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# Adenovirus Induced Rhabdomyolysis Causing Hemodialysis Dependent Acute Renal Failure

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## Background

- Adenoviruses are double-stranded DNA viruses belonging to the family Adenoviridae.
- An extremely hardy virus, adenovirus is ubiquitous in human and animal populations, survives long periods outside a host, and is endemic throughout the year. It is transmitted via direct inoculation to the conjunctiva, fecal-oral route, aerosolized droplets, or exposure to infected tissue or blood.
- The clinical syndromes commonly associated with adenovirus (ADV) infection, which is usually in children, are febrile pharyngitis with or without conjunctivitis, severe and often fatal pneumonia, keratoconjunctivitis, acute hemorrhagic cystitis and asymptomatic intestinal infection.
- In adults, it causes acute respiratory disease, which varies from mild, febrile pharyngitis and tracheitis to severe, fatal pneumonia and rarely encephalitis, meningitis, myocarditis and rhabdomyolysis.
- Rhabdomyolysis is a syndrome characterized by severe muscle injury causing elevated serum concentrations of creatine phosphokinase (CPK) and myoglobinuria leading to electrolyte imbalances, acute renal failure (ARF), and DIC.
- Most common causes of Rhabdomyolysis are traumatic muscle injury, drugs and toxins, ischemic, inflammatory disorders. Among non-traumatic causes infectious etiology is very rare.
- However sporadic cases of infectious myoglobinuria are reported, with most common causative agent being Influenza [accounting for 33 to 44% of adult cases].<sup>1,2</sup>
- Adeno virus has been implicated as a causative agent for Rhabdomyolysis only in 2 case reports, based on literature review.<sup>5,6</sup>
- This case report describes a "Severe case of Rhabdomyolysis induced renal failure requiring Hemodialysis and the causative agent was concluded to be Adeno virus".
- A high index of suspicion for rare viral etiology is required when other causes of myositis is ruled out in a patient presenting with acute febrile illness and severe rhabdomyolysis.

## Case Presentation

We report a case of healthy 39 year old African American male who presented with acute febrile illness which was preceded with symptoms suggestive of viral conjunctivitis.

Past medical history significant for essential hypertension for which he takes valsartan.

The patient was in his usual state of health until approximately 2 weeks before his hospital admission when he noticed erythema and drainage in his left eye consistent with a viral conjunctivitis. He had associated self remitted diarrheal illness.

Shortly thereafter in the next couple of days he developed severe muscle aches to an extent of impaired ambulation and associated with increased fatigability, subjective fevers with chills.

He had around this time developed "Dark urine" for which he was evaluated at his PCP's office where a urine dipstick was positive for blood. He was given a script for Trimethoprim-sulfamethoxazole empirically for presumed urinary tract infection.

The hematuria continued afterwards. He eventually became oliguric, for which he presented to ER at our facility and was found to be in frank Rhabdomyolysis.

On further questioning he said his symptoms were not preceded by any specific medication changes, denied statin use, excessive alcohol use, recreational drug abuse, seizure activity, prolonged immobilization, severe physical exertion, eating wild game, crush injury or compartment syndrome.

Family history was significant for kidney disease of unknown etiology in his Mother but no family history of muscle disorder-myopathies/muscular dystrophy.

On physical examination, his blood pressure was 150/82 mmHg, heart rate was 85 beats per minute, temperature 96.30 F, and oxygen saturation 96% on room air.

On presentation he was found to have oliguric renal failure with creatinine of 5.04 [previous unknown baseline] with significant anemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. The serum CPK level was elevated at 857,200 U/L (normal < 35).

Laboratory data during course of the patient's illness are given in Table 1 and Table 2.

His urinalysis was positive for protein and blood. Urine myoglobin was positive. Multiplex real-time RT-PCR assay performed on respiratory specimens was negative for influenza but positive for adenovirus DNA. The patient was diagnosed with Rhabdomyolysis and oliguric renal failure due to Adenoviral infection after excluding all other potential etiologies.

