

Exertional rhabdomyolysis-induced “normokalemic” severe acute kidney injury. A case report and a brief literature review

Alper Tuna Güven¹, Rüya Özelsancak²

¹Department of Internal Medicine, Division of General Internal Medicine, Başkent University Faculty of Medicine, Ankara, Turkey

²Department of Internal Medicine, Division of Nephrology, Başkent University Adana Hospitals, Adana, Turkey

ABSTRACT

Rhabdomyolysis is the breakdown of the muscle cells with the resultant leakage of intracellular components. Hyperkalemia and hyperphosphatemia may occur during the disease course, as well as acute kidney injury due to blockade of the tubules by myoglobin released from the muscle cells. Electrolyte disturbances are generally more severe than acute kidney injuries. We would like to report a patient who was diagnosed with exertional rhabdomyolysis-induced acute kidney injury due to vigorous swimming and who required hemodialysis but lacked hyperkalemia. The discrepancy between the severe acute kidney injury and lack of hyperkalemia was remarkable. A brief literature search also revealed several patient reports with hypo- and normokalemia despite experiencing acute kidney injury. Pathophysiologic explanations for this discrepancy include exercise-induced increased kaliuresis and intracellular shifting of potassium.

Keywords: Rhabdomyolysis, acute kidney injury, potassium, exercise, dialysis

Rhabdomyolysis is a disorder characterized by muscle necrosis and the release of muscle contents into the circulation. There are multiple causes of rhabdomyolysis, including but not limited to exercise, trauma, drugs, toxins, electrolyte disturbances, and inherited metabolic or muscle disorders. Rhabdomyolysis severity may range from asymptomatic muscle enzyme elevations to life-threatening disease due to electrolyte imbalances (i.e., hyperkalemia and hyperphosphatemia) and acute kidney injury (AKI).¹ In the event of an AKI, the severity of hyperkalemia is expected to become disproportionate to the severity of kidney injury.² Exertional rhabdomyolysis is associated with unique pathophysiologic changes regarding kidney injury and

potassium since vigorous exercise has been shown to lower potassium levels by several mechanisms.^{3, 4, 5} Herein, we present a case of exertional rhabdomyolysis-induced acute kidney injury that we think is of particular importance due to the reversely disproportioned severity between acute kidney injury (AKI) and potassium levels.

CASE PRESENTATION

The patient is a 27-year-old male who was admitted to the emergency department with recent-onset nausea and vomiting. He states he had cola-colored urine output after swimming for long hours four days ago,

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Address for correspondence: Alper Tuna Güven, MD., Taşkent Caddesi (Eski 1. Cadde) 77. Sokak (Eski 16. Sokak) No:11 06490 Bahçelievler, Ankara, Turkey
E-mail: alper.tuna.guven@gmail.com

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Table 1. Exertional rhabdomyolysis induced acute kidney injury patients in the PubMed search

