Exertional rhabdomyolysis in a 21-year-old healthy man resulting from lower extremity training
A case report
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Abstract
Rationale: The incidence of exercise-induced rhabdomyolysis is increasing in the healthy general population. Rhabdomyolysis can lead to the life-threatening systemic complications of acute kidney injury (AKI), compartment syndrome, and disseminated intravascular coagulopathy.

Patient concerns: A 21-year-old man had bilateral lower limb pain and soreness, dark brown urine after lower extremity training. Laboratory results showed that creatinine kinase (CK) and myoglobin (Mb) increased to 140,500 IU/L and 8632 mg/L, respectively, with elevated liver enzymes, Scr, and proteinuria.

Diagnoses: Exercise-induced rhabdomyolysis with AKI.

Interventions: The patient was hospitalized and treated with vigorous hydration and sodium bicarbonate for 6 days.

Outcomes: After 6 days of treatment, the patient had a significant decrease in the CK and Mb levels. His renal function returned to normal. His laboratory tests had completely normalized during 2-week follow-up.

Lessons: Exercise-induced rhabdomyolysis can cause serious complications such as AKI. Delayed diagnosis can be critical, so timely manner should be taken to achieve a favorable prognosis.

Abbreviations: AKI = acute kidney injury, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BUN = blood urea nitrogen, CK = creatinine kinase, ER = exertional rhabdomyolysis, KDIGO = Kidney Disease: Improving Global Outcomes, LDH = lactate dehydrogenase, Mb = myoglobin, Scr = serum creatinine.

Keywords: acute kidney injury, creatinine kinase, exercise, myoglobinuria, rhabdomyolysis

1. Introduction
Exertional rhabdomyolysis (ER) has been increasingly identified in the healthy general population after exercise.[1,2] Rhabdomyolysis is a syndrome caused by disruption of skeleton muscle with the release of muscle tissue content into the circulation that can lead to the life-threatening systemic complications of acute kidney injury (AKI), compartment syndrome, and disseminated intravascular coagulopathy.[3] Here we present a case of exercise-induced rhabdomyolysis caused by a lower extremity training.

1.1. Consent statement
Written informed consent was obtained from the patient for the publication of this study.

2. Case report
A 21-year-old man presented to the emergency department with a 2-day history of lower extremity pain and soreness and 1 day of gross hematuria. He reported that the pain began the 2nd day after he went to the gym doing lower extremity exercise training. The day prior to his presentation, the patient developed gross hematuria, without back pain and fever. He reported no history of previous medical conditions or medications.

Physical examination showed muscle tenderness but no edema. Urinalysis showed protein 2+ and urine occult blood +/−. Laboratory work-up demonstrated a creatinine kinase (CK) of 140,500 IU/L, alanine aminotransferase (ALT) of 316 IU/L, aspartate aminotransferase (AST) of 1319 IU/L, and myoglobin (Mb) of 8632 μg/L. His blood urea nitrogen (BUN) and serum creatinine (Scr) were 7.38 mmol/L and 94 μmol/L, respectively.
Based on his markedly elevated CK, myalgia, and myoglobinuria, he was diagnosed and hospitalized with exercise-induced rhabdomyolysis. After treatment with vigorous hydration and sodium bicarbonate, his pain improved and his CK, ALT, AST, Mb, BUN, and Scr decreased to 124,600 IU/L, 1594.0 IU/L, 1279 IU/L, 6062 μg/L, 1594.0 IU/L, and 94 μmol/L, respectively. His urine color returned to normal without urinalysis abnormalities. After 6 days of hydration, his CK, ALT, AST, Mb, and lactate dehydrogenase (LDH) decreased to 2750 IU/L, 129 IU/L, 291 IU/L, 84.4 μg/L, and 291 IU/L (Table 1), respectively. So the patient was discharged.

By 2 weeks postdischarge, his Scr was 70 μmol/L. His CK level, liver enzymes and other laboratory tests had normalized.

