CASE REPORT

Massive Rhabdomyolysis and Acute Renal Failure after Acetonitrile Exposure

Kazuhiko Muraki, Yasushi Inoue, Itsuro Ohta, Kaori Kondo*, Yasutoshi Matayoshi* and Toshiaki Kamei**

Abstract

A case of systemic rhabdomyolysis after acetonitrile exposure is reported. A 35-year-old previously healthy man suffered from vomiting, convulsion and consciousness loss 15 hours after exposure to acetonitrile. Since acetonitrile is known to be metabolized into cyanide, antidote therapy against cyanide poisoning was given. On admission, pain and all-over muscle swelling were marked. Although the initial therapy was effective, rhabdomyolysis and then acute renal failure developed. Renal function improved very slowly after six weeks of hemodialysis, but atrophy of the muscles remained. The rhabdomyolysis may have been caused by toxicity of the cyanide itself in combination with hypoxia and convulsion.

(Internal Medicine 40: 936-939, 2001)

Key words: cyanide, poisoning, hemodialysis

Introduction

Rhabdomyolysis is a syndrome that results in the destruction of skeletal muscle. The mechanism of this syndrome is still unclear (1, 2), but it often occurs under some special conditions such as severe exercise, hypophosphatemia, hypokalemia, alcoholism (3), sepsis (4), and the habitual use of illegal drugs such as heroine or cocaine (5).

Tissue hypoxia is also responsible for rhabdomyolysis in only a minority of patients. A few cases of rhabdomyolysis have been reported in patients with carbon monoxide (6) or cyanide (7, 8) poisoning and the pathological mechanism is more complicated in these cases. Not only the toxicity of chemicals, but also hard muscle work, such as systemic convulsion, are responsible for the morbid steps.

To our knowledge, this is the first full case report of severe rhabdomyolysis after accidental acetonitrile poisoning.

Case Report

A 35-year-old previously healthy man, employed at a chemical plant, was transferred to our hospital on July 17, 1999 because of suspected cyanide poisoning. The day before the transfer, the patient had washed the inside of a reactor kiln using acetonitrile to remove the precipitated by-products for an hour at around noon. At that time, he had worn a facemask and a rubber-coated over-all, and fresh air was pumped into the reactor continuously. At 3:00 AM the next day (15 hours after the exposure ended), he suffered from severe nausea, frequent vomiting, diarrhea and muscle weakness. At 8:30 AM he went to a nearby hospital and routine blood studies were normal except for a slight increase in creatine phosphokinase (CPK) activity (346 IU/l) (Table 1). In the course of observation, generalized weakness continued, and at the next hospital visit, muscle tenderness was noted. After a CPK level of 3,426 IU/l was reported, he was brought to our hospital immediately.

Laboratory data on admission to the local hospital (left panel) and to our hospital (right panel). Normal ranges are shown in parentheses.

Table 1. Laboratory Data on Admission

<table>
<thead>
<tr>
<th></th>
<th>Local hospital</th>
<th>Our hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb (14-17 g/dl)</td>
<td>14.6</td>
<td>11.6</td>
</tr>
<tr>
<td>WBC (4,000-9,500/µl)</td>
<td>8,600</td>
<td>15,200</td>
</tr>
<tr>
<td>Platelet (14-33x10^4/µl)</td>
<td>23.8</td>
<td>20.1</td>
</tr>
<tr>
<td>Blood chemistry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein (6.5-8.0 g/dl)</td>
<td>7.4</td>
<td>5.8</td>
</tr>
<tr>
<td>Albumin (3.8-5.0 g/dl)</td>
<td>4.5</td>
<td>3.0</td>
</tr>
<tr>
<td>AST (6-35 IU/l)</td>
<td>27</td>
<td>70</td>
</tr>
<tr>
<td>ALT (5-30 IU/l)</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>LDH (106-211 IU/l)</td>
<td>197</td>
<td>9,521</td>
</tr>
<tr>
<td>Total bilirubin (0.2-1.0 mg/dl)</td>
<td>0.6</td>
<td>1.0</td>
</tr>
<tr>
<td>Total cholesterol (130-200 mg/dl)</td>
<td>242</td>
<td>168</td>
</tr>
<tr>
<td>Creatinine (0.5-1.1 mg/dl)</td>
<td>1.1</td>
<td>2.8</td>
</tr>
<tr>
<td>BUN (8-20 mg/dl)</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>Na (136-146 mmol/l)</td>
<td>139</td>
<td>155</td>
</tr>
<tr>
<td>K (3.6-4.8 mmol/l)</td>
<td>3.3</td>
<td>4.1</td>
</tr>
<tr>
<td>Cl (100-107 mmol/l)</td>
<td>102</td>
<td>99</td>
</tr>
<tr>
<td>CPK (29-203 IU/l)</td>
<td>346</td>
<td>3,426</td>
</tr>
</tbody>
</table>

