Case Report



# Unusually high creatine kinase in a case of rhabdomyolysis without acute kidney injury: a case report

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**Background:** While rhabdomyolysis frequently leads to hospital admissions, typically following trauma, recurrent occurrences are relatively rare, accounting for just 10% of cases. For young patients experiencing repetitive episodes without an apparent cause, a comprehensive investigation into the possible etiologies is crucial. Recognizing the atypical nature of recurrent rhabdomyolysis is crucial and a thorough workup encompassing evaluations for potential endocrine, inflammatory, and metabolic etiologies is recommended. Additionally, acute kidney injury is a common complication with severe rhabdomyolysis, hence early recognition and intervention is crucial.

**Case Description:** Herein we present a case of a 30-year-old young African American male patient with recurrent rhabdomyolysis with the highest ever reported creatine kinase (CK) to our knowledge. A notable aspect of this case is the surprising absence of acute kidney injury, despite the severity of CK elevation. We also delve into the extensive workup done for rhabdomyolysis of unclear etiology.

**Conclusions:** Our case underscores the importance of looking into non-traumatic factors behind recurrent rhabdomyolysis, especially in young patients. We also stress the significance of early detection and intervention, showcasing the potential to prevent acute kidney injury even in the presence of markedly elevated CK levels. Timely recognition and appropriate management can prove instrumental in mitigating the severity of complications associated with rhabdomyolysis.

**Keywords:** Rhabdomyolysis; case report; highest ever; creatine kinase (CK)

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## Introduction

Rhabdomyolysis results from breakdown of skeletal muscle, and its diagnosis can be made based on clinical symptoms and diagnosis is confirmed by creatine kinase (CK) levels 5–10 times the upper limit of normal (1,2). Etiologies of rhabdomyolysis are classified as either traumatic or non-traumatic secondary to drugs, toxins, infections, and metabolic, endocrine, and electrolyte disturbances, as well as myopathies. Some cases are also multifactorial. Recurrent episodes of rhabdomyolysis or very high levels of CK are very rare and should raise concerns of other etiologies. We present a case of a young male patient with recurrent rhabdomyolysis with the highest ever reported CK levels so far. With this case report we aim to educate readers about etiology, diagnosis and management of rhabdomyolysis. We present this article in accordance with the CARE reporting

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checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-23-172/rc).

## Case presentation

A 30-year-old African American male came to our emergency department complaining of body pains, generalized weakness, and discolored urine for the last 4 days. He reportedly was walking to his car 4 days prior when he slipped on ice and fell onto his buttocks. The patient reports having been mostly taking bed rest at home since the fall and reported pain in both of his legs and both of his arms. His past medical history was significant for rhabdomyolysis with no obvious etiology 2 years ago, obesity with a body mass index (BMI) of 38 kg/m$^2$, and mild intermittent asthma. Unfortunately, no records were available in regards to his prior episode. The patient denied any alcohol or smoking history but did report occasional recreational marijuana and vaping. Family history was unremarkable. The patient denied any home medications. The physical exam was grossly benign except for diffuse muscle soreness. Vitals showed a heart rate of 89 beats/min, respirations of 18 breaths/min, blood pressure of 145/89 mmHg, and afebrile. Laboratory studies done showed normal hemoglobin and mildly elevated white blood cell count (WBC) 11,200/mm$^3$. Chemistry showed significantly elevated critical CK of 275,685 U/L. The renal function panel was normal with potassium 4.2 mEq/L, blood urea nitrogen (BUN)/creatinine (Cr) 11/0.8 mg/dL. Transaminases were elevated at aspartate transaminase (AST) 779 U/L, alanine transaminase (ALT) 275 U/L. CK myoglobin binding (MB) isoenzyme was mildly elevated at 17.8 ng/mL. Urinalysis showed evidence of large blood but negative red blood cell (RBC) or WBC. Extensive imaging with computed tomography of chest, abdomen pelvis were unremarkable. The urine drug screen was positive for tetrahydrocannabinol (THC). He was given 2 L of normal saline (NS) bolusand after that started on maintenance fluids with NS at 200 mL/h. On hospital day 2, CK continued to trend up to 293,162 U/L. Given uptrending CK, the rate of fluids was increased to NS at 250 mL/h. Surprisingly, renal function was still normal with BUN/Cr 11/0.7 mg/dL. Transaminases uptrended to AST 1,385/ALT 785 U/L. Patient had a urine output of 7.2 L on this day.

On hospital day 3, the patient became more tachycardic with worsening muscle aches. Labs showed an extremely high critical CK of 4,570,630 U/L. Chemistry also showed evidence of hyperkalemia with K 6.2 mEq/L. Transaminases continued to trend up with AST 1,474/ALT 570 U/L. Renal function BUN/Cr 11/0.6 remained normal. Temporizing measures were initiated for hyperkalemia with albuterol nebulization, Lokelma, and bicarbonate. The patient was started on bicarbonate based fluids with D5 at 100 mL/h and NS was continued at 100 mL/h. A dose of furosemide was also given to facilitate kaliuresis. Further workup was sent namely thyroid stimulating hormone (TSH), anti-Jo antibody, antinuclear antibody, aldolase, anti-Smith, inflammatory myositis panel, protein electrophoresis, and hemoglobinopathy evaluation. Inflammatory markers like C-reactive protein were mildly elevated at 4.5 mg/dL (normal <1 mg/dL) and the sedimentation rate was normal. Orthopedics also evaluated the patient and compartment syndrome was ruled out.

