CASE REPORT

High Anion Gap Metabolic Acidosis after a Suicide Attempt with Cyanide: The Rebirth of Cyanide Poisoning

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Abstract

A 33-year-old woman was admitted to our emergency department in a state of unconsciousness after attempting suicide with unknown substances. Severe metabolic acidosis (pH: 6.81), with a high anion gap (36.2) and high lactate level (20.2 mmol/L), was observed. After four hours of intensive medical treatment, the patient regained consciousness, with a return of the arterial pH to 7.42. Finally, cyanide intoxication was diagnosed based on the detection of a serum cyanide level of 3.5 mg/L. The presence of a high anion gap associated with severe lactic acidosis is a clue for making a rapid differential diagnosis of acute cyanide intoxication. Providing intensive and immediate supportive management is also crucial, even in cases without obtainable specific antidotes.

Key words: cyanide poisoning, metabolic acidosis, anion gap, lactic acidosis

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Introduction

Cyanide poisoning may result in severe medical complications and a high mortality rate, whether caused by ingestion or inhalation (1-4). The definitive diagnosis of cyanide poisoning is made by measuring the serum cyanide level. Nevertheless, as cyanide poisoning is relatively uncommon, few laboratories offer real-time serum cyanide assays (4-6), and it is not easy for the general population to obtain sodium or potassium cyanide. Consequently, acute cyanide poisoning is difficult to identify in the emergency department (ED). The detection of metabolic acidosis, especially that induced by drug intoxication, often leads to an accurate and rapid differential diagnosis (7, 8). In addition to an obvious history of contact and typical signs and symptoms, such as unexplained acute confusion, respiratory failure, seizures and even coma, the only clue available in most emergency settings is the presence of high anion gap metabolic acidosis combined with a high lactate level. The lethal oral dose of cyanide salts is 200±300 mg, and a whole serum cyanide level in excess of 3.0 mg/L is associated with coma and may be potentially lethal (1-4). We herein present the rare case of a patient who survived without antidotal therapy following severe potassium cyanide intoxication.

Case Report

A 33-year-old woman was brought to our ED soon after attempting suicide by ingesting unknown substances. She was in a semi-comatose state upon presentation, with a Glasgow coma scale (GCS) score of E1M1V2. She was afebrile, with a blood pressure of 78/40 mmHg, pulse rate of 44 beats per minute and respiratory rate of 23 breaths per minute. Pulse oximetry showed 97% oxygenation while breathing ambient air. A detailed neurological examination revealed no pathological reflexes, while the pupils were dilated to 6 mm bilaterally and light reflexes were sluggish. A 12-lead electrocardiogram revealed first-degree atrioventricular block with a heart rate of 40 beats per minute, whereas the serum liver enzyme, creatine kinase and troponin I levels were all within the normal ranges. The relevant laboratory

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continued to recover and was extubated on the second hospital
neously increased toward the normal range (Table). She con-
arterial pH was detected, and the bicarbonate level simulta-
consciousness, with a GCS score of E4M6Vt. A normal serum
ment with intravenous sodium bicarbonate, adequate hydra-
TC-
conduction velocity assessments of the peripheral nerves or
detected on magnetic resonance imaging of the brain, nerve
she was found to be well. No neurological sequelae were
seven days later. When last seen six months after discharge,
finally told the physician that she had taken a small amount
nide concentration in the ED was 3.5 mg/L, as measured at
results are shown in Table.
Thirty minutes after admission, generalized tonic-clonic
seizures were observed. Endotracheal tube intubation was
performed, and no focal lesions were detected on unen-
hanced cranial computed tomography. An arterial blood gas
(ABG) analysis was repeated on a ventilator with 100%

