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CASE REPORT

Four Cases of Acute Kidney Injury Requiring Dialysis in Ultramarathoners

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Transient acute kidney injury (AKI) following ultraendurance footraces is a common biochemical diagnosis. However, severe AKI requiring renal replacement therapy is uncommon in ultramarathoners. We report 4 runners (3 men; mean age, 44 ± 3 y) who required prolonged (10–42 d) dialysis following the Western States 100 Mile Endurance Run over a 3-y span (0.38% of starters). The maximum ambient temperatures on the race day ranged from 36.6° to 38.3°C. The runners presented to local hospitals 17 to 32 h after running, with laboratories confirming rhabdomyolysis, hyponatremia (mean serum sodium concentration, 127±2 mmol·L^{-1}), and AKI (mean serum creatinine concentration, 8.5±2 mg·dL^{-1}). The case-cluster report highlights the potential synergistic effects of high ambient temperatures, muscle damage, and electrolyte imbalance on protracted renal dysfunction in ultramarathoners competing in a warming world.

Keywords: ultramarathon, rhabdomyolysis, acute renal failure, heat nephropathy

Introduction

Although mild-to-moderate acute kidney injury (AKI) and exertional rhabdomyolysis (ER) are common following ultramarathons, severe AKI with prolonged hospitalization and dialysis is rare.[1,2] A 2022 systematic review of 1113 ultrarunners over the last 15 y reported an overall incidence of mild AKI of 42%, with only 1 case (0.01%) meeting the criteria for severe renal failure but not requiring dialysis.[3] In addition, a systematic review of case reports identified only 27 runners who developed severe AKI following marathon or ultramarathon running.[2] Of the 27 runners, only 15 required dialysis.

Given the low historical risk of developing severe renal injury because of running ultramarathons, it is concerning that over the last 3 y of the Western States 100 Mile Endurance Run (WS100), 4 runners out of 1053 starters (0.38%) required prolonged dialysis treatment for AKI with ER. It remains unclear which features of the WS100, including extreme heat and a considerable net downhill course, exacerbate risk factors for AKI necessitating dialysis. This case cluster highlights the emerging potential for heat stress nephropathy to impact ultramarathoners competing in extreme environments hypothetically as an athletic variant of Mesoamerican nephropathy, as suggested elsewhere.[4]

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Case Report

The WS100 is a 100-mile (161 km) trail running race which traverses the Sierra Nevada mountains and includes 5486 m of ascent and 7010 m of descent. Roughly 315 to 400 annual starters have 30 h to complete the race distance. Ambient temperatures typically range between 4 and 37°C.

Table 1 summarizes the demographics, training history, medical history, and select laboratory values of the 4

Table 1. Summary of 4 runners requiring dialysis after WS100

Variable	*Runner A*	*Runner B*	*Runner C*	*Runner D*
Age at time of race (y)	47	47	43	41
Year running WS100	2018	2018	2021	2021
Sex	M	F	M	M
Number of ultramarathons run prior to race	14	4	54	36
Number of 100-mile races run prior to race	8	1	8	7
Finished WS100	Y	Y	N (dropped mile 85)	Y
Previous medical issues	Hypertension	Hydronephrosis but no renal damage	None	None
Time from stopping running to presentation in ED	19.5 h	32 h	28 h	17 h
BUN ($mg \cdot dL^{-1}$)	101	109	108	92
Serum creatinine ($mg \cdot dL^{-1}$)	8.94	5.19	10.3	9.39
Sodium levels ($mmol \cdot L^{-1}$)	125	128	126	128
Potassium ($mmol \cdot L^{-1}$)	7.7	4.6	5.2	7.5
Calcium ($mg \cdot dL^{-1}$)	5.8	7.3	6.1	6.4
Magnesium ($mg \cdot dL^{-1}$)	3.3	n/a	n/a	4.2
AST ($U \cdot L^{-1}$)	5365	780	1040	5956
ALT ($U \cdot L^{-1}$)	1526	450	4098	962
CPK ($U \cdot L^{-1}$)	292,500	>16,000	153,900	>37,580
Time on dialysis	10 d	4 wk	4 wk	6 wk
Hospital complications	Atrial fibrillation, complete heart block	None	None	Respiratory failure, jugular venous thrombosis
Back running	Y	Y	Y	Y
Completed ultramarathon since being on dialysis	Y	Y	N	N

WS100, Western States 100 Mile Endurance Run; M, male; F, female; Y, yes; N, no; ED, emergency department; BUN, blood urea nitrogen; n/a, not available; AST, aspartate transaminase; ALT, alanine transaminase; CPK, creatine phosphokinase.

runners who required dialysis after the race during 2 "hot" years (2018 and 2021, with the 2020 race canceled because of COVID-19). In 2018, the maximum temperature was 36.6°C, and in 2021, the maximum temperature was 38.3°C. All 4 runners reported nausea and vomiting, dark urine, and muscle cramping during the race. One runner ingested 2 doses of 200 mg of ibuprofen, whereas the other runners did not ingest nonsteroidal anti-inflammatory (NSAID) or other medications during the race. Two runners reported consuming salt tablets. Because of the elevated risk of developing hyponatremia during ultradistance running, we promote the "drink to thirst" guidelines outlined by the Wilderness Medical Society.[5] All 4 runners reported drinking fluids according to the dictates of thirst, ingesting a combination of water, Coca-Cola, Sprite, and sports drinks.

