Six Cases of Sudden Cardiac Arrest in Alcoholic Ketoacidosis

Youichi Yanagawa, Toshihisa Sakamoto and Yoshiaki Okada

Abstract

We report herein 6 cases of sudden cardiac arrest in alcoholic ketoacidosis (AKA). All cases displayed evidence of prolonged excessive alcohol consumption and elevated β-hydroxybutyric acid levels and exhibited pulseless electrical activity (PEA) upon collapse. Severe metabolic acidosis was also seen in all cases. Some cases also displayed concomitant respiratory acidosis, hypothermia, hypoxia and/or hemorrhage. No evidence of myocardial infarction, tamponade or right heart strain, which would suggest pulmonary embolism, was found on cardiac ultrasonography. As PEA in AKA is induced by severe metabolic acidosis, aggressive correction of acidosis may represent a useful therapeutic strategy for such patients.

Key words: sudden cardiac arrest, alcoholic ketoacidosis, pulseless electrical activity

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Introduction

Alcoholic ketoacidosis (AKA) occurs following prolonged excessive alcohol consumption, and is caused by a relative depletion of insulin, mainly due to starvation and glycogen depletion, extracellular fluid volume depletion and an elevated NADH/NAD rate secondary to alcohol metabolism (1-3). The main symptoms of this condition are nausea, vomiting and/or abdominal pain (1). These symptoms are usually improved by the infusion of 5% dextrose and thiamine. AKA is occasionally associated with multiple complications and treatment in such cases requires a multidisciplinary approach (4). Medico-legal autopsies have revealed that AKA accounts for 7% of deaths due to chronic alcoholism (5). In such cases, forensic pathologists sometimes encounter unexpected deaths among alcoholics for which the anatomical causes are unclear. Pathological abnormalities in such cases are usually a fatty liver with or without fibrosis, elevated levels of β-hydroxybutyric acid and insignificant blood alcohol (2, 6). We have previously reported only 1 case that documented the progress of a patient with sudden cardiac arrest due to AKA (7). We therefore report herein the AKA cases encountered at our institute to elucidate the etiology of cardiac arrest due to AKA.

Case Report

AKA was considered present in a patient displaying evidence of prolonged excessive alcohol consumption and elevated β-hydroxybutyric acid levels as revealed by biochemical analyses upon arrival to the hospital. Six cases of AKA with cardiac arrest are briefly described below.

Case 1: A 51-year-old woman had been drinking alcohol throughout the day. An ambulance was called after she displayed disturbance of consciousness. When the emergency medical technicians (EMT) checked the patient, she was in a state of shock but could still speak. After vomiting, she suddenly collapsed. Electrocardiography (ECG) performed at the scene revealed pulseless electrical activity (PEA). Basic cardiac life support was initiated and the patient was transported to our department. Upon arrival, she had already regained spontaneous circulation. As arterial blood gases demonstrated severe combined acidosis, bicarbonate was infused. Complicated multiple organ failure developed, therefore a multidisciplinary approach to treatment was implemented, including artificial ventilation. The patient was finally discharged on foot on hospital day 31.

Case 2: A 56-year-old man had been drinking alcohol all day. As he experienced abdominal pain and several bouts of vomiting, an ambulance was called. By the time EMT
Table 1. Background, Chief Complaint and Vital Signs of Subjects Upon Arrival

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Complaint</th>
<th>CPA</th>
<th>GCS</th>
<th>Temp.</th>
<th>MAP</th>
<th>HR</th>
<th>RR</th>
<th>APACHEII</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51</td>
<td>F</td>
<td>Vomiting, unconsciousness</td>
<td>OH-ROSC (PEA)</td>
<td>13*</td>
<td>35.1*</td>
<td>50*</td>
<td>104*</td>
<td>30*</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>56</td>
<td>M</td>
<td>Abdominal pain, vomiting</td>
<td>CPA-GA (PEA)</td>
<td>7*</td>
<td>27.2*</td>
<td>40*</td>
<td>100*</td>
<td>30*</td>
<td>47</td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>M</td>
<td>Epigastalgia, visual loss</td>
<td>CPA-OW (PEA)</td>
<td>9*</td>
<td>33.3*</td>
<td>70*</td>
<td>40*</td>
<td>12*</td>
<td>44</td>
</tr>
<tr>
<td>4</td>
<td>63</td>
<td>M</td>
<td>Hematemesis, melena</td>
<td>CPA-AA (PEA)</td>
<td>14</td>
<td>35.0</td>
<td>40</td>
<td>106</td>
<td>30</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>44</td>
<td>M</td>
<td>Backache, headache, visual loss</td>
<td>CPA-AA (PEA)</td>
<td>14</td>
<td>31.9</td>
<td>70</td>
<td>112</td>
<td>28</td>
<td>19</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>M</td>
<td>Unconsciousness</td>
<td>CPA-AA (PEA)</td>
<td>6</td>
<td>33.3</td>
<td>50</td>
<td>95</td>
<td>34</td>
<td>29</td>
</tr>
</tbody>
</table>


