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Carnitine Palmitoyltransferase II Deficiency, a Rare Cause of Rhabdomyolysis: A Case Report

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ABSTRACT

Introduction: Muscle weakness and rhabdomyolysis have a wide range of differential diagnosis. In many situations, they are induced by seizure, trauma, drugs, and toxins. They could also be due to inflammatory or metabolic myopathies. Identifying the exact cause is crucial and sometimes challenging.

Case Presentation: A 23-year-old man was admitted to our hospital with muscle weakness, fatigue, dyspnea, and dark urine, all preceded by flu-like symptoms, myalgia, and fever. Due to reduced muscle strength, dark urine, elevated serum creatine kinase, and serum creatinine, he was diagnosed with rhabdomyolysis and acute kidney injury. Muscle biopsy was performed three years before for the patient, due to a history of similar episodes and exercise intolerance. Because of recurrent episodes of muscle weakness and rhabdomyolysis along with the negative muscle biopsy for inflammatory myopathies, we suspected metabolic myopathy as a cause. Therefore, metabolic screening was performed for the patient, and he was diagnosed with metabolic myopathy known as Carnitine Palmitoyltransferase II (CPT II) deficiency.

Conclusion: In patients with recurrent rhabdomyolysis, we should consider inherited myopathies, especially carnitine palmitoyltransferase II deficiency and glycogen storage disease type V (McArdle disease) as likely causes. CPT II deficiency is regarded as a preventable cause of recurrent rhabdomyolysis. Therefore, by early diagnosis of this disorder we could prevent recurrent episodes of rhabdomyolysis and ultimately avoid life-threatening complications like acute kidney injury.

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Introduction

Muscle weakness and rhabdomyolysis have a wide range of differential diagnosis. In many situations, they are induced by seizure, trauma, drugs, and toxins [1]. They could also be due to inflammatory or metabolic myopathies. Identifying the exact cause is crucial and sometimes challenging.

Idiopathic inflammatory myopathies are a group of autoimmune disorders that present with symmetrical proximal muscle weakness and inflammatory infiltrates on muscle biopsy. A combination of clinical, serological, and pathological data is mandatory to diagnose and manage this type of myopathies [2].

Metabolic myopathies are genetic disorders of glycogen, lipid, and mitochondrial metabolism that result in impaired energy production. The three main categories include fatty acid oxidation defects, glycogen storage diseases, and mitochondrial myopathies [3, 4].

Case Presentation

A 23-year-old man was admitted to our hospital with muscle weakness, fatigue, dyspnea, and dark urine. He had a history of flu-like symptoms, myalgia, and fever started a few days before admission. He had no history of seizure, trauma, or medication usage. On his physical examinations, his muscle strength in upper and lower extremities was 3 out of 5. There was no neurological deficit or skin involvement. The initial laboratory findings were as follows: blood urea nitrogen of 30 mg/dL, plasma creatinine of 1.7mg/dL, plasma creatine kinase of 376 mg/dL, plasma lactate dehydrogenase of 9923 mg/dL. Urine analysis showed bloody urine that was positive for protein, blood, bilirubin, urobilinogen, and negative for red blood cells. Table 1 presents his complete lab test results. The patient was diagnosed with rhabdomyolysis and acute kidney injury. The patient was not a candidate for emergent hemodialysis, so conservative management started with intravenous fluids.

His past medical history was positive for Arnold-Chiari malformation, which was resolved with surgery two years ago. He had previous episodes presenting similar symptoms, exercise intolerance, and rhabdomyolysis since three years ago. Due to his muscle weakness, he was worked up for polymyositis, and muscle biopsy showed no significant histochemical pathologic findings other than some moth-eaten fibers with no necrosis, regeneration, and inflammation, which were inconclusive. His family medical history was negative, except for consanguineous marriage in his parents.

In the days following admission, the patient's symptoms, including his muscle weakness reduced, and his muscle strength improved up to four out of five. In the fourth day of hospitalization, his muscle weakness completely resolved, and muscle strength examinations became normal. Upon further detailed investigations we discovered that he had done prolonged exercise (dancing) the night before coming to the hospital.

During hospitalization, his plasma creatinine increased up to 3mg/dL, hence he underwent kidney biopsy due to lack of reduction in serum creatinine level despite full hydration. The biopsy showed mild tubulointerstitial nephritis. Ultrasonography of kidneys showed normal size kidneys without any evidence of abnormal echo and structure. Echocardiography, ventilation-perfusion scan, and spirometry were also performed due to his dyspnea and blood pressure rise during his hospitalization. Ventilation-perfusion scan was negative for pulmonary thromboembolism; the echocardiography showed Left Ventricle Ejection Fraction (LVEF) of 45% with normal valves, and the spirometry was inconclusive due to the patient's lack of cooperation.

According to recurrent episodes of rhabdomyolysis and muscle strength recovery without any treatment other than hydration, metabolic myopathies were suspected; thus, Electromyography (EMG), Nerve Conduction Velocity (NCV), and metabolic screening test with carnitine profile were performed for him. EMG and NCV results were within the normal range. Metabolic investigations showed deficiencies of carnitine translocase, carnitine palmitoyltransferase I and II. The patient was diagnosed with a genetic disorder, carnitine palmitoyltransferase deficiency type II.

The patient was discharged from the hospital with stable hemodynamic and good condition. We recommended him to avoid heavy activities to prevent recurrent episodes of rhabdomyolysis and prescribed him carnitine supplement. On his follow up visit, he was in good condition, and his serum creatinine decreased to 1.2mg/dL.