### 3. Discussion

Lower extremity exercise training in gyms requires strenuous leg movements such as kick-back, squats, and prone leg bending with body-building apparatus. The heat in the gyms, dehydration, and the excessive muscle activities increase susceptibility to rhabdomyolysis. Moreover, recurrence to rhabdomyolysis is thought to be related to specific genetic defects and more than 60 monogenic genes have been found associated with rhabdomyolysis. Increasing cases have reported ER caused by conditioning requiring dialysis. Meanwhile, reports showed low-intensity exercise and low-load high-repetition resistance exercise can also cause ER.

Our patient had a presentation of elevated CK of 140,500 IU/L, myoglobinuria, and myalgia. Clinically, a triad of symptoms was described including myalgia, weakness, and dark brown urine. Although there is not a clearly consistent cutoff threshold of CK levels, a concentration 5 times the upper limit of normal, ranging from 1500 to over 100,000 IU/L is used by most clinicians. Detection of Mb in urine may be absent in 25% to 30% of patients with rhabdomyolysis.[10] A consensus criteria of rhabdomyolysis definition is needed to support clinical studies and diagnosis.

The Scr of our patient was 94 μmol/L at admission, and decreased to a baseline value between 60 and 70 μmol/L during hospitalization and follow-up visits. Initially, his Scr increased by 0.3 mg/dL (≥26.5 μmol/L) within 48 hours. According to Kidney Disease: Improving Global Outcomes, any item that conforms to the following can be defined as AKI: Scr increased by 0.3 mg/dL (≥26.5 μmol/L) within 48 hours; Scr increased to 1.5 times over the baseline value, which is known or presumed to have occurred within the previous 7 days; urine output 0.5 mL/ (kg·h) for 6 hours. Based on the guideline, he had AKI. He was diagnosed 2 days after exercise and treated with early vigorous hydration, and did not develop subsequent severe kidney injury. Although the Scr value can be within the normal range of the general, the baseline value is different for each individual and possible AKI may be overlooked. Thus, timely diagnosis of AKI is necessary.

The AKI is rarely reported in young ER patients without underlying renal diseases. Alpers and Jones found that the lower incidence of AKI in patients with ER vs rhabdomyolysis from other causes in a retrospective cohort.[15] In addition, Kenney et al reported that patients with exertional rhabdomyolysis were younger, generally healthier, had higher elevation of CK than those who developed rhabdomyolysis from other etiologies, but had a lower incidence of severe complications.[16] But some cases progressed rapidly and violently. Bhalla and Dick-Perez reported a man with rhabdomyolysis and evidence of renal insufficiency, developed bilateral compartment syndrome and renal failure requiring dialysis.[17] Therefore, it is important to diagnose AKI timely.

Some studies reported the predictors of AKI and mortality in patients with rhabdomyolysis. It is reported that initial Scr levels were associated with progression to AKI and mortality at 30 days.[18] A study indicated that the value of serum Mb was a more sensitive marker of acute myoglobinuric kidney injury and considered 15 to 20 mg/L as an appropriate Mb cutoff.[19] A retrospective study suggested that the Mb/CK ratio more than 0.2 was related to the increased development of AKI.[20] Some studies found that serum CK levels had been regarded as a predictor of AKI and mortality in severe rhabdomyolysis with elevated serum CK levels of more than 10,000 IU/L.[21,22] However, some conflicted results were reported. Clarkson et al presented data on measures of renal function (potassium, osmolality, BUN, Scr, phosphorus, and uric acid) in 203 subjects who performed 50 maximal eccentric contractions of the elbow flexor muscles.[23] None of these participants developed AKI, though 111 of them had CK values at 4 days postexercise >2000 IU/L, and 51 had values >10,000 IU/L. Another retrospective cohort analysis showed that CK levels did not predict mortality.[18] McMahon et al proposed a risk prediction score to identify high-risk patients with rhabdomyolysis.[24] The risk prediction score model

