

## Acute kidney injury followed by seizure induced rhabdomyolysis

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### Abstract

Rhabdomyolysis is a potentially life-threatening syndrome which is caused by muscle injury and characterized by the leakage of muscle cell contents, including electrolytes, myoglobin and other sarcoplasmic proteins into circulation. Rhabdomyolysis may develop from a variety of causes such as trauma, muscle disease, drugs and toxins etc. Acute kidney injury is the most frequent lethal complication of rhabdomyolysis. Seizures especially generalized tonic-clonic type can rarely cause rhabdomyolysis by the muscle forces generated during seizure episode. In this case, we represent a rarely seen case of acute renal failure due to rhabdomyolysis after seizure episodes with full recovery.

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## **Introduction**

Rhabdomyolysis is characterized by the leakage of muscle-cell contents, including electrolytes, myoglobin and other sarcoplasmic proteins (e.g., creatine kinase (CK), aldolase, lactate dehydrogenase (LDH), alanine aminotransferase (ALT) and aspartate aminotransferase (AST)) into circulation (1). It is a potentially life-threatening syndrome which may develop from a variety of causes such as trauma, muscle diseases, drugs and toxins, neuroleptic malignant syndrome, seizures etc (2,3). Rhabdomyolysis is characterized clinically by myalgias, red to brown urine due to myoglobinuria and elevated serum muscle enzymes (creatine kinase, LDH etc) (4).

It can cause fluid and electrolyte abnormalities, many of which precede or occur in the absence of kidney failure. Hepatic injury and cardiac dysrhythmias, some other complications such as acute kidney injury, compartment syndrome and disseminated intravascular coagulation may develop laterally in the course (5,6) .

Acute kidney injury (AKI) is the most common potentially lethal complication of rhabdomyolysis (1,2). Frequency of AKI due to rhabdomyolysis ranges between 15% to 50% (3,7). It is caused by a number of different reasons such as volume depletion, tubular obstruction and injury due to pigment casts, and free iron (8,9).

Seizures, especially generalized tonic-clonic type can rarely cause rhabdomyolysis by the muscle forces generated during seizure episode. We report here a rarely seen case of acute renal failure due to rhabdomyolysis after seizure episodes.

## **Case report**

A 19 years old female patient was admitted to emergency service with the complaints of nausea, vomiting and deterioration of oral intake. These complaints was started after 3 episodes of generalized tonic-clonic seizures in the previous week. In the personal history of the patient, she has a mild mental retardation and has been tonic-clonic seizure attacks since childhood. She has never gone to specialist for this reason. There was no history of hypertension, diabetes mellitus or another chronic disease and chronic usage of a drug in the past medical history of the patient.

At the time of admission, she was conscious, oriented, afebrile with a pulse rate of 80/min. Blood pressure was 135/75 mmHg and respiratory rate was 15/min. Neurological examination was normal with no signs of meningeal irritation and focal neurological deficit and there was no significant sign in other system examinations.

In the patient's initial laboratory, evaluation showed a total leucocyte count of 11000/mm<sup>3</sup>, urea 247 mg/dl, serum creatinine 7.43 mg/dl, CK:23681 U/l, LDH:632 U/L, ALT 138 u/l, AST 363 U/L, albumin 1.98 g/dl. In arterial blood gas analysis; pH 7.33, HCO<sub>3</sub> 19.2 mmol/l. In urine evaluation; it was dark brown coloured and showed 1 + protein and 6-7 red blood cells (RBCs) per high power field, but no casts. HBsAg, HCV, and HIV serology were negative. Abdominal - renal usg and two dimensional echocardiography were normal. Magnetic resonance imaging of the brain showed no abnormalities and the patient was transferred to nephrology clinic with the preliminary diagnosis of acute kidney injury due to rhabdomyolysis.

In clinical follow up, a central venous catheter was opened and one session of hemodialysis was made. Symptomatic therapy was started. The patient was managed with optimum rehydration and forced alkaline diuresis. EEG was performed and patient was reconsulted to neurology and levetiracetam therapy was started. After optimal therapy, laboratory tests of the patient came back to the normal levels in a period of two weeks (table 1). Patient was discharged with the proposal of outpatient control.

