Rhabdomyolysis Associated with Crohn’s Disease

Mitsuro Chiba, Kiyoshi Igarashi, Hiromasa Ohta, Michiro Ohtaka, Hiromichi Arakawa and Osamu Masamune

Three cases of Crohn’s disease (CD) which showed an elevation of creatine phosphokinase (CPK) during the course were reported. In two cases, elevations of serum myoglobin and aldolase were also observed which indicated rhabdomyolysis. Rhabdomyolysis occurred unrelated to the activity of CD and it was asymptomatic. It was unable to identify an apparent known cause for rhabdomyolysis. All three cases were under elemental diet (ED) but the causality of ED for rhabdomyolysis was uncertain. So far as we know, there is no report on rhabdomyolysis during ED treatment and there are only two reports in which rhabdomyolysis was documented in CD. The latter was rhabdomyolysis due to electrolyte depletion secondary to malabsorption in CD which was not encountered in our cases. Our department dealt only three cases of CD and all of them had an elevation of CPK which had been measured as one of routine blood chemistry in our hospital. These observations led to a following conclusion that subclinical rhabdomyolysis may be one of extra-intestinal complications of CD.

Key Words: Rhabdomyolysis, Crohn’s disease, Myoglobinemia, Creatine phosphokinase (CPK), Extra-intestinal complication

We had three cases of Crohn’s disease (CD) in which creatine phosphokinase (CPK) was elevated during the course without any muscle symptoms and without any discernible cause. In two of those three cases, elevations of serum myoglobin and aldolase were also seen. This indicated that subclinical rhabdomyolysis might be associated with Crohn’s disease, so far as we know, which has not been described previously.

CASE REPORT

Case 1. Y.K., Male.

Family history showed no family member who had myoglobinuria and past history showed neither myoglobinuria nor cramps on exertion. He was diagnosed as having Crohn’s disease at age of eighteen on 1980. He was admitted four times and the last three admissions were ones to our clinic. He had lesions of Crohn’s disease in duodenum, ileum, and colon (enterocolitis). The clinical course including Crohn’s disease activity index (CDAI),1 the treatment, and values of serum CPK is depicted in Fig. 1. He was admitted on Jan. 12, 1984 because of fever and abdominal pain. CDAI of the admission was 252. He was given 2500 Calorie/d. of elemental diet (ED),2 Elental (Ajinomoto Co. Ltd., Tokyo, Japan) and the symptoms became gradually improved. On Feb. 27, an elevation of serum CPK was first noticed (Fig. 2) and it reached to a peak, 2827 U/L (normal 40–210 U/L, rate assay of Rosalki) on March 7, 1984 (Fig. 2). Following the change of 2500 Cal of ED to 1200 Cal of ED and about 900 Cal of rice gruel (Fig. 1) CPK became rapidly normal. An elevation of CPK was associated with elevations of serum myoglobin 170 ng/ml (normal < 60 ng/ml) and serum aldolase 12.3 mU/ml (normal 0.5–3.1 mU/ml) (Table 1). The isozyme of CPK was normal; MM was identified at 92% and CPK-MB and CPK-BB were not increased (Table 1). Two weeks ahead of CPK elevation, serum alkaline-phosphatase (ALP) increased slightly, while at the same time of

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Table 1. Laboratory data of CPK, myoglobin, and aldolase

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
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<tbody>
<tr>
<td>CPK (40–210 U/L)</td>
<td>2827</td>
<td>572</td>
<td>1269</td>
</tr>
<tr>
<td>BB (&lt;1%)</td>
<td>0</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>MB (0–2)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>MM (92–99)</td>
<td>92</td>
<td>98</td>
<td>93</td>
</tr>
<tr>
<td>Albumin (1–6)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Band</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Myoglobin (&lt;60 ng/ml)</td>
<td>170</td>
<td>81</td>
<td>140</td>
</tr>
<tr>
<td>Aldolase (0.5–3.1 mU/ml)</td>
<td>12.3</td>
<td>tested</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1.7–5.7 IU/L/37°C)</td>
<td>5.6</td>
<td>10.2</td>
</tr>
</tbody>
</table>
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had myoglobinuria and past history showed neither myoglobinuria nor cramps on exertion. He developed loose stool and weightloss as age of eighteen on 1981. He was once diagnosed as ulcerative colitis and was treated with Salazopyrin by some hospital. He was referred to our clinic because of prolonged diarrhea, fatigability, weightloss, and abdominal pain and was admitted on April 21, 1986. He had lesions in the ileum and the colon and was diagnosed as CD (ileocolitis). The clinical course including CDAI, the treatment, and values of serum CPK is shown in Fig. 3. CDAI was decreased following an administration of 2400 Cal/d. of ED (Fig. 3). An elevation of CPK was noticed on June 23 and it was reached to a peak 1436 U/L on July 17, when he was given 2400 Cal/d. of ED and 4 g/d. of Salazopyrin (Figs. 3, 4). The calorie of ED was decreased to 2100 Cal/d. on July 23 and about 300 Cal/d. of rice gruel was supplemented (Fig. 3). CPK measured on July 24 showed a decrease to 1024 U/L (Fig. 4). Then CPK became rapidly normal (Fig. 4). Elevations of CPK were associated with elevations of serum myoglobin and aldolase when they were measured twice (Table 1). The higher in the value of CPK, the more increases in myoglobin and aldolase were observed (Table 1). The isozyme of CPK was normal on the twice (Table 1). Serum ALP did not change during CPK elevation and it was normal. GOT and GPT were slightly increased in parallel with CPK. There was no change in other laboratory data mentioned in case 1. There were neither complaints nor changes in physical examination.

