CLINICAL VIGNETTE

Rhabdomyolysis: An Unfortunate Complication of Intermittent Fasting

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Case Presentation

A 36-year-old woman with obesity (BMI 35) and no other significant medical history presented with a 3-day history of headache, nausea, lightheadedness and one day of bilateral leg pain and weakness so severe she required assistance walking. She denied recent fevers, chills, rashes, vomiting, and diarrhea. She reported no recent trauma, injuries, episodes of syncope, nor infections. She works as a nurse in a medical clinic and had no known recent COVID-19 exposures. She had no chest pain nor shortness of breath at rest or with exercise. She denied dysuria, hematuria, and dark colored urine. She denied prior history of muscle weakness nor family history of myopathies. She was not taking any new medications, illicit drugs or supplements. She had recently decreased her alcohol consumption to 2 servings per week. Her medications included fish oil, probiotics, and a multivitamin.

The patient had begun a new weight loss plan in the past month. She walked on the treadmill one hour daily for five days per week. She fasted except for one meal daily in the early afternoon. Her diet included primarily vegetables and lean proteins totaling approximately 500 kcal daily. On the day of presentation at 12pm, she had only consumed 8 oz of black coffee and no water.

On examination, she had orthostatic hypotension with blood pressure decreasing from 134/89 (supine) to 113/74 (standing) and heart rate increasing from 89 (supine) to 105 (standing). She was unable to ambulate across the room without assistance due to thigh pain. Bilateral quadriceps strength was decreased (4+/5). Strength in bilateral upper extremities was intact as was sensation in all four extremities.

To further evaluate her acute symptoms of headache, nausea, myalgias and weakness laboratory testing was ordered. These included negative nasal PCR testing for COVID19. Laboratory tests showed elevated creatine kinase (CK) and liver enzyme (see Table 1). Her complete blood panel and comprehensive metabolic panel were normal, and urinalysis was negative for both hemoglobin and myoglobin. She was admitted to her local hospital for treatment of acute rhabdomyolysis. Her CK and liver function tests improved over the next two days with IV fluid hydration, improvement in caloric intake, and cessation of exercise. Her renal function remained normal and her symptoms slowly improved. After discharge, the patient continued increased fluid and food intake. At 4-month follow up, she had complete resolution of symptoms.

Date	**Time**	**Creatine Kinase (38-282 U/L)**	**Creatinine (0.6-1.3mg/dL)**	**AST (13-47 U/L)**	**ALT (37-113 U/L)**
Day 1 (outpatient)	11:01	6818	0.62	240	63
Day 1 (hospital)	23:30	5277	0.84	235	76
Day 2 (hospital)	5:12	4661			
Day 2 (hospital)	20:20	3892			
Day 3 (hospital)	6:46	3194	0.66	163	73
Day 6 (outpatient)	16:15	263	0.65	81	94
Day 125 (outpatient)	16:41	66	0.71	23	19

Discussion

Intermittent fasting strategies are a current popular health and fitness trend. The diet focuses on a daily or weekly pattern of cycling between fixed time periods of eating and fasting instead of restricting particular foods. Common intermittent fasting methods such as time restricted feeding (TRF) involve fasting for 16 hours per 24-hour period - often involving skipping breakfast and limiting food intake to an 8-hour period of the day. By reducing the overall caloric intake, participants can lose weight as long as they do not overcompensate by eating more calories during the 8-hour eating period.[1,2] Intermittent fasting appears to be comparable to continuous energy restriction strategies for short term weight loss in overweight and obese adults.

The physiologic benefits of fasting include:

1. Increased human growth hormone to help with fat loss and muscle gain.[3]
2. Decreased insulin levels, allowing fat cells to release stored sugar to be used as energy and improving insulin sensitivity.[4]
3. Increased release of the fat-burning hormone nor-epinephrine which may increase metabolic rate.[5]

In this patient, extreme caloric restriction led to rhabdomyolysis. Rhabdomyolysis has not been well-described in patients on intermittent fasting weight loss strategies.[6,7] However, rhabdomyolysis has been described in case reports of patients with altered eating patterns due to bulimia nervosa.

Signs and symptoms of rhabdomyolysis range from mildly symptomatic muscle aches to potentially lethal multi-organ damage causing cardiac arrest, acute kidney injury, and compartment syndrome. Classically, rhabdomyolysis presents with myalgias, muscle weakness, and muscle swelling that develops over hours to days due to necrosis of striated muscle from a number of causes. Some patients may also report dark colored urine caused by excreted myoglobin from muscle breakdown. Rhabdomyolysis is commonly caused by:

1. Trauma or muscle compression; such as crush injuries or prolonged immobilization
2. Non-traumatic exertion; such as malignant hyperthermia or prolonged exercise
3. Non-traumatic non-exertion; such as from infections, toxins (such as carbon monoxide poisoning, snake/insect venom), alcohol, and drugs (including statins, colchicine, fibric acid derivatives, neuroleptics, and stimulants), and rare metabolic myopathies.

The diagnosis is commonly established by significant elevation of serum CK levels or by the appearance of myoglobin in the urine. Urinalysis, which is readily available in the office setting, can suggest myoglobinuria when heme is detected but there are no observed red blood cells.[8] Urinalysis showing negative or trace amounts of blood can reliably predict the absence of clinically significant myoglobinuria, preventing the need for expensive urine myoglobin testing. Commonly, serum CK will rise 2-12 hours after onset of muscle injury, peak at 3-5 days, and then decline over 6-10 days.[9] Early complications of rhabdomyolysis include fluid and electrolyte abnormalities such as hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia which can occur before or even in the absence of kidney or liver failure.[10] In the setting of severe electrolyte abnormalities, patients may develop cardiac arrhythmias as an early complication of rhabdomyolysis. Late complications of rhabdomyolysis typically include acute renal failure and disseminated intravascular coagulation.

Treatment for rhabdomyolysis focuses on early and aggressive fluid resuscitation to avoid intratubular cast formation and to maintain renal perfusion to prevent ischemic injury. Patients should continue with intravenous hydration until plasma CK values are stable and decreasing. To avoid fluid overload or pulmonary edema, patients' volume status and urine output should be monitored carefully during hospitalization.[11] Familial, metabolic, and inflammatory myopathies are rare, but should be considered in patients with recurrent episodes of rhabdomyolysis.

Conclusion

Intermittent fasting strategies can be an effective method for patients to lose weight. However, as in this patient, combining severe calorie restriction with intermittent fasting can cause dangerous complications like rhabdomyolysis. Diagnosis of rhabdomyolysis should be made early with aggressive fluid hydration to avoid significant end organ complications. Guidance from medical providers for patients wishing to lose weight by intermittent fasting on timing, amount of caloric restriction, and monitoring can prevent severe complications such as rhabdomyolysis.

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