**Table 1.** Laboratory results of the patient

	13.05.14	15.05.14	16.05.14	18.05.14	20.05.14	23.05.14	31.05.14
Urea (mg/dl)	247	236	222	116	79	34	20
Creatinine (mg/dl)	7.43	7.22	7.61	5.4	3.95	1.64	0.86
CK (U/L)	23681	13732	>4267	>4267	2709	1802	145
LDH (U/L)	682	662	599	450	373	418	186
AST (U/L)	363	232	169	78	35	29	18
ALT (U/L)	138	106	88	51	34	23	15
Albumin (g/dl)	1.98	1.8	2	2.37	2.2	2.96	3.3

## Discussion

Rhabdomyolysis is a potentially life-threatening syndrome that may develop from multiple potential traumatic (multiple trauma, crush injuries, surgery, immobilization etc.) and non-traumatic causes (extreme exertion, hyperkinetic states, seizures, drugs, toxins, neuropathies, malignant neuroleptic syndrome etc.). The mechanism responsible for the rhabdomyolysis is the muscle cell death, which may be triggered by any of a variety of initiating events. The final common pathway for injury is an increase in intracellular free ionized cytoplasmic and mitochondrial calcium which may be caused by depletion of adenosine triphosphate (ATP), the cellular source of energy, and/or by direct injury and rupture of the plasma membrane (10). ATP depletion leads to myocyte injury and the release of intracellular muscle constituents, including CK and other muscle enzymes (aldolase, AST,ALT, LDH ETC), myoglobin, and various electrolytes. In this case, the cause which was responsible for the rhabdomyolysis was seizure episodes. A seizure episode can cause rhabdomyolysis by the extreme muscular activity which results in a state in which ATP production cannot keep up with the demand, subsequently exhausting cellular energy supplies leading to a disruption of muscle cell membranes.

Rhabdomyolysis can cause a variety of clinical manifestations and complications by the mechanisms above mentioned. The classical triad of muscular aches, generalized weakness and tea colored urine are non-specific and may not always be found. So, diagnosis of rhabdomyolysis is based on high index of suspicion and also laboratory tests are important for diagnosis. In the laboratory findings, the hallmark of rhabdomyolysis is an elevation in CK and other serum muscle enzymes. The other characteristic finding is the reddish-brown urine of myoglobinuria, but because this may be observed in only half of cases, its absence does not exclude the diagnosis.

CK levels are the most sensitive indicator of myocyte injury in the rhabdomyolysis. Normal CK enzyme levels are 45–260 U/l. CK rises in rhabdomyolysis within 12 hours of the onset of muscle injury, peaks in 1–3 days, and declines 3–5 days after the cessation of muscle injury. CK has a serum half-life of about 1.5 days and declines at a relatively constant rate of about 40 to 50 percent of the previous day's value (11). Usually, CK levels are at least five times the upper limit of normal, but range from approximately 1500 to over 100,000 international units/L. In a study by Melli G et al., the mean peak CK was reported for each of a variety of

different causes and for patients with both single and multiple causes ranged from approximately 10,000 to 25,000 (7). In our patient, CK level at admission was 23681 U/l which is consistent with CK values of clinically significant rhabdomyolysis cases. Other laboratory results such as urea, creatinine, alanine aminotransferase and aspartate aminotransferase were also changed significantly. In our patient, CK level was started to fall progressively in the follow-up. Also other laboratory tests were return to normal in clinical follow-up. The urine analysis of our patient at admission was dark brown coloured because of myoglobinuria in consistent with rhabdomyolysis urine findings. In supportive treatment with saline and bicarbonate, urine colour was gone to the normal progressively.

