

Rhabdomyolysis Secondary to Severe Hypokalemia, a rare association

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Abstract: Rhabdomyolysis denotes a clinical and laboratory syndrome that results from a rapid breakdown of skeletal muscle cells. Rhabdomyolysis results from acute necrosis of skeletal muscle fibers and consequent leakage of muscle constituents into the circulation. It ranges from an asymptomatic state to a severe condition associated with extreme elevations in creatine kinase, myoglobinuric acute renal failure, disseminated intravascular coagulation, or cardiac arrest. Reported etiologies of rhabdomyolysis include alcohol abuse, drugs, muscle trauma and muscle overexertion. Less common causes include muscle enzyme deficiencies, electrolyte abnormalities, infectious causes, toxins and endocrine disorders. Severe hypokalemia is a well known, yet rare cause of rhabdomyolysis. Here we report an unusual presentation of rhabdomyolysis secondary to severe hypokalemia in a healthy adult with no previous history of any medical illness. Excessive occupational heat exposure and strenuous exercise were the only attributable etiology detected and a residual damage affecting the renal function persisted despite the aggressive emergency treatment.

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Key Words: Rhabdomyolysis, hypokalemia, myoglobinuria.

Case Report:

A 36-year-old construction worker living in Jeddah, KSA was admitted to the Department of Internal Medicine complaining of generalized muscle weakness and pain involving predominantly his thighs, calves, and arms. This progressed to paralysis involving all the extremities; the patient also had myalgia, muscle cramps and mild stiffness, he also noticed his urine was tea colored, infrequent and small in amount. The symptoms evolved over three days prior to admission, without any history of trauma or falls. He denied nausea, vomiting, diarrhea, fever, headache or loss of consciousness. Patient had no history of alcohol abuse, any drug intake (including diuretics), and ingestion of liquorice or any herbal medicine.

Two years prior to this admission, the patient experienced similar but milder symptoms which resolved spontaneously in few days without any medication nor investigations, family and past medical histories were also unremarkable. On physical examination, his blood pressure was 122/80 mmHg, heart rate 80 beats/min and regular, but hypokalemic ECG changes were noted (Figure 1), respiratory rate 16 breaths/min, and body temperature 37.9°C., no signs of dehydration could be noted, Cardiopulmonary and abdominal examination were unremarkable. There was a symmetric flaccid paralysis with areflexia in the

upper and lower extremities. No fasciculations, myoclonus, nor muscular atrophy and the remainder of the physical examination were normal. The major biochemical abnormalities are shown in *table 1*. Laboratory tests showed severe hypokalemia (1.5 mmol/L) and marked muscle enzymes abnormalities (CK/CPK 12807U/L, CKMB 189.3 U/L) (Table 1) all compatible with diagnosis of rhabdomyolysis induced acute renal injury secondary to severe hypokalemia due to occupational heat exposure and strenuous muscular exercise at his work.

Management included bolus Potassium IV, followed by continuous potassium infusion until the normal range was reached, and then was gradually tapered, and stopped when the potassium reached 3.6 mmol/L, within 3 days. The patient was put on daily ultra filtration since hypokalemia was initially predominant, then he was shifted to intermittent hemodialysis together with generous intravenous fluids, forced diuresis with mannitol and furosemide to avoid volume overload. Strict ICU monitoring to his heart rhythm and other vital signs at the first 4 days of admission which passed uneventfully and the patient was discharged after 3 weeks with residual renal dysfunction and creatinine clearance ranging from 30 to 40 ml/min, to be followed up at the nephrology outpatient clinic as a chronic renal impairment patient.

