ILLUSTRATIVE CASE

A Case of Exertional Rhabdomyolysis: A Cheer for Standardizing Inpatient Management and Prevention

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CASE

A 17-year-old girl presented to the emergency department with bilateral triceps pain, swelling, and stiffness after participating in 2 days of summer cheerleading camp in August 2015. Serum creatine kinase (CK) was measured at 32 531 IU/L. The patient was diagnosed with exertional rhabdomyolysis (ER). A full chemistry panel (serum electrolytes, serum urea nitrogen/creatinine, glucose, calcium, magnesium, phosphate), serum CK, and urinalysis with microscopy was obtained. The patient received 2 L normal saline (NS) by intravenous (IV) bolus in the emergency department and was admitted to the inpatient ward. As she was one of several patients subsequently admitted from her cheerleading training camp, the pediatric hospitalist and nephrology services created a standardized inpatient management protocol according to which all admitted patients were treated (Table 1). This protocol delineated admission criteria, approach to inpatient management with contingency planning, and discharge criteria. It is based on current adult and pediatric literature on rhabdomyolysis and clinician expertise.[1–5]

Question What Is Currently Known About ER and Its Optimal Management?

DISCUSSION

Acute rhabdomyolysis is a potentially fatal illness, defined by the triad of muscle weakness, myalgias, and elevation in serum CK.[6] Causes of rhabdomyolysis include infectious, traumatic, medication-induced, exertional, metabolic, and genetic.[2] Viral infection is the most common cause in school-aged children, whereas in adolescents, trauma is the most common cause.[8] ER, or exercise-induced rhabdomyolysis, is a subset of rhabdomyolysis, and therefore a potential cause of acute kidney injury (AKI) and subsequent need for renal replacement therapy. Although the pathogenesis of ER is not completely understood, tissue injury is thought to occur when muscle energy requirements exceed maximal adenosine triphosphate production. Consequent muscle necrosis results in the release of intracellular calcium, potassium, and myoglobin, the latter of which causes AKI.[9]

www.hospitalpediatrics.org
DOI:10.1542/hpeds.2016-0082

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HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

Drs Carter, Cook, and Schwartz were responsible for constructing the inpatient management protocol with guidance from Dr Paul; Dr Yang performed acquisition of the data, and drafted the initial manuscript; and all authors made substantial contributions to conception, design, and analysis and interpretation of data, as well as revising the article critically for important intellectual content, gave final approval of the version to be published, and agree to be accountable to 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.

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TABLE 1. Inpatient Management Protocol for Exertional Rhabdomyolysis

Initial evaluation

- Obtain baseline full chemistry panel,[a] CK, and urinalysis with microscopy on presentation.
- Administer 2 L NS bolus.

Continuing inpatient management

- Total fluid intake per day: minimum 2 times maintenance rate (as calculated by the Halliday-Segar method), titrate IV fluids and oral intake to goal.
- Use LR unless specified by contingency plan below.

If:	Then:
Urine pH <5.5	Check full chemistry panel
Serum Ca <8	Add albumin to serum sample, start calcium carbonate 500 mg PO QID, give 50 000 IU vitamin D
UOP <100 mL/h and TBB[b] positive	Give furosemide 10 mg IV
UOP <100 mL/h and TBB negative	Give NS 1 L bolus IV
Urine pH <5.5 and serum bicarbonate <20 on recheck after fluid resuscitation	Switch to 1/2 NS with 75 mEq/L of sodium bicarbonate

Discharge

- Criteria for hospital discharge:
  - o Serum CK <5000 IU/L with consistent trend down, and normal renal function and electrolytes with UOP >2 mL/kg/h
  - o Urine dip must be heme negative, or if clearly menstruating, must contain intact red blood cells on urinalysis with microscopy and discuss with attending
  - o Must demonstrate good oral fluid intake of at least 3–4 L per day
- Follow-up with primary care provider for repeat serum CK, full chemistries, and urinalysis with microscopy at 2–3 d postdischarge and weekly until serum CK <500
- Strict activity restrictions until serum CK < 500

PO, oral; QID, 4 times a day; TBB, total body balance; UOP, urine output.
[a] Serum electrolytes, serum urea nitrogen/creatinine, glucose, calcium, magnesium, phosphate.
[b] TBB = 24-h PO/IV fluid input subtracted by 24-h UOP.

