While fluid overloading can lead to poor outcomes, overt dehydration is also harmful for HS patients. No fixed protocol can be directly applied to all HS patients with multi-organ dysfunction. Fluid resuscitation in HS patients should be carefully managed and adjusted frequently for ensuring appropriate levels of hydration.

Key Words: Heat stroke, pulmonary edema, cardiac dysfunction, acute kidney injury

Introduction

Heat stroke (HS) is a life-threatening disease that is defined by a core temperature greater than 40.6°C (105.1°F) and accompanied by central nervous system (CNS) disturbances. The typical symptoms of HS include dry and hot skin, rapid heart rate, extremely high fever, CNS dysfunction (delusion, delirium, convulsions, or coma), and possible multi-organ dysfunction.1 In the United States, HS incidence varies from 17.6 to 26.5 cases per 100,000 population.2 However, in Saudi Arabia, this incidence varies from 22 to 250 cases per 100,000 population, and the HS mortality rate in Saudi Arabia is approximately 50%.3 Fluid resuscitation is an important component

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in the treatment of patients with HS. However, pulmonary edema is a frequent complication encountered among HS patients. Here, we have described 5 cases of HS complicated by pulmonary edema and proposed a strategy for optimal fluid management in patients of HS.

**Case reports**

**Case 1**
A 22-year-old man, with no prior medical history, presented to our emergency department (ED) due to disturbed consciousness with agitation, after running 1000 meters. High core temperature (40.6°C) and low blood pressure (82/36 mmHg) were noted, and fluid resuscitation with approximately 2500 mL of normal saline was applied in 6 h. Subsequently, acute pulmonary edema complicated with acute respiratory failure developed on the same day; therefore, emergent endotracheal (ET) intubation was performed. Acute kidney injury (blood creatinine 1.8 mg/dL), and high creatine phosphokinase (CPK) levels (6445 U/L) were also recorded. After admission to the intensive care unit, we used central venous pressure (CVP) levels for guiding fluid resuscitation. The initial CVP level was 20 mmHg; therefore, mannitol and furosemide were prescribed. Echocardiography on day 2 of hospital admission showed global hypokinesis of the left and right ventricles with impaired left and right ventricular systolic function. We adjusted the furosemide and saline dosages according to the CVP level and urine output. After 2 days of therapy, pulmonary edema subsided and the patient was extubated. Subsequent echocardiography revealed improved left and right ventricular systolic function as compared to the initial echocardiogram. Renal function and CPK levels recovered comparison to admission day after medical therapy. This patient was transferred to the ordinary ward after 4 days of ICU hospitalization and charged after 7 days of ordinary ward hospitalization.

**Case 2**
A 20-year-old man, with no prior medical history, presented to our ED with altered consciousness after running 5000 meters. A core temperature of 41.3°C and hypotension (88/17 mmHg) were noted. ET intubation was performed following loss of consciousness. Fluid resuscitation therapy was administered with approximately 5500 mL of normal saline for correcting the hypotension and oliguria. Acute pulmonary edema was recorded after the fluid challenge in the ED. Further, poor renal function and elevated CPK levels were also noted. After admission to the intensive care unit, the CVP was measured and fluid supplementation was adjusted according to the CVP levels. The initial CVP level was 15 mmHg, and mannitol and furosemide were accordingly prescribed. Echocardiography was performed on day 2 of admission; this indicated normal systolic and diastolic function. We adjusted the furosemide and saline dosages according to the urine output and CVP levels. Following medical therapy, pulmonary edema, impaired renal function, and CPK levels improved, and we extubated the patient after 2 days of admission in the ICU. This patient was transferred to the ordinary ward after 5 days of ICU hospitalization.

