Abstract

We report 3 patients with alcoholic ketoacidosis (AKA). All had a history of excessive intake and abrupt termination of alcohol. They showed tachypnea, tachycardia, abdominal tenderness, and epigastralgia. Metabolic acidosis with an increased anion gap, decreased PaCO₂ and ketonemia were present. One patient whose ratio of 3-hydroxybutyric acid to acetoacetic acid was 4.0 was associated with diabetic ketoacidosis. All patients were successfully hydrated with electrolyte, glucose and thiamine. Complications such as liver dysfunction, lactic acidosis, acute pancreatitis, Wernicke’s encephalopathy, rhabdomyolysis and heart failure were present. Attention should be paid to multiple complications in the treatment of AKA.

Case Report

Case 1

The patient was a 50-year old woman. She had been a severe alcoholic for the previous 10 years. She had been diagnosed with chronic alcoholic hepatitis. Nausea and vomiting occurred on July 3, 2002. She kept vomiting overnight. The following morning, she was admitted to Misato Kenwa Hospital. She was 151 cm tall and weighed 41 kg. Vital signs were body temperature of 37.3°C, blood pressure of 104/70 mmHg, respiratory rate of 24/min, and regular pulse of 130/min with clear consciousness. Her palms were erythematous, and she had vascular spider. She complained of epigastralgia. Laboratory data on admission are summarized in Table 1. Urinalysis showed proteinuria (+), hematuria (+) and ketonuria (3+) without glycosuria. The white blood cell count (WBC) was 11,000/μl, hemoglobin; 9.74 g/dl. Total bilirubin was 1.41 mg/dl, aspartate aminotransferase (AST); 319 IU/l, alanine aminotransferase (ALT); 109 IU/l, γ-glutamyltransferase (γ-GTP); 911 IU/l, and plasma glucose; 73 mg/dl. The serum concentration of acetoacetic acid (AcAc) and 3-hydroxybutyric acid (3-OHB) were 1,400 μmol/l (normal range [NR]: <70) and 10,900 μmol/l (NR: <70), respectively. The serum concentration of lactic acid and pyruvic acid were 98.6 mg/dl (NR: 3.3–15.6) and 1.5 mg/dl (NR: 0.4–1.2), respectively. Arterial blood gas analysis in room air showed pH 7.140, PaCO₂ 25.6 mmHg, PaO₂ 117.7 mmHg, HCO₃⁻ 8.5 mmol/l. She was diagnosed with AKA and lactic acidosis. Endoscopic examination of the upper digestive tract revealed esophagitis, erosive gastritis and duodenitis. After hydration with 5% glucose solution...
containing electrolyte and thiamine (Table 2), her metabolic acidosis was improved quickly. Subsequently, she had 2 recurrent episodes of AKA.

**Case 2**

The patient was a 62-year-old man. He had been diagnosed with type 2 DM when he was 48 years old. Insulin therapy had been introduced using biphasic isophane insulin (10 units in the morning and 6 units in the evening). Diabetic retinopathy was absent, but intermittent proteinuria and diabetic neuropathic pain in his legs were present. He had been consuming excessive alcohol for years. Gastric pain occurred and worsened after binge drinking. He could not drink alcohol because of severe epigastralgia for 3 days and was admitted to our hospital on July 3, 2002. He was 165 cm tall and weighed 40 kg. Vital signs were body temperature of 35.3°C, blood pressure of 166/90 mmHg, respiratory rate of 28/min, and regular pulse of 105/min. His consciousness was drowsy and palms were erythematous. Abdominal examinations revealed tenderness in the epigastrium. Laboratory data on admission are summarized in Table 3. Urinalysis showed glycosuria (4+), proteinuria (2+), hematuria (2+) and ketonuria (2+). The platelet count was 3.9x10^4/μl. Total bilirubin was 2.09 mg/dl, AST; 244 IU/l, ALT; 134 IU/l, lactate dehydrogenase (LDH); 497 IU/l, γ-GTP; 3,246 IU/l, amylase; 1,308 IU/l and plasma glucose; 428 mg/dl. His hemoglobin A1c was 7.3%. The serum concentration of AcAc and 3-OHB were 3,100 μmol/l and 10,900 μmol/l, respectively. Serum concentration of lactic acid and pyruvic acid were 29.1 mg/dl and 1.6 mg/dl, respectively. Arterial blood gas analysis in room air showed pH 7.179, PaCO₂ 12.2 mmHg, PaO₂ 117.7 mmHg, HCO₃⁻ 8.5 mmol/l. The anion gap (Na-[Cl+HCO₃⁻]) was 35.2 mEq/l. Abdominal CT revealed swelling of the pancreas. He was diagnosed with DKA because of hyperglycemia, acidemia, decreased bicarbonate, positive urinary ketones, increased serum ketones and increased anion gap. In addition, acute pancreatitis was present. Initial treatment consisted of intravenous infusion of regular insulin (8 units injection followed by 8 units/hour) and a large volume of saline (mainly 0.9% NaCl 1 l/first 2 hours) containing thiamine (Table 2). Two hours later, his plasma glucose became as low as 91 mg/dl. Therefore, insulin infusion was reduced and 0.9% NaCl was replaced by 5% glucose solution. At that time, we diagnosed him as having AKA concomitantly. Acute pancreatitis was treated simultaneously with gabexate mesilate and antibiotics (cefmetazole sodium). His metabolic acidosis and pancreatitis were cured. However, his drowsiness persisted. Brain computed tomography revealed slight brain atrophy. Although vitamin B1 was not measured, the cause of his consciousness disturbance might be Wernicke’s encephalopathy considering the clinical course.

