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Recurrent Rhabdomyolysis and Extreme Exercise - A Case Study

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Objective: To present the case of recurrent rhabdomyolysis in an active female. **Background**: A healthy 21 year old female developed severe fatigue and peripheral edema in the upper extremities after an extreme exercise workout session. 4 ½ months later she participated in a similar exercise session with a personal trainer and experienced the same symptoms. **Differential Diagnosis**: In the initial case, upon physical examination and review of blood work a diagnosis of rhabdomyolysis was made. After the second exercise session athlete was diagnosed with recurrent rhabdomyolysis and was advised to seek treatment at the local emergency room. **Treatment:** In the initial case the athlete was told by medical personnel to increase fluid intake and rest. In the second case athlete was treated at the emergency room with IV fluids. **Uniqueness:** The athlete was female, and most cases of rhabdomyolysis occur in males. Athlete was treated for rhabdomyolysis and recurrent rhabdomyolysis, however these diagnosis were made 4 ½ months apart. Also, both cases appear to be the result of the same type of exercise session. **Conclusion**: There does not appear to be a definitive protocol for an accurate diagnosis of rhabdomyolysis. Guidelines for return to activity should be evaluated on a case by case basis, and a conservative increase in intensity of exercise is warranted to prevent a case of recurrent rhabdomyolysis.

Key words: *rhabdomyolysis, extreme exercise, recurrent, exertional*

Introduction

The purpose of this case study is to examine current diagnostic criteria of rhabdomyolysis and determine applicability in specific cases, as well as to analyze the process of recurrent rhabdomyolysis and to investigate the mechanisms for prevalence in certain populations. Guidelines for returning to activity are also examined following a case of exertional rhabdomyolysis.

A developing trend in the exercise industry is participation in extreme-type high intensity workouts. These forms of workouts can be performed individually or in a class-type setting. Currently, many exercise facilities are being established based on this concept. Workout sessions are generally guided by an instructor who may dictate the specific exercises, sets and repetitions performed during that particular session. With an emphasis on proper form combined with gradually increasing intensity levels, this type of workout has been shown to provide positive outcomes on the health and fitness levels of the participants. [1,2,3]

However, intense exercise along with an emphasis on eccentric contractions has been shown to increase muscle damage in the body, thereby increasing the risk of injury.[4,5] One study showed that the acute injury rate from participating in a particular style of extreme exercise was approximately 20%.[6]

When an injury and/or subsequent muscle damage becomes severe, a diagnosis of rhabdomyolysis may be suspected. Rhabdomyolysis is a clinical condition characterized by acute destruction of skeletal muscle resulting in myoglobinuria and increasing the risk of acute kidney injury (AKI).[7] Exertional rhabdomyolysis (ER) refers to skeletal muscle damage induced by exercise, most often from strenuous and eccentric exercises.[8] The exact mechanism, or pathway of ER has not been clearly determined. However, it does appear that a "cascade" of events may contribute to this condition. These events include the depletion of adenosine triphosphate (ATP), impaired function of the sodium-potassium ATPase system, intracellular excess calcium accumulation, sarcolemma damage and release of intracellular proteins into the blood.[9] This may result in muscle weakness, extreme fatigue, and edema in the affected areas. While no single exercise or even type of exercise has been shown to specifically cause this condition, it appears that certain types of training and activities can have a greater disposition to facilitate severe muscle damage. Endurance-type muscular activities (example:

performing multiple sets of curl-ups, followed by push-ups and squat/stand repetitions) have been shown to cause this type of damage in certain population groups.[10] Also, simply performing repetitive pushups has been shown to facilitate upper body damage.[11]

Rhabdomyolysis is often diagnosed by measuring the level of creatine kinase (CK) in the blood. Normal levels of CK are generally considered between 50 and 200 U/L.[12] However, there does not appear to be a concise clinical level for CK levels for definitive diagnosis of rhabdomyolysis. Some clinicians have defined rhabdomyolysis as 5 times the upper limit of normal (ULN).[13] Because normal values of CK at approximately 200 U/L are the upper limit, a diagnosis at levels greater than 1,000U/L could be made. However, others place the diagnosis at 10 times ULN.[14] Still others indicate a diagnosis should be made when CK levels are greater than 5,000 IU/L,[15] 10,000 U/L,[16] or even 20,000 U/L.[17] It is, however, well accepted that a definitive diagnosis of rhabdomyolysis should not be made by simply evaluating CK levels as clinical markers and other blood level values may have some significance. Clinical indications are generally not specific but can include muscle pain, soreness, weakness and edema in affected areas. An accurate diagnosis may not be possible without utilizing other clinical markers including increased levels of myoglobin, as well as dark or discolored urine (hematuria).

