CASE REPORT

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Rhabdomyolysis Associated with Concomitant Use of Fusidic Acid and Statin

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ABSTRACT Rhabdomyolysis is a complex condition resulting from muscle necrosis, where the breakdown products within the cells are released into circulation, causing systemic effects. This condition can be identified through the use of muscle damage markers. A 70-year-old male patient presented to the emergency department with complaints of muscle pain, weakness, and difficulty walking persisting for 3 days. Laboratory values showed increased transaminase levels and severely elevated creatine kinase levels. The patient, who had a history of surgery due to lumbar spinal stenosis, was using fusidic acid 3 months due to post-surgical wound infection. And he was also taking statin drugs for atherosclerotic heart disease. In cases of rhabdomyolysis, it should be remembered that laboratory values may significantly exceed literature averages. Adequate fluid resuscitation and urine alkalinization are crucial for preserving kidney function. Additionally, a meticulous evaluation of the patient's drug history and consideration of possible drug-drug interactions are essential.

Keywords: Rhabdomyolysis; myoglobinuria; statin; fusidic acid; creatine kinase

Rhabdomyolysis (RML) occurs as a result of the release of breakdown products from muscle necrosis into the circulation. Muscle pain, weakness, and dark urine comprise the classical triad. Fluid-electrolyte imbalance, kidney and liver damage, compartment syndrome, and widespread intravascular coagulation can manifest as complications of RML.[1] Through the presentation of our patient who presented to the emergency department with complaints of muscle pain, weakness, and difficulty walking, the aim is to emphasize the etiology, treatment, and follow-up of RML.

CASE REPORT

A 70-year-old male patient presented to the emergency department with complaints of muscle pain, weakness, and difficulty walking for 3 days. His medical history included coronary artery disease and lumbar spinal stenosis, for which he underwent surgery. Vital signs were stable. Respiratory and cardiovascular examinations were unremarkable. Abdomen was soft, with no organomegaly detected. Pretibial edema was noted as ++/++. No rash was observed on the skin. His urine was dark brown in colour (Figure 1). Laboratory findings were as follows: aspartate aminotransferase (AST): 1,787 U/L, alanine aminotransferase (ALT): 523 U/L, creatine kinase (CK): 70,742 U/L, C-reactive protein (CRP): 87 mg/dL, sedimentation rate: 95 mm/hr, lactate dehydrogenase (LDH): 2,345 U/L, glucose: 173 mg/dL, urea: 47 mg/dL, creatinine: 0.72 mg/dL, leukocytes: 7,800 µL, neutrophils: 6,500 µL, lymphocytes: 900 µL, hemoglobin: 9.6 g/dL, mean corpuscular volume: 68 fl, platelets: 346,000 µL. Urine analysis revealed pH: 7.0, negative for leukocytes, erythrocytes, ketones, nitrites, and protein.

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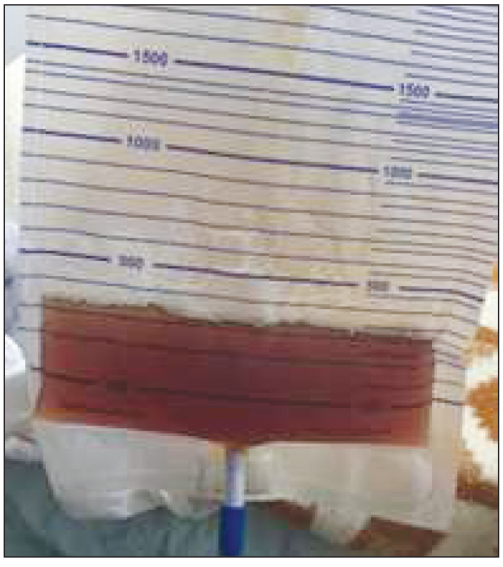

FIGURE 1: The appearance of myoglobinuric urine upon presentation

The patient was admitted with a preliminary diagnosis of RML. He was using fusidic acid for wound infection following surgery, in addition to statin therapy for concomitant coronary artery disease. Both fusidic acid and statin therapy were discontinued. Normal saline support was planned at a rate of 200 mL/hour. Grade 1 hepatosteatosis was detected on abdominal ultrasonography. Serological tests were negative.

The patient had a history of elevated CK levels (5,600 U/L) one week prior, and his laboratory values continued to rise during the first 48-72 hours. Considering the possibility of an underlying muscle disease, tests for inflammatory myopathy-associated autoantibodies were requested. Compartment syndrome was ruled out based on physical examination findings. The prolonged elevation of CK was attributed to ongoing muscle damage. CK, AST, ALT, LDH, and CRP levels started to decrease after the 3rd day (Table 1). Urine colour began to lighten (Figure 2). The patient's muscle pain improved, and he started walking on the 10th day. There were no developments of renal damage or hyperkalemia during follow-up. In motor conduction studies, tibial and peroneal motor conduction amplitudes are low, conduction velocity and distal latency are normal. Electromyography (EMG) revealed low-amplitude motor unit potentials with early interference patterns, particularly in proximal muscles such as the vastus lateralis and rectus femoris. Prominent fibrillation and positive sharp waves were noted at rest, which could be seen in inflammatory myopathic conditions and acute denervation. These findings were considered consistent with ongoing muscle fiber instability. Magnetic resonance imaging of the thigh area showed heterogeneity in the adductor muscle group attached to the inferior pubic ramus, with suggested correlation to myositis.

