Acute Rhabdomyolysis

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Lecture goals

› Identify the causes of rhabdomyolysis in an athletic population
› Differentiate between acute and delayed onset
Rhabdomyolysis
What is Rhabdomyolysis?

› Rhabdo: a word of Greek definition meaning rod

› Myolysis: destruction of muscle tissue

› Injured muscle releases a variety of proteins and enzymes into the blood stream causing a cascade of pathologic reactions
Exertional Rhabdomyolysis and Acute Renal Impairment -- New York City and Massachusetts, 1988

During the summer and fall of 1988, outbreaks of exertional rhabdomyolysis (the breakdown of muscle fiber) with renal impairment occurred in New York and Massachusetts among candidates or trainees for public safety positions. In each of the outbreaks, risk for illness was lower in persons who were accustomed to vigorous exercise; however, incidence rates, the relation to dehydration, and settings differed.

On June 14, 1988, the New York City (NYC) Department of Health was notified of one death and three hospitalizations among candidates for the NYC Fire Department (NYCFD) who had taken the NYCFD competitive physical fitness test within the previous 2 weeks. The fatality occurred in a young man with sickle cell trait who died because of uncontrollable hyperkalemia secondary to rhabdomyolysis within 6 hours of taking the fitness test; the three other hospitalized candidates had rhabdomyolysis and renal insufficiency.

The firefighter physical fitness test is usually administered during a 2- to 3-month period every 4 years to approximately 25,000-30,000 men and women who are aged 19-29 years and who have passed the NYCFD written employment examination. The test, which was given indoors in a temperature-controlled environment, required the candidates to wear a 20-lb vest and a 20-lb oxygen tank while consecutively performing 11 activities that simulate typical firefighter tasks. Completion of the test in less than or equal to 7 minutes earned a passing score, and completion in less than or equal to 4 minutes earned a special recognition.

In another outbreak in Massachusetts, 39 candidates were hospitalized within 24 hours of taking a similar physical fitness test, with one fatality. The median interval between the test and rhabdomyolysis was 60 minutes (range 5-180 minutes), and the median interval between the test and renal insufficiency was 120 minutes (range 60-240 minutes).
Exertional Rhabdomyolysis in Seven Division-1 Swimming Athletes

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Key Words: rhabdomyolysis, overexertion, upper extremity, swimming


INTRODUCTION

Rhabdomyolysis is a syndrome in which injury to muscle leads to breakdown of muscle fibers and the release of intracellular elements from myocytes into the systemic circulation. Although rhabdomyolysis has many etiologies, extreme physical exercise is 1 preceding circumstance that may be easily identified from the history.1 Exertional rhabdomyolysis classically occurs in individuals who are physically untrained, but it may occur in young, healthy, and competitive athletes who acutely increase their activity.2

CASE REPORT

A 21-year-old Division-1 male swimming athlete presented to the emergency department 24 hours after missing a daily swimming practice due to injury. He experienced complete upper extremity weakness, muscle cramping, and mild urinary retention. He was admitted for inpatient management to receive intravenous fluids, closely monitor renal function and urine output, and provide adequate pain control. In addition, no student athletes had local parental supervision and the medical staff felt uncomfortable discharging each to a dormitory or apartment.

Aggressive saline resuscitation was provided; serial CPK and AST values improved, and SCR levels remained normal. Clinical symptoms improved during the inpatient stay and the athletes were discharged after Day 6, 4, and 3 for swimmers 1, 2–5, and 6–7, respectively. CPK levels were followed to less than 5000 U/L, and once symptoms had resolved, they were allowed to slowly progress into conditioning, exercise, and swimming. Each is currently active swimming in intercollegiate competitions.
Thirteen University of Iowa football players remain hospitalized after becoming ill with what the university says is a little-known muscle syndrome called rhabdomyolysis. Rhabdomyolysis occurs when muscle is destroyed and the pigment in it that makes it red, called myoglobin, gets into the kidneys and can damage them.
Mystery Illness Hits Oregon High School Team

Extreme Swelling in Upper-Arms Sends 19 Football Players to Hospital; Baffles Doctors

(CBS/AP) A doctor sums up the illness that hit 19 members of a northwest Oregon high school football team as "very weird." They all suffered muscle damage after a preseason camp.

Three of the McMinnville High School players also were diagnosed with possible cases of a rare soft-tissue condition called "compartment syndrome," which caused painful soreness and extreme swelling in their triceps. They underwent surgery to relieve the pressure.