### Table 1

| Variable               | Hospital admission | Day 1 | Day 3 | Day 6 | Follow-up (3 wks after admission) |
|------------------------|--------------------|-------|-------|-------|----------------------------------|
| CK, IU/L               | 124,600            | 75,866| 27,624| 2750  | 220.4                            |
| CK-MB, IU/L            | n/a                | 572.5 | 187.5 | 40.2  | 13.1                             |
| AST, IU/L              | 1279               | 950   | 521   | 97    | 19                                |
| ALT, IU/L              | 304                | 296   | 235   | 129   | 14                                |
| Mb, IU/L               | 6062               | 1594.0| 226.4 | 84.4  | <21                              |
| LDH, IU/L              | n/a                | 1304.5| 513.9 | 291   | 205.7                            |
| α-HBDH, IU/L           | n/a                | 533   | 357   | n/a   | n/a                              |
| Scr, μmol/L            | 94                 | 57.2  | 61.9  | 71    | 70                               |
| BUN, mmol/L            | 7.38               | 4.99  | 3.73  | 3.1   | 3.45                             |

ALT = alanine aminotransferase; AST = aspartate transferase; BUN = blood urea nitrogen; CK = creatine kinase; CK-MB = creatine kinase-MB; Mb = myoglobin; LDH = lactate dehydrogenase; α-HBDH = α-hydroxybutyrate dehydrogenase; Scr = serum creatinine.
included age, sex, race, cause of rhabdomyolysis, and independent risk factors such as initial Scr, CK >4000 IU/L, calcium, bicarbonate, phosphate, and inpatient laboratory work-up. It was validated among more than 2000 patients with rhabdomyolysis and turned out that a score of <5 was of low risk of renal replacement therapy or in-hospital mortality, whereas a score of >10 was of high risk. It needs more studies to confirm these.

Clinically, major management of rhabdomyolysis is fluid therapy with NaCl 0.9%.[13] It relieves the obstruction of Mb to the necrotic regions.[27] Some studies presented cases of regenerate after a few weeks and grow well with good circulation balance disorder.[13] These were confirmed very useful in our patient. Our patient was treated with early vigorous replacement with saline and bicarbonate to improve urine pH and urine output, and received favorable prognosis.

The recurrence of well-healed young patients with ER is low.[15] It has been shown that destructed muscle fibers regenerate after a few weeks and grow well with good circulation to the necrotic regions.[27] Some studies presented cases of recrudescence, especially in patients with underlying sickle cell trait, malignant hyperthermia, carnitine palmitoyltransferase II deficiency, or other hereditary diseases.[28,29] To enable patients return to sport without recurring ER, Schleich et al outlined a 4-phase progressive program implemented to successfully return each athlete to sport after an ER diagnosis requiring hospitalization.[30] Athletes returned to activities of daily living for 2 weeks after discharge in phase I and were not allowed to train until the CK level was below 5 times normal (1000 IU/L). Then, it moved forward to phases II to IV, in which recovery training began from low-load exercise to high-resistance training. No athletes in the program had a relapse of rhabdomyolysis and it suggested an individual regime based on patients’ improvement of physical and laboratory indicators.

Global exercise is a trend, and anyone participates in sports is likely to develop ER. To improve the prognosis of ER, we hope that there will be more authoritative consensus in diagnosis, more effective, and accurate prediction system of AKI.