On hospital day 4, the patient started to feel better. CK trended down to 529,693 U/L. Renal function remained normal. He was maintained on continuous intravenous hydration with NS at 250 mL/h and bicarbonate fluid was discontinued given metabolic alkalosis. By hospital days 5 and 6, the patient continued to improve and CK improved to 37,098 U/L at discharge. His renal function remained normal and transaminases improved to AST/ALT 451/438 U/L at discharge (*Table 1*).

All work up including TSH, anti-Jo antibody, antinuclear antibody, aldolase, anti-Smith, hemoglobinopathy evaluation, myositis panel, HMG-CoA reductase and protein electrophoresis came back negative. *Table 2* summarizes the extensive pertinent testing done on the patient.

The patient had an outpatient follow-up with neurology

### Highlight box

**Key findings**

- Here we report extreme elevations of creatine kinase (CK) that can be seen in patients.

**What is known and what is new?**

- Recurrent rhabdomyolysis is rare and seen in only 10% of cases. High levels of CK are seen usually in metabolic myopathies.
- This manuscript reports on the highest ever reported CK level so far and educates readers about possible etiologies of recurrent rhabdomyolysis.

**What is the implication, and what should change now?**

- In cases of recurrent rhabdomyolysis, further investigations into rare causes should be undertaken and a multidisciplinary approach among specialties is needed to figure out the cause and guide appropriate management of patients.

**Table 1** Electrolyte values during clinical course

| Electrolyte | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 |
|---|---|---|---|---|---|---|
| Na (mmol/L) | 138 | 137 | 136 | 134 | 133 | 134 |
| K (mmol/L) | 4.2 | 5.1 | 6.2 | 5.6 | 4.8 | 4.4 |
| Cl (mmol/L) | 99 | 101 | 100 | 100 | 101 | 104 |
| $CO_2$ (mmol/L) | 32 | 29 | 27 | 31 | 32 | 29 |
| BUN (mg/dL) | 11 | 11 | 11 | 14 | 16 | 14 |
| Cr (mg/dL) | 0.9 | 0.7 | 0.7 | 0.6 | 0.6 | 0.6 |
| ALT (U/L) | 157 | 375 | 580 | 636 | 541 | 438 |
| AST (U/L) | 779 | 1,389 | 1,474 | 1,204 | 670 | 451 |
| CK (U/L) | 275,685 | 293,162 | 4,570,630 | 529,693 | 98,977 | 37,098 |

Na, sodium; K, potassium; Cl, chloride; BUN, blood urea nitrogen; Cr, creatinine; ALT, alanine transaminase; AST, aspartate transaminase; CK, creatine kinase.

and nephrology in 2 weeks and his CK had improved to 355 U/L. Outpatient testing such as electromyography, and nerve studies were also unremarkable. Given this was a recurrent episode with extreme elevations of CK unexplained by mild trauma, he was referred to a neuromuscular specialist for further evaluation with a muscle biopsy, after which the patient was lost to follow up.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent for publication of this case report was not obtained from the patient or the relatives after all possible attempts were made.

## Discussion

Rhabdomyolysis is a medical condition characterized by muscle necrosis and the release of intracellular muscle constituents into the circulation. The disruption of skeletal muscle integrity leads to the direct release of intracellular muscle components, including myoglobin, CK, and electrolytes into the bloodstream (1,2). While most cases of rhabdomyolysis are secondary to trauma, other causes like extreme exertion, drugs, infections, and toxins also play a role. Inherited metabolic or mitochondrial disorder, sickle cell trait, and muscular dystrophies also are known to cause rhabdomyolysis in about 10% of cases. Only about 11% of cases, like our case, are recurrent and these are usually associated with metabolic muscle conditions (3). Although it can occur in all age groups and sexes, it is most commonly seen in African American males (4).

The clinical presentation is extremely variable ranging from mild symptoms to life-threatening complications. The classic triad of symptoms includes myalgia, weakness, and red or brown urine, which is seen in only 10% of cases (1,5,6). Certain life-threatening complications associated with extreme elevations in CK, electrolyte imbalances, acute renal failure, cardiac arrhythmias, acute liver injury, and coagulopathy have also been reported (7,8).