**Case 3**

The patient was a 53-year-old man. He was admitted to a hospital due to alcoholic hepatitis and had never been diagnosed with DM. He had been consuming excessive alcohol. Vomiting because of gastric irritation occurred and worsened on November 18, 2001. He kept vomiting frequently for 2 days, and then, was transferred to our hospital on November...
metabolic ketoacidosis was improved quickly. Nevertheless, the patient received gabexate mesilate and antibiotics (cefmetazole sodium). His albumin was reported to be common (8, 16).

In Case 1, her casual blood glucose was 163 cm tall and weighed 49 kg. Vital signs were body temperature of 33.8°C, blood pressure of 110/72 mmHg, respiratory rate of 36/min, and regular pulse of 108/min. His consciousness was drowsy and palms were erythematous. The bulbar conjunctiva showed icterus. Abdominal examinations revealed tenderness and slight defense in the right hypochondriac region. Laboratory data on admission were summarized in Table 4. Urinalysis showed glycosuria (3+), proteinuria (2+) and hematuria (3+). The WBC and platelet count were 20,400/μl and 9.8×10⁴/μl, respectively.

All 3 patients presented in this paper shared a common clinical picture of massive alcoholic intake, which had been terminated a few days before admission by repeated vomiting or abdominal pain, resulting in acute starvation and severe dehydration. For these patients, alcohol is almost the only source of calorie intake, so the cessation of alcohol caused starvation. Pathophysiologically, acute starvation, ethanol abuse and dehydration were direct causes of AKA, leading to the accumulation of ketone bodies (8, 14, 15). Taking the history of not only excessive intake but also abrupt cessation of alcohol is very important for the correct diagnosis of AKA. Recurrence of AKA as in Case 1 is reported to be common (8, 16).

The precise pathogenesis of AKA is not clear. In Cases 2 and 3, DM was diagnosed. In Case 1, her casual blood

### Table 3. Laboratory Data (Case 2, July 2002)

<table>
<thead>
<tr>
<th>Urinalysis</th>
<th>Blood chemistry</th>
<th>Arterial blood gas analysis (room air/rest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (3+)</td>
<td>Total bilirubin 2.09 mg/dl</td>
<td>pH 7.179</td>
</tr>
<tr>
<td>Protein (2+)</td>
<td>AST 244 IU/μl</td>
<td>PaCO₂ 12.2 mmol/l</td>
</tr>
<tr>
<td>Occult blood (2+)</td>
<td>ALT 134 IU/μl</td>
<td>PaO₂ 119.4 mmol/l</td>
</tr>
<tr>
<td>Ketone (2+)</td>
<td>LDH 497 IU/μl</td>
<td>HCO₃ 5.8 mmol/l</td>
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</tbody>
</table>

### Table 4. Laboratory Data (Case 3, November 2001)

<table>
<thead>
<tr>
<th>Urinalysis</th>
<th>Blood chemistry</th>
<th>Arterial blood gas analysis (room air/rest)</th>
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<tbody>
<tr>
<td>Glucose (3+)</td>
<td>Total bilirubin 2.74 mg/dl</td>
<td>pH 6.934</td>
</tr>
<tr>
<td>Protein (2+)</td>
<td>AST 98 IU/μl</td>
<td>PaCO₂ 12.6 mmol/l</td>
</tr>
<tr>
<td>Occult blood (3+)</td>
<td>ALT 29 IU/μl</td>
<td>PaO₂ 157.6 mmol/l</td>
</tr>
<tr>
<td>Ketone (3+)</td>
<td>LDH 785 IU/μl</td>
<td>HCO₃ 2.6 mmol/l</td>
</tr>
</tbody>
</table>

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20. The color of urine changed into dark brown, oliguria developed and his potassium rose to 5.8 mEq/l. Acute renal failure due to rhabdomyolysis was strongly suspected, because CPK on admission was very high. Subsequently, hypoxia and acute heart failure developed, then mechanical ventilation and hemodialysis were introduced. Subsequently, his general condition was improved, but his drowsiness, probably due to Wernicke’s encephalopathy, persisted.

### Discussion

All 3 patients presented in this paper shared a common clinical picture of massive alcoholic intake, which had been terminated a few days before admission by repeated vomiting or abdominal pain, resulting in acute starvation and severe dehydration. For these patients, alcohol is almost the only source of calorie intake, so the cessation of alcohol caused starvation. Pathophysiologically, acute starvation, ethanol abuse and dehydration were direct causes of AKA, leading to the accumulation of ketone bodies (8, 14, 15). Taking the history of not only excessive intake but also abrupt cessation of alcohol is very important for the correct diagnosis of AKA. Recurrence of AKA as in Case 1 is reported to be common (8, 16).