Table 1: Laboratory Data

TEST	RESULT
Urine Toxic Screen	Negative for Cocaine
URINE MYOGLOBIN	POSITIVE
URINE ANALYSIS	POSITIVE FOR BLOOD
Serum Level: Alcohol	Negative
Serum Level: Salicylates	Negative
Blood Culture x 2	No growth in 5 days
HIV	Negative
Comprehensive Hepatitis Panel	Negative
CMV and Mycoplasma	Mild elevations of IgM, WITH elevations of IgG
EBV and VCA	IgG antibody
Influenza A and B	Negative
ADENO VIRUS DNA	POSITIVE

Table 2: Laboratory Data

TEST	DAY 1	DAY 2	DAY 3	DAY 4	DAY 64
Sodium (mmol/L)	125	124	122	129	137
Potassium (mmol/L)	4.7	7.3	6.7	6.4	4.1
Chloride (mmol/L)	89	83	84	94	102
Bicarbonate (mmol/L)	17	20	26	23	26
BUN (mmol/L)	40	52	58	43	17
Creatinine (mg/dL)	5.04	5.79	8.50	7.02	1.32
CPK	857,200	1,360,000	1,149,533	900,500	245
Phosphorus (mg/dL)	14.4	>16	14.6	9.9	3.5
Calcium (mg/dL)	5	<5	<5	<5	9.4

## Discussion Follow-up and Conclusions

### DISCUSSION

- The classic triad of symptoms of Rhabdomyolysis consists of myalgia, weakness, and tea-colored urine. The muscle mass of the patient, the concentration of urine, and glomerular function can affect the color of the urine.
- Among various causes of Rhabdomyolysis, Infectious specifically Viral etiology is uncommon.
- Influenza is the most common viral etiology followed by HIV infection and Enterovirus infection.<sup>1</sup> Adenovirus is a rarely reported cause.
- Precise pathophysiology underlying virus induced myoglobinuria is unknown. However two mechanisms have been postulated: direct viral invasion of muscle fiber causing muscle necrosis and toxin or cytokine generation.<sup>1</sup>
- Renal dysfunction associated with rhabdomyolysis arises from a variety of factors. Myoglobin obstructs tubules and is a direct renal toxin. Cortical ischemia and decreased glomerular filtration are also injurious, and when these conditions are combined with hypovolemia, oliguric renal failure can result.
- 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<sup>16</sup> 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<sup>17</sup> nor the peak CPK level<sup>11,13,14</sup> are predictive of the need for renal replacement therapy.
- The incidence of acute kidney injury among hospitalized patients with rhabdomyolysis is estimated between 13% and 50%.<sup>11,12,13</sup> Nearly 4% of patients suffering acute kidney injury from rhabdomyolysis require hemodialysis,<sup>14</sup> but the majority recover renal function.<sup>15</sup>
- One of the most important goal of Rhabdomyolysis treatment is to avoid Acute Renal failure.
- Aggressive fluid management to aim urinary output goal of 200 mL/h, urine pH >6.5, and plasma pH <7.5 should be achieved.
- Renal replacement therapy should be promptly started in patients who fail to respond to fluid management.

### FOLLOW-UP

- Despite aggressive volume resuscitation, the patient remained oliguric and hyperkalemic, and was initiated on hemodialysis (HD) on hospital day 2. 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.
- He was still dependent on hemodialysis on the day of discharge and eventually HD was stopped and his last known CPK was 245.

### CONCLUSIONS

Adenovirus infection can be a rare but fatal cause of Rhabdomyolysis which in turn is a life threatening condition with complications like Acute renal failure and compartment syndrome. A very high index of suspicion for Viral etiology is required while working up a case of rhabdomyolysis. A comprehensive viral panel is warranted when appropriate clinical presentations is present. 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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