RHABDOMYOLYSIS IN PATIENTS WITH HYPOGLYCEMIC COMA: THREE CASES STUDY

Michio Nishino, Akihiro Yoshida, Tsugiyasu Kanda, Isao Kobayashi

*Department of Laboratory Medicine, Gunma University School of Medicine*

**Abstract**: We showed the three cases in rhabdomyolysis according to hypoglycemic coma. The measurements of creatine phosphokinase, creatine phosphokinase isozyme, myoglobin, and cardiac myosin light chain I are useful for diagnosing the rhabdomyolysis in patients with diabetes mellitus.

**Key words**: Rhabdomyolysis, Myoglobin, Myosin light chain I


**INTRODUCTION**

Rhabdomyolysis is defined as a clinical laboratory syndrome resulting from skeletal muscle injury with release of muscle all contents into the circulation. There are many reports that measurements of creatine phosphokinase (CPK) or myoglobin for the determination of rhabdomyolysis in cases with diabetic ketoacidosis. Whereas there have been no reports about rhabdomyolysis in case of prolonged hypoglycemic coma, as far as we know.

In this report, we measured the values of CPK, CPK isozyme, myoglobin, and cardiac myosin light chain I for the detection of rhabdomyolysis. After metabolic control and gradual decrease of creatine kinase levels, they presented a progressive improvement of renal function. We emphasize nontraumatic rhabdomyolysis as a poorly recognized pathogenic factor for acute renal failure in diabetic ketoacidosis and suggest that a better understanding of its mechanisms should be understood. Moreover, we would like to emphasize the early application of measurements of cardiac enzymes to the diagnosis of rhabdomyolysis.

**CASE REPORTS**

We studied 3 patients who visited hospital due to hypoglycemic coma, deteriorated, and admitted to hospital. The criterion of rhabdomyolysis in this study was a serum creatine kinase concentration greater than 500 IU/L during the hospitalization (normal range ≤ 85 IU/L). Patients were excluded from analysis if evidence existed for a myocardial infarction or cerebral vascular accident unless the laboratory documented the presence of only MM isozymes of CPK.

**Case 1**

The patient was an 81-year-old woman who had been pointed to be diabetes mellitus for 20 years and when the hypoglycemic coma emerged, she had been taken orally a hypoglycemic drug and alpha-glucosidase inhibitor. Consciousness disorder appeared from the day before the admission. It healed by taking sugar solution, but her consciousness was coma from the next morning of admission, blood pressure (BP) was 210mmHg in systolic and 92mmHg in diastolic phase, and blood sugar (BS) was 45mg/dl in hypoglycemic coma (Fig. 1). She was admitted because her BS recovery was not efficient by outpatient allowance. Although drip infusion was administered, her BS was still 27mg/dl. Inspection report on admission was as follows: GOT 25mU/ml, GPT 12mU/ml, LDH 171mU/ml, ALP 107mU/ml, CPK 108mU/ml, BUN 39mg/dl, Cr 2.4mg/dl, Na 142mEq/l, K 5.3mEq/l, Cl 107mEq/l, Ca 9.1mEq/dl. The levels of CPK rose up to 108mU/ml and 117mU/ml on day 1 and 2, respectively. From the day 3, it decreased gradually. The values of myoglobin and cardiac myosin light chain I increased up to 120ng/ml and 6.6ng/ml (fig. 2). As for CPK isozyme, 97.8% of those were CPK-MM.
Case 2

The patient was 55-year-old woman who had been pointed to be DM for 15 years. When the hypoglycemic coma emerged, she had injected insulin subcutaneously. The day of admission, she injected insulin in the morning, had a breakfast and then got out to gather mountain plants with her husband in the afternoon. But she lay unconscious 1 hour after exercise. She came to emergency visit in the evening. She was in coma, BP was 160mmHg in systolic and 100mmHg in diastolic, her BS was 41mg/dl (Fig. 1). General prostration was also found and she was admitted to our hospital. Inspection report on admission was as follows; GOT 36mU/ml, GPT 34mU/ml, LDH 362mU/ml, ALP 91mU/ml, CPK 682mU/ml, BUN 21mg/dl, Cr 0.8mg/dl, Na 139mEq/l, K 3.5mEq/l, Cl 103mEq/l, Ca 87mg/dl. The levels of CPK rose up to 682mU/ml and 265mU/ml on day 1 and 2 after hypoglycemic coma, respectively. The value of myoglobin rose up to 190ng/ml on day 2 (Fig. 2). The circulating level of cardiac myosin light chain I significantly rose up to 11ng/ml and 5.1ng/ml on day 1 and 2. Those cardiac enzymes became within normal limit within several days. As for CPK isozyme, all of that was MM.