**Case 3**
A 24-year-old man, with no prior medical history, presented to our ED for disturbed consciousness and high fever (40.7°C) after bayonet drill exercises. Attack behavior and convulsions were also reported. Emergent fluid challenge with approximately 2500 mL was prescribed for resuscitation. Since unconsciousness, oliguria, and CO2 retention were present, ET intubation with mechanical ventilation support was performed. Chest radiograph revealed acute pulmonary edema, and blood tests showed poor renal function and abnormal CPK levels. After admission to the intensive care unit, the initial CVP level was 5 mmHg. Echocardiography on day 2 of admission showed mild hypokinesis of the septal wall. We closely monitored the patient’s urine output and CVP levels for adjusting the
dose of diuretic drugs and the hydration levels. Pulmonary edema subsided after medical therapy; however, ischemic bowel disease was suspected on the fifth day of hospitalization. Elevated levels of serum amylase and lipase (204 and 794.6 U/L, respectively) were detected, and abdominal computed tomography revealed fluid and free air accumulation over bilateral subphrenic regions, with wall thickening of small intestinal segments as well as of the large intestine. Emergent exploratory laparotomy was performed, which revealed rupture of the splenic flexure of the colon with peritonitis; this was considered to be induced by ischemic injury. Aggressive medical therapy was administered for resuscitation. The patient was transferred to the ordinary ward after 1 month of intensive care.

**Case 4**

A 21-year-old man, with no prior medical history, presented to the ED following sudden collapse after military training involving running for 1000 meters. Disturbed consciousness, high body temperature (41°C), and a seizure attack were recorded. Emergent ET intubation and fluid hydration of approximately 9500 mL were administered for resuscitation. Acute pulmonary edema was noted on the chest radiograph. Moreover, impaired renal function and elevated CPK levels were also detected. Echocardiography on day 2 of admission revealed normal wall motion with adequate systolic and diastolic function. After 2 days of medical therapy, pulmonary edema subsided and the renal function improved gradually. The patient was extubated on day 6 of hospitalization.

**Case 5**

A 19-year-old man, with no prior medical history, presented to our ED with high fever and disturbed consciousness following military training exercises. Acute respiratory failure developed, and ET intubation was prescribed for resuscitation. The core temperature was 41.6°C, and adequate cooling and intravenous hydration with 1500 mL were administered for treatment. He was admitted to the intensive care unit since HS with multi-organ dysfunction was suspected. After fluid supplementation of over 4000 mL during 5 h, chest radiograph revealed pulmonary edema, and blood tests revealed impaired renal function. Mannitol and furosemide were prescribed for treating the pulmonary edema. Echocardiography on day 2 of admission showed normal systolic and diastolic function. We closely monitored the urine output and electrolyte levels for evaluation of hydration and adjusted the dose of the diuretics accordingly. Following medical therapy, pulmonary edema regressed and renal function gradually recovered.

**Table 1.**

<table>
<thead>
<tr>
<th>Age/Gender</th>
<th>BH/BW</th>
<th>BP, PR</th>
<th>BT</th>
<th>Fluid amount/duration</th>
<th>Initial CVP</th>
<th>Echocardiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>22/Male</td>
<td>170/77</td>
<td>82/36, 124</td>
<td>40.6</td>
<td>2500 mL/6 h</td>
<td>20 mmHg</td>
</tr>
<tr>
<td>Case 2</td>
<td>20/Male</td>
<td>183/77</td>
<td>88/17, 98</td>
<td>41.3</td>
<td>5500 mL/1.5 h</td>
<td>15 mmHg</td>
</tr>
<tr>
<td>Case 3</td>
<td>24/Male</td>
<td>172/78.6</td>
<td>128/50, 142</td>
<td>40.7</td>
<td>2500 mL/2 h</td>
<td>5 mmHg</td>
</tr>
<tr>
<td>Case 4</td>
<td>21/Male</td>
<td>189/88.9</td>
<td>105/55, 135</td>
<td>41.0</td>
<td>9500 mL/5 h</td>
<td>None</td>
</tr>
<tr>
<td>Case 5</td>
<td>19/Male</td>
<td>163/66.9</td>
<td>81/48, 107</td>
<td>41.6</td>
<td>4000 mL/5 h</td>
<td>None</td>
</tr>
</tbody>
</table>

