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Rhabdomyolysis in a Female Caucasian Adolescent Distance Runner: A Case Report

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We present the case of an adolescent female collegiate distance runner competing in her first 6K race. She presented with multiple systemic symptoms of dizziness, nausea, confusion, muscle cramping, and syncope. The patient was immediately treated for heat stroke and, on follow-up, reported to the AT with a headache, lack of appetite, muscle aches, and dark-colored urine. Rhabdomyolysis should be considered following a heat illness event with necessary treatments performed immediately. Symptomatic patients must be referred to a physician for evaluation and laboratory testing. We present recommendations for a supervised return-to-participation protocol and acclimatization to safely return to competition readiness. **Key Words:** heat illness, return-to-participation protocol, creatine kinase, myoglobinuria

Exertional rhabdomyolysis is a poorly understood clinical syndrome involving excessive muscular exertion and requiring a careful return-to-participation program. Rhabdomyolysis is a pathologic syndrome associated with the disintegration of striated muscle leading to the excretion of muscle contents, including creatine kinase (CK) and myoglobin, into the circulatory system.[1] This condition is caused by trauma, toxicological factors, certain drugs, infectious disease, metabolic abnormalities, extreme muscle exertion, and heat-related illnesses in which the body's core temperature elevates to dangerous levels.[1] Heat stroke is a common cause of exertional rhabdomyolysis in an athlete excessively exercising outdoors.[2]

Athletes competing outdoors with extreme exertion and in heat or humidity that present with a triad of symptoms such as diffuse myalgia, weakness, and brown, tea-colored urine (myoglobinuria)[3] might be suffering from rhabdomyolysis, and this should be considered in the differential diagnosis. This condition is diagnosed from serum CK elevations; however, disagreement[4,5] exists relating to diagnostic criteria for CK elevations in athletes. Normal resting CK reference levels for men are 30–260 U/L and 32–170 U/L for women,[6] although athletes may have higher CK because of greater muscle mass[4,7] and intensity of exercise.[8,9] Some authors agree that CK levels greater than 5–10 times the upper limit of normal (ULN) are necessary for diagnosing exertional rhabdomyolysis (ranging from 1,300–2,600 U/L for men and 850–1,700 U/L for women).[4–6] Within 2–12 hr following the muscle injury, CK levels begin to rise and peak at 24–72 hr before decreasing at a steady rate.[10] After surpassing the plasma protein binding capacity, myoglobin appears in the urine resulting in the classic diagnostic sign of myoglobinuria.[10] Additional factors such as electrolyte imbalances, severe muscle tenderness, and edema may present along with CK levels that may be greater than 50 times baseline in exercising individuals who develop rhabdomyolysis.[5,11] Accurate diagnosis of rhabdomyolysis is important as the syndrome can possibly lead to acute compartment syndrome and acute renal failure. In addition, limited return-to-play criteria and protocols exist in the literature for athletes who suffer from this syndrome.[6,12,13] The purpose of

this case report is to describe the unusual scenario in which exertional rhabdomyolysis developed in a female collegiate runner and to present a suggested protocol for a safe return to participation.

Case Report

History

A 17-year-old White female collegiate distance runner (height = 162 cm, weight = 57 kg) with a history of hypoglycemia and training participated in her first 6K race at a meet (timeline of symptom onset is provided in Table 1). The patient was recovering from an upper respiratory infection 2 weeks prior and was taking her prescribed antibiotic (ampicillin 500 mg q.d.). Approximately 1 week before the meet, the patient's diet had not returned to normal; she was limited to light, bland foods, and maintaining hydration had been a challenge due to diarrhea. She was reintroduced to team practices in the week leading up to race day but was struggling with dehydration and had dark (lemonade color) urine. She appeared healthy on race day, having taken in her normal precompetition hydration and prerace meal. Her liquids and electrolytes were monitored by the athletic trainer (AT). The environmental conditions were not excessively hot or humid during the race (73 °F, 58 % relative humidity), with moderate cloud coverage. On race day, the patient suffered a heat illness (possibly heat stroke) and was removed from the race so she could be evaluated in the medical tent.

Physical Exam Findings

Initial examination findings by the AT and emergency personnel included dizziness, nausea, headache, confusion, muscle cramping, muscle soreness, syncope, and moments of unexplained outbursts by the patient. She was immediately treated for exertional heat illness with cold-water immersion on site, monitored for systemic decline, and was allowed to return home with the team.

