Severe Rhabdomyolysis Secondary to Adenovirus Infection

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Severe Rhabdomyolysis Secondary to Adenovirus Infection

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INTRODUCTION

- Rhabdomyolysis presents with weakness, myalgias, and dark urine. There is severe muscle injury with extrusion of myocyte contents into the blood.
- There have been several reports of viral myositis resulting in rhabdomyolysis. The most common viral cause of rhabdomyolosis is influenza, accounting for 33-42% of adult cases.[1,2] Viral myositis causing rhabdomyolysis have also been reported in children.[3] In viral myositis causing rhabdomyolysis, CPK elevations can exceed 800,000 U/L.[2,4]
- Adenovirus is a double-stranded DNA virus of the *Adenoviridae* family most commonly implicated in pediatric upper respiratory illness. Uncommonly, adenovirus can cause encephalitis, meningitis, hemorrhagic cystitis, myocarditis, and rhabdomyolysis.
- Only 2 cases of rhabdomyolysis from adenovirus have been reported in the literature.[5,6] Adenovirus most commonly manifests as a febrile illness with pharyngitis and cervical adenitis.
- The diagnosis of viral myositis precipitating rhabdomyolysis is based on characteristic clinical features, results of viral culture and PCR, and exclusion of other causes of rhabdomyolysis.

CASE

A 38-year-old African American male presented to the emergency department with a 4-day history of generalized weakness, decreased appetite, subjective fever, chills, and diffuse myalgias to the point of impaired ambulation. The patient did not report difficulty speaking or swallowing. Two and a half weeks prior to presentation he had erythema and drainage in his left eye consistent with viral conjunctivitis. Several days later he noticed that his urine was dark and of decreased volume. The patient denied any strenuous activity, prolonged immobility, statin medication use, seizure activity, or illicit drug use. Review of systems was negative for paresthesias, peri-oral numbness, and muscle cramps. He took Losartan for essential hypertension. On physical examination, his blood pressure was 150/82 mmHg, heart rate was 85 beats per minute, temperature 96.3ºF, and oxygen saturation 96% on room air. His weight was 117 kg.

Laboratory data during course of the patient's illness are given in Table 1. He was in oliguric renal failure. Despite unknown baseline creatinine his presenting serum creatinine was 5.04, with hyperkalemia, hyperphosphatemia, and hypocalcemia. The serum CPK level was elevated at 857,200 U/L (normal <351). His urinalysis was positive for protein and blood. Urine myoglobin was positive. The patient was diagnosed with rhabdomyolysis and oliguric renal failure. In the setting of recent conjunctivitis symptoms and diffuse myalgias a viral panel was ordered and was positive for adenovirus. Other potential causes were excluded. Due to hyperkalemia, and oliguria he was initiated on hemodialysis.

DISCUSSION

- The pathogenesis of viral myositis is not well understood. Direct myocyte infection by the virus is one proposed mechanism, though visualization of viral inclusions on muscle biopsy is inconsistent.[7]
- In most cases, identification of the specific viral pathogen will not impact management or inform prognosis; thus, the benefit of serologic testing is uncertain. Oseltamivir is commonly used in the treatment of influenza, where it has been shown to reduce symptoms, including myalgias.[8] However, case reports suggest oseltamivir is not effective in preventing or treating influenza-associated rhabdomyolysis, and may even contribute to the pathogenesis of muscle injury.[9,10]
- The incidence of acute kidney injury among hospitalized patients with rhabdomyolysis is estimated between 13% and 50%.[11,12,13] Nearly 4% of patients suffering acute kidney injury from rhabdomyolysis require hemodialysis,[14] but the majority recover renal function.[15]
- Predicting incidence and severity of renal impairment, need for renal replacement therapy, and mortality based on CPK level has been studied. In a study of critically ill patients with rhabdomyolysis, de Meijer and colleagues[16] found a positive correlation between the degree of CPK elevation and of the incidence of acute kidney injury. However, other studies have shown neither the CPK level on presentation[17] nor the peak CPK level[11,13,14] are predictive of the need for renal replacement therapy.
- Hypocalcemia in rhabdomyolysis is due to movement of extracellular calcium into damaged muscle cells, and subsequent complexing with intracellular phosphate and soft tissue calcification.[18] Low levels of 1,25(OH)$_2$ Vitamin D and skeletal resistance to parathryroid hormone may also contribute to hypocalcemia in this setting.[19] Calcium supplementation is usually avoided unless hypocalcemia is symptomatic to minimize the development of hypercalcemia during the recovery phase. Hypocalcemia should be treated with intravenous calcium if carpopedal spasm, tetany, or seizures develop.