Once a diagnosis is made, and the patient is subsequently treated for rhabdomyolysis, it is critical that the individual be allowed to fully recover before resuming potentially harmful activities. There is no definitive criteria established as to when an individual should return to activity, or even resume training after an initial case of rhabdomyolysis. Cleary and colleagues[18] propose a seven question guideline that will assist athletes, coaches, and medical practitioners with recommendations for returning to activity:

1) Is the athlete afebrile?
2) Does the athlete feel good (no flu-like symptoms)?
3) Is the athlete well hydrated?
4) Are the CK levels within normal limits?
5) Is myoglobin no longer present in serum and urine?
6) Is urine color clear or pale yellow, or less than 4 on a urine color chart?
7) Has muscle pain diminished to no pain?

If the athlete answers YES to all of the questions then they may resume mild physical activity.[18] Once released to return to activity, the intensity of the exercise sessions should be gradually increased. Athletes may be asymptomatic and therefore believe they can begin their exercise program at the same intensity level as previously maintained. If an athlete returns too quickly to activity or increases the intensity too early in the exercise protocol, a second (recurrent) case of rhabdomyolysis may occur.

The incidence rate of recurrent exertional rhabdomyolysis is not well researched, and there exists variability in the reported recurrence rates. One study found a recurrence rate in .08% of patients[19], while another study indicated a recurrence rate of 5% in a 6 year follow up.[20] Another study found a recurrence rate of 11%.[21] Obviously the recurrence rate is difficult to exactly measure or potentially comprehend. It does appear that certain clinical situations may predispose individuals to a secondary case of rhabdomyolysis. But does an initial case predispose an individual to a recurrent case? Currently no evidence based guidelines exist to assist the provider in identifying who may return safely to play or activity from those who are potentially at higher risk for a repeat occurrence of rhabdomyolysis.[22] It is well established and accepted that the athlete should fully recover in order to decrease the risk of recurrent rhabdomyolysis. However, there does not seem to be an exact consensus on what “fully recovered” actually entails. Granted, there are general protocols that can assist practitioners guiding an athlete’s return to play or activity. Should both the criteria for diagnosis and guidelines for returning to activity be individually evaluated on a case by case basis?

Background

A healthy 21 year old Caucasian female was participating in an organized, extreme exercise workout session conducted at a fitness center. The athlete engaged in an exercise session consisting of performing a designated number of pushups in one minute. The protocol dictated 5 pushups in the first minute, 10 in the second, and adding 5 pushups each minute until participants can no longer continue. She recalls completing 6 rounds of increasing repetitions in each minute, thereby performing 105 pushups in 6 minutes. At this point she indicated that she was unable to continue that protocol. Athlete described her form as "questionable" especially during final stages of the exercise protocol.

The next day upon visual inspection, the elbow areas of both arms were observed to have significant edema. The athlete self-reported extreme fatigue and muscle soreness, and indicated her arms were "warm" upon palpation. On day 2 post activity, athlete reported visually observing and palpating a "bump" on the posterior aspect at the elbow.

Athlete reported that she had been physically active her whole life, but not accustomed to intense exercise. Athlete expressed that she had been participating in this particular organized class for approximately one week prior to performing the pushup progression. Athlete indicated that she was not taking any medications or supplements throughout her exercise history.

Approximately 4 ½ months after the initial visit to the physician, the athlete was exercising with a personal trainer at a fitness center. Athlete indicated to her first personal trainer (personal trainer A) that she was previously diagnosed with rhabdomyolysis from performing an extreme pushup progression. Based on that information the personal trainer A did not have athlete engage in strenuous types of extreme workouts. Personal trainer A subsequently discontinued working at the facility and athlete began training with new trainer (personal trainer B). Athlete indicated that she did not inform personal trainer B of previous diagnosis of rhabdomyolysis. According to athlete, personal trainer B was gradually increasing the intensity of the athletes' exercise program. As the program progressed, during one workout session the athlete was asked to perform a maximum number of pushups completed on the ground alternating with a maximal amount of pull ups completed on a weight assisted pull up machine. Athlete indicated that she was able to do this protocol for approximately 7-8 minutes before exhaustion. Athlete indicated she finished the rest of that particular workout at a lower intensity. The following day she experienced similar muscle soreness as she had 4 ½ months earlier, however reported edema was not as severe as the after initial exercise session.

Differential Diagnosis

In the initial case, upon physical examination and review of blood work a diagnosis of rhabdomyolysis was made. After the second exercise session athlete was diagnosed with recurrent exertional rhabdomyolysis (RER) and was advised to seek treatment at the local emergency department (ED).

Treatment

Athlete presented to her primary care physician (PCP) subsequent to the first exercise session. A physical examination was administered, and blood and urine samples were taken. All blood values were within normal limits except for her CK, measured at 7,816 U/L. PCP prescribed rest and increased fluid consumption. Athlete had a follow up blood draw the next day and the CK level had decreased to 4,286 U/L. The PCP felt that the situation was resolving and recommended rest and increased fluid consumption continue until athlete felt better. Athlete indicated that she consumed fluids and rested. In several days athlete felt like she was "back to normal". She then waited an additional two weeks before resuming light physical activity.