Case ^{ref.}	Age/Sex	Body Temperature (°C)	Creatinine (mg/dL)	Potassium (mmol/L)	CK (U/L)	Underlying disease	Medication - Herbal products	Rhabdomyolysis cause	Possible additional factors	Mortality
1 ⁶	21/M	41.0	2.1	4.2	1100	-	-	Military training	Heat stroke	-
2 ⁷	21/M	37.3	1.9	4.5	426	-	Herbal supplement	Military training	Ephedra	-
3 ⁸	25/M	38.2	2.3	*	5555	-	-	Military training	Influenza infection	-
4 ⁹	19/M	36.1	2.3	5.2	536	Sickle cell trait	-	Football training	Sickle cell trait	+
5 ¹⁰	31/M	41.7	1.9	6.7	7482	-	-	Obstacle marathon	Heat stroke	-
6 ¹¹	36/M	39	2.1	6.2	2975	-	Ephedrine	Half marathon run	Ephedrine	-
7 ¹²	50/M	N/A	1.8	*	2306	Hypertension, gastroesophageal reflux disease, osteoarthritis, insomnia	Hydrochlorothiazide, omeprazole, sildenafil, Hydroxyzine, fat burn X	Daily sports exercise	Fat burn X	-
8 ¹³	25/M	36	1.1	5.5	38280	-	Androgenic steroids	Gym exercise	Androgenic steroids	-
9 ¹⁴	N/A/M	N/A	4.9	3.1	>40000	N/A	NSAID	Endurance run	-	-
10 ¹⁴	N/A / M	N/A	3.4	4.9	38218	N/A	NSAID	Endurance run	-	-
11 ¹⁴	N/A / M	N/A	4.4	2.8	>40000	N/A	NSAID	Endurance run	-	-
12 ¹⁵	41/M	40.3	12	5.3	112300	-	-	10 km run	Heat stroke	-
13 ¹⁶	19/M	37.1	8.3	6.2	10127	hereditary renal hypouricemia	-	Gym exercise	-	-
14 ¹⁷	19/M	37.0	1.9	4.2	587600	-	-	26 km run	-	-
15 ¹⁸	39/M	N/A	8.1	4.9	26320	-	-	4 km run	Alcohol Abuse	-
16 ¹⁹	32/M	N/A	1.3	4.6	>100000	N/A	N/A	Endurance run	Diarrhea	-
17 ¹⁹	47/F	N/A	1.1	4.1	15636	-	N/A	Endurance run	-	-
18 ¹⁹	35/M	N/A	4.8	5.2	>100000	-	N/A	Endurance run	-	-
19 ¹⁹	41/M	N/A	7.1	5.9	122347	-	N/A	Endurance run	-	-
20 ²⁰	20/M	39.4	2.8	2.1	27947	Sickle cell trait	-	Military training	Heat stroke	+
21 ²¹	19/M	36.7	13.6	3.5	850	-	-	Wrestling	Dextroamphetamine use	-
22 ²²	25/M	40.5	8.1	4.8	6409	-	-	Police recruitment training	Heat stroke	+
23 ²³	33/F	N/A	12.2	6.1	11500	Hypothyroidism	Levothyroxine	Marathon run	Hypothyroidism	-
24 ²⁴	19/M	N/A	1.6	3.2	2545	-	-	Football play	Cold water immersion	-
25 ²⁵	26/M	37.5	2.7	5.6	2112	Sickle cell trait	-	Military training	Sickle cell trait	+
26 ²⁶	23/M	N/A	1.5	5.8	36640	Graves' disease	-	Weight lifting	Thyrototoxicosis	-
27 ²⁷	33/M	38.3	2.3	4.8	133240	-	Creatine, ephedrine.	Military training	Crash diet, Creatine, ephedrine	+
28 ²⁸	25/F	>40	3.2	3.0	1600000	-	protein supplements, caffeine, pseudoephedrine,	Hiking	Heat stroke	-
29 ²⁹	31/M	N/A	1.3	4.5	59159	-	-	Resistance training	Protein supplements, caffeine, pseudoephedrine	-
30 ³⁰	19/M	38.3	1.9	4.6	408545	Sickle cell trait, asthma	-	Football play	Sickle cell trait, heat stroke	-
31 ³¹	20/M	40	3.2	4.7	23500	-	-	Military training	Heat stroke	-
32 ³²	32/M	N/A	2.8	5	114383	Hypertension, hypothyroidism, gastroesophageal reflux disease, inflammatory bowel disease	Esomeprazole, levothyroxine, irbesartan-hydrochlorothiazide, metoprolol succinate, metoclopramide, dicyclomine, oxycodone, acetaminophen, phentermine	Furniture lifting	Phentermine	-
33 ³³	25/M	N/A	4.4	4.4	2268	-	-	Military training	-	-
34 ³⁴	57/M	N/A	9.4	6.4	3389	Hypertension, hyperlipidemia	Ramipril, atorvastatin	Trekking	Atorvastatin	-
35 ³⁵	59/M	Afebrile	2.5	4.6	>18000	N/A	N/A	Brisk walk	Alcohol	-
36 ³⁶	22/M	37.3	6	4.2	100000	Sickle cell trait	-	Military training	Sickle cell trait, diarrhea	+