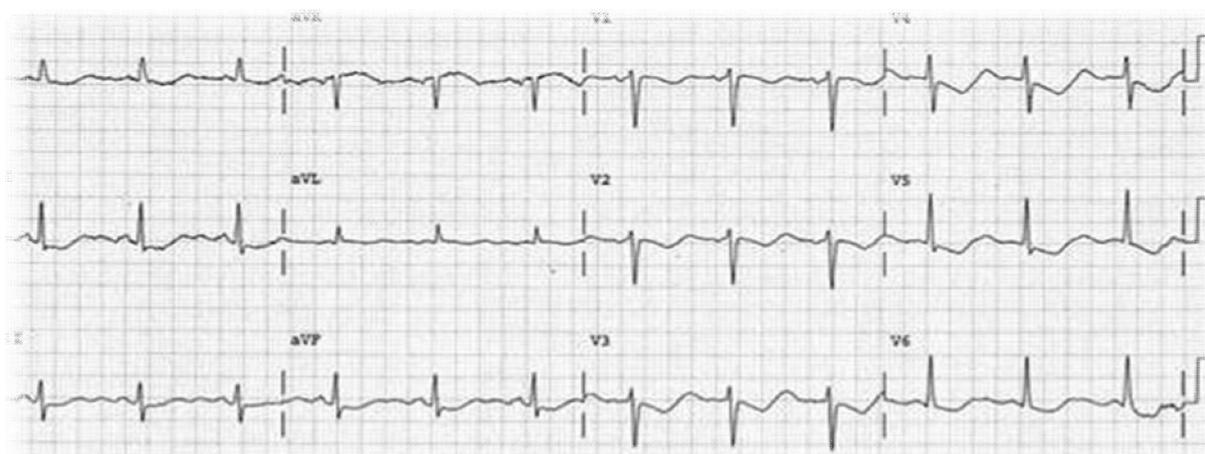


Figure (1) ECG at day 1 of admission, marked st depression and T inversion, U wave also noted specially at LII.

Table 1. Serum biochemistry of the patient along the 3 weeks of admission:

	Reference range	Admission	4 th day	8 th day	12 th day	16 th day	20 th day	At discharge
Na	136 - 145 mmol/L	141	137	137	135	133	134	127
k	3.5 - 5.3 mmol/L	1.5	3.3	4.95	3.8	4.59	4.2	3.6
CPK	21 – 331 U/L	12807	7604	363	114	318	315	385
Urea	2.5 – 6.4 mmol/L	32.4	21.6	25	31.9	36.8	41.4	40.9
Creatinine	53 – 123 umol/L	698.5	504	842	557.9	491	417.1	250.1
AST	10 – 50 U/L	691	131	114	36.4	40.6	38	35.6
ALT	30 – 46 U/L	512	277	216	101.8	92.5	81.5	77.3
Bicarbonate	22 – 26 mmol/L	26.1	24.2	22.8	27.2	30.2	26.6	24.8
WBC	4.5 – 10.5 K/uL	12.49	16.4	13	9.31	7.55	8.24	7.8
RBC	5.5 – 6.5 M/uL	5.85	4.82	5.15	5.07	4.88	5.17	5.5
Hb	12.5 – 18.5 g/dL	15	12.9	14.2	13.1	12.6	13.3	13.1
Plt	150 – 450 K/uL	314	243	210	405	506	539	473

Discussion:

Rhabdomyolysis denotes a clinical and laboratory syndrome that results from a rapid breakdown of skeletal muscle cells. This releases potentially toxic muscle cell components into the circulation which may cause life threatening complications including myoglobinuric acute renal failure, cardiac arrest or disseminated intravascular coagulation.⁽¹⁾ Rhabdomyolysis may result from a wide variety of causes, including primary muscle disease (metabolic and muscular dystrophy), infection, trauma, connective tissue disease, strenuous exercise, drug overdose, drug reaction, seizures, ischemia, and electrolyte derangements. Electrolyte abnormalities that lead to rhabdomyolysis include hypokalemia, hypocalcaemia, hypophosphataemia, hyponatraemia, hypernatraemia⁽³⁾, of which hypokalemia the most common, accounting for 14% - 28% of cases of rhabdomyolysis due to electrolyte abnormalities. However, hypokalemia may go unrecognized as the

cause of rhabdomyolysis due to the release of potassium from damaged muscle into the circulation which is considered a compensatory increase in serum potassium levels caused by rhabdomyolysis itself.⁽⁵⁾⁽⁸⁾

Rhabdomyolysis is defined as a pathological condition of skeletal muscle cell damage leading to the release of toxic intracellular material into the blood circulation, such as CPK, myoglobin, aspartate aminotransferase, alanine aminotransferase and potassium. The syndrome generally presents with the triad of muscular pain, weakness and reddish brown urine.

