

# Rhabdomyolysis Causing Acute Kidney Injury in a Patient with Multiple Risk Factors and an Underlying Inflammatory Muscle Disease: A Case Report

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## ABSTRACT

A 33 year-old Caucasian male with underlying type one diabetes mellitus, dyslipidemia, hypothyroidism, and nephrotic syndrome secondary to membranous glomerulonephropathy (GN), presented with new onset tonic-clonic seizures (lasting one minute) after an episode of binge drinking in which there was a considerable period of immobilization. The patient was taking 80 mg of atorvastatin daily at the time of presentation. The patient was intubated and ventilated and initial laboratory investigations confirmed a creatine kinase (CK) of 12,000 U/L (normal 20-220 U/L) and creatinine of 3.1 mg/dL (normal 0.7-1.3 mg/dL), and associated symptomatic hyperkalemia of 5.6-5.9 mmol/L (normal 2.5-5.0 mmol/L). The patient developed acute kidney injury (AKI) presumed secondary to rhabdomyolysis, and required renal replacement therapy. His CK eventually peaked at 153,741 U/L on the seventh day of admission. The patient regained consciousness and improved clinically over the following weeks. A muscle biopsy performed on the 29th day of admission showed changes consistent with polymyositis. On follow-up testing, the patient's TSH was noted to be 101.99 mIU/L (normal 0.5-5.0 mIU/L) with a T4 of 5.5 pmol/L (normal 8.5-15.2 pmol/L) indicating uncontrolled hypothyroidism. This case highlights multiple potential etiologies causing rhabdomyolysis that may occur concurrently in a patient and contribute to AKI.

**KEYWORDS:** *rhabdomyolysis, AKI, polymyositis, CRRT*

## INTRODUCTION

Rhabdomyolysis is a condition in which skeletal muscle cells break down, releasing intracellular proteins, including creatine kinase and myoglobin, intravascularly. Clinical symptoms may include the classical triad of muscle pain, weakness, and brown urine. Rhabdomyolysis has multiple etiologies and accounts for 7-10% of AKI in the United States.<sup>1</sup> Of these etiologies, statin use, alcohol use, seizures, immobilization and hypothyroidism have been well-documented in the literature.<sup>2</sup> Polymyositis induced rhabdomyolysis has also been documented.<sup>3</sup> There is an increased incidence of rhabdomyolysis in patients possessing multiple risk factors.<sup>4</sup> While most patients afflicted with rhabdomyolysis causing AKI recover renal function, some studies have suggested that those patients in ICU settings have a mortality rate nearing 59%.<sup>5</sup>

We report here on a patient who developed rhabdomyolysis secondary to a combination of all of the above-mentioned

etiologies and subsequently required the administration of continuous veno-venous hemodiafiltration during an extended ICU admission.

## CASE REPORT

A 33 year-old Caucasian male presented to a community hospital after a grand-mal seizure occurring twenty-four hours after an episode of binge drinking, in which he consumed approximately 12 oz of liquor.

His medical history included a diagnosis of membranous GN proven by biopsy in 1998 as well as in 2009. He was showing signs and symptoms consistent with nephrotic syndrome two months prior to presentation. Prior to admission, the patient's baseline creatinine was 1.07 mg/dL with 4.20 g/day urine protein (normal <0.15 g/day). His nephrotic syndrome was also complicated by dyslipidemia. Medications on admission included insulin aspart 14 units TID, insulin glargine 26 units qhs, fosinopril 40 mg po od, ECASA 81 mg daily, atorvastatin 80 mg daily, candesartan 16 mg daily and levothyroxine 50 mcg daily. He was a one pack-per-

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day smoker and admitted to regular bouts of binge drinking.

The patient was intubated without sedation and physical exam showed no abnormalities except mild peripheral edema. Initial blood work showed a creatine kinase of 12,000 U/L and creatinine of 3.09 mg/dL. Intermittent hemodialysis was started and his potassium levels remained elevated between 5.6-5.9 mmol/L, which in turn was associated with a wide complex tachycardia. Head CT was normal. A bronchoscopy was also performed at this time and bronchial washing culture grew *Streptococcus pneumoniae* and *Haemophilus influenzae*.

The patient became anuric with refractory hyperkalemia despite daily intermittent hemodialysis and was diagnosed at that time with rhabdomyolysis causing AKI. He was hypotensive and was started on dopamine and norepinephrine infusion to maintain adequate perfusion. On day three of presentation, the patient was transferred to a tertiary care centre ICU and was started on continuous veno-venous hemodiafiltration secondary to persistent and rising potassium levels with EKG changes (Table 1). He was initially treated with Dilantin for seizure prophylaxis that was subsequently switched to valproic acid after he developed an apparent allergic reaction to Dilantin. Cefotaxime and vancomycin were started for treatment of his respiratory infection. The patient's liver function tests at time of transfer, aspartate transaminase (AST; normal values 0-35 U/L) and alanine transaminase (ALT; normal values 3-36 U/L) were 1511 U/L and 522 U/L, respectively. The patient's creatine kinase peaked at 153,741 U/L and creatine at 7.03 mg/dL on the seventh day of admission. The patient spent eighteen days in ICU, was dialyzed for approximately 26 days, and was discharged from hospital approximately three days after discontinuation of dialysis. On the day of discharge, lab work showed a creatinine value of 2.06 mg/dL, creatine kinase of 151 U/L, and LFT's within normal range.