On follow-up at the AT clinic the next morning, the patient presented with fatigue, increased muscle soreness, muscle weakness, lack of appetite, dark-colored urine, and headache. The day after returning from the track meet, the university team physician examined the patient and referred her to University Health Services for severe dehydration, fatigue, and increased muscle soreness. The patient's signs and symptoms are listed in Table 2. Her vital signs were within normal limits and are presented in Table 3.

Table 1 Timeline of Heat Event and Exertional Rhabdomyolysis in a Female Distance Runner

Day	Timeline
Before race	
14 days	Patient suffers upper respiratory infection and is prescribed antibiotic treatment. Training is limited and diet is altered to include only light, bland foods due to nausea.
7 days	Patient still having difficulty maintaining normal diet regimen. Concern for dehydration due to diarrhea with dark urine (light-lemonade).
1 day	Patient able to eat prerace meal and participate in all premeet activities with team. Liquid and electrolyte intake monitored by athletic trainer (AT).
Race day	Patient suffers heat illness event during race and is removed from race before finishing. Treated for heat illness and monitored on return flight.
After race	
1 day	Patient reports to AT facility still suffering symptoms of fatigue/dehydration and complaining of increased muscle soreness. Evaluated by team physician, blood laboratory analysis confirmed (Table 3), and patient is diagnosed with rhabdomyolysis. Removed from all physical activities and monitored on outpatient basis.
4 days	Patient has follow-up blood analysis. Creatine kinase (CK) levels decreased, but still above normal range. Patient remains restricted from physical activities.
8 days	Follow-up blood analysis indicates CK decreased to within normal ranges. Physician clears patient return to play protocol supervised by AT.

Table 2 Symptoms for Differential Diagnosis[25] for Female Distance Runner

Condition	Differential Diagnosis Symptoms	Patient's Symptoms
Fatigue	Muscle weakness, muscle soreness, and grogginess	Muscle weakness, muscle soreness, lethargy
Dehydration	Headache, fatigue, muscle cramps, dark-yellow urine	Headache, fatigue, muscle cramps, dark urine
Heat exhaustion	Normal or elevated core body temperature, dizziness, lightheadedness, syncope, headache, nausea, diarrhea, decreased urine output, persistent muscle cramps, weakness	Dizziness, syncope, headache, nausea, muscle cramps, weakness
Heat Stroke	High core body temperature (> 40 °C), dizziness, confusion, irritability, hysteria, apathy, aggressiveness, weakness, tachycardia, hypotension, vomiting, diarrhea	Dizziness, confusion, irritability, delirium, weakness, dry skin
Rhabdomyolysis	Muscle soreness, muscle weakness, myoglobinuria, dark discolored urine, CK levels > 5× upper limit normal	Muscle soreness, muscle weakness, discolored urine (dark orange), CK = 1327 U/L

Abbreviation: CK = creatine kinase.

Table 3 Laboratory Analysis Results and Vital Signs of Female Distance Runner with Exertional Rhabdomyolysis

Test Normal Reference Range	1 Day Postincident	4 Days Postincident	8 Days Postincident
CK 38–176 U/L*	1,327	236	87
CK MB 0–5.0 ng/mL	30.6	8.3	2.8
Aspartate aminotransferase 11–32 U/L	203	66	26
Alanine aminotransferase 8–33 U/L	237	138	55
Myoglobin, 14–66 ng/mL	34	Not reported	Not reported
Urine color	Dark orange	Not reported	Not reported
Blood pressure, mmHg	134/66		
Pulse, bpm	55		
Intravenous fluids	3 L saline solution	3 L saline solution	1.5 L saline solution
Medications	Acetaminophen, 500 mg Ondansetron,** 4 mg		

Abbreviations: CK = creatine kinase; MB = myoglobin.

*According to laboratory norms.

**Prescribed for nausea and vomiting.

Differential Diagnosis

At the initial time of the incident the patient's differential diagnosis included fatigue, dehydration, heat exhaustion, and heat stroke. The AT documented the incident as a heat illness, probably heat stroke, although no core body temperature was recorded before cold-water immersion. Her initial blood test results were CK = 1,327 U/L, creatine kinase myoglobin (CK-MB) = 30.6 U/L, aspartate aminotransferase (AST) = 203 U/L, and alanine aminotransferase (ALT) = 237 U/L; laboratory results and normal ranges are presented in Table 2. At this time, the patient was diagnosed with rhabdomyolysis. The patient was treated on

an outpatient basis. A review of the patient's preparticipation physical examination by the AT staff and team physician indicated that she tested negative for sickle cell trait and had no other predisposing conditions, except the aforementioned infection.