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ED</th>
<th>4 hours after ED</th>
<th>Normal value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/dL)</td>
<td>13.3</td>
<td>12.6</td>
<td>12–16</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>6</td>
<td>7</td>
<td>6–20</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.9</td>
<td>1.0</td>
<td>0.5–0.9</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>146</td>
<td>148</td>
<td>136–145</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>4.6</td>
<td>4.2</td>
<td>3.5–5.1</td>
</tr>
<tr>
<td>Chloride (mmol/L)</td>
<td>106</td>
<td>109</td>
<td>98–107</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>367</td>
<td>NA</td>
<td>74–109</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>20.2</td>
<td>1.0</td>
<td>0.5–2.2</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>6.81</td>
<td>7.42</td>
<td>7.35–7.45</td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>24.7</td>
<td>26.7</td>
<td>35–45</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>3.8</td>
<td>17.1</td>
<td>24±2</td>
</tr>
<tr>
<td>Osmolality (mOsm/kg)</td>
<td>308</td>
<td>NA</td>
<td>275–295</td>
</tr>
<tr>
<td>Anion gap (AG)</td>
<td>36.2</td>
<td>21.9</td>
<td>12±2</td>
</tr>
<tr>
<td>Ketone bodies (mmol/L)</td>
<td>1.1</td>
<td>NA</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>Prothrombin time (second)</td>
<td>11.0</td>
<td>NA</td>
<td>8–12</td>
</tr>
<tr>
<td>International normalised ratio (INR)</td>
<td>1.1</td>
<td>NA</td>
<td>-</td>
</tr>
</tbody>
</table>

Anion Gap = Na⁺ – Cl⁻ – HCO₃⁻
BUN: Blood urea nitrogen
NA: Not available

Discussion

It is difficult to diagnose acute cyanide intoxication
swiftly and accurately if the emergency staff lacks informa-
tion regarding the patient’s contact history. Measuring the
serum anion gap can be of use, as it identifies abnormal
electrolyte concentrations and acid-base disorders and can be
used to rapidly evaluate patients with suspected intoxication
with unknown drugs (7, 8).

Acute cyanide poisoning generally has a high mortality
rate, especially in cases involving the intentional ingestion
of cyanide compound, although cyanide exposure also fre-
quently occurs in patients with smoke inhalation from resi-
dential or industrial fires (1–4). A common source of acute
cyanide intoxication is smoke inhalation during the burning
of rubber, plastic, silk and other substances. Occupational
risks are common in people working in industries such as
chemical research, gold and silver industries, synthetic plas-
tic and/or metal processing, electroplating and jewelry pol-
ishing. Bitter almonds smell like cyanide, as they contain
some of this compound, and severe cyanide poisoning has
been reported following the ingestion of lethal amounts of
bitter almonds (9, 10). Cyanide is a rapidly acting poison,
particularly when inhaled. The mechanism of toxicity in-
volves the binding of cyanide to cellular cytochrome oxidase
and resultant interference with aerobic oxygen utiliza-
tion (1–4). Cyanide may cause cellular hypoxia, with a large
increase in lactic acid production, consequently resulting in
metabolic acidosis associated with an elevated anion gap.
Tissues most dependent on oxidative phosphorylation, in-
cluding the heart and brain, are the most severely and
quickly affected. Therefore, the initial symptoms may in-
clude the manifestation of functional deficits of the central
nervous system. Inhibition of the respiratory center leads to
transitory hyperventilation, followed by respiratory depres-
sion, respiratory failure, coma and death. Myocardial depres-
sion induces further hypoxia, a decreased cardiac output and
shock. A blood cyanide level of >0.5 mg/L is considered to
indicate toxicity, and a level of >3.0 mg/L is regarded as le-
thal. The relationship between the blood cyanide level and
ultimate outcome is of obvious importance (1–4). In the ED,
clinicians can be alert to cyanide poisoning early based on
the detection of symptoms such as the rapid onset (within
minutes to hours) of coma, seizures, fixed dilated pupils
and cardiopulmonary dysfunction in the presence of severe lactic
acidosis or elevated mixed venous oxygen saturation
(10–12).