Hypokalemia might play an important role in muscle cell damage. Local potassium levels in capillaries are important regulators for vascular tension (2). Severe hypokalemia contracts capillaries, reduces muscle blood supply and finally results in lysing of muscle cells and muscle cell damage. Frank rhabdomyolysis usually occurs only when serum potassium values are below 2.0 mmol/L, which

possibly induces cardiac arrhythmia and needs emergency treatment.⁽⁴⁾

Conversely, subclinical rhabdomyolysis may be missed; biochemical evidence of rhabdomyolysis was documented in 32% of hypokalemic patients in one study.⁽³⁾

Rhabdomyolysis and myoglobinuria occur commonly in men who sustain environmental heat injury during intensive physical training in hot climates (10). These also occur in patients with potassium depletion. Since physical training in hot climates may be accompanied by serious loss of body potassium, the possibility was considered that performance of strenuous exercise when potassium was deficient might enhance susceptibility to rhabdomyolysis.⁽⁴⁾

The main clinical presentation is weakness. Weakness refers to a decrease in muscle strength. It is encountered in a number of medical and psychiatric disorders but it is highly a non-specific symptom (14). Therefore, evaluation and differential diagnosis of weakness in the emergency room is often difficult and time consuming⁽¹⁵⁾.

Hypokalemia is one of the electrolyte problems that can lead to weakness. When hypokalemia is determined, underlying causes should be investigated (18).

Although the mechanism by which potassium deficiency leads to rhabdomyolysis has not been elucidated, impressive evidence has accumulated that potassium release from contracting skeletal muscle cells into interstitial fluid of the muscle directly dilates the adjoining arterioles, and thereby, the potassium ion may be a major factor mediating the rise of muscle blood flow which normally occurs with exercise. Accordingly, it might be postulated that if potassium release from potassium-deficient skeletal muscle is impaired during intense exercise, muscle injury or frank necrosis could occur as a consequence of relative ischemia.⁽¹⁾

Potassium is released from contracting skeletal muscle fibers and its rising concentration in interstitial fluid is thought to dilate arterioles thereby mediating the normal rise of muscle blood flow during exercise. If potassium release from deficient muscle were subnormal, exercise would not be accompanied by sufficient muscle blood flow and rhabdomyolysis could occur by ischemia.⁽¹⁾ This hypothesis was examined by comparing the effect of electrically stimulated exercise on muscle blood flow, potassium release, and histology of the intact gracilis muscle preparation in normal and potassium-depleted dogs. In normal dogs, muscle blood flow and potassium release rose sharply during exercise (12). In contrast, muscle blood flow and potassium release were markedly subnormal in depleted dogs despite brisk muscle

contractions (13). Although minor histological changes were sometimes observed in non-exercised potassium-depleted muscle, frank rhabdomyolysis occurred in each potassium-depleted animal after exercise. These findings support the hypothesis that ischemia may be the mechanism of rhabdomyolysis with exercise in potassium depletion.⁽⁶⁾ Approach to management of acute renal failure in hypokalemic rhabdomyolysis is different from management of all other causes of rhabdomyolysis induced acute renal injury (18) since potassium replacement is needed, but forced diuresis using furosemide, sodium bicarb and/or hemodialysis will cause further critical decline in potassium level and thus should be contraindicated at least till potassium is corrected, on the other hand, volume overload due to the vigorous IV fluids administration necessitates different modalities for water removal without electrolytes from blood, and hence hemofiltration is preferred and should be available for management of such a case., Once potassium level is corrected by replacement, then hemodialysis and other measures of forced diuresis can be applied but with caution since liability for recurrence of hypokalemia is unpredictable, no universal guidelines had been authored for steps of management in this scenario most probably due to rarity of presentation of hypokalemia with rhabdomyolysis (16).

Recurrent subclinical rhabdomyolysis especially in high risk occupations due to heat exposure and strenuous muscular exercise may predispose to chronic occult renal damage and renal failure in a previously healthy individuals (3), this necessitates health awareness for plenty of fluids and potassium containing nutrients intake in high risk group for such a condition.

Conclusion:

This case should always remind the physicians to bear in mind the risk of hypokalemia-induced rhabdomyolysis especially with strenuous exercise at hot climates and occupational heat exposure. Rhabdomyolysis is usually associated with hyperkalemia due to renal failure, but hypokalemia as a preventable cause of rhabdomyolysis and ARF is usually missed, and Approach in early management is totally different.

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