The patient underwent tests for inflammatory myopathy, with the suspicion that they could explain the clinical picture. Antinuclear antibodies, Anti-Jo-1, Anti-Mi-2, Anti-Ro/SSA, anti-La/SSB, anti-Sm, anti-ribonucleoprotein antibodies, anti-PM-Scl, and anti-Ku antibodies were all found to be negative.

During post-discharge outpatient follow-up, the patient's CK, AST, ALT, LDH, CRP, and sedimentation levels were normal. Motor nerve conduction studies for median, ulnar, tibial, and peroneal nerves were normal. The amplitudes of the examined sensory nerves were low, while nerve conduction velocities were normal. No myopathic discharges were detected on needle EMG.

Gastrointestinal system screening for anemia revealed internal hemorrhoids. No other pathology was detected.

TABLE 1: Laboratory monitoring

	1st day	2nd day	3rd day	4th day	5th day	6th day	7th day
CK	70,742	94,198	132,011	44,300	24,719	8,130	2,938
AST	1,787	1,834	2,341	1,898	916	409	210
ALT	523	550	772	755	636	491	362
LDH	2,345	2,053	3,373	2,241	926	560	382
CRP	87	95	120	84	68	37	17

CK: Creatine kinase (U/L); AST: Aspartate aminotransferase (U/L); ALT: Alanine aminotransferase (U/L); LDH: Lactate dehydrogenase (U/L); CRP: C-reactive protein (mg/L)

FIGURE 2: : The colour of urine after hydration

DISCUSSION

The characteristic triad of complaints in RML is muscle pain, weakness, and dark urine.[11] Although an elevation of 5 times the upper limit (~1,000 U/L) is considered diagnostic of RML, there is no definitive cut-off value. Additionally, CK levels have a wide spectrum.

It is crucial to recognize that laboratory values in cases of RML may exceed the averages reported in the literature. Elevated markers such as high CK levels, increased LDH, and rising myoglobin levels can reflect the severity of muscle breakdown. Elevated CK levels may persist despite treatment, indicating ongoing muscle damage or the presence of an underlying muscle disease. Severe elevation in CK levels may also be a sign of compartment syndrome development.[10]

Therefore, regular and meticulous laboratory monitoring should form the cornerstone of appropriate treatment and follow-up in patients diagnosed with RML.[8,9]

Appropriate fluid support and urine alkalinization play a critical role in preserving kidney function.[2] Fluid support can reduce myoglobinuria, thereby preventing kidney damage, and urine alkalinization has been shown to reduce tubular epithelial deposition of myoglobin, thereby preventing nephrogenic systemic fibrosis.[6,7]

The patient's medication history is important for identifying RML risk factors and evaluating potential triggers. Drug interactions such as those involving fusidic acid and statins should be considered.[3-5]

In recent years, fusidic acid, commonly used in the treatment of methicillin-resistant *Staphylococcus aureus* infections, has been increasingly associated with muscle toxicity, especially when combined with statin therapy. This drug interaction has been well-documented in pharmacovigilance databases and clinical reports. A pivotal case series analyzing 75 patients from the French Pharmacovigilance Database revealed a 22% mortality rate due to RML caused by fusidic acid and statin co-administration.[12] Similarly, an analysis of 182 cases from the World Health Organization global database reported a 24% mortality rate, emphasizing the seriousness of this interaction.[14]

The underlying mechanism is believed to involve the inhibition of hepatic uptake transporters—notably OATP1B1 and OATP1B3—by fusidic acid, which leads to elevated plasma levels of statins and a heightened risk of myotoxicity. This was experimentally demonstrated by Eng et al., who showed that fusidic acid significantly impairs the hepatic clearance of statins like rosuvastatin, thereby increasing systemic exposure.[13]

Furthermore, a population-based cohort study by Rönnqvist et al. found that the risk of statin-associated myopathy increased nearly sevenfold when fusidic acid was co-administered.[15] Despite the widespread use of statins in cardiovascular disease management, clinical awareness of this dangerous interaction remains limited. Given the consistent reports of high mortality and the pharmacological basis of this toxicity, temporary discontinuation of statins should be strongly considered when fusidic acid treatment is necessary.

The management of RML cases should not be limited to symptom control alone. It should also include regular monitoring of laboratory values and preservation of kidney function. This comprehensive approach provides a comprehensive treatment strategy to best preserve the patient's health.

Idiopathic inflammatory myopathies were suspected in the differential diagnosis, and non-charac-

teristic findings were observed on EMG. In particular, tibial and peroneal motor conduction amplitudes were found to be decreased in the initial evaluation. These reductions may reflect transient muscle fiber injury due to acute RML or early denervation associated with toxic myopathy from fusidic acid-statin interaction. Similar EMG findings (including reduced compound muscle action potential amplitudes) have been documented in patients with statin-associated RML, with recovery observed upon drug discontinuation and clinical improvement.[16] Upon improvement of the clinical picture, repeated EMG did not show these findings. It is known that muscle biopsy is utilized in cases where diagnosis is challenging. However, due to the favorable clinical course, muscle biopsy was not deemed necessary.

The presented case demonstrates that laboratory values in RML cases can exceed the averages reported in the literature. Appropriate fluid support and urine alkalinization play a critical role in preserving kidney function. Close monitoring of urine output and fluid support helped in the regression of myositis damage. The emphasis on the potential for RML due to the combination of fusidic acid and statins highlights the need for clinical professionals to pay closer attention to medication history and to be more cautious when prescribing these drugs.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

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