GCS: Glasgow Coma Scale, Temp: temperature, MAP: mean arterial pressure, HR: heart rate, RR: respiratory rate

*: prehospital data

checked the patient, he had already entered a state of both shock and semicoma. During transportation to our department, he collapsed and was administered basic cardiac life support. ECG showed PEA. On arrival, the patient remained in cardiac arrest. After infusion of epinephrine, he regained spontaneous circulation. However, he suffered complicated multiple organ failure and died the following day.

Case 3: A 53-year-old man had been drinking alcohol all day. After complaining of abdominal pain and visual disturbance following disturbance of consciousness, an ambulance was called. When the EMT checked the patient, he was in a state of shock but could speak. During transportation to our department, he collapsed and was given basic cardiac life support. ECG showed PEA. On arrival, he remained in cardiac arrest and displayed dilated non-reactive pupils, but regained spontaneous circulation after infusion of epinephrine. After correcting severe acidosis with an infusion of bicarbonate, the pupils became reactive to light. Due to complicated multiple organ failure, a multidisciplinary approach to treatment was applied, including artificial ventilation and continuous hemofiltration. Finally, the patient was discharged on foot on hospital day 80.

Case 4: A 63-year-old man had been drinking alcohol all day. He developed hematemesis and an ambulance was called. When EMT checked the patient, he was alert but in a state of shock, and he remained in a state of shock on arrival at our department. After infusion of 1 L lactated Ringer solution, his blood pressure increased to 120/60 mmHg and the hemoglobin level was 7.8 g/dl. Before commencement of emergency gastroenteroscopy, he received 5 mg of diazepam due to restlessness and a systolic blood pressure of 160 mmHg. After diazepam infusion, the patient suddenly collapsed. ECG showed PEA. Immediate advanced cardiac life support failed to restore spontaneous circulation.

Case 5: A 44-year-old man who had been drinking alcohol all day presented with blindness and collapsed after admission. ECG showed PEA. After infusion of epinephrine and bicarbonate, he regained spontaneous circulation and rapid resolution of blindness. He suffered complicated multiple organ failure (for a more detailed description, see reference 7). Finally, the patient was discharged on foot on hospital day 59.

Case 6: A 46-year-old man had been drinking alcohol all day. An ambulance was called after he exhibited disturbance of consciousness. When the EMT checked the patient, he was in a state of shock, and he remained in this state on arrival. However, he was resuscitated with infusion of 2 L lactated Ringer solution, 250 ml of bicarbonate, dopamine and mechanical ventilation, he collapsed. ECG showed PEA. Repeated infusion of epinephrine and cardiac massage failed to restore spontaneous circulation. Although an autopsy revealed fatty liver, fatty kidney, atrophic pancreas and erosive esophagitis, the heart demonstrated no abnormalities and the anatomical cause of death was unclear.

Summary of the 6 cases

Table 1 shows the age, sex, vital signs and APACHE II and SOFA scores for the 6 cases (8, 9). Table 2 shows the results of biochemical analyses and Table 3 shows the use of bicarbonate, complications and outcomes. All cases exhibited PEA upon collapse, and all patients underwent cardiac ultrasonography. However, no evidence of myocardial infarction, tamponade or right heart strain, which would suggest pulmonary embolism, was found. Regarding ECG monitoring during prehospital care by the EMT and then while receiving treatment during hospitalization, no life-threatening arrhythmia was observed.