Case 3. T.N., Male.
slight elevation when CPK showed the highest value on May 14 (Fig. 6). The isozyme of CPK was normal (Table 1). Serum myoglobin and aldolase were not measured. He did not recognize any change in the body during the periods of CPK elevations.

**DISCUSSION**

Muscle damage causes the leakage of enzymes (CPK, aldolase, GOT, LDH) and myoglobin within muscle into the blood. We have reported here three cases of CD in which CPK was elevated. Two of them were associated with elevations of myoglobin and aldolase and it was sure that rhabdomyolysis occurred in our cases. However, since we are uncertain whether CPK elevation in case 3 was due to playing soccer or due to a same factor as case 1 and case 2, we restrict our discussion mainly to case 1 and case 2.

Rhabdomyolysis is characterized by injury of muscle and excretion of myoglobin in the urine. Recently rhabdomyolysis has been proposed as a more precise term for myoglobinuria. Rhabdomyolysis is seen when there are extensive trauma, crush injuries, and nontraumatic various situations. The latter includes: increased muscle oxygen consumption (heat stroke, severe exercise, and seizures); decreased muscle energy production (hypokalemia, hypophosphatemia, and genetic enzymatic deficiency); muscle ischemia (arterial insufficiency, coma after suicidal ingestion of barbiturates or carbon monoxide intoxication); progressive muscle disease; viral infections; direct toxin of alcohol, heroin, and the bite of Malayan sea snake; malignant hyperthermia. Rhabdomyolysis listed above causes symptoms of muscle (weakness, pain, cramps, swelling) with or without pigmenturia (gloss myoglobinuria). However the recent development of measuring myoglobin in serum and urine in the order of ng/ml made it possible to detect rhabdomyolysis which is neither associated with pigmenturia nor muscle symptoms. The characteristic of rhabdomyolysis in our cases was asymptomatic and our cases might be another example of subclinical rhabdomyolysis. We could not find any apparent cause for rhabdomyolysis listed above. Although our patients were not studied for muscle enzymes (phosphorylase, phosphofructokinase) responsible for rhabdomyolysis, it was improbable because none of our cases had a history of cramps or myoglobinuria on exertion which is common in disorders of genetic enzymatic deficiency.

To our knowledge, there have been two reports...
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on rhabdomyolysis in CD.\(^12,13^\) Heitzman et al\(^12^\) reported a case with cramps, muscle weakness and gross myoglobinuria. Meharg\(^13^\) reported a case with muscle weakness and CPK elevation. Both cases were caused by severe potassium depletion (2.3 mEq/L in the former case and 2.1 mEq/L in the latter case), calcium depletion (5.3 mg/dl and 4.8 mg/dl respectively), and possible other deficiency secondary to malabsorption due to CD. Our cases were different from these two cases because our cases developed rhabdomyolysis without electrolyte depletion.

CPK elevation in all our cases was observed during ED treatment. In the first episode of case 1, the decrease of CPK was observed following the decreasing the calorie of enteral feeding suggesting that hyperalimentation by ED might be related to CPK elevation. In case 2, it is hard to judge whether the decrease of CPK occurred spontaneously or due to decreasing calorie of ED because the decrease of CPK was observed just 1 day after the decrease of ED calorie. However CPK elevation was also observed even when the calorie of ED was 900 Cal/d. in the second episode of case 1. So far as we know there has not been a report describing CPK elevation or rhabdomyolysis during ED. However an elevation of CPK was described during total parenteral nutrition (TPN)\(^14,15^\) and it was observed at a time of starting TPN. Our cases did not have TPN.

The isozyme pattern of CPK\(^16,17^\) in our cases was normal and the most of CPK was found to be an origin of striated muscle. An origin of intestinal muscle was denied because of normal CPK-BB and CPK-MB each of which accounted for about a third of total CPK in the intestine.\(^17^\)

In our hospital, CPK has been one of routine blood chemistry, therefore we could observe the value of CPK in CD. Otherwise we might have been unaware of CPK elevation because patients were asymptomatic. Apart from CPK elevation, the decrease of CPK less than the lower limit of normal value was observed in all three patients with CD before treatment. It was repeatedly observed in case 1 who had the history of CD for six years. The decrease of muscle activity in combination with or without the atrophy of striated muscle due to undernutrition in CD might explain the low level of CPK.

Although rhabdomyolysis occurred in muscle other than the digestive tract in our cases, it is noteworthy that several viral infections have been shown to induce rhabdomyolysis\(^18-23^\) since some unknown microbial agent including a viral agent is thought to be involved in the etiology of CD.\(^24^\)

Our department has seen only three patients with CD and all of them had CPK elevation. Although rhabdomyolysis in our cases was obviously unrelated with the activity of CD, it is likely that subclinical rhabdomyolysis is one of extra-intestinal complication of CD.\(^25,26^\) To confirm this, a study in a large scale is needed.

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REFERENCES