Treatment

The patient was prescribed hydration, rest, and food as tolerated. Her timeline of symptom presentation and resolution is described in Table 1. The patient remained at University Health Services for outpatient treatment and monitoring but she was not hospitalized overnight. During her outpatient treatment at the University Health Services, she was administered three 1 L bags of intravenous (IV) saline, and blood analysis was initiated. She was also given acetaminophen for her headache as well as ondansetron to prevent nausea and vomiting. Laboratory results yielded normal complete blood count and myoglobin levels, but elevated CK-MM and CK-MB levels and liver function tests (ALT and AST). The patient's urine was discolored with a dark orange tint despite the IV treatments and abundant intake of fluids. Follow-up laboratory tests performed 3 days later revealed decreases in ALT, AST, CK, and CK-MB isoenzymes, but the levels were still above normal range (Table 3). All physical activity, except walking to class, was eliminated for 1 week and increased fluid intake was strongly encouraged. Eight days after the initial blood tests, the patient's CK levels had returned to normal ranges and she was allowed to begin a rehabilitation program.

Rehabilitation and Return to Participation

The initial return-to-participation protocol (Figure 1) included stationary cycling without resistance, slowly increasing to a 35-min duration at a moderate pace, with no signs or symptoms immediately following or appearing the following day. The patient rested the next day before beginning a running progression. However, after 6 days of incremental increases in running intensity and duration, she became symptomatic, complaining of muscle soreness and cramping in the