The 19 players all had elevated levels of the enzyme creatine kinase, or CK, which is released by muscles when they're injured, said Dr. Craig Winkler of Willamette Valley Medical Center in McMinnville. High CK levels can lead to kidney failure if not properly treated.

"To have an epidemic like this is very weird," Winkler said.
History

› First reported in the battlefield by German physicians during WW I.

› Dr Eric Bywaters, a British physician gave the syndrome its first name, “crush injury” while treating victims of Luftwaffe Air Raids during the Battle of Britain of WWII.
Rhabdo: a leading cause of death in earthquakes

Crush Injuries in Haiti

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By RangeMD

After being trapped under the rubble of her house in Port-au-Prince, a 5-year-old girl died within 24 hours of being rescued. She had been a Argentiners worked to save her. The only injuries mentioned were to the organs and no indication of massive bleeding or overwhelming.
MYOGLOBIN

› Myoglobin is a large muscle protein that is released into the bloodstream when muscle is injured

› Myoglobin is very similar to Hemoglobin: Hgb carries oxygen in blood: myoglobin carries oxygen in muscle

› Myoglobin is what makes red meat red
Acute Renal Failure from Myoglobin

› Blood is filtered in the kidney

› Myoglobin in the urine
Other Causes of Rhabdomyolysis

› Medications and Toxic Substances
› Infectious, Inflammatory, Metabolic and Endocrinologic Causes
› Genetic Causes of Rhabdomyolysis
› Heat Related and Exertional Causes
Medications and toxins

› Cholesterol lowering drugs
› Corticosteroids (prednisone)
› Alcohol
› Snake venom
› Mushroom poisoning
› Cocaine, Meth, Ecstasy
› Neuroleptic malignant syndrome
Infectious and Endocrinologic

› Influenza
› Mononucleosis
› Staph and Strep infections
› Hypothyroidism
› Diabetes (ketoacidosis)
Genetic Causes

- Muscular Dystrophy
- Mitochondrial enzyme deficiencies
- Carbohydrate metabolic enzyme deficiency
- Malignant Hyperthermia

Interestingly, horses and humans are the only known species to suffer Acute Rhabdomyolosis
Exertional heat stroke, rhabdomyolysis and susceptibility to malignant hyperthermia

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Key words
malignant hyperthermia, heat stroke, rhabdomyolysis, pharmacogenetics, genetic testing.

Abstract
Unexpectedly severe exertional heat stroke and rhabdomyolysis should prompt a clinician to look for susceptibility to malignant hyperthermia. We report a case of exertional heat stroke and rhabdomyolysis in a man later determined to have the malignant hyperthermia phenotype. We review the existing literature regarding this association and suggest future research that could address areas of remaining clinical uncertainty.

Malignant hyperthermia (MH) is a life-threatening disorder of skeletal muscle calcium metabolism. This pharmacogenetic disease is triggered by depolarising muscle relaxants and volatile anaesthetic agents. The condition has an approximate 3.5-fold predominance for males and occurs in 1 in 73,000 to 100,000 anaesthetised adults. Susceptibility to malignant hyperthermia (MH) has an estimated prevalence of between one in 2000 and 10,000 individuals, but figures range widely. The condition demonstrates autosomal dominant inheritance with variable penetrance. There are at least 30 known causative mutations of the type 1 ryanodine receptor (RYR1) gene on chromosome 19q 13.1-13.2, which are almost to certainty 90-95% of cases and hypercarbia if untreated, myocardial necrosis with hyperkalaemia and myoglobinuria develop. Complications can include disseminated intravascular coagulation, congestive cardiac failure and limb compartment syndromes. Management protocols advise discontinuation of the anaesthetic, administration of the RYR1 antagonist dantrolene, and supportive measures.

MH is diagnosed on characteristic clinical and laboratory findings during the period of anaesthesia. The definitive diagnostic investigation for MH is in vitro contracture testing (IVCT), which is reported to be 97-99% sensitive and 78-94% specific. This involves excising muscle bundles from the vastus lateralis under local anaesthesia and exposing their extracellular compartment to caffeine.
“Tying Up” Syndrome in Thoroughbreds

ACUTE MUSCLE SWELLING IN THE HAUNCHES

ETIOLOGY
› High Potassium diet
› Selenium deficiency
› Muscle Calcium regulatory disorders
› Genetic tendencies
› Affects about 5% of thoroughbreds
Exercise Causes of Rhabdomyolysis

› Heat Stroke
› Sickle Cell Trait
› Eccentric Muscle contractions
Heat Stroke

“THE PERFECT STORM”