Four and one half months later the athlete experience a recurrence of similar symptoms. The athlete visited a PCP (same medical practice, different physician) and was advised to discontinue the exercise regimen and blood was subsequently drawn. CK level was measured at 15,231 U/L. PCP recommended athlete go to the local ED for evaluation and treatment. Athlete was seen in ED and subsequently was transferred to a level two trauma center facility approximately 30 miles from the first facility. At the second facility a subsequent blood draw was performed and the athlete's CK level had risen to 21,948 U/L. Athlete did not have any renal compromise and tolerated all nutritional intake. Athlete stayed in second facility the majority of the day, and IV fluids were administered. Athlete indicated she experienced extreme fatigue throughout this process. Athlete was subsequently discharged, however she indicated that she did not feel "normal" for approximately 2-3 days post treatment.

Uniqueness

Several factors combine to make this case somewhat unique in nature. First, the athlete was female, and evidence indicates that rhabdomyolysis is significantly more common in males than in females.[11] One study that compared increases in CK levels after exercise in men and women found that the mean increase in CK levels was significantly greater in men. This could indicate that female muscle is less susceptible to damage by adverse factors and that estrogen may act as a CK–protective factor.[10,23] Another unique factor in this case is that the athlete was treated for over-exertion in the upper extremity as a result of multiple push-ups during both exercise sessions. Interestingly, her CK levels doubled as a result of the same exercise, of similar format and intensity. The separate diagnoses of rhabdomyolysis occurred approximately 4 ½ months apart. There is no specific timeline established for return to activity after a diagnosis of rhabdomyolysis is made. However, in the absence of significant clinical markers and other subjective information from the athlete (example: absence of muscle pain, athlete maintaining proper hydration levels), an 18 week convalescence would generally be considered sufficient recovery time to return to normal activity levels. It is important to note that a convalescent blood draw to measure CK levels was not taken before the athlete resumed her activity. This case also represents a systemic misunderstanding of how to identify and manage individuals with suspected exertional rhabdomyolysis and recurrent exertional rhabdomyolysis. A "cascade" of events precipitated the athlete's primary and subsequent bouts. First, the athlete was not aware of the indicators of overexertion and rhabdomyolysis. Next, the second personal trainer did not obtain an adequate history or background on their client before beginning the particular exercise regimen. Third, the medical community appears to be in disagreement on definitive diagnostic criteria for this condition. Finally, all contributors may not be in agreement when determining adequate return to play guidelines for individuals who experience exertional rhabdomyolysis and recurrent exertional rhabdomyolysis.

Conclusions

Approximately 26,000 cases of rhabdomyolysis are reported each year in the United States.[21] However, this figure is often considered low, as others believe a much greater number of cases are simply not reported.[24] This particular case reiterates the necessity of both proper instruction and adequate adjustment/acclimation periods when beginning and continuing any extreme exercise program.

Individuals who begin exercise programs often experience delayed onset muscle soreness, associated with participating in an unusual or intense activity. This soreness may be exacerbated by intense movements, specifically eccentric-type exercises. Excessive exercise can lead to increased muscle damage, resulting in high CK levels and a diagnosis of rhabdomyolysis being made.

There exists variability in recommendations on how to properly treat exertional rhabdomyolysis. In addition to monitoring CK levels, it is important to review other clinical markers of potential compartment syndrome or acute renal failure. Taken in combination, a definitive diagnosis can be made with resulting guidelines being offered for returning to activity.

However, at what time point is it absolutely safe to return to activity? Most athletes and avid exercisers desire to return to activity as soon as possible. Four and ½ months would probably be considered adequate convalescent time for full and complete recovery, if guidelines for returning to activity as suggested by Cleary and colleagues[18] are followed. Alpers and Jones[19] suggest a graduated return to previous physical activity one month after a diagnosis if: 1) their condition is medically uncomplicated (example: no associated renal failure), 2) a normal neurological examination 3) no personal history of prior episodes of rhabdomyolysis or other muscle diseases, 4) no familial rhabdomyolysis, and 5) a return of CK levels to within normal limits. Yet this particular athlete, while performing the same activity as she performed previously, experienced increases in CK levels over twice the level of the first diagnosis. Again, it is important to note that a blood draw was not performed on the athlete at any time during her recovery. Even though one particular exercise may precipitate increased muscle damage, gradual increase after convalescence would be prudent when returning to activity. Physicians and exercise practitioners might discourage this athlete from performing multiple pushups in the future. Is this experienced situation indicative of this athlete's future inability to perform this type of activity? Perhaps even a more gradual return to activity should be implemented after an initial diagnosis of rhabdomyolysis has been made. Medical professionals and exercise practitioners should work together with athletes in order to ensure safer outcomes of training programs. Therefore, further research is necessary in order to identify individuals who may be at risk for both rhabdomyolysis and exertional rhabdomyolysis. Additional studies should be initiated in order to refine identification methods of athletes that are particularly at-risk of ER, as well as to identify other signs and symptoms of this condition. Also, further studies should address criteria for return to activity protocols in athletes who experience ER and RER. In conclusion, the information presented in this case study warrants further review and development of more precise clinical values to adequately diagnose rhabdomyolysis.

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