Discussion

Rhabdomyolysis is a critical and potentially life-threatening event. The patients with rhabdomyolysis present with myalgia, muscle weakness, myoglobinuria, and elevated serum creatine kinase [1, 5]. Rhabdomyolysis may result in serious complications, including acute kidney

Table 1. The patient's laboratory test results during hospitalization

Date Lab Tests	February 24	February 25	March 8	March 9	March 10	March 11	March 12	March 13	March 14
White Blood Cell Count (cells/µL)	15500	16900	-	-	5100	-	4200	4600	6800
Red Blood Cell Count (g/dL)	19.7	19.9	-	-	13.6	-	14.8	14.3	14.7
Hematocrit (%)	52.7	52.5	-	-	37.7	-	40.9	41.5	40.4
Platelet (cells/µL)	141000	114000	-	-	227000	-	274000	275000	268000
Sodium (mEq/L)	131	132	139	142	138	135	136	136	135
Potassium (mEq/L)	6.9	4.7	3.9	4.4	4.3	4	4.6	4.1	4.8
Urea (mg/dL)	60	65	100	80	56	40	37	37	36
Creatinine (mg/dL)	1.7	1.4	3	2.3	2.6	2.5	2.6	2.6	2.5
Calcium (mg/dL)	7.6	-	8.8	8.5	8.4	8.8	9	8.8	9.7
Phosphorus (mg/dL)	5	-	5.7	4.8	4.8	5	4.6	4.3	5.5
Magnesium (mg/dL)	2.8	-	2.4	2.5	2.2	2.3	2.2	2	2.1
Uric Acid	-	-	8.1	7.2		4.8	4.7	5.4	5.4
Creatinine Kinase	376	-	-	-	-	-	-	-	-
Lactate Dehydrogenase	9923	-	-	-	-	-	-	-	-
PH	7.2	-	7.46	7.37		7.36	7.34		-
HCO3 (mmol/L)	18.8	-	34.2	30.5		25.3	24.9		-
PCO2 (mmHg)	47.4	-	48.1	51.9		44.4	44.8		-
PT (Prothrombin Time) (Sec)	12.9	-	-	-	12.6	-	-	11.1	-
PTT (Partial Thromboplastin Time) (Sec)	25	-	-	-	30	-	-	25	-
INR (International Normalized Ratio)	1.16	-	-	-	1.03	-	-	1.03	-
Albumin (g/dL)	4	-	-	-	-	-	-	-	-
Urine analysis	Bloody Protein: 4+ Blood: 2+	-	Yellow Blood: 1+ RBC: 6-8	-	-	-	Yellow Blood: 1+ RBC: 6-8	-	Normal
ANA (Antinuclear Antibody) Anti-ds DNA (Anti-double strand DNA) CH50 (50% Hemolytic Complement) HBS Ag (Hepatitis B Surface Antigen) Anti HCV Ab (Anti Hepatitis C Virus Antibody) HIV Ab, Ag (Human Immunodeficiency Virus Antibody, Antigen)	Negative	-	-	-	-	-	-	-	-

injury and respiratory failure [6]. Thus, early diagnosis, treatment, and also prevention of rhabdomyolysis are of prime importance. Most of the patients experience only one episode of rhabdomyolysis triggered by seizure, medications, or trauma; however, several patients may experience recurrent episodes [1].

The two important differential diagnoses for recurrent muscle weakness and rhabdomyolysis are glycogen storage disease type V (McArdle disease) and Carnitine Palmitoyltransferase II (CPT II) deficiency [7-12]. It is crucial to differentiate between these groups of metabolic myopathies according to the history and physical examination of the patient. McArdle disease is typically induced by short duration and high intensity exercise, while CPT II deficiency is triggered by prolonged and mild exercise, fasting, cold, infections, and anesthesia [1].

In our case, the patient has no history of trauma, medication usage, or seizure. He also noted that he had recurrent episodes of muscle weakness after exercise. His history of exercise-induced muscle weakness and rhabdomyolysis, as well as a previous negative muscle biopsy for inflammatory myopathies, led us to consider metabolic myopathies (McArdle disease and CPT II deficiency) as the probable causes. The patient had mild but prolonged exercise (dancing), and on his physical examinations, no muscle spasm or contracture was found; thus, we considered CPT II deficiency as the first probable diagnosis. The metabolic screening with carnitine profile was performed, and the patient was found to have CPT II deficiency.

CPT II deficiency is an autosomal recessive long-chain fatty-acid oxidation disorder. There are three clinical phenotypes: The first and second types are lethal forms with multisystemic involvement, which manifest in neonatal and infancy, respectively. The third and most common form is the myopathic type that can present from infancy to adulthood. It is characterized by recurrent episodes of muscle pain, weakness, and rhabdomyolysis, triggered by exercise, infection, fasting, stress, and cold. The adult-onset CPT II deficiency can be preventable by many methods. Patients diagnosed with CPT II deficiency should avoid infections, general anesthesia, and changes in body temperature, fasting, stress, exercise, and drugs like ibuprofen, diazepam, and valproic acid [8, 13-15]. A low-fat diet enriched with medium-chain triglycerides and carnitine, carnitine supplementation, and medium-chain fatty acid triheptanoin may be useful and should be considered in the prevention and treatment of adult-onset CPT II deficiency [16].

Conclusion

In patients with recurrent rhabdomyolysis, we should always consider inherited myopathies (carnitine palmitoyltransferase II deficiency and McArdle disease) as essential causes. CPT II deficiency is regarded as a preventable cause of recurrent rhabdomyolysis. By early diagnosis of this disorder, we could prevent recurrent episodes of rhabdomyolysis and ultimately avoid life-threatening complications like acute kidney injury.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article.

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Conflict of interest

The authors declared no conflict of interest.

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