CK: Creatine Kinase, N/A: Not applicable
* Potassium level was written as "normal"

but the urine had turned to its normal color the day after. He was deconditioned, and strenuous swimming took place on a very hot and humid day. He did not have any prior disease or medication history, and he denies substance abuse. He did not have any diarrhea or abdominal pain prior to admission. His vital signs, including body temperature, were in the normal range. Blood tests revealed stage 3 AKI (creatinine = 8.07 mg/dL), moderate transaminase elevation (ALT = 214 U/L, and AST = 384 U/L), and marked creatine kinase (CK) elevation (CK = 14.851 U/L). Urinalysis showed mild protein and moderate hemoglobin and myoglobin but a lack of red blood cells. The electrolyte levels were as follows: sodium = 132 mmol/L, potassium = 4.0 mmol/L, and phosphorus = 6.7 mg/dL. The uric acid level was 13.1 mg/dL, the TSH level was 0.94 mIU/L, and the blood gas analysis was unrevealing. Abdominal ultrasound showed mild hepatosteatosis and increased renal echogenicity. He was diagnosed with exertional rhabdomyolysis-induced AKI, so vigorous hydration was started. After hydration, he became fluid overloaded and his creatinine did not improve; therefore, hemodialysis was initiated. He was discharged after a week with residual kidney impairment.

DISCUSSION

We presented an untrained young man who swam for several hours during a hot and humid weather and experienced exertional rhabdomyolysis. Our patient is noteworthy with regards to the discordance between the level of kidney injury and potassium levels. One would expect hyperkalemia during a rhabdomyolysis course that has caused stage 3 AKI. There are several explanations for this discrepancy and include several mechanisms: Firstly, heat and exercise-induced sweating, and tachypnea caused direct potassium loss and intracellular potassium shift, respectively. Secondly, exercise-generated heat and exercise-induced water loss led to aldosterone overproduction and resultant kaliuresis.³ Finally, ongoing urine output and vomiting might have played a role in potassium loss.

A brief literature review was performed via PubMed in order to compare our case with the existing literature. Search keywords were as follows: ((exercise) OR (exertional)) AND (rhabdomyolysis). Only case reports, letters, and observational studies

that were conducted in humans over 18 years old were included. Search results included 441 studies. Studies that included patients without acute kidney injury, patients without data regarding kidney function and potassium level, patients with inherited metabolic disorders, inborn errors of metabolism, storage disorders, muscle disorders, malignant hyperthermia, drug-related rhabdomyolysis, and non-exertional rhabdomyolysis were excluded. Of the remaining 31 studies,⁶⁻³⁶ patients were found to have exertional rhabdomyolysis with acute kidney injury. Of the 36 patients, 4 were hypokalemic, 18 were normokalemic, and 14 were hyperkalemic. Creatinine levels, mortality, body temperature, and CK levels upon admission to the emergency department were not different between these 3 groups. Table 1 illustrates the characteristics of these patients.

Further systematic reviews should be conducted to search for and describe the features associated with non-hyperkalemic exertional rhabdomyolysis. Findings may challenge the dogma that clinicians should expect hyperkalemia during rhabdomyolysis regardless of the kidney injury and assert the finding that hypokalemia or normokalemia may occur during exertional rhabdomyolysis even in the presence of severe kidney injury.

CONCLUSION

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors' Contribution

Study Conception: ATG; Supervision; RÖ; Data Collection and/or Processing: ATG; Literature Review: ATG; Critical Review: RÖ; Manuscript preparing: ATG.