Author contributions

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References

[1] Knaff EG, Hughes JA, Dimeski G, et al. Rhabdomyolysis: patterns, circumstances, and outcomes of patients presenting to the emergency department. Ochsner J 2018;18:215–21.
[2] Aalborg C, Rod-Larsen C, Leiro I, et al. An increase in the number of admitted patients with exercise-induced rhabdomyolysis. Tidsskr Nor Laegeforen 2016;136:1332–6.
[3] Furman J. When exercise causes exertional rhabdomyolysis. JAAPA 2015;28:38–43.
[4] Scako RS, Gardiner AR, Pitecaithy RD, et al. Rhabdomyolysis: a genetic perspective. Orphanet J Rare Dis 2015;10:31.
[5] Cutter TS, DeFilippis EM, Unterbrink ME, et al. Increasing incidence and unique clinical characteristics of spanning-induced rhabdomyolysis. Clin J Sport Med 2016;26:429–31.
[6] Meyer M, Sundaram S, Schaalfalter-Zoppoth I. Exertional and crossfit-induced rhabdomyolysis. Clin J Sport Med 2018;28:92–4.
[7] Gagliano M, Corona D, Guiffrida G, et al. Low-intensity body building exercise induced rhabdomyolysis: a case report. Cases J 2009;2:7.
[8] McKay BD, Yeo NM, Jenkins N, et al. Exertional rhabdomyolysis in a 21-year-old healthy woman: a case report. J Strength Cond Res 2017;31:1403–10.
[9] Shaprio ML, Baldea A, Luchette FA. Rhabdomyolysis in the intensive care unit. J Intensive Care Med 2012;27:335–42.
[10] Chavez LO, Leon M, Einav S, et al. Beyond muscle destruction: a systematic review of rhabdomyolysis for clinical practice. Crit Care 2016;20:135.
[11] Wakabayashi Y, Kikuno T, Ohwada T, et al. Rapid fall in blood myoglobin in massive rhabdomyolysis and acute renal failure. Intens Care Med 1994;20:109–12.
[12] Mellii G, Chaudhry V, Cornbluth DR. Rhabdomyolysis: an evaluation of 475 hospitalized patients. Medicine (Baltimore) 2005;84:377–85.
[13] Cervellin G, Comelli I, Lippi G. Rhabdomyolysis: historical background, clinical, diagnostic and therapeutic features. Clin Chim Lab Med 2010;48:749–56.
[14] Group AKI/Sector 2: AKI definition. Kidney Int Suppl 2012;2:19–36.
[15] Alpers JP, Jones LJ. Natural history of exertional rhabdomyolysis: a population-based analysis. Muscle Nerve 2010;42:487–91.
[16] Kenney K, Landau ME, Gonzalez RS, et al. Serum creatine kinase after exercise: drawing the line between physiological response and exertional rhabdomyolysis. Muscle Nerve 2012;45:356–62.
[17] Bhalla MC, Dick-Perez R. Exercise induced rhabdomyolysis with compartment syndrome and renal failure. Case Rep Emerg Med 2014;2014:735–820.
[18] Baeza-Trinidad R, Brea-Hernando A, Morera-Rodriguez S, et al. Creatinine as predictor value of mortality and acute kidney injury in rhabdomyolysis. Intern Med J 2015;45:1173–8.
[19] Premru V, Kovac J, Ponikvar R. Use of myoglobin as a marker and predictor in myoglobinuric acute kidney injury. Ther Apher Dial 2013;17:391–5.
[20] Vangstad M, Bjornas MA, Jacobsen D. Rhabdomyolysis: a 10-year retrospective study of patients treated in a medical department. Eur J Emerg Med 2019;26:199–204.
[21] de Meijer AR, Fikkers BG, de Keijzer MH, et al. Serum creatine kinase as predictor of clinical course in rhabdomyolysis: a 5-year intensive care survey. Intens Care Med 2005;31:1121–5.
[22] Safari S, Yousefzadeh M, Hashemi B, et al. The value of serum creatine kinase in predicting the risk of rhabdomyolysis-induced acute kidney injury: a systematic review and meta-analysis. Clin Exp Nephrol 2016;20:153–61.
[23] Clarkson PM, Kearns AK, Rouzier P, et al. Serum creatine kinase levels and renal function measures in muscular exercise damage. Med Sci Sport Exer 2006;38:623–7.
[24] McMahon GM, Zeng X, Waikar SS. A risk prediction score for kidney failure or mortality in rhabdomyolysis. JAMA Intern Med 2013;173:1821–8.
[25] Petropoulou M, Mikkelsen UK, Raadast T, et al. Leucocytes, cytokines and satellite cells: what role do they play in muscle damage and regeneration following eccentric exercise? Exerc Immunol Rev 2012;18:42–97.
[26] Hannah-Shmouni F, McLeod K, Sirs S. Recurrent exercise-induced rhabdomyolysis. CMAJ 2012;184:426–30.
[27] Samboughi N, Mungunsukh O, Ren M, et al. Pathogenic and rare deleterious variants in multiple genes suggest oligogenic inheritance in recurrent exertional rhabdomyolysis. Mol Genet Metab Rep 2018;16:76–81.
[28] Schleich K, Slayman T, West D, et al. Return to play after exertional rhabdomyolysis. J Athl Training 2016;51:406–9.