Laboratory data on admission to the local hospital (left panel) and to our hospital (right panel). Normal ranges are shown in parentheses.

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Received for publication November 20, 2000; Accepted for publication April 23, 2001
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Internal Medicine Vol. 40, No. 9 (September 2001)
convulsion and reduced consciousness occurred. Arterial blood gas analysis showed severe acidosis: pH 6.559, PO₂ 103.9 mmHg, PCO₂ 31.1 mmHg, HCO₃⁻ 2.6 mmol/l, base excess (BE) -39.8 mmol/l. Mechanical ventilation with 100% oxygen was started at 10:19 AM, and sodium bicarbonate and dopamine were given. Since acetonitrile can be metabolized into cyanide in the liver, cyanide poisoning was suspected. The patient was transferred to the emergency center in our hospital at 13:05 to receive antidotes against cyanide.

On arrival, he was drowsy but restless, complaining of severe muscle pain and tenderness over his whole body. Muscle swelling was marked, especially in extremities. He also complained of dyspnea because of the weakness of respiratory muscles. Blood pressure was 97/40 mmHg, heart rate was 145/min (dopamine: 19 μg/kg/min) and his temperature was 38.4°C. A complete blood count showed anemia and leukocytosis. Blood chemistry showed a mild elevation in aspartate aminotransferase (AST) and renal dysfunction (blood urea nitrogen 27 mg/dl, creatinine 2.8 mg/dl) (Table 1). Arterial blood gas analysis showed: pH 7.260, PaO₂ 515 mmHg, PCO₂ 36.6 mmHg, HCO₃⁻ 15.9 mmol/l, BE -9.8 mmol/l. Twenty ml of 10% sodium nitrite and repeated boluses of 10% sodium thiosulfate (170 ml in total) were given. The concentration of cyanide in the blood could not be determined. A brown discoloration of urine was detected and benzidine test was positive. Urinary protein (200 mg/dl) was present. Brain lesion was not detected by CT scan. Propofol, a sedative, was infused at the rate of 3 mg/kg/h for 6 days to continue mechanical ventilation because the patient complained of severe dyspnea and muscle pain.

The next day (Day 2), oliguria and then anuria developed in spite of a large amount of fluid transfusion. Blood level of CPK activity was markedly high (325,000 IU/l) and MM isozyme was dominant. Myoglobin was detected in the blood at high concentrations (340,000 ng/ml) (normal range: less than 60 ng/ml). In the urine, it was also markedly elevated (1,000,000

Figure 1. Changes in urine volume and serum levels of CPK and creatinine. CPK: creatine phosphokinase activity (closed circle), creatinine: closed square, Light and dark shaded areas indicate normal ranges of CPK and creatinine, respectively. CHDF: continuous hemodiafiltration, HD: hemodialysis.
ng/ml) (less than 10 ng/ml). Values for AST, alanine aminotransferase (ALT) and lactate dehydrogenase (LDH) were 4351, 813 and 9521 IU/l, respectively. All these parameters reached their peaks at Day 2. Serum creatinine level rose gradually and reached a peak of 8.9 mg/dl on Day 18. Continuous hemodiafiltration was started on Day 2.

One-week of continuous hemodiafiltration and 5-week intermittent hemodialysis (three times initially and then twice a week) were required before CPK activity and myoglobin levels in the blood or urine returned to their normal ranges. Serum creatinine level did not return completely and remained around 2.0 mg/dl on discharge (Fig. 1).