REFERENCES

1. McMahon GM, Zeng X, Waikar SS. A risk prediction

- score for kidney failure or mortality in rhabdomyolysis. *JAMA Intern Med.* 2013;173(19):1821-1828. doi:10.1001/jamainternmed.2013.9774
2. Lordon RE, Burton JR. Post-traumatic renal failure in military personnel in Southeast Asia. Experience at Clark USAF hospital, Republic of the Philippines. *Am J Med.* 1972;53(2):137-147. doi:10.1016/0002-9343(72)90124-6
 3. Poortmans JR. Exercise and renal function. *Sports Med.* 1984;1(2):125-153. doi:10.2165/00007256-198401020-00003
 4. Wang AY, Li PK, Lui SF, Lai KN. Renal failure and heatstroke. *Ren Fail.* 1995;17(2):171-179. doi:10.3109/08860229509026254
 5. Aizawa H, Morita K, Minami H, Sasaki N, Tobise K. Exertional rhabdomyolysis as a result of strenuous military training. *J Neurol Sci.* 1995;132(2):239-240. doi:10.1016/0022-510x(95)00144-q
 6. Pereira F, Moraes R, Bavel D, Lorenzo AR, Tibirica E. Exertional Rhabdomyolysis after Military Training Paralleled by Systemic Microvascular Dysfunction and Plasma Cytokine Increase: A Case Report. *Arq Bras Cardiol.* 2019;113(2):294-298. Published 2019 Sep 2. doi:10.5935/abc.20190165
 7. Stahl CE, Borlongan CV, Szerlip M, Szerlip H. No pain, no gain--exercise-induced rhabdomyolysis associated with the performance enhancer herbal supplement ephedra. *Med Sci Monit.* 2006;12(9):CS81-CS84.
 8. Tseng GS, Hsieh CY, Hsu CT, Lin JC, Chan JS. Myopericarditis and exertional rhabdomyolysis following an influenza A (H3N2) infection. *BMC Infect Dis.* 2013;13:283. Published 2013 Jun 21. doi:10.1186/1471-2334-13-283
 9. Anzalone ML, Green VS, Buja M, Sanchez LA, Harrykissoon RI, Eichner ER. Sick cell trait and fatal rhabdomyolysis in football training: a case study. *Med Sci Sports Exerc.* 2010;42(1):3-7. doi:10.1249/MSS.0b013e3181ae0700
 10. Aquilina A, Pirotta T, Aquilina A. Acute liver failure and hepatic encephalopathy in exertional heat stroke. *BMJ Case Rep.* 2018;2018:bcr2018224808. Published 2018 Jul 30. doi:10.1136/bcr-2018-224808
 11. Rhidian R. Running a risk? Sport supplement toxicity with ephedrine in an amateur marathon runner, with subsequent rhabdomyolysis. *BMJ Case Rep.* 2011;2011:bcr1120115093. Published 2011 Dec 13. doi:10.1136/bcr.11.2011.5093
 12. Hannabass K, Olsen KR. Fat burn X: burning more than fat. *BMJ Case Rep.* 2016;2016:bcr2015213374. Published 2016 Jan 25. doi:10.1136/bcr-2015-213374
 13. Braseth NR, Allison EJ Jr, Gough JE. Exertional rhabdomyolysis in a body builder abusing anabolic androgenic steroids. *Eur J Emerg Med.* 2001;8(2):155-157. doi:10.1097/00063110-200106000-00015
 14. Bruso JR, Hoffman MD, Rogers IR, Lee L, Towle G, Hew-Butler T. Rhabdomyolysis and hyponatremia: a cluster of five cases at the 161-km 2009 Western States Endurance Run. *Wilderness Environ Med.* 2010;21(4):303-308. doi:10.1016/j.wem.2010.06.012
 15. Hart LE, Egier BP, Shimizu AG, Tandan PJ, Sutton JR. Exertional heat stroke: the runner's nemesis. *Can Med Assoc J.* 1980;122(10):1144-1150.
 16. Chakraborty S, Sural S. A young patient of hereditary renal hypouricaemia presenting with exercise-induced rhabdomyolysis and acute kidney injury. *Ann Clin Biochem.* 2013;50(Pt 3):271-273. doi:10.1258/acb.2012.012017
 17. Al Badi A, Al Rasbi S, Alalawi AM. Exercise-Induced Rhabdomyolysis: A Case Report and Literature Review. *Cureus.* 2020;12(8):e10037. Published 2020 Aug 26. doi:10.7759/cureus.10037