BH: body height, BW: body weight
Discussion

Most cases of exertional HS occur in outside environs, particularly during military training and exercise. When a patient with HS is admitted to the emergency department, dry skin turgor, high fever, and hypotension are almost always present. Massive hydration is frequently prescribed for correcting the unstable hemodynamic status. A chest radiograph often reveals pulmonary edema or pulmonary congestion if the HS is not treated appropriately. Therefore, we reviewed the HS cases admitted to our hospital from January 2006 to January 2013, and observed that 5 of the 20 cases (25%) were complicated by pulmonary edema. The reasons leading to pulmonary edema in patients of HS in this case series included fluid overload, endothelial injury with leakage, acute kidney injury, and transient cardiac dysfunction.

Effective thermolysis via the skin leads to active cutaneous vasodilataion. When a patient presents with hyperthermia, cooling techniques are aimed at lowering the body temperature to below 39.5°C, using ice packs, ice or cold water immersion, or cooling sprays using air conditioners and electric fans. However, if no prompt cooling is provided, such peripheral vasodilatation may lead to hypotension. Aggressive fluid challenge is often administered for ensuring optimal blood pressure support, which is beneficial for organ perfusion. However, such fluid challenge may be harmful in the presence of cardiac dysfunction and/or enhanced vascular permeability induced by hyperthermia. A previous study demonstrated normal or elevated CVP levels in 64.7% patients of HS on admission. In Saudi Arabia, where HS is fairly frequent, initial fluid resuscitation involves 3-4 L of saline administered over 1-2 h; here, a high frequency of pulmonary edema has been reported.

In HS patients, blood shifts from the mesenteric circulation to active muscles and skin, leading to ischemia of the visceral organs, which can subsequently result in intestinal hyperpermeability, altered intestinal immune and barrier functions, and endotoxin leakage. These alterations increase the production of inflammatory cytokines that then stimulate endothelial-cell activation and induce the release of endothelial vasoactive factors. HS patients with such endothelial injury have an increased risk of pulmonary edema and brain edema and require careful monitoring and calibrated fluid administration to prevent acute pulmonary edema.

Acute kidney injury is frequently detected in patients with HS due to volume depletion, poor organ perfusion, and rhabdomyolysis, which is commonly caused by tissue destruction believed to result from mechanical muscle fiber injuries. Myoglobinemia can possibly exacerbate renal hypoperfusion under a state of acute volume depletion. Therefore, early aggressive fluid hydration is indicated in the case of volume depletion and rhabdomyolysis, wherein 1-1.5 L/h of normal saline infusion is recommended. However, close monitoring of the urine output is essential, especially in patients with cardiac dysfunction, presenting unstable hemodynamic status.

Cardiac dysfunction, whether transient or persistent, is commonly observed in HS patients. The pathophysiology of cardiac dysfunction in HS is not entirely clear; however, it is considered to be related to heat-induced tissue injury, neurohormonal factors, and central nervous system reflexes. Pathological examination in such patients has revealed myocardial injury, including subendocardial hemorrhage, cardiac dilatation, and cardiac muscle degeneration.

Although fluid overloading may cause pulmonary edema in HS patients, dehydration is equally or more harmful. Inotropic agents are frequently used in HS patients for hemodynamic stability; however, these can potentially worsen the splanchnic circulation. In patients in whom high-dose inotropic agents are administered, dehydration would further decreased organ perfusion. In case 3 in the present series, the patient suffered colonic ischemia after intentional dehydration for treatment of pulmonary edema. Dehydration and subsequent circulatory collapse with splanchnic vasoconstriction may thus
induce colonic ischemia. Therefore, the aim of fluid supplementation in HS patients should be maintaining euvolemic status. In a patient with collapsed circulation, the aim is to achieve a blood pressure of 90/60 mmHg or MAP > 65 mmHg by rapid fluid challenge with 200 to 400 mL saline infusion. According to previous reports, a total of 1000-1200 mL of normal saline, on average, is necessary to reach an optimal state of hydration in early resuscitation phase. If despite the fluid challenge, MAP < 65 mmHg or persistent shock is observed, 100-250 mL/h fluid supplementation is recommended. In such situations, CVP is necessary as a guiding indicator for monitoring hydration.