ER is not well-represented in the pediatric literature beyond case reports and scant case series. Case series that have described ER include mainly adult patients. In a series of military recruits, 2% to 40% developed acute ER in the first 6 days of basic training. In a series of adult ultramarathon runners, 57% had clinical and laboratory evidence of ER.[10] Pediatric case reports and 1 case series have primarily focused on ER in male patients.[10–16]

Literature on inpatient management and postdischarge recommendations for ER are also scarce, with no established standard of care. One previous publication has advocated for IV hydration with NS (1–2 L/h) to goal urine output of 200 mL/h and serial laboratory studies.[17]

Our protocol used an initial bolus of IV NS, followed by a longer infusion of lactated Ringer's (LR) solution. Although some authors have suggested a theoretical benefit to alkalinizing the urine to reduce precipitation of protein–myoglobin complexes (Tamm–Horsfall complex), which are responsible for tubular injury, prospective trials have not supported this hypothesis.[1–4] Although LR does contain alkali, we chose LR for our protocol not for purposes of urinary alkalinization, but rather in an effort to avoid the hyperchloremic acidosis induced by prolonged NS infusions. This approach is also supported by 1 small randomized controlled trial of LR versus normal saline in toxin-induced rhabdomyolysis that demonstrated less metabolic acidosis in those treated with LR.[5] Calcium-containing LR was selected over NS formulated with sodium bicarbonate because of the known higher risk for physiologic hypocalcemia on administration of sodium bicarbonate. LR contains potassium and lactate, which can potentiate hyperkalemia and metabolic acidosis, respectively. Both can increase risk for AKI. However, both potassium and anion gap were trended daily for all patients, without any clinically significant consequences. For our purposes, the standard formulation of readily available LR facilitated the rapid and efficient treatment of several patients simultaneously without taxing our pharmacy's resources for customized IV fluids. After their initial fluid resuscitation with NS, all patients were maintained on LR for the duration of hospitalization without complication.

CASE CONTINUED

Our patient's CK on admission was 32 531 IU/L, and peaked 4 days after the start of training camp, to 47 500 IU/L. Her estimated glomerular filtration rate (eGFR), as calculated by the Modified Schwartz Equation, on admission was 89.4 mL/min/1.73 m^2, and on discharge was 116.5 mL/min/1.73 m^2.[18] Her total length of stay (LOS) was 7 days. She adhered to the goal of a total of twice maintenance oral and IV fluid intake.

Question What Are the Current Recommendations for Return to Activity After ER?

DISCUSSION

The patient was discharged to home once her serum CK was <5000 IU/L. The postdischarge plan was based on serial laboratory monitoring and home oral hydration. She was instructed to refrain from further sports participation until serum CK levels were <500 IU/L (roughly 3 times the upper limit of normal defined as 150 IU/L in our institution's laboratory). Although no standard guidelines exist for return to physical activity, at least 1 publication supports a graded approach to return to play.[9] For our patient, a gradual return to exercise under physician supervision was recommended, as described in Table 1.

CASE CONTINUED

Our patient initially presented to care because one of her cheerleading teammates had been admitted to our hospital and had posted on social media about her condition and hospital admission. Over the next 2 days, a total of 9 young women from the same cheerleading camp presented to the emergency department for evaluation of identical symptoms. All subsequent patients were found to have CK levels >2000 IU/L.

Question What Factors Contribute to Pediatric ER and How Might These Be Mitigated in the Future?

DISCUSSION

There have been multiple case series as well as lay press reports of high school and college athletes presenting with ER after a training hiatus, requiring hospital admission, typically in the summer months. August has the highest rate of dehydration and heat-related illness in high school athletes, which corresponds to the start of high school and college fall sports seasons.[14,19,20]

In our series, a total of 9 patients, ages ranging from 15 to 18 years old, were admitted to our facility's inpatient unit for further treatment. These patients started cheerleader training camp 1 day before the first admission, after a 5-month training hiatus. On the first day of the training camp, they performed triceps exercises with concentric and eccentric muscle contraction. The facility where they trained did not have air conditioning, and outdoor temperatures on the first and second days of training were 90°F and 86°F, respectively. All 9 patients presented over a 48-hour period. Four patients had taken at least 1 dose of ibuprofen for myalgias within 72 hours of presentation, and all patients denied drug use or infectious symptoms. On examination, the patients had triceps swelling, tightness, and limited range of forearm extension. Two patients had pigmenturia on urinalysis. None had clinically significant concerns for neurovascular compromise or compartment syndrome.