Case 3

The patient was 52-year-old man who had been pointed to be diabetes mellitus for 17 years. When the hypoglycemic coma emerged, he had been taken oral hypoglycemic agents. His renal function was remarkably deteriorated, and pointed the need of insulin injection and hemodialysis. Somnolence and dysarthria were observed from the day before admission and he recovered temporarily by taking a meal. But the
next day, somnolence and dysarthria were also observed, and he was admitted to our hospital in the early morning. On the admission, he opened his eyes, verbal contact was intact and hemiplegia was present. His BP was 180mmHg/96mmHg, and BS was 30mg/dl (Fig. 1). He recovered conscious and hemiplegia by taking sugar solution, and he was admitted to our hospital because he had renal dysfunction. Inspection report on admission was as follows; GOT 21mU/ml, GPT 15mU/ml, LDH 220mU/ml, ALP 112mU/ml, CPK 552mU/ml, BUN 54mg/dl, Cr 9.6mg/dl, Na 143mEq/ml, K 3.1mEq/l, Cl 115mEq/l, Ca 7.5mg/dl. The value of CPK rose up to 552mU/ml and 357mU/ml on day 1 and 2 after hypoglycemic coma. From the day the CPK gradually decreased but over normal limit. The value of myoglobin increased to more than 500ng/ml on day 1 (Fig. 2). The value of cardiac myosin light chain I was 4.2ng/ml. As for CPK isozyme, 97.8% and 96.8% of those were CPK-MM on day 1 and 8 after hypoglycemic coma. From the day 1 (Fig. 2). The value of cardiac myosin light chain I rose up to 19ng/ml and 17ng/ml on day 1 and 3, respectively. On day 8 after coma, myosin light chain I was 4.2ng/ml. As for CPK isozyme, 97.8% and 96.8% of those were CPK-MM on day 1 and 8 after coma, respectively.

**DISCUSSION**

We experienced three diabetic patients, who had hypoglycemia with rhabdomyolysis. It was first described by Waters and Beall that rhabdomyolysis was associated with crush injuries during the second world war. And then it has been recognized as the cause of cases of acute renal failure. The three most common presumed pathogenic disorders causing rhabdomyolysis in patients were alcohol abuse, muscle compression and generalized seizures. Meanwhile, metabolic derangement can also cause rhabdomyolysis. It is known that in case of diabetic ketoacidosis, rhabdomyolysis often appears and the circulating levels of CPK and myoglobin increase. Among them, Kodama et al. announced that the cause of rhabdomyolysis is advanced dehydration and severe distal circulation dysfunction. 

CPK is the most sensitive marker of muscle injury and is readily determined in most hospital laboratories. Cardiac myosin light chain is a kind of structural protein that flow out to the blood when cardiac muscle have some damage, and reflects the degree of the myocardial damage at the acute myocardial infarction. Furthermore, myosin light chain is a good marker to evaluate the effect of reperfusion therapy. Myosin light chain is classified into 3 parts by physiological function and binding site with heavy chain, and further according to the kind of muscle, the types of light chain is different. Cardiac myosin light chain I is referred to show cross-reaction with 17.6% of all skeletal muscle myosin light chain, since cardiac type of myosin light chain exists in both myocardium and red muscle of skeletal muscle. Consequently, it is reasonable that ventricular myosin light chain I rises without the increase of CPK, the increase of myosin light chain I depends on skeletal muscle destruction rather than myocardial disorder. Since the red muscle fiber of skeletal muscle contains myoglobin and mitochondria more than white muscle fiber, this structure favors aerobic metabolism, accompany with several capillary muscles.

Hypoglycemia and hypoglycemic coma are sometimes found on usual practice, among patients using insulin or taking oral hypoglycemic drug. However, most patients recover by outpatient allowance, and few patients admit. Patients tending to become hypoglycemic coma are almost long-time patient, and suffer diabetic complication such as diabetic nephropathy, retinopathy, and neuropathy. Consequently, if these patients are taken with hypoglycemic coma, we should consider about rhabdomyolysis. As a practical matter, patients suffer from severe renal failure is considered to show significant elevation of CPK, myoglobin, and cardiac myosin light chain I.

About the possibility that prolonged hypoglycemia directly causes the elevation of CPK, no literature was found. But Libby et al. observed the circulating CPK was not elevated in dogs with insulin induced hypoglycemia after coronary occlusion. Only a literature states that minute-long hypoglycemia does not cause the elevation of CPK. Meanwhile the elevation of CPK is observed on the condition that muscle cannot chronically consume glucose such as III, V or VII type of glycogen storage disease. If CPK elevation is observed on hypoglycemic coma, we must determine if convulsion exists first. If it exist, the cause of the elevation of CPK is convulsion. None of 3 patients is said to go into convulsion, but their family did not always look at them. So the possibility of going into convulsion is not able to deny. Next, in case 2, she climbed a quite steep mountain earlier than hypoglycemic coma. In other words exercise might cause the elevation of CPK. As a practical matter, many papers showed that hard exercise causes the elevation of CPK and myoglobin. Kosano et al. reported the change of CPK and myosin light chain I by long time exercise. Our case showed the higher value of myosin light chain I than CPK.

In patients with severe renal failure receiving hemodialysis, CPK, myoglobin, and cardiac myosin light chain are described to remarkably elevate. In case 3, the value of circulating creatinine is 9.6mg/dl on
admission. Obviously we must consider about the effect of renal failure, however, the level of circulating creatinine hardly changed. On the contrary, CPK and cardiac myosin light chain I were remarkably reduced in the short term. So it is difficult to explain the decrease of cardiac enzymes by the effect of renal failure.

The common complications of these 3 cases are hypertension and that GOP and GPT are in normal limit. Serum K was 3.1 to 5.3mEq/l, and serum Ca was 7.5 to 9.1mEq/l, showing no certain tendency. Furthermore, there is a question that the cause of the elevation of CPK and myoglobin is whether the accentuation of membrane permeability or dissolution of muscle fiber. The value of cardiac myosin light chain I did not much more elevate compared to CPK and myoglobin. Consequently, the cause is thought to be the accentuation of membrane permeability14). Rhabdomyolysis may be complicated with diabetic patients more frequently than non-diabetic ones.

In conclusion, the stress of long time hypoglycemia may trigger the release of CPK, myoglobin, and cardiac myosin light chain I. Physicians who care diabetic patients should be cautious to the rhabdomyolysis accompanying with hypoglycemic coma.

REFERENCES