The complications of rhabdomyolysis can be classified as early and late complications. The early complications include hyperkalemia, hypocalcemia, elevated liver enzymes, cardiac dysrhythmias and cardiac arrest, while the late complications include AKI and disseminated intravascular coagulation. AKI is a common complication with a frequency ranges from 15% to over 50 % (12). dehydration and aciduria are important contributing factors for AKI development in rhabdomyolysis. Renal vasoconstriction with diminished renal circulation, intraluminal cast formation and direct heme protein-induced cytotoxicity are the main mechanisms responsible for AKI development (6). Among patients with rhabdomyolysis and AKI; long-term survival is close to 80% and majority of patients with rhabdomyolysis induced AKI recover renal function (13).

If creatine kinase levels are less than 15 000 U/L at admission; the risk of acute kidney injury is low (14). Although acute kidney injury may develop with lower creatine kinase values ( as low as 5000 u/l), this is rarely seen (15). Acute kidney injury was developed in our patient at admission and CK values of the patient was 23618U/l. This value was consistent with the CK values of patients in the literature who developed AKI after rhabdomyolysis. Renal functions of the patient was returned to normal after appropriate treatment especially with saline and bicarbonate treatment.

In conclusion, rhabdomyolysis can lead to different clinical manifestations and complications. Therefore, clinical suspicion and laboratory tests have an important role in the diagnosis of rhabdomyolysis. Seizures, especially generalized tonic-clonic types can rarely cause rhabdomyolysis and acute kidney injury as a result of this. So, our aim to report this case is to draw attention to these complications in patients with seizure attack

## References

- 1- Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med* 2009; 361: 62-72.
- 2- Khan FY. Rhabdomyolysis: a review of the literature. *Neth J Med* 2009; 67: 272-283.
- 3- Gabow PA, Kaehny WD, Kelleher SP. The spectrum of rhabdomyolysis. *Medicine* 1982; 61 (3): 141-152.
- 4- Knochel JP. Rhabdomyolysis and myoglobinuria. *Annu Rev Med* 1982; 33: 435-443.
- 5- Akmal M, Massry SG. Reversible hepatic dysfunction associated with rhabdomyolysis. *Am J Nephrol* 1990; 10: 49–52.
- 6- Huerta-Alardin AL, Varon J, Marik PE. Bench-to-bedside review: Rhabdomyolysis — an overview for clinicians. *Crit Care* 2005; 9: 158-169.
- 7- Melli G, Chaudhry V, Cornblath DR. Rhabdomyolysis: an evaluation of 475 hospitalized patients. *Medicine (Baltimore)* 2005; 84: 377-385.
- 8- Odeh M. The role of reperfusion-induced injury in the pathogenesis of the crush syndrome. *N Engl J Med* 1991; 324:1417-1422.
- 9- Zager RA, Burkhardt KM, Conrad DS, Gmur DJ. Iron, heme oxygenase, and glutathione: effects on myohemoglobinuric proximal tubular injury. *Kidney Int* 1995; 48: 1624-1634.
- 10- Giannoglou GD, Chatzizisis YS, Misirli G. The syndrome of rhabdomyolysis: pathophysiology and diagnosis. *Eur J Intern Med* 2007; 18: 90–100.
- 11- Mikkelsen TS, Toft P. Prognostic value, kinetics and effect of CVVHDF on serum of the myoglobin and creatine kinase in critically ill patients with rhabdomyolysis. *Acta Anaesthesiol Scand* 2005; 49: 859-864.
- 12- Veenstra J, Smit WM, Krediet RT, Arisz L. Relationship between elevated creatine phosphokinase and the clinical spectrum of rhabdomyolysis. *Nephrol Dial Transplant* 1994; 9 (6): 637-641.
- 13- Woodrow G, Brownjohn AM, Turney JH. The clinical and biochemical features of acute renal failure due to rhabdomyolysis. *Ren Fail* 1995; 17: 467-474.

14- de Meijer AR, Fikkers BG, de Keijzer MH, van Engelen BG, Drenth JP. Serum creatine kinase as predictor of clinical course in rhabdomyolysis: a 5-year intensive care survey. *Intensive Care Med* 2003; 29: 1121-1125.

15- Ward MM. Factors predictive of acute renal failure in rhabdomyolysis. *Arch Intern Med* 1988; 148: 1553-1557.