Table 1. Laboratory Data

Serum Parameter	Day 1	Day 2[a]	Day 3	Day 4[b]	Day 10	Day 17[c]	Day 64[d]
Sodium (mmol/L)	125	124	122	129	139	136	137
Potassium (mmol/L)	4.7	7.3	6.7	6.4	4.3	4.2	4.1
Chloride (mmol/L)	89	83	84	94	103	104	102
Bicarbonate (mmol/L)	17	20	26	23	24	24	26
BUN (mmol/L)	40	52	58	43	56	40	17
Creatinine (mg/dL)	5.04	5.79	8.50	7.02	6.52	9.52	1.32
CPK (U/L)	857,200	360,000	1,149,533	900,500			245
Phosphorus (mg/dL)	14.4	>16	14.6	9.9	4.3		3.5
Calcium (mg/dL)	5	<5	<5	<5	11.6	8.2	9.4
Ion. Calcium (direct)			<2.24	2.4	6.7		

[a]Day 2 - hemodialysis initiated
[b]Day 14 - switched from HD to continuous renal replacement therapy
[c]Day 17 - hospital discharge, still dialysis-dependent
[d]Day 64 - **outpatient follow-up, off dialysis**

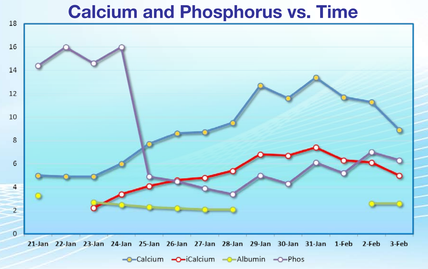

Table 2. Major Causes of Rhabdomyolysis

Category	Specific Causes
Traumatic	• Crush syndrome • Limb compression • High-voltage electrical injury • Prolonged immobility
Exertional	• Seizure • Alcohol withdrawal • Exercise • Amphetamine overdose
Genetic	• Disorders of glucogenolysis and glycolysis • Disorders of lipid metabolism • Mitochondrial disorders
Infectious	• Influenza A & B • Coxsackievirus • Epstein-Barr virus • Primary Human Immunodeficiency Virus • Legionella species • Adenovirus
Body Temperature Deregulation	• Heat stroke • Hypothermia • Malignant hyperthermia • Malignant neuroleptic syndrome
Metabolic Derangements	• Hypophosphatemia • Hypokalemia • Hypocalcemia • Nonketotic Hyperosmotic Disorders • Diabetic ketoacidosis • Primary adrenal insufficiency • Hypothyroidism • Hyperthyroidism
Drugs and Toxins	• Fibrates • Statins • Antipsychotics • Alcohol, heroin, cocaine, amphetamine • Snake and insect venom
Autoimmune	• Polymyositis • Dermatomyositis

HEMODIALYSIS, CALCIUM and PHOSPHATE MANAGEMENT

- Despite aggressive volume resuscitation, the patient remained oliguric and hyperkalemic, and was initiated on hemodialysis (HD) on hospital day 2. His initial dialysis treatment consisted of 2 hours with a blood flow rate of 200 ml/min and a dialysate flow rate of 300 cc/hr, against a 2 mEq/L potassium bath and 2.5 mEq/L calcium bath. After 2 HD treatments, the patient remained hyperkalemic (K = 6.4 mEq/L) and hypocalcemic (Ca < 5.0 mg/dL) and was therefore changed to continuous veno-venous hemodialysis (CVVHD) on hospital day 4. He was maintained on CVVHD until the potassium normalized, and he was transitioned back to intermittent HD on hospital day 7. On admission the patient weighed 111 kg. His peak body weight was 118.5 kg on hospital day 9, reflecting accumulated volume from fluid resuscitation. On day of discharge the patient weighed 110 kg.
- Our patient developed severe hypocalcemia by hospital day 2, without signs of neuromuscular irritability. Initially, severe hyperphosphatemia precluded calcium supplementation for fear of exacerbating calcium-phosphate precipitation. By hospital day 4, hyperphosphatemia resolved but hypocalcemia persisted, and oral supplementation with calcium acetate was initiated. This, together with positive calcium balance on CVVHD (Prismasate calcium concentration 2.5 mEq/L), may have contributed to the development of hypercalcemia on hospital day 9 (Ca = 12.7 mg/dL). At this point, his calcium supplementation was discontinued, and his dialysate calcium was changed to 2.0 mEq/L. His vitamin D 25-OH level was 7 and intact parathyroid hormone 22.6. His serum calcium level peaked at 13.4 mg/dl, then gradually returned to the normal range (See figure 1).

CONCLUSION

Adenoviral infection can lead to rhabdomyolysis with severe acute kidney injury. Respiratory viral panel should be included in workup of rhabdomyolysis when no other cause is evident. Treatment includes supportive care, intravenous fluid resuscitation, and renal replacement therapy. Continuous renal replacement therapy should be considered in severe cases for management of severe electrolyte abnormalities and volume status.

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