The onset time is a clue to the differential diagnosis of
other common causes of lactic acidosis. Lactic acidosis re-
sulting from hypoperfusion or tissue hypoxia, such as that
associated with shock, regional ischemia or carbon monox-
id poisoning, is termed type A (fast) lactic acidosis. In con-
trast, type B (slow) lactic acidosis generally comprises lac-
tate metabolism without hypoxia. In experimental animal
and clinical human studies, apparent type A lactic acidosis is
observed hours to days after shock (13–15). The degree of
serum lactate elevation (mmol/L) is usually categorized as
low (<2), intermediate (2–3.9) or high (> or = 4) in clinical
shock patients and assessed in terms of the mortality
rate (14–16). However, in most reported animal models and
human cases of cyanide intoxication, severe type A lactic acidosis develops within only minutes after ingestion or inhalation (17-19). In the literature, a plasma lactate concentration of >8 mmol/L has been reported to be sensitive (94%) and moderately specific (70%) for a toxic blood cyanide concentration (>1.0 mg/L) (18). Cyanide is a fast-acting poison that is usually fatal. The minimum lethal dose of cyanide after oral ingestion is approximately 50 mg, and inhalation of a concentration of 0.13 mg/L can cause death within one hour (19). In most patients with methemoglobin overdose, severe type B lactic acidosis occurs within 4-9 hours after ingestion. In human immunodeficiency virus patients, treatment with nucleoside reverse transcriptase inhibitors may result in severe type B lactic acidosis after several months of use (20-22). Hence, obtaining an accurate and prompt diagnosis of acute cyanide intoxication is necessary, and, importantly, a new field sensor for the diagnosis of cyanide exposure was recently reported (6).

Providing general supportive measures is crucial in cases of acute cyanide intoxication. There is experimental evidence that oxygen has a specific antidotal activity. For example, it can accelerate the reactivation of cytochrome oxidase and may increase tissue oxygen delivery. Treatment with artificial ventilation with 100% oxygen is recommended, although for no longer than 24 hours at this concentration. The administration of sodium bicarbonate and inotropic agents is also suggested. Furthermore, monitoring the ABG values, fluid and electrolyte balance, GCS changes and parameters of the circulatory status, including the central venous pressure, is essential, as well as providing intensive support of the respiratory function (23-25).

The administration of specific antidotes, such as sodium nitrite, sodium thiosulfate, dimethylaminophenol and hydroxocobalamin, together with supportive therapy has been shown to be even more effective in patients with acute cyanide intoxication. The outcome depends on the dose ingested and the availability of the antidote (23-25). The current patient was transported to our ED immediately after attempting suicide. She experienced bradycardia, generalized tonic-clonic seizures and severe lactic acidosis secondary to the ingestion of unknown toxic agents approximately half an hour after admission. We did not apply any specific antidotes in the ED because we were not certain of the exact toxic agent she had ingested. However, her clinical condition, including the coma, shock and severe lactic acidosis, improved significantly after providing intensive supportive management. Is it possible that most of the lactate production in this case was the result of severe hypotension rather than acute cyanide poisoning itself; thus, the rapid administration of supportive therapy targeting the hypotension and acidosis was sufficient to improve her clinical situation. The level of cyanide in our patient was confirmed to be high (3.5 mg/L). Importantly, the serum cyanide level is related to the dose of ingestion and time at which the blood specimen is drawn. To our knowledge, only three patients (including our patient) with well-documented severe cyanide poisoning (blood cyanide level ≥3.5 mg/L) have survived following treatment with supportive therapy alone (26-28). However, our patient demonstrated the fastest consciousness recovery time (within four hours) among these three cases.

The present case highlights the importance that physicians be alert to the possibility of acute cyanide poisoning in patients presenting with the impenetrable rapid onset of coma, seizures and cardiopulmonary dysfunction in the presence of severe lactic acidosis. Early recognition and the provision of prompt intensive supportive measures are also imperative, even in cases without accessible specific antidotes. In patients with suspected severe cyanide poisoning, an additional intravenous antidote should be administered as soon as possible.

The authors state that they have no Conflict of Interest (COI).

References