Once high suspicion of rhabdomyolysis is clinically suspected, diagnosis is mainly based on serum CK levels. Serum CK levels at the presentation of rhabdomyolysis are usually at least five times the upper limit of normal, ranging from 1,500 to 100,000 U/L with levels peaking in 24 to 72 h. CK levels as high as seen in our patient is very uncommon and to our knowledge, our case with CK level of 4.5 million U/L represents the highest ever reported in literature (9). Although most cases of initial episode are likely secondary to specific etiology, in patients with recurrent rhabdomyolysis like seen in our patient further investigation into other causes such as metabolic myopathies, inflammatory or congenital myopathies, muscular dystrophies should be pursued. Metabolic myopathies such as mitochondrial disorders, fatty acid oxidation disorders, glycogen metabolism disorders have been known to cause recurrent non traumatic rhabdomyolysis (10,11). Inflammatory myopathies such as polymyositis have been rarely reported to cause rhabdomyolysis. This was ruled out to be the cause in

**Table 2** Laboratory and investigative work up

| Test | Value/result | Reference range/result |
|---|---|---|
| CK | 4,570,630 | <500 U/L |
| AST | 1640 | <45 U/L |
| ALT | 636 | <45 U/L |
| Urine drug screen | THC positive | Negative |
| TSH | 2 | 0.5–5 mU/L |
| ANA | Negative | Negative |
| Anti-Jo Ab | Negative | Negative |
| Aldolase | Negative | Negative |
| Anti-Smith Ab | Negative | Negative |
| SPEP | Normal pattern | Normal |
| HIV 1/2 Ab and P24 Ag | Negative | Negative |
| SAE1 Ab | Negative | Negative |
| NXP2 Ab | Negative | Negative |
| MDA5 (CADM-140) Ab | Negative | Negative |
| TIF-1 gamma Ab | Negative | Negative |
| Mi-2 antibody | Negative | Negative |
| P155/140 antibody | Negative | Negative |
| PL-12 (alanyl-tRNA synthetase) antibody | Negative | Negative |
| PL-7 (threohyl-tRNA synthetase) antibody | Negative | Negative |
| OJ (isoleucyl-tRNA synthetase) antibody | Negative | Negative |
| SRP Ab | Negative | Negative |
| EJ (glycyl-tRNA synthetase) antibody | Negative | Negative |
| PM-Sc1 antibody, ID | Negative | Negative |
| SSA 52 (Ro) (ENA) antibody IgG | 0 | 0–40 AU/mL |
| SSA 60 (Ro) (ENA) antibody IgG | 0 | 0–40 AU/mL |
| Fibrillarin (U3 RNP) Ab, IgG | Negative | Negative |
| RNP (U1) (ENA) antibody IgG | 2 | 0–19 U |
| HMG-CoA reductase Ab | <3 | 0–19 U/L |

CK, creatine kinase; AST, aspartate transaminase; ALT, alanine transaminase; TSH, thyroid stimulating hormone; ANA, antinuclear antibody; SPEP, serum protein electrophoresis; HIV, human immunodeficiency virus; SAE1, SUMO activating enzyme; NXP2, nuclear matrix protein-2; TIF, transcriptional intermediary factor; SRP, signal recognition particle; ENA, extractable nuclear antigen; IgG, immunoglobulin G; RNP, ribonucleic protein; HMG, β-hydroxy β-methylglutaryl.

our patient given that his antibody testing was negative. There have also been case reports mentioning the role of synthetic cannabinoids with rhabdomyolysis, although pathophysiology of this is still poorly understood (12). In our patient, although ground level fall triggered the cascade there is likely an undiagnosed secondary cause that contributed to such extreme elevation of CK. While preliminary testing was reassuring, if followed upon, muscle biopsy would have given more diagnostic information.

The crux of the management of rhabdomyolysis relies

on aggressive intravenous hydration. Isotonic saline is the fluid of choice for resuscitation and in some severe cases, fluid rates of 1 to 2 L/h are given to counteract and prevent kidney injury while maintaining adequate urine output of at least 200 to 300 mL/h (7,13). Electrolyte abnormalities like hyperkalemia and hypocalcemia can manifest with or without acute kidney injury and hence close attention is to be paid to electrolyte abnormalities and corrective measures should be taken to prevent the risk of fatal arrhythmias. Other treatment measures include bicarbonate to alkalinize the urine to pH >6.5, for the purpose of minimizing the toxic effects of myoglobin on the renal tubules, preventing cast formation, and decreasing the risk for hyperkalemia (7,13). Although theoretically, it makes sense, some studies have shown that alkalinization with bicarbonate did not improve clinical outcomes (14). Some other measures like mannitol have not shown any established benefit, hence their use remains controversial (15). In about 33% of cases acute renal failure develops due to rhabdomyolysis and some patients need dialysis to manage hyperkalemia, volume overload, and acidemia. This emphasizes that overall prognosis remains favorable with almost all patients recovering renal function on long-term follow-up (13,16).

## Conclusions

We describe a case of a young male with recurrent rhabdomyolysis with highest ever reported level of CK. Recurrent cases of rhabdomyolysis are very uncommon and especially in young people, should raise concerns about the need for further investigation into metabolic causes. Our case also highlights that despite such high levels of CK, early recognition and intervention might avert renal failure.

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## Footnote

*Reporting Checklist:* The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-23-172/rc

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent for publication of this case report was not obtained from the patient or the relatives after all possible attempts were made.



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