 18. Daher Ede F, Silva Júnior GB, Brunetta DM, Pontes LB, Bezerra GP. Rhabdomyolysis and acute renal failure after strenuous exercise and alcohol abuse: case report and literature review. *Sao Paulo Med J.* 2005;123(1):33-37. doi:10.1590/s1516-31802005000100008
 19. Ellis C, Cuthill J, Hew-Butler T, George SM, Rosner MH. Case report: exercise-associated hyponatremia with rhabdomyolysis during endurance exercise. *Phys Sportsmed.* 2009;37(1):126-132. doi:10.3810/psm.2009.04.1693
 20. Ferster K, Eichner ER. Exertional sickling deaths in Army recruits with sickle cell trait. *Mil Med.* 2012;177(1):56-59. doi:10.7205/milmed-d-11-00106
 21. Hamilton RW, Gardner LB, Penn AS, Goldberg M. Acute tubular necrosis caused by exercise-induced myoglobinuria. *Ann Intern Med.* 1972;77(1):77-82. doi:10.7326/0003-4819-77-1-77
 22. Hassanein T, Perper JA, Tepperman L, Starzl TE, Van Thiel DH. Liver failure occurring as a component of exertional heatstroke. *Gastroenterology.* 1991;100(5 Pt 1):1442-1447.
 23. Nelson SR, Phillips AO, Hendry BM. Hypothyroidism and rhabdomyolysis in a marathon runner. *Nephrol Dial Transplant.* 1993;8(4):375-376.
 24. Kahanov L, Eberman LE, Wasik M, Alvey T. Exertional rhabdomyolysis in a collegiate american football player after preventive cold-water immersion: a case report. *J Athl Train.* 2012;47(2):228-232. doi:10.4085/1062-6050-47.2.228
 25. Kerle KK, Nishimura KD. Exertional collapse and sudden death associated with sickle cell trait. *Mil Med.* 1996;161(12):766-767.
 26. Kim HR, Kim SH, Oh DJ. Rhabdomyolysis after a regular exercise session in a patient with Graves' disease. *Nephrology (Carlton).* 2012;17(3):307-308. doi:10.1111/j.1440-1797.2011.01528.x
 27. Kuklo TR, Tis JE, Moores LK, Schaefer RA. Fatal rhabdomyolysis with bilateral gluteal, thigh, and leg compartment syndrome after the Army Physical Fitness Test. A case report. *Am J Sports Med.* 2000;28(1):112-116. doi:10.1177/03635465000280010401
 28. Pattison ME, Logan JL, Lee SM, Ogden DA. Exertional heat stroke and acute renal failure in a young woman. *Am J Kidney Dis.* 1988;11(2):184-187. doi:10.1016/s0272-6386(88)80210-5
 29. Pearcey GE, Bradbury-Squires DJ, Power KE, Behm DG, Button DC. Exertional rhabdomyolysis in an acutely detrained athlete/exercise physiology professor. *Clin J Sport Med.* 2013;23(6):496-498. doi:10.1097/JSM.0b013e318291d39e
 30. Shelmadine BD, Baltensperger A, Wilson RL, Bowden RG. Rhabdomyolysis and acute renal failure in a sickle cell trait athlete: a case study. *Clin J Sport Med.* 2013;23(3):235-237. doi:10.1097/JSM.0b013e3182625a37
 31. Sherner JH, Yuan CM. A 20-year-old army private with leg pain, fever, and collapse during a forced road march. *Mil Med.* 2002;167(4):363-366.
 32. Steidl KE, Darko W, Probst LA, Noviasky JA, Nasser S. Rhabdomyolysis associated with phentermine. *Am J Health Syst Pharm.* 2010;67(22):1929-1932. doi:10.2146/ajhp090395
 33. Tietjen DP, Guzzi LM. Exertional rhabdomyolysis and acute renal failure following the Army Physical Fitness Test. *Mil Med.* 1989;154(1):23-25.
 34. Unnikrishnan D, Satish B. Exertion-induced rhabdomyolysis in a patient on statin therapy. *Nephrol Dial Transplant.* 2005;20(1):244. doi:10.1093/ndt/gfh578

35. West H. Rhabdomyolysis associated with compartment syndrome resulting in acute renal failure. *Eur J Emerg Med.* 2007;14(6):368-370. doi:10.1097/MEJ.0b013e32823a3c8b
36. Zimmerman J, Granatir R, Mummert K, Cioffi R. Sickie crisis precipitated by exercise rhabdomyolysis in a patient with sickle cell trait: case report. *Mil Med.* 1974;139(4):313-315.