Nonoliguric Acute Renal Failure Caused by Doxylamine-Induced Rhabdomyolysis

In this report a case of nonoliguric acute renal failure caused by doxylamine-induced rhabdomyolysis for suicide is presented and literature data reviewed.

Key Words: Doxylamine, Rhabdomyolysis, Nonoliguric acute renal failure

Ethanolamine derived doxylamine is a drug frequently used for treatment of insomnia because of its hypnotic effect. We report a case of rhabdomyolysis complicated by nonoliguric acute renal failure associated with high dose doxylamine ingestion for suicidal purpose.

Case Report

A 37 years old man taking drug for suicide was applied to emergency department and he was conscious and cooperated. It was learned that he complained sleeplessness and, for this reason, he used Unisom (doxylamine succinate 25 mg) irregularly for one year. He took 25 tablets of doxylamine 2 hours before suicide. There was no pathologic finding in the physical examination. Following gastric lavage, activated charcoal (Haemocol) was adjusted via nasogastric tube. At performed investigations serum creatinine and lactate dehydrogenase (LDH) levels were found high (Table 1). The patient was observed for 10 hours without complication and he was transferred to the clinic.

When he was admitted to service he complained generalized lumbal and muscular pain. There was no property in the systemic examination. In history it was learned that he did not take any drug or substance except doxylamine. There was no trauma or exercise history. In investigations done after 2nd day of his admission not only LDH but also urea, uric acid and creatine phosphokinase (CPK) levels were increased (Table 1). Serum calcium, phosphorus and potassium levels were normal. In urinary examination: density is 1008, protein and glucose negative, and in urinary sediment
1-2 leukocytes and 2-3 eritrocytes were found. Myoglobinuria was not recorded. Oliguria did not develop. During the following day, urea and creatinine levels increased. Daily urine volume was over 1000 cc, but creatinine clearance was found 3 ml/min in investigations done at the 3rd day. With these findings non-oliguric acute renal failure caused by rhabdomyolysis was thought. Treatment was performed to enable excessive diuresis and to make urine alkaline. Serum creatinine, CPK, and LDH levels decreased gradually. At the 14th day: creatinine, 1.8 mg/dl; creatinine clearance 54 ml/min were recorded. At the 20th day, all abnormal laboratory findings were normal and patient was sent to psychiatrics clinic. The patient was normal at control done 8 months later.

**Discussion**

Rhabdomyolysis is a picture resulted from entrance of myoglobin, CPK and urate into circulation and, it also occurs after the effects of a prolonged coma (with or without a trauma), heavy exercise, infection, various drugs or substances (1,2). In nontraumatic cases, the mechanism of muscle destruction is not known precisely but direct toxic effects on striated muscles is thought. One of the complications of rhabdomyolysis is acute renal failure. Acute renal failure can be seen in 33% of patients with nontraumatic rhabdomyolysis observed in hospital, and dialysis is required in 15% of the cases (1).

The most sensitive test for diagnosis of rhabdomyolysis is the increment in serum CPK level. There is an obvious correlation between serum myoglobin and CPK levels (3). But myoglobin in urine is found only in 57% of patients during the initial stage of rhabdomyolysis (4). The elevation in transaminases and LDH found in skeletal muscle during routine examinations can be the first laboratory sign leading to diagnosis (5).

In Turkey, antihistaminic hypnotics have used widely since they are sold with normal prescription. An ethanalamine derived doxylamine is a drug used for treatment of insomnia frequently because of its hypnotic effect. Rhabdomyolysis which is due to antihistaminic drug toxicity was firstly reported by Hampel et al. They reported in 34 years old-male patient developed renal failure due to myoglobinuria following excessive diphenhydramine usage and with CPK level 30 000 U/L (6). Rhabdomyolysis following doxylamine usage was firstly reported by Mendoza et al. In this report, 16 years old-male patient had CPK level increased to 126 400 U/L and mild non-oliguric renal failure determined at 5th day of doxylamine usage (7).

Köppel et al. observed only one rhabdomyolysis case associated with temporary renal failure in 109 doxylamine intoxication reports. But there was no correlation between the taken amount or plasma level and the frequency or severity of symptoms. So, this makes us think that personal differences play an important role in the sensitivity against doxylamine (8). Again Köppel et al. observed 7 rhabdomyolysis cases which had phosphokinase level between 980 U/L -634 000 U/L in 442 patients and also in 3 of them temporary creatinine el-

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**Table 1. Biochemical dates**

<table>
<thead>
<tr>
<th></th>
<th>Urea (10-40% mg)</th>
<th>Creatinine (0.5-1.4% mg)</th>
<th>Uric acid (2.4-7% mg)</th>
<th>Lactate Dehydrogenase (160-480 U/L)</th>
<th>Creatine phosphokinase (0-190 U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>28</td>
<td>2.5</td>
<td></td>
<td>620</td>
<td></td>
</tr>
<tr>
<td>2. day</td>
<td>62</td>
<td>4.4</td>
<td></td>
<td>848</td>
<td>4973</td>
</tr>
<tr>
<td>3. day</td>
<td>113</td>
<td>6.2</td>
<td></td>
<td>9.1</td>
<td>563</td>
</tr>
<tr>
<td>6. day</td>
<td>93</td>
<td>6.1</td>
<td></td>
<td>12.4</td>
<td>644</td>
</tr>
<tr>
<td>7. day</td>
<td>156</td>
<td>6.2</td>
<td></td>
<td>6.1</td>
<td>1118</td>
</tr>
<tr>
<td>8. day</td>
<td>157</td>
<td>5.4</td>
<td></td>
<td>11.9</td>
<td>435</td>
</tr>
<tr>
<td>10. day</td>
<td>138</td>
<td>3.5</td>
<td></td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>14. day</td>
<td>92</td>
<td>1.8</td>
<td></td>
<td>6.1</td>
<td>410</td>
</tr>
<tr>
<td>16. day</td>
<td>57</td>
<td>1.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. day</td>
<td>40</td>
<td>1.2</td>
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</table>
evation were noted (9). Frankel et al. reported rhabdomyolysis dependent on acute renal failure in two patients coming to hospital in status epilepticus state following diphenhydramine and doxylamine ingestion for suicide (10).

Although the findings like unconsciousness, agitation or disorientation were generally seen in cases of doxylamine intoxication in the literature, neuropsychiatric examination was totally normal in our case. It was diagnosed with CPK analysis performed upon the finding of creatinine and LDH increment in the routine biochemical laboratory analysis. Renal failure regressed in 20th day and the patient was sent to home without any sequel.

Because other potential causes (e.g., hemodynamic disorders) of the patient's acute renal failure was detected, it was believed to be related to rhabdomyolysis. Because there was no evidence of trauma, infectious diseases, muscular compression, convulsions, or metabolic disorders known to be responsible for rhabdomyolysis (1), this rhabdomyolysis was attributed to the doxylamine itself.

In conclusion, this case shows us that whatever the clinical picture is in every patient coming with doxylamine intoxication, the possibility of rhabdomyolysis must be considered and the patient must be observed for probable risk of renal failure.

REFERENCES