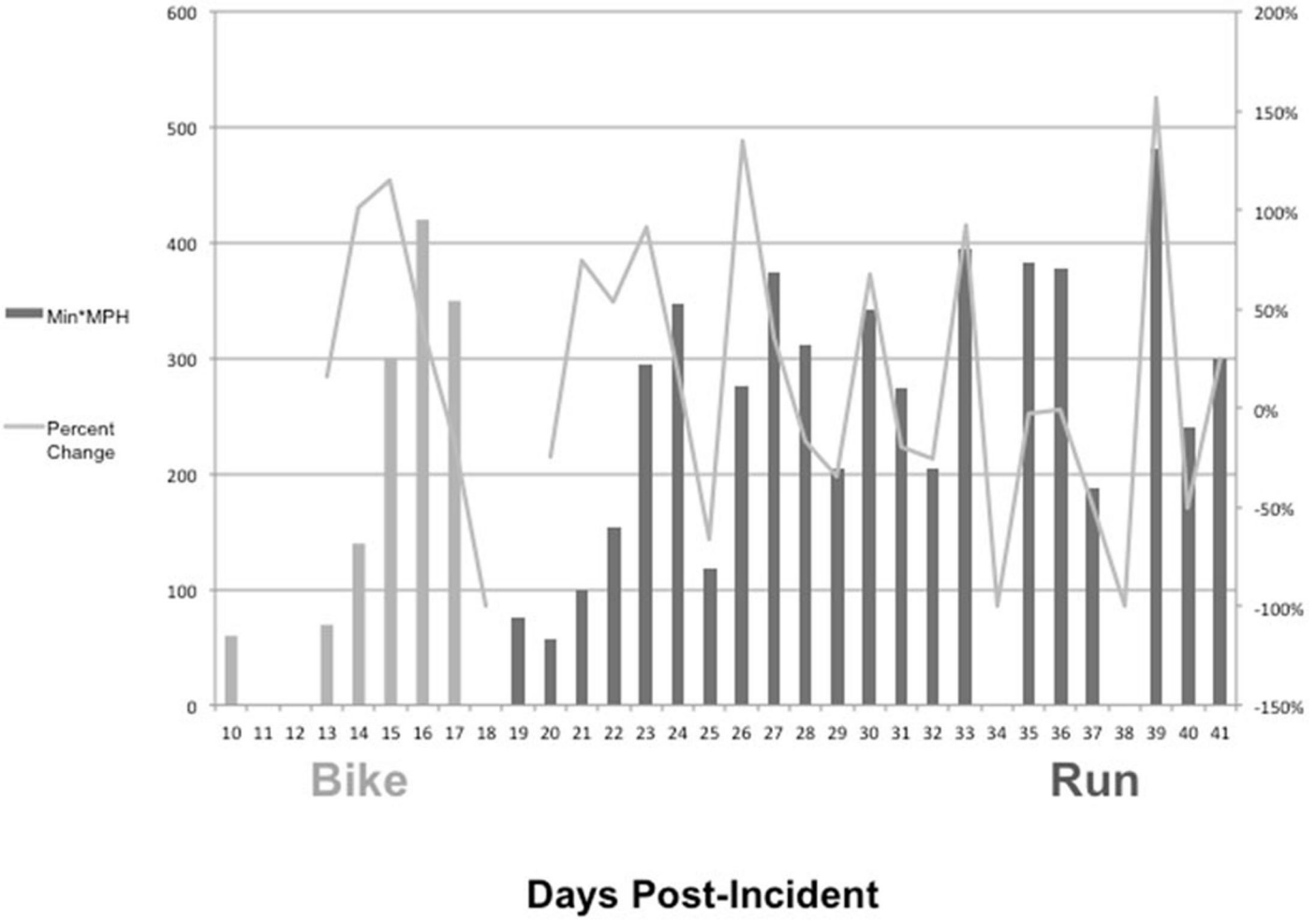

Figure 1 Return to running progression.

evening following the workout. The patient was eager and determined to return to full participation as soon as possible and she exercised with intensity and effort such that the workouts were excessively challenging. In retrospect, the patient's return-to-participation protocol should have been more gradually increased and included mandatory rest days as a safeguard to prevent recurrence of symptoms. A gradual increase of 10% intensity and duration with mandatory rest/active recovery days should be implemented every 2–3 days of the return-to-participation protocol (Table 4). If at any time symptoms recur, the patient should cease activity until asymptomatic and then resume at the previous asymptomatic level of intensity and duration.

Discussion

Rhabdomyolysis is a rare condition in younger populations,[14] although still a possibility with 37 of 165,000 adolescent patients diagnosed with rhabdomyolysis in a pediatric emergency department.[3] The clinical presentation of rhabdomyolysis may be subtle, but a high index of suspicion is prudent when assessing individuals with a triad of muscle weakness, muscle pain, and dark urine.[15] Exertional rhabdomyolysis may develop when an athlete exercises at an intensity and duration to which she is unaccustomed, usually at the urging of a coach or personal trainer.[15,16] Strenuous exercise, including distance running,[8,9,17] can result in damage to skeletal muscle cells. In most cases, this damage is resolved without consequence; however, profound damage, or exercising while heat stressed or dehydrated, can cause a release of muscle proteins into the blood, specifically CK and myoglobin. In high concentrations and under certain conditions (such as dehydration and heat stress), myoglobin can precipitate in the kidneys, thereby resulting in acute renal failure.[17] Fortunately, although long-distance running is a grueling physiological challenge, with races sometimes run in hot and humid weather, acute renal

Table 4 Recommended Return-to-Participation Protocol for Low-Risk Exertional Rhabdomyolysis Patients

Phase One
• Rest for 72 hr and encourage oral hydration
• Hydrate, sleep 8 hr/night consecutively, and remain in thermoneutral environment if the episode was related to heat injury
• Follow-up in 72 hr for repeat CK tests, when CK < 5× ULN, begin phase two
• If phase one exceeds 2 weeks, refer for expert consultation
Phase Two
• Begin aqua therapy, no strenuous exertion; if well tolerated (no recurrence of symptoms), progress the patient. With exacerbation of symptoms, stay with aqua therapy until asymptomatic.
• Begin stationary cycling at own pace/duration. As tolerated, increase intensity and duration daily but not to exceed 10%. Include rest days as needed.
• If no return of clinical symptoms, then begin progression to weight bearing exercise, walking, or jogging at own pace/duration as tolerated in thermoneutral environment.
• Increase intensity and duration of running no more than 10% each session; if well tolerated, progress to outdoor training avoiding midday ambient heat/humidity.
• Begin phase three when there is no significant muscle weakness, swelling, pain, or soreness and patient tolerates outdoor exercise in warm/humid conditions.
• If muscle pain persists > 4 weeks, consider specialty evaluation
Phase Three
• Gradually return to regular training; use caution when training with heavy weight lifting and environmental heat/humidity exposure
• Follow up with AT as needed.

Abbreviations: CK = creatine kinase; ULN = upper limit of normal; AT = athletic trainer.

Note. Based on O'Connor et al.[13]

failure is infrequent. From case reports, a high proportion of marathon runners who developed acute renal failure had taken analgesics, had a viral[14] or bacterial infection, or had a preexisting condition,[17] as was the case in this report. Clinicians should be aware of the increased risk of rhabdomyolysis with analgesic use and compromised prerace health status.