Our patient's CK level peaked on day 4. For the overall group, their CK levels peaked 2 to 5 days after the start of training camp (Fig 1). Median CK on admission was 6975 IU/L (range 1915–32 531 IU/L). The median peak CK during hospitalization was 13 692 IU/L (range 5170–47 500 IU/L). The median eGFR on admission was 85.9 mL/min/1.73 m^2 and median eGFR was 115.2 mL/min/1.73 m^2 on discharge. One patient required furosemide to reverse her positive fluid body balance and low urine output. None of the patients developed significant electrolyte abnormalities. Three patients were in the "risk" category, as defined by the pediatric risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function, end-stage renal disease criteria. These criteria have been used to determine AKI in pediatric patients based on estimated creatinine clearance and urine output. The risk category is defined as a decrease in estimated creatinine clearance by 25%, or urine output <0.5 mL/kg/h for 8 hours.[21,22]

Deconditioning and high ambient temperatures likely contributed to the timing and severity of these patients' presentations. These athletes resumed highly strenuous activity after a prolonged training hiatus rather than gradually increasing exercise intensity. Our series, taken in combination with previous reports, suggests that safety guidelines for high school and college sports training programs may be warranted.

The median LOS for the 9 patients was 6 days (range 3–8 days). Altogether, this case series accrued a total of 54 inpatient

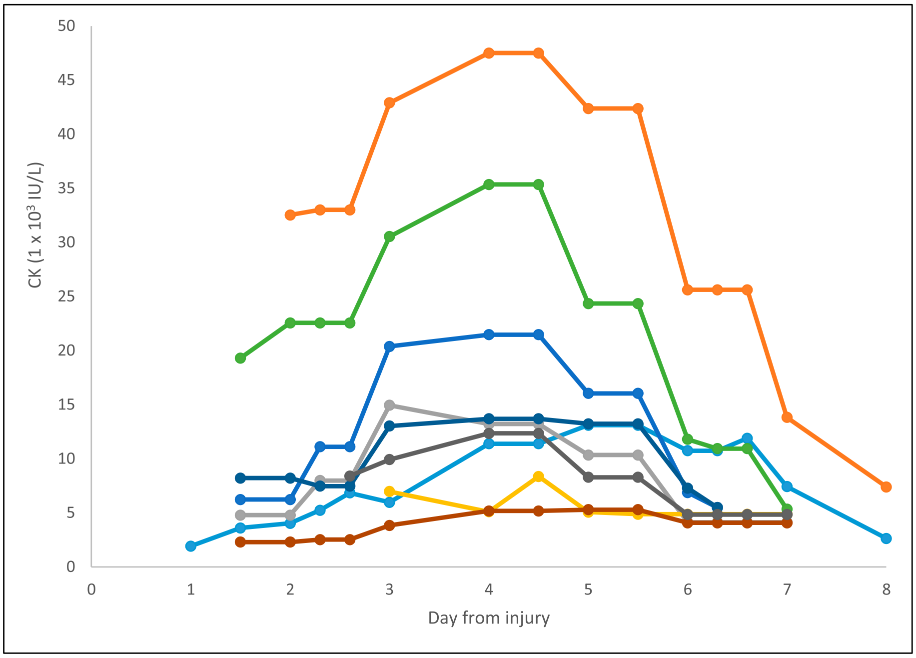

FIGURE 1 CK levels of individual patients during hospitalization.

hospitalization days. Of the 5 patients with whom follow-up data are available, return to activity lasted up to 17 days postinjury (as determined by serum CK <500 IU/L). For this cohort, 1 episode of ER could potentially keep an athlete out of activity for 2.5 weeks. Given the LOS and time of return to activity, prevention could help decrease morbidity associated with ER, as well as health care costs. Annual physical examinations may be an ideal time for primary care physicians to educate adolescent athletes about the dangers of overexertion.

CONCLUSIONS

Pediatric ER is not well understood, but presents a danger to adolescent athletes, with potentially serious consequences. The management protocol used in the case presented here and 8 similar cases admitted simultaneously is based on current literature and clinical expertise. Prospective multicenter studies can be conducted comparing this inpatient protocol with NS infusions or oral hydration alone to determine efficacy and costs, as well as overall utility of inpatient hospitalization. Further examining preventive strategies for ER can help guide the development of evidence-based recommendations for physical training in young athletes, particularly in the setting of recent inactivity or other environmental factors that may predispose to developing ER. Future research should examine optimal inpatient management, discharge criteria, and return to activity guidelines for children with rhabdomyolysis.

Acknowledgments

We thank Dr Chadi El-Saleeby and Dr Brian Cummings for their editorial assistance on the manuscript.

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Hospital Pediatrics 2016;6;753

DOI: 10.1542/hpeds.2016-0082 originally published online November 9, 2016;

Hospital Pediatrics®

AN OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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