CASE REPORT

Rhabdomyolysis and Acute Renal Failure Associated with Salmonella Food Poisoning
Al Ani A.M., Mudather M. and Asim M.
Department of Medicine, Hamad Medical Corporation
Doha, Qatar

Abstract:
A young man with Salmonella food poisoning developed rhabdomyolysis complicated by acute renal failure. This is an uncommon but potentially fatal extra-intestinal manifestation of Salmonellosis. He responded to alkaline diuresis and antibiotic therapy and made a complete recovery.

A discussion of the case, the pathophysiological mechanisms involved in myoglobinuric renal failure and the management is presented.

Key words and abbreviations: Rhabdomyolysis; ARF=Acute Renal Failure; Salmonella; CPK=Creatinine Phosphokinase

Introduction:
Rhabdomyolysis refers to disruption of the striated muscle integrity resulting in the release of intracellular constituents into the circulation. This syndrome is characterized by an elevated serum concentration of the enzyme creatinine phosphokinase (CPK) and by myoglobinuria. The manifestations can be as mild as a subclinical rise in CPK or as severe as myoglobinuric acute renal failure (ARF) or compartment syndrome. However, it is important to realize that rhabdomyolysis does not always imply irreversible necrosis of muscle(1); damaged myocytes can undergo repair if the insult is not severe or long lasting.

In German medical literature, cases of rhabdomyolysis were reported during World War I but in modern English medical literature, Bywaters first described it in victims of crush injury during the blitz of London in World War II(2). Non-traumatic causes of rhabdomyolysis were recognized only in the 1970s. These include alcohol abuse, seizure activity, soft tissue compression, drugs, electrolyte disturbances and a variety of infections.

Address for correspondence:
Dr. Ahmed M. Al Ani, MRCP(UK), FRCP(Glasg)
Consultant Physician, Department of Medicine
Hamad Medical Corporation, P.O. Box 3050, Doha, Qatar
E-mail: ahmda@yahoo.com

Case Report:
A previously fit 32-years-old Sri Lankan man presented to the emergency department of Hamad General Hospital with a three day history of gastroenteritis and mild upper abdominal pain. He had been passing 15-20 non-bloody watery stools daily. This was accompanied by vomiting 2-3 times a day. Apart from oral rehydration solution he was not receiving any other medication. There was no history of alcohol intake. On the day of admission he developed pain and weakness in both legs and also noted that his urine had turned brown in color.

Physical examination showed that he was afebrile and in no apparent distress. Blood pressure was 150/90 and pulse 102/min. Lower limb muscles were tender on palpation. However the limbs were warm and foot pulses were of good volume. The power in the lower limbs was grade 4/5 but this was attributed to muscle pain; there were no other neurological signs. The rest of the physical examination was unremarkable.

Serum biochemistry showed advanced renal insufficiency (Table 1) and a high anion gap metabolic acidosis. LDH was elevated at 1696 IU/l (normal range: 230-460 IU/l) but the striking feature was a spectacular rise in serum CPK at 28260 IU/l (normal: ≤190 IU/l). Examination of the peripheral blood film did not show schistocytes or thrombocytopenia. Hepatic transaminases, serum amylase, prothrombin time and partial thromboplastin time were all normal. HIV, hepatitis B & C serology was negative. Urinary pH was 5.0. Urinalysis showed protein 75 mg/dl and 5-50 red blood cells/ mm³. Spot urinary sodium was 37 mmol/l and osmolality 237 mosmol/l. Myoglobinuria was detected; myoglobin level in blood was raised at 11,348 ng/ml (normal range 23-72 ng/ml). Stool examination did not show presence of blood, mucous, ova cyst or parasite.

A diagnosis of myoglobinuric ARF secondary to rhabdomyolysis was made and alkaline rehydration therapy was instituted. Empirical therapy with intravenous Ciprofloxacin 400mg once a day and metronidazole (Flagyl; Aventis Pharma) 500 mg eight hourly was also commenced. No signs of compartment syndrome were seen on serial examinations. Three consecutive stool cultures were negative for any enteric pathogens or Clostridium difficile. Abdominal ultrasound was normal. On day 3, blood cultures taken at the time of hospitalization yielded
Table 1: Blood Chemical and Enzymes Values