The precise pathogenesis of AKA is not clear. In Cases 2 and 3, DM was diagnosed. In Case 1, her casual blood
glucose became 163 mg/dl when AKA was cured, indicating that she had glucose intolerance. Considering that all of the present 3 cases possessed glucose intolerance, it might be an important factor for the onset of AKA. It was reported that insulin secretion is delayed and decreased in untreated AKA and that insulin secretion is normalized when AKA was treated (11). This suggests the possibility that hormonal imbalance (relative deficiency in insulin, relative surplus in counter-regulatory stress hormones including glucagon) might be an important mechanism underlying this disorder. Plasma insulin concentration should have been measured in these 3 cases to better understand the pathophysiology of AKA.

Physical examinations revealed that all 3 patients showed tachypnea, tachycardia and erythematous palm. Tachypnea often in the form of Kussmaul respiration, is commonly present in AKA (8, 9), compensating for metabolic acidosis. Tachycardia reflects intravenous dehydration. Erythematous palm is a typical characteristic of an alcohol abuser. In Cases 2 and 3, tense, tender abdomen and epigastralgia were present. Diffuse or localized abdominal tenderness and epigastralgia, caused by acute pancreatitis as in Cases 2 and 3, or acute gastritis as in Case 1, are usually found (2, 7, 8, 14). Hypothermia as in Cases 2 and 3 could occur (2, 17).

Metabolic acidosis with an increased anion gap (Case 1; 33.5, Case 2; 35.2, Case 3; 48.4, respectively), decreased PCO2, and increased level of serum ketone bodies were present in these 3 cases. The ratio of 3-OHB to AcAc of Case 2 was lower than that of Cases 1 and 3 (Case 1; 7.8, Case 2; 4.0, Case 3; 12, respectively). Considering that Case 2 was associated with DKA, this has clinically important significance.

It has been reported that the ratio of 3-OHB to AcAc is higher in patients with AKA than in those with DKA. In AKA patients, this ratio averages 7.2 (3) or 5.2 (4), compared with an average of 3 (16) or 2.85 (18) among the DKA patients. If a patient with AKA is presenting with hyperglycemia and whose 3-OHB/ AcAc ratio is less than 5, the coexistence of DKA must be considered.

Treatment within 24 hours after arrival at our hospital for these 3 cases is shown in Table 2. As mentioned above, alcohol abuse, starvation and dehydration play a crucial role in the pathogenesis of AKA. Consequently, hydration with electrolytes and administration of glucose and thiamine are the fundamental treatments of AKA. Glucose is essential to stop ketogenesis and to replete glycogen stores in the liver (2, 7). Thiamine is necessary because some patients have thiamine deficiency, which could be the cause of lactic acidosis and Wernicke’s encephalopathy (4, 7–9).

Theoretically, AKA patients without DM do not require insulin. Furthermore, there are opinions that insulin should be contraindicated because of the risk of hypoglycemia (8, 14, 19, 20). It has been reported that most patients with AKA do not have concomitant DM (6, 9) and it has been considered that the co-existence of AKA and DKA is exceptional (14). As in Case 2, however, the co-existence of both conditions could happen. Therefore, it is prudent to treat hyperglycemic AKA patients with insulin under careful monitoring of plasma glucose, because DKA could be fatal.

During the treatment of Case 2, 24 units of insulin lowered his plasma glucose from 428 mg/dl to 91 mg/dl in only 2 hours. The reason for this phenomenon is not clear. Malnutrition, glycogen depletion in the liver and decrease in gluconeogenesis might be involved. Ohshiro et al reported an AKA case whose plasma glucose was very changeable (11). In their report, only 6.7 grams of glucose raised the patient’s plasma glucose from 30 mg/dl to 280 mg/dl in 40 minutes. Considering the above, blood glucose might be changeable and should be monitored carefully during the treatment of AKA.

In uncomplicated AKA, the prognosis is reported to be very good (2, 7–9). But multiple complications as in our cases could be present. All 3 cases in this paper showed liver dysfunction. Lactic acidosis was found in Case 1. Acute pancreatitis and suspected Wernicke’s encephalopathy were present in Cases 2 and 3. Rhabdomyolysis and heart failure probably due to beriberi heart were present in Case 3. AKA is far from a simple disease. We should pay attention to possible multiple organ failure in the treatment of AKA.

In conclusion, awareness of this syndrome and taking a typical history of drinking are essential for the correct diagnosis of AKA. AKA is an important differential diagnosis among heavy drinkers with metabolic acidosis. Attention should be paid to complications involving multiple organs. DKA is not only an important differential diagnosis but also a possible complication of AKA.

References

12) Kreisberg RA. Diabetic ketoacidosis: New concepts and trends in
3 Cases of Alcoholic Ketoacidosis