Discussion

In this case study, all of the cases exhibited PEA upon sudden cardiac arrest. The main diseases that may result in PEA are coronary thrombosis, pulmonary thrombosis, tension pneumothorax, cardiac tamponade, drug intoxication, massive hemorrhage, hypothermia, abnormality of serum potassium, hypoxia and acidosis (10). Among these diseases,
Table 2. Results of Biochemistry Upon Arrival

<table>
<thead>
<tr>
<th>Case</th>
<th>β-HBA</th>
<th>AAA</th>
<th>pH</th>
<th>PaCO₂</th>
<th>HCO₃⁻</th>
<th>PaO₂/ FiO₂</th>
<th>Na</th>
<th>K</th>
<th>Cl</th>
<th>Glucose Alcohol</th>
<th>Anion gap</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4320</td>
<td>2290</td>
<td>6.746</td>
<td>89</td>
<td>11</td>
<td>72</td>
<td>131</td>
<td>5.3</td>
<td>87</td>
<td>132</td>
<td>0.8</td>
</tr>
<tr>
<td>2</td>
<td>1510</td>
<td>468</td>
<td>6.684</td>
<td>103</td>
<td>5</td>
<td>154</td>
<td>142</td>
<td>5</td>
<td>94</td>
<td>10</td>
<td>n.e.</td>
</tr>
<tr>
<td>3</td>
<td>1190</td>
<td>332</td>
<td>6.497</td>
<td>51</td>
<td>3.8</td>
<td>427</td>
<td>129</td>
<td>3.7</td>
<td>74</td>
<td>241</td>
<td>n.e.</td>
</tr>
<tr>
<td>4</td>
<td>729</td>
<td>80</td>
<td>7.352</td>
<td>21</td>
<td>11.5</td>
<td>625</td>
<td>139</td>
<td>5.4</td>
<td>98</td>
<td>546</td>
<td>8.3</td>
</tr>
<tr>
<td>5</td>
<td>245</td>
<td>11</td>
<td>6.707</td>
<td>13</td>
<td>1.6</td>
<td>660</td>
<td>132</td>
<td>5.2</td>
<td>81</td>
<td>117</td>
<td>74</td>
</tr>
<tr>
<td>6</td>
<td>1710</td>
<td>80</td>
<td>7.231</td>
<td>22</td>
<td>9.4</td>
<td>414</td>
<td>125</td>
<td>5.0</td>
<td>45</td>
<td>357</td>
<td>5.1</td>
</tr>
</tbody>
</table>

Table 3. Bicarbonate Use, Complications, SOFA Score and Outcomes

<table>
<thead>
<tr>
<th>Case</th>
<th>Bicarbonate</th>
<th>Complication</th>
<th>SOFA</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>Shock, ARDS, Liver dysfunction, Renal failure, Thrombocytopenia, Rhabdomyolysis</td>
<td>19</td>
<td>Survival</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>Shock, ARDS, Liver dysfunction, Renal failure, Thrombocytopenia, Rhabdomyolysis</td>
<td>15</td>
<td>Death (MOF)</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>Shock, Liver dysfunction, Renal failure, Thrombocytopenia, Rhabdomyolysis</td>
<td>15</td>
<td>Survival</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>Shock</td>
<td>2</td>
<td>Death (GI Bleeding)</td>
</tr>
<tr>
<td>5</td>
<td>No</td>
<td>Shock, ARDS, Liver dysfunction, Thrombocytopenia, Rhabdomyolysis</td>
<td>15</td>
<td>Survival</td>
</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>Shock, ARDS, Liver failure, Renal failure, Thrombocytopenia, Rhabdomyolysis</td>
<td>14</td>
<td>Death (MOF)</td>
</tr>
</tbody>
</table>

ARDS: Acute respiratory distress syndrome

coronary thrombosis, pulmonary thrombosis, tension pneumothorax and cardiac tamponade were excluded based on the results of radiological, biochemical and sonographic tests in this study. In cases where alcohol levels were measured, the levels were too low to result in PEA (0.8-74 mg/dl). In general, the alcohol level is low if the level of β-hydroxybutyric acid is high. The possibility of alcohol representing the main cause of PEA in this study was thus minimal (1, 6). The main cause of PEA in Case 4 might have been massive gastrointestinal hemorrhage, but the remaining cases did not exhibit melena on arrival or any evidence of massive hemorrhage as based on blood cell counts.

The serum sodium levels in Cases 3, 5 and 6 were low. Hyponatremia is commonly reported among patients with chronic alcoholism. Liamis et al (11) reported hyponatremia (serum sodium <134 mmol/l) in 22 of 127 patients (17.3%). The most common cause of hyponatremia in that cohort was hypovolemia due to vomiting or diarrhea in chronic alcoholic patients. Severe hypovolemia also has the potential to lead to PEA (12), and cases of sudden cardiac arrest may also be attributed to this mechanism. In Cases 1 and 2, hypoxia was recognized after vomiting, which may have induced aspiration and cardiac arrest, thus causing PEA. Body temperature in all cases was low. In fact, hypothermia may have been one of the causes of PEA in this report. However, as the minimum temperature among the 6 cases was 27°C, temperature was not considered the sole factor inducing PEA.