In conclusion, exertional HS is an emergent clinical entity requiring first-line medical professional treatment. Rapid cooling is the mainstay of treatment; however, adequate hydration is crucial to resuscitation. However, as the present case series demonstrates, pulmonary edema occurs frequently in HS patients following fluid resuscitation. Fluid overload, endothelial injury with leakage, acute kidney injury, and transient cardiac dysfunction may induce pulmonary edema in HS patients. In the ED, administration of 1000-1200 mL saline may be adequate for early resuscitation; however, further fluid supplementation should be based on the patient’s blood pressure, fluid input, and urinary output. Inappropriate fluid supplementation may lead to pulmonary edema and respiratory impairment. In patients with persistent hypotension after fluid challenge, CVP is beneficial as a guiding indicator for fluid resuscitation.

Key messages
• Heat stroke (HS) is a life-threatening disease that is defined by a core temperature greater than 40.6°C (105.1°F) and accompanied by central nervous system (CNS) disturbances.
• The reasons leading to pulmonary edema in patients of HS in this case series included fluid overload, endothelial injury with leakage, acute kidney injury, and transient cardiac dysfunction.
• In a patient with collapsed circulation, the aim is to achieve a blood pressure of 90/60 mmHg or MAP > 65 mmHg by rapid fluid challenge with 200 to 400 mL saline infusion.
• According to previous reports, a total of 1000-1200 mL of normal saline, on average, is necessary to reach an optimal state of hydration in early resuscitation phase.
• If despite the fluid challenge, MAP < 65 mmHg or persistent shock is observed, fluid supplement guided by CVP monitoring is recommended.

List of abbreviations
HS, heat stroke; PE, pulmonary edema; CNS, central nerve system; ED, emergency department; ET, endotracheal; CPK, creatine phosphokinase; CVP, central venous pressure.

Competing interests
There are no competing interests.

Author Contribution
The work presented here was carried out in collaboration between all authors. All authors have contributed to, seen and approved the manuscript.

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None

References
運動型熱中暑併發肺水腫之案例討論

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摘要

引言：熱中暑為一個由高中心體溫及混亂意識狀態所表現出的急症，輸液給予合併迅速降溫是治療熱中暑的不二法門。然而，我們在治療此類病患時，肺水腫常可在熱中暑病人的臨床表現中發現。

病例呈現：我們回顧了自西元2006年一月至2013年一月住院的所有熱中暑案例中發現，總共20個熱中暑案例就有5個出現肺水腫情形，同時合併多器官功能不全。此篇文章中，我們摘要這5個案例並分析可能造成肺水腫的原因，包括輸液過多、血管內皮傷害併滲漏、急性腎損傷以及暫時性的心臟功能不全。

討論及結論：在急診，最初的治療，靜脈輸液量約1000-1200 mL生理食鹽水可能就已足夠，更多的輸液必須依病患的平均動脈壓和進出量來評估，若是不適當的輸液可能會造成肺水腫以及呼吸障礙。在經過輸液治療及降溫處理後仍為低血壓的病患，中心靜脈壓力可以做為進一步輸液治療的指引。然而，過多的輸液會造成不好的結果，過度的脫水對於熱中暑的病患也是有害的！因此對於熱中暑合併多器官功能不全的病人，沒有固定的治療步驟可以套用在這類病人上面。

輸液的給予對於治療熱中暑病人必須是謹慎小心的並且時常的調整，以確保病人體內的水分是處於適當的狀態。

關鍵詞：熱中暑，肺水腫，心臟功能不全，急性腎損傷