Muscle biopsy was done from the anterior tibial muscle on Day 3. Destruction of the normal structure and lysed fibers were proven later (Fig. 2). The patient’s body weight, 68 kg initially, decreased to 45.5 kg on the 50th day. He was discharged on Day 96 after rehabilitative training.

Discussion

Acetonitrile, CH₃CN, is a volatile colorless liquid widely used as a material or solvent in chemical plants and laboratories. Acetonitrile is believed to have little toxicity, but it is metabolized into cyanate compounds in the liver by cytochrome P-450 enzyme system (9-12); thus, it displays delayed toxicity.

Reports of human poisoning with acetonitrile had been rare until several authors described accidental or suicidal poisoning with acetonitrile-containing nail glue remover (13-17). The clinical features of vomiting, convulsions, coma and acidosis seem common to all cases reported and are believed to be caused by cyanide not acetonitrile. The time lag between the ingestion of acetonitrile and the onset of the symptoms seemed to range from 3 to 12 hours. Mueller and Borland (13) measured successively the serum concentrations of cyanide and calculated the cyanide half-life as 44 hours in a 39-year-old woman who swallowed 25 g acetonitrile in a suicidal attempt. In a case of 2-year-old boy who ingested sculptured nail remover, Caravati and Litovitz (17) reported that the cyanide was eliminated in a biphasic manner. The initial half-life was 6.3 hours, followed by a 24-hour plateau phase, then a terminal half-life of 6.0 hours. The patient should be carefully observed and repeatedly evaluated for a few days after acetonitrile poisoning.

In the industrial fields, only two reports on human poisoning with acetonitrile have been published. Amdur reported accidental group exposure to acetonitrile (18), in which 16 workers were exposed to acetonitrile vapor in a 5,000 gallon tank. Four hours after the exposure ended, one worker experienced nausea, vomiting, and chest pain, followed by a convulsive seizure, and finally died. Cyanide was detected in postmortem blood. Although another 2 coworkers showing similar symptoms were hospitalized, they survived after therapy with fluids, oxygen by nasal cannula, whole blood, ascorbic acid and sodium thiosulfate. Dequidt et al reported the death of a worker exposed to acetonitrile in a photographic laboratory (19). Four hours after the exposure the worker experienced nausea and emesis. He vomited throughout the night, and became comatose the following morning. Cardiopulmonary arrest occurred, with death occurring 6 days later.

The conditions of the accident in the present case resemble those reported by Amdur (18). The above clinical courses are similar to those in the present case except for a longer lag time. The symptoms and laboratory findings are consistent with those in cyanide poisoning, as is the effectiveness of sodium thiosulfate therapy. This case is unique in that the acetonitrile poisoning was accompanied by severe and systemic rhabdomyolysis,
Rhabdomyolysis after Acetonitrile Exposure

which took the patient more than 3 months to recover from. Rhabdomyolysis had not been described in previous acetonitrile-poisoning cases, except for a brief abstract in which the details were not shown (20). The patient had been in a good health and had not been receiving any drugs, nor was he an alcoholic, or an illegal drug user. Propofol has been reported as a possible drug that may cause rhabdomyolysis (21) in children; however, the CPK level was markedly high in this case even before the use of the drug. Thus, it seemed that propofol was not causative for rhabdomyolysis. We concluded that the patient had acetonitrile poisoning followed by severe rhabdomyolysis, although the serum cyanide level was not measured.

Cyanide can cause rhabdomyolysis by itself (7) or in the combination with carbon monoxide in the cases of fire victims (8). The mechanism of muscle destruction by cyanide is not clear, but hypoxia and severe exercise (convulsion) seem to play an important role. In the present case, we speculated that systemic hypotension and generalized convulsion aggravated the pathological steps. Then, rhabdomyolysis seems to cause acute renal failure mainly by obstructing renal tubuli and in part by hypoxia and dehydration.

Rhabdomyolysis in the present case was severe. Whole muscles were swollen and tender, the blood level of CPK was extremely high and the loss of muscle tissue was marked. The patient also lost more than 20 kg in weight in a few weeks. In cases of acetonitrile poisoning, we must pay attention not only to the management for cyanide poisoning, but also to possible rhabdomyolysis.

**References**