Rhabdomyolysis patients can be categorized as high-risk or low-risk.[13] According to the classification described by O'Connor et al,[13] this patient would be considered low-risk for recurrence of an episode of exertional rhabdomyolysis. To be considered a 'low-risk athlete, none of the high-risk conditions should exist (including sickle cell trait, previous history, complicated recovery, and serum CK ≥ 100,000 U/L). Further, the patient had several of the criteria for the low-risk category, including rapid clinical recovery and CK normalization after exercise restrictions. She was a sufficiently fit, well-trained athlete with a history of very intense training/exercise session. She had no personal or family history of rhabdomyolysis or previous reporting of debilitating exercise-induced muscle pain, cramps, or heat injury, but she did have a documented concomitant viral illness.[13] One recommended return-to-participation protocol for low-risk athletes is outlined in Table 4.

Return-to-play protocols following an episode of exertional rhabdomyolysis should be individually developed and implemented using caution and symptom recurrence as a guide. When heat illness is involved, as in this case, increasing the athlete's heat tolerance with gradual acclimatization from a thermo-neutral environment to warm, then to hot environments, along with gradual increases in intensity and duration of exercise, is advised. The recommended three-phase guideline adapted from O'Connor et al[13] is outlined in Table 4 for athletes considered low-risk for recurrence. Phase one of the protocol should begin with 8-hr of full sleep, hydration, and rest in an air-conditioned environment for at least 72 hr.[6] When CK has returned to normal, the athlete may begin phase two of the protocol. Each phase should include short- and long-term goals with specific criteria for progression. If the athlete experiences exacerbated symptoms during the rehabilitation protocol, activity should be reduced until asymptomatic. Once asymptomatic, the athlete may begin the progression at the previous intensity and duration, then gradually progress without exceeding a 10 % increase while adhering to basic progression principles.

Although the athlete may be eager to return to full activity as quickly as possible, the clinician has the responsibility to keep the patient's short- and long-term health as the primary objective in safely completing the return-to-participation protocol. For distance runners, athletes' progress should begin with aqua therapy, such as running in a pool,[12] followed by exercise on a stationary cycle without resistance in an air-conditioned location. This strategy will enable the athlete to improve tolerance to cardiovascular duration and intensity before progressing to jogging with full weight bearing. Intensity and duration of running should gradually be increased with exposure to a warm/humid environment (similar to competition conditions). Finally, in phase three, the athlete should gradually progress to running for a longer duration, then gradually increase intensity, building up to competition readiness.

This case is unusual for several reasons. Rhabdomyolysis is less common in women, although a few cases have been described in female collegiate rowers (lay media reports), swimmers,[15] and lacrosse players,[18] where the intensity of the training was greater than the individual's level of fitness. In addition, rhabdomyolysis is more likely to occur in group or team exercise in which athletes might be urged beyond their capabilities by a coach or authority figure. The patient in this case was a female long-distance runner, an individual sport athlete; however, she was new to the team and possibly was attempting to perform at a *heroic* level[19] to impress her coach or maintain her position on the track team. Reports of distance runners *trying to keep up with the pack*[20] illustrate the mental and emotional pressures on runners. Further complicating this case was the previous viral illness causing this patient to lose valuable training time before her first track meet as a college athlete. Viral and other systemic illnesses, particularly those causing seizures and violent, forceful muscle contractions, have caused rhabdomyolysis in sedentary patients[21,22] and after intense activity.[14,23] This patient had almost completely recovered from her illness and, after missing several days of training, participated in a strenuous running event, leading to her exertional rhabdomyolysis. Athletes recovering from illness and subsequently competing in distance running events leading to exertional rhabdomyolysis have been rarely reported in the literature.[21,22] Clinicians should be aware that acute rhabdomyolysis is uncommon,[22] but recent episodes of viral infection,

use of analgesics, detraining, dehydration, and heat stress can result in acute rhabdomyolysis.

Clinical Bottom Line

Rhabdomyolysis in distance runners is rare and may be attributed to a "perfect storm" when several exacerbating factors (heat stress, dehydration, nonsteroidal anti-inflammatory or other drug/analgesic use, and viral/bacterial infection)[17,24] come together to create poor patient outcomes. This case illustrates the necessity of rapidly and accurately recognizing, even in trained athletes, the presentation of rhabdomyolysis and to initiate the appropriate care to avoid complications. Although renal failure is a potentially serious complication of rhabdomyolysis, high levels of serum CK/myoglobin do not usually lead to renal failure,[15] which was fortunate in this case. These findings can be helpful in counseling and discussing the possible complications of rhabdomyolysis with patients and may be a useful tool in the clinical decision-making and rehabilitation process.[12,15] Patients should complete a supervised, individualized return-to-participation protocol that slowly reintroduces intensity and duration of exercise to safely return to competition readiness. ▮

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