- Heat generating muscles
- Fluid Depletion
- Heroic effort
- Hyperthermia

KOREY STRINGER
The pathophysiology of heat stroke has many similarities with the sepsis syndrome. When blood is redistributed from the splanchnic circulation to the periphery in an attempt to lose heat and supply skeletal muscle, there is a risk of gut ischaemia. This facilitates the absorption of bacterial endotoxins. Inflammatory mediators, which appear in the circulation in response to endotoxaemia, are soluble tumour necrosis factor, interleukins 1, 2, 6 and 8, platelet-activating factor, vasoactive amines and arachidonic acid metabolites. Their targets are widespread throughout the body; this, combined with direct thermal injury, accounts for the multiple organ dysfunction seen in heat stroke. Blood purification therapy (continuous venovenous haemofiltration and plasma exchange) may have a role in the treatment of heat stroke. The removal of proinflammatory cytokines during blood purification may improve survival.
Sickle Cell Trait: Role of Oxygen

› When the red blood cell has oxygen attached, sickle HgB functions normally.

› When the red blood cell gives up its oxygen to muscle, the HgB deforms and the HgB molecules stick to one another in a line.
Sickled Hemoglobin
Sickle Cell Trait

› Sickled Hemoglobin
Sickled Cell
When does sickling occur?

- Sickling players may be on-field only briefly, sprinting only 800-1,600 meters, often early in the season.
- Sickling can also occur during repetitive running of hills or stadium steps, during intense sustained strength training, if the tempo increases late in intense one-hour drills, or at the end of practice when players run “gassers.”
- Sickling can occur (rarely) in the game, as when a running back is in constant action during a long, frantic drive downfield.
Eccentric Muscle Contraction

› Muscle myofibril

• Muscle sheath
Micro structure of muscle myofibril
Examples of Potentially Damaging Eccentric Activities

- Repeated squatting activities
- Walking/running downhill
- Going down a ladder
- Decline pullups

(Activities where gravity opposes effort in the vertical plane)
Exercise-Induced Rhabdomyolysis

CITATION:

AUTHORS:
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ABSTRACT:
Study objective: To describe the syndrome of exercise-induced rhabdomyolysis and to investigate the relation between exercise-induced rhabdomyolysis and the development of acute renal failure.

Design: Retrospective chart analysis on all patients with a discharge diagnosis of rhabdomyolysis from January 1988 to January 1993.

Setting: An urban tertiary care center with 225,000 annual emergency department visits.

Type of participants: Thirty-five patients met the inclusion criteria for exercise-induced rhabdomyolysis: a history of strenuous exercise, creatine phosphokinase level more than 500, and urine dipstick positive for blood without hematuria. We excluded patients with a history of trauma, myocardial infarction, stroke, or documented sepsis. Charts also were examined for the presence of nephrotoxic cofactors (i.e., hypovolemia and/or acidosis).

Results: All 35 patients were men without significant past medical history and were an average age of 24.4 years. The average admission creatine phosphokinase was 40,471 U/L. No patient presented with or developed nephrotoxic cofactors during hospitalization. None of our study patients experienced acute renal failure.

Conclusion: Previous literature has described a 17% to 40% incidence of acute renal failure in rhabdomyolysis. None of our patients developed acute renal failure, signifying a much lower incidence of acute renal failure in exercise-induced rhabdomyolysis without nephrotoxic cofactors than in other forms of rhabdomyolysis.
White Collar Rhabdo: “Delayed onset muscle soreness”

- Phrase coined from working population most likely to use health club facilities with personal trainers or high intensity workout programs
- Patients present with swollen painful extremities usually 1-2 days after a hard workout
- Workout emphasized eccentric activities with multiple sets
Is Eccentric Exercise Rhabdo different than other rhabdo?

› No
  - Muscle enzyme levels just as high or higher
  - Soreness and myoglobinuria present

› Yes
  - No development of acute renal failure
  - Symptoms are not acute in onset
  - No change in K+, renal function, acid base balance
  - No systemic release endo-toxins, inflammatory mediators
Treatment for Exercise Induced Rhabdo

› Check blood levels for muscle enzymes CPK, Myoglobin, K⁺
› Evaluate Renal Function
› Push fluids
› Minimize strenuous activity
› Light exercise
› Requires 8-10 days for muscle healing to occur
› Restrict training till muscle soreness and swelling gone
Conclusions

› Acute Rhabdomyolysis has many causes: in an athletic department always think of two things:
  – Heat related problems
  – Sickle Cell Trait crises

› Delayed Rhabdomyolysis is almost always eccentric exercise related
  – Rarely causes significant problems
  – Occurs very frequently
  – Don’t blame the athlete