A remaining possible cause of PEA is acidosis. In this case study, all cases demonstrated metabolic acidosis. In AKA patients, elevated NADH/NAD rates lead to decreased fatty acid oxidation, blockade of glucogenesis and suppression of the citric acid cycle. As a result, an energy crisis may occur and AKA patients thereafter tend to show dramatic increases in β-hydroxybutyric acid levels, leading to severe metabolic acidosis with a high anion gap. In addition, PCO₂ levels in Cases 1-3 were high. Respiratory acidosis may be induced by aspiration of vomitus, fatigue of the respiratory muscles or obstruction of the airways due to disturbance of consciousness or sedative drugs. In addition, a canine study has proven that diaphragmatic pressure is reduced under conditions of metabolic acidosis, which may also subsequently lead to respiratory acidosis (13). PEA during AKA in these cases may have been induced by severe metabolic acidosis with additional respiratory acidosis. Another animal study demonstrated that severe acidosis causes a decrease in ventricular performance by a direct depressant effect on the myocardium, impaired myocardial response to catecholamines, decreased cardiac muscle contractility and endocardial damage (14-17). Accordingly, extremely severe acidosis could lead to PEA as a result of extremely low cardiac output. An energy crisis induced by impairment of fat and glucose metabolism or direct injury to the mitochondria (18), due to excessive ethanol intake might directly suppress
cardiac output, but no studies have yet proven this hypothesis. The low cardiac output induced by severe acidosis is also exacerbated by hypovolemia, hypoxia and/or hypothermia, with each different factor also leading to low cardiac output. Accordingly, clinical findings such as blood pressure, temperature or factors causing respiratory failure are thought to represent important signs of cardiac arrest in AKA. To prevent the occurrence of sudden cardiac arrest in critical AKA conditions, aggressive correction of acidosis and energy crisis may prove useful.

Chronic alcoholism is often combined with vitamin B deficiency, as such patients tend to have a poor diet and alcohol affects thiamine uptake and other aspects of thiamine utilization (19, 20). However, vitamin B levels in the present Cases 2, 5 and 6 were 7.172 [MS1] and 3.2 μg/dl, respectively (normal, 2.0-7.2 μg/dl). All cases underwent an infusion of vitamin B on arrival. The cardiovascular complications induced by vitamin B deficiency are thought to improve quickly after infusion of vitamin B (21). However, none of our cases demonstrated immediate recovery from unstable circulation. The contribution of vitamin B deficiency to the occurrence of PEA was thus minimal, at least after admission.

In these 6 cases, elevations in β-hydroxybutyric acid and acetocetatic acid varied greatly. Kanetake et al reported that if β-hydroxybutyric acid levels exceed 1,000 μmol/L, a diagnosis of death caused by ketoacidosis would be reasonable if autopsy failed to explain the cause of death (22). However, they also reported that cardiac arrest occurred among AKA patients even with low levels of β-hydroxybutyric acid (22). In addition, production of ketone bodies is accelerated by multiple pathophysiological states such as excessive alcohol intake, diabetes, poorly nourished state, infection and/or hypothermia, similar to our findings (22).

Most patients in this study displayed complications of rhabdomyolysis and renal failure. An association between alcohol use and episodes of rhabdomyolysis has long been recognized, but the mechanism underlying this phenomenon remains poorly understood. Riggs hypothesized that some alcohol-associated myotoxicity could be related to induction of skeletal muscle cytochrome P450 by ethanol, leading to the production of toxic metabolites of other compounds that then injure the muscle (23). Trounce et al verified that a combination of prolonged alcohol intake and a short fast could induce alcoholic myopathy experimentally (24). They hypothesized that acute rhabdomyolysis may arise from superimposed mitochondrial failure, resulting in a severe energy crisis in muscle. Conversely, acute renal failure due to rhabdomyolysis has been widely described and the main pathophysiological mechanisms have been reported as renal vasoconstriction, intraluminal cast formation and direct myoglobin toxicity (25). Accordingly, severe chronic alcoholism has often been reported to be associated with rhabdomyolysis and renal failure (4).

Conclusion

This case series suggests that when AKA patients experience sudden cardiac arrest, the ECG shows PEA. As PEA in AKA appears to be induced by multiple pathophysiological disorders such as severe metabolic acidosis plus additional respiratory acidosis, hypothermia, hypoxia and/or hemorrhage, aggressive correction of acidosis may offer a useful treatment strategy for such patients.

References


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