There was an improvement clinically over the following weeks and a biopsy of the left deltoid muscle was performed on the day of discharge approximately thirty days after presentation. The results of this biopsy showed a chronic endomysial inflammatory infiltrate with degenerating fibers most consistent with polymyositis. This inflammatory picture showed a predominance of lymphocytic infiltrate which is consistent with the diagnosis of polymyositis, and not with alcohol or statin induced myopathy. On follow-up with a rheumatologist approximately five weeks after presentation, it was noted the patient did not present clinically with signs of polymyositis. In further follow-up, it was noted that since the time of his admission his TSH level had risen to 101.99 mIU/L from 16.16 mIU/L and his free T4 level dropped from 10.2

pmol/L to 5.5 pmol/L. The patient was discharged home on an increasing dose of thyroid replacement therapy, erythropoietin 4000 units IV weekly and the atorvastatin was discontinued. Creatinine returned to a stable value of 154 umol/L three months after presentation while the creatine kinase remains elevated at 854 U/L. The patient is clinically well.

## DISCUSSION

While the etiological components leading to rhabdomyolysis are diverse, a common pathway of myocyte injury has been elucidated.<sup>6</sup> The most fatal end result of this condition being AKI, with a mortality rate reported to be as high 50%.<sup>2</sup> The effects of these intracellular proteins on the kidney are multifactorial, with important components being hypovolemia, luminal obstruction by both myoglobin and uric acid casts, ischemia due to vasoconstriction<sup>7</sup> as well as direct damage by ferrihaemate.<sup>6</sup>

Our patient presented after an episode of binge drinking associated with a tonic-clonic seizure and period of immobilization. There was an underlying component of chronic kidney disease and polymyositis as well as hypothyroidism. He was also taking a statin and had an underlying respiratory infection. One study described the top three causes of rhabdomyolysis were illicit drug and alcohol use, prescribed pharmaceuticals, and trauma.<sup>4</sup>


Interestingly, this group<sup>4</sup> was the first to look at muscle diseases in a hospitalized population. They found that not only is polymyositis the most frequent muscle disease associated with rhabdomyolysis, but those with muscle diseases tend to develop rhabdomyolysis *de novo* and suffer from recurrent episodes. This finding is consistent with two case reports of a 39 year-old woman<sup>3</sup> and 57 year-old woman<sup>8</sup> who presented with distinct episodes of rhabdomyolysis in the context of an underlying polymyositis with no other risk factors.

Our patient's creatine kinase value was noted to be grossly elevated following admission to a tertiary care hospital. In most instances creatine kinase values rise shortly after muscle injury from 2-12 hours, peak in 1-3 days<sup>9</sup> and then decline 39% per day.<sup>10</sup> Persistently elevated levels may indicate ongoing muscle insult or the development of compartment syndrome.<sup>11</sup> Serum creatine kinase concentrations are not used to definitively define rhabdomyolysis, but many large-scale studies have assigned a value of five times normal as a diagnostic criterion.<sup>6</sup> There is a linear relationship between creatine kinase levels and serum creatinine levels. However, there is conflicting evidence regarding the association of CK levels with AKI<sup>12</sup> and it is generally accepted that factors such as age and multiple insults influence AKI independent of creatine kinase. Patients suffering from multiple insults have been found to have an increase incidence of AKI independent of creatine kinase levels.<sup>4</sup>

The patient described here presented with multiple risk factors for rhabdomyolysis. His underlying chronic conditions set the stage for a sub-clinical myopathy that was exacerbated by alcohol, seizure, and immobilization. Muscle biopsy is an infrequently employed technique of diagnosing rhabdomyolysis but may have further clinical value if there is an underlying muscle disease. Few cases of polymyositis induced AKI have been described,<sup>14,15</sup> but in the setting of acute on chronic muscle

**Table 1.** Indications for Dialysis<sup>16,17</sup>

Acid base	Acidemia (pH < 7.1)
Electrolyte abnormalities	Hyperkalemia (>6.5 meq/L or rapidly rising), hypercalcemia (>3.5 mmol/L), tumour lysis syndrome
Ingestion	Methanol, ethylene glycol, ASA, lithium
Overload	CHF
Uremia	Pericarditis, neuropathy, encephalopathy, bleeds

injury this condition would likely contribute significantly. The most frequently used diagnostic test, serum creatine kinase, may not predict who will develop AKI in patients who suffer from multiple insults.<sup>4</sup> The sustained increase in creatine kinase levels on follow-up two months later may indicate that there may be a sustained muscle insult, stemming from sub-optimal treatment of hypothyroidism or ongoing polymyositis. 

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# Elective Report: A European Take on Neuro-Anesthesia

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ABSTRACT

The LKH-Universitätsklinikum Hospital lies within Graz, Austria, a small city of approximately 250,000 residents. From a North American perspective this is an unrecognized medical university. It has an incredible dedication to teaching and is frequently visited by both European and Asian medical students as a part of their medical training. My opportunity to complete a four-week elective in the Department of Neuro-anesthesia was an invaluable opportunity that improved my understanding of this particular anesthesia subspecialty and the technological advancements specific to it. Unlike the more popular third world electives carried out by many of my peers, the focus of interest was not on the development of underprivileged healthcare systems. Rather, it was on the importance of international collaboration towards the betterment of medical care.

KEYWORDS: *anaesthesia, neuro-anaesthesia*

ELECTIVE REPORT

Graz, Austria, is well-known throughout Europe as a university town with upward of 44,000 students who attend the six universities situated within Graz.<sup>1</sup> Although a popular site of study for those residing in Europe, it is largely unknown internationally. With over 2,000 research profiles and

60,000 publications, it is surprising that the Faculty of Medicine in Graz remains largely hidden from international recognition and affiliation.<sup>2</sup> Furthermore, the faculty's extensive experience with the education and training of European medical students suggests that the University of Graz is a well-qualified site for Canadian medical student's elective experience.

Luckily, I was granted the opportunity to spend four weeks in the Department of Neuro-anesthesia at the LKH-Universitätsklinikum Hospital in Graz. During this period, my

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