<table>
<thead>
<tr>
<th>Day of Admission</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>5</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN (mmol/l)</td>
<td>22.5</td>
<td>28.4</td>
<td>32.3</td>
<td>30</td>
<td>15.6</td>
<td>6.9</td>
</tr>
<tr>
<td>Serum creatinine (umol/l)</td>
<td>752</td>
<td>745</td>
<td>648</td>
<td>449</td>
<td>171</td>
<td>108</td>
</tr>
<tr>
<td>Serum Na (umol/l)</td>
<td>130</td>
<td>124</td>
<td>129</td>
<td>131</td>
<td>142</td>
<td>137</td>
</tr>
<tr>
<td>Serum Cl (umol/l)</td>
<td>89</td>
<td>92</td>
<td>95</td>
<td>100</td>
<td>108</td>
<td>105</td>
</tr>
<tr>
<td>Serum K (mmol/l)</td>
<td>5.6</td>
<td>4.5</td>
<td>3.9</td>
<td>3.5</td>
<td>5</td>
<td>4.3</td>
</tr>
<tr>
<td>Serum HCO3 (mmol/l)</td>
<td>10</td>
<td>11</td>
<td>14</td>
<td>28</td>
<td>24</td>
<td>29</td>
</tr>
<tr>
<td>Serum Ca (mmol/l)</td>
<td>2.24</td>
<td>1.86</td>
<td>1.61</td>
<td>1.75</td>
<td>2.12</td>
<td>2.21</td>
</tr>
<tr>
<td>ALT (IU/l)</td>
<td>88</td>
<td></td>
<td>96</td>
<td>26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST (IU/l)</td>
<td>411</td>
<td></td>
<td>146</td>
<td>43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDH (IU/l)</td>
<td>1696</td>
<td></td>
<td>1170</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPK (IU/l)</td>
<td>28260</td>
<td>31380</td>
<td>14384</td>
<td>8095</td>
<td>2469</td>
<td>153</td>
</tr>
<tr>
<td>Uric acid (mmol/l)</td>
<td>951</td>
<td></td>
<td>333</td>
<td>328</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum PO4 (mmol/l)</td>
<td>1.56</td>
<td></td>
<td>1.36</td>
<td>1.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein (g/l)</td>
<td>74</td>
<td></td>
<td>74</td>
<td>75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum albumin (g/l)</td>
<td>37</td>
<td></td>
<td>37</td>
<td>42</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Salmonella group D; sensitive to Ciprofloxacin. Metronidazole was stopped and Ciprofloxacin continued for another ten days. Diarrhea decreased in frequency and subsided on day 6. The patient maintained good urine output throughout the illness, averaging 2.5 liters per day, and his renal parameters improved as shown in Table 1. Ten days after admission he was discharged with normal renal function. By this time serum CPK level had normalized and urinary abnormalities had disappeared.

Discussion:

Myoglobinuric ARF is common and, in some hospitals, has accounted for as many as eight per cent of all cases of acute renal failure. Alcohol and drugs account for most of the cases of rhabdomyolysis. An infectious origin is diagnosed in about five per cent of cases.

Rhabdomyolysis can develop during the course of viral and bacterial infections. Influenza is a common viral cause (25 cases reported in the English literature) with acute renal failure developing in 44% of these patients.

Legionella, streptococcal and Francisella tularensis infections are common bacterial causes. Between 1976 and 1983 fourteen cases were reported, most of which were due to Legionella species. Rhabdomyolysis has been reported as a complication of non-typhoidal salmonellosis. Only eight such cases were found in a review of the English literature and renal failure was observed in each one.

Our patient had advanced renal impairment following severe diarrhea. Muscle pain and tenderness was a prominent feature of his illness. Markedly elevated serum CPK level and myoglobinuria established the diagnosis of rhabdomyolysis. Salmonella infection was felt to be the likely etiology; no intra-muscular injections had been administered.

The mechanism of Salmonella induced rhabdomyolysis has not been clearly elucidated. Proposed mechanisms include decrease in activation of glycolytic and oxidative enzymes, direct bacterial invasion and production of endotoxins.

ARF develops in 30-40% of patients with rhabdomyolysis. The etiology is multifactorial. Ferrihemate, a product of myoglobin, is directly tubulo-toxic. Renal blood flow is altered in response to activation of rennin-angiotensin system, increased renal sympathetic tone, decreased production of vasodilatory prostaglandins and deposition of microthrombi. In addition, tubular obstruction secondary to precipitation of myoglobin, protein and uric acid crystals is an important factor. This is made worse by the production of acidic urine in volume-depleted patients. Alkaline rehydration is thus the cornerstone of treatment. This maneuver also ameliorates hyperkalemia and metabolic acidosis.

Myoglobinuric ARF, as seen in our patient, is frequently accompanied by marked elevation in serum urate concentration.
and notable hypocalcemia (even early in the course of renal failure\(^1\)). Hyperuricemia results from purines released from injured muscles and converted to uric acid in the liver. Calcium salts are deposited in damaged muscles and various other abnormalities of the calcium-vitamin D-parathyroid axis also lead to hypocalcemia\(^{13,14}\). In the presence of hyperkalemia, severe hypocalcemia may lead to cardiac arrhythmias and seizures. Calcium salts should only be administered to treat toxic effects of elevated serum potassium or to treat symptomatic hypocalcemia. Treatment of asymptomatic hypocalcemia is discouraged as it promotes calcium deposition in the injured muscles. Unnecessary administration of calcium can also make rebound hypercalcemia in the recovery phase more likely. There was but only a slight elevation of serum phosphate. Highest values are reported in rhabdomyolysis due to crush syndrome or exhaustive exercise.

Salmonella food poisoning is usually a self-limiting disease and antibiotic therapy does not appear to decrease the duration of symptoms or consistently eliminate stool carriage. Bacteria develop in less than 5% of cases and these patients require antibiotics. Quinolines should be included in the antibiotic regimen until susceptibility patterns are known\(^{16}\). Acute myoglobinuric renal failure has got an excellent prognosis and complete renal recovery can be expected unless complicated by cortical necrosis from prolonged hypotension\(^{13,17,18}\).

**Conclusion:**

Myalgias are sometimes misinterpreted as a part of bacterial infection and the presence of red blood cells in the urine of many patients with rhabdomyolysis may falsely reassure the physician that hematuria accounts for the urine color and prevent a search for rhabdomyolysis. Myoglobinuria and its potentially important sequelae should be considered in patients seriously ill with Salmonella infections. A high index of suspicion is required for timely diagnosis and prompt treatment. We recommend determination of serum CPK level in patients with acute gastro-enteritis requiring hospitalization.

**References:**