All 4 runners reported feeling "worse" after the race than after similar events. However, none of the runners required acute care or immediate hospitalization. Three runners traveled back to the race start or their hometowns before seeking medical care for persistent fatigue, severe myalgias, nausea, and vomiting. Hematemesis occurred in 1 of the runners. The time to seek medical care ranged from 17 to 32 h after they stopped running. All 4 runners required dialysis for a minimum of 10 d to a maximum of 6 wk. All the runners have subsequently returned to training, without lingering medical issues.

Discussion

The pathophysiologic combination of ER, hyponatremia, and AKI requiring hospitalization has been reported after ultramarathons, including a previous WS100, but is rare.[1] Only 15 similar cases have been reported in the literature.[2] Exertional rhabdomyolysis with mild AKI is a recognized, transient phenomenon following ultramarathon footraces and typically does not require dialysis.[6] Research on the prevalence of severe AKI after endurance running has been limited to case reports and data from research studies focusing on changes in renal function due to endurance running. As a result, there is

no accurate estimate of the incidence of severe AKI after distance running. Nevertheless, our incidence of 0.38% is concerning. This group of runners who required protracted (2−6 wk) dialysis raises concerns about a potential new medical challenge, ultramarathon running in an era of global warming.[4]

High ambient temperatures, during the 2018 and 2021 WS100 races, are a known risk factor for AKI and ER and likely contributed to renal injury. Muscle-damaging exercise before running in the heat exacerbates both the inflammatory response and renal stress.[7] Of potential concern for ultramarathon runners, especially those who live and train at high temperatures, are the results of an indirectly related study performed on otherwise young (median age, 34 y), healthy sugarcane workers who developed chronic kidney disease (CKD) after 12 mo of repeated hard, physical labor.[8] Thus, correct identification of interventions that help preserve renal function while training and racing in the heat requires further investigation.

One common strategy directed at preserving renal function during ultramarathon running is hydration. However, the relationship between hydration, ER, and AKI remains complex and underappreciated. Although dehydration is classically associated with heat stress, runners with nephropathy were hyponatremic at their initial hospital presentation.[8] It remains unclear whether or not hyponatremia on admission preceded AKI because of hypervolemia or was a renal consequence of AKI, as similarly described.[1,9]

Another risk factor for AKI and rhabdomyolysis may be the elevation profile, specifically the net descent of the WS100, which portends a more significant mechanical load. In 1 study, volunteers running in the heat for 60 min at a grade of −10% had more inflammation and renal stress than runners running on a flat surface.[7] Although other ultramarathons take place in severe heat, a race such as the Badwater 135 is a net uphill race with a notably lower total descent of 1433 m.[10] The marked downhill profile of the WS100 likely leads to more eccentric muscle damage and higher levels of rhabdomyolysis. Combined with extreme temperatures, WS100 runners are at a significantly higher risk of ER.

We have been educating runners about the potential harms of NSAIDs during ultramarathons. Compared with previous studies in which two thirds of runners presenting with AKI had used NSAIDs, only 1 of our runners had ingested an NSAID and took a relatively low dose.[2]

Another challenging aspect for the medical team is runners' clinical presentation at the finish line. All 4 runners complained of gastrointestinal distress and myalgias, but these were not severe enough to require care in medical tents. Furthermore, these signs and symptoms are common during and after ultramarathons.[11] Previous studies have shown >75% of runners with severe AKI because of distance running presented in a delayed fashion, sometimes up to a week after the race.[2] Further study is required to identify risk factors that may inform clinicians of poor renal outcomes. It is crucial for medical directors of endurance events to keep in contact with athletes for up to a week after the event is over to monitor AKI cases. With only 15 runners requiring dialysis previously reported in the literature, there may be underreporting of severe AKI cases in runners because of this delayed presentation and medical teams being unaware of hospitalization.

Although all 4 runners had elevated creatine phosphokinase (CPK) levels, they were within the range of laboratory values seen previously in the WS100.[1,6] While markedly elevated CPK levels almost invariably result in hospital admission, most runners with elevated CPK levels have normalization of their laboratory values without medical interventions. Improved identification of risk factors for severe, symptomatic AKI due to ER may prevent unnecessary hospitalizations by initiating treatments, such as IV fluid resuscitation, before athletes leave the race venue.

Although it is concerning that these runners required protracted dialysis, their kidney dysfunction resolved completely, and all have resumed running. Normalization of kidney function has been previously demonstrated in runners with less severe kidney injury.[12] It remains unclear whether repeated bouts of exercise-related AKI can eventually lead to CKD, as seen in Mesoamerican nephropathy and other forms of recurrent AKI.[8] Longitudinal follow-up of renal function is recommended in runners with severe AKI.

Moving forward, we are considering methods to help our medical team better guide runners to complete the WS100 while avoiding hospitalization and dialysis. Current considerations may be point-of-care urine testing or using iStat devices for blood testing.[13,14] Before implementation, we must determine laboratory value thresholds at which runners would be held or disqualified. Finally, we have made a practice of limiting IV fluids and encouraging oral postrace hydration. We are now reconsidering this practice, especially for runners with persistent nausea and vomiting. More aggressive hydration with hypertonic saline in the face of hyponatremia or normal saline if runners have normal serum sodium levels could potentially reduce the incidence and severity of AKI. In the future, measurement of baseline electrolytes and renal function markers will allow us to better

understand the trajectory of chronic heat stress on renal function during ultramarathon running.

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