

CLINICAL VIGNETTE

Acute Renal Failure from Rhabdomyolysis Brought on by Influenza A Infection: A Rare but Dangerous Complication of a Common Infection

Gregory Bierer, MD and M. Iain Smith, MD

The diagnosis and management of influenza has received increased attention since the H1N1 pandemic of 2009. In addition to the well-known risks for respiratory failure, influenza infection can be associated with extrapulmonary manifestations such as myocarditis, pericarditis and encephalitis. Rhabdomyolysis is another rare, but potentially dangerous complication of influenza A infection. We present a case of rhabdomyolysis induced by influenza infection, which resulted in acute renal failure.

Case Report

A 70-year-old man with life-long deafness and type 2 diabetes was doing well at home until a few days prior to admission when he developed cough and fever. He was seen by his primary doctor and given azithromycin for presumed chest infection. The following day he was feeling “weaker” and more short of breath (although no falls, no muscle pains, and still ambulatory). His friends called paramedics to have him brought to the hospital. At arrival in the emergency room he denied chest pain, or productive sputum. He was having no muscle pain. He stated he was taking his prescribed medications including metformin, hydrochlorothiazide, levothyroxine, sitagliptin, atenolol, amlodipine, simvastatin, quinapril, and diazepam and the newly prescribed antibiotic. He was taking no over the counter medications, herbal medications or NSAIDs.

In the emergency room his temperature was 101.6, his blood pressure 95/66 and he was requiring 6 L/min face-mask to maintain oxygen saturation greater than 95%. His exam was notable for diffuse rhonchi throughout his lung fields. There was no muscle tenderness or signs of trauma. His laboratories showed an elevated WBC (18,000 with left shift) with normal hematocrit and platelet count.

His chemistries showed Na 123, K 5.1, CO₂ of 15 with a gap of 20 and a bun of 44 with a creatinine of 3.7 mg/dl. His CK value was 30,000 and his lactate value 60. Urine and serum toxicology studies were negative.

His CXR at admission showed some patchy densities (Figure 1) and he was admitted to the ICU on broad spectrum antibiotics, oseltamivir and vigorous intravenous fluids. Initially he was anuric, with bedside ultrasound showing normal sized kidneys and no hydronephrosis. A central line was placed which showed a CVP of 14 mm Hg, and an echocardiogram showed normal wall motion. A call to his outside doctor revealed he had normal blood chemistries (including normal creatinine) a few months ago, and other than the new antibiotic his medications had been unchanged for several years. The following day the patient began to make scant amounts of urine and his laboratories remained with an elevated CK value of 24,000 and creatinine increased at 5.7 mg/dl. Urinalysis showed minimal sediment or cells, but did have a positive reaction for pigment. A urine myoglobin returned later with a high value of 388 mcg/L (nl > 28 mcg/L). Sputum obtained at admission showed no bacterial growth, but PCR from a nasal swab was influenza A positive.

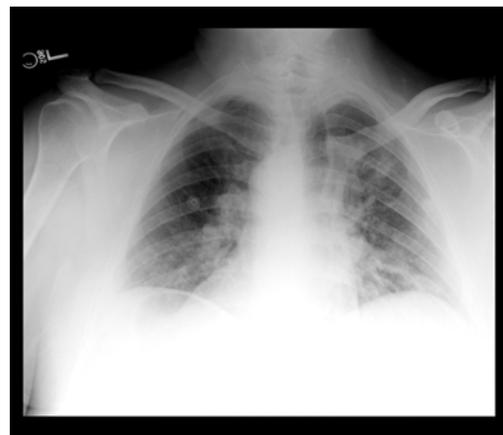


Figure 1

The patient's urine output gradually improved, creatinine kinase levels gradually came down and his creatinine returned to near normal over the subsequent week of hospitalization. He completed a full course of oseltamivir and returned home after discharge feeling well.

Discussion

Acute rhabdomyolysis can result in enough muscle breakdown to cause renal injury and failure. The myoglobin released from the muscle is believed to be directly toxic to the kidney. Compression injury and trauma are well known to causes of severe muscle injury. This patient had no trauma or cause for compression injury. Less obvious causes of acute rhabdomyolysis include drugs, toxins, electrolyte abnormalities, endocrinopathies and infections. This patient's toxicology screen was negative. There are certain prescription drugs which have been implicated in causing rhabdomyolysis. HMG CoA inhibitors (such as simvastatin- taken by this patient) can induce severe muscle injury. Muscle symptoms of pain and tenderness typically develop after several months of treatment with these agents in susceptible patients. Large reviews have estimated the risk for progression of such muscle injury to rhabdomyolysis from this class of drugs at 1.6 patients per 100,000 patient-years¹. Interestingly, in the rare cases where this does occur, a second drug has often been prescribed and is implicated as aggravating the effects of these agents on the muscles (in 60% of the cases in one series)². Azithromycin (the antibiotic recently prescribed to our patient) has been reported in at least one case as causing rhabdomyolysis in a patient taking an HMG CoA inhibitor³. Although we cannot entirely rule out drug effects in our patient, muscle injury to this degree would be quite rare and is typically heralded by symptoms developing over the course of months. It would also be somewhat surprising to develop problems with this agent after so many years of use.

The more likely cause of rhabdomyolysis in our patient was acute infection. His cough, fever, lung findings and CXR were most consistent with pneumonia. Several chest infections have been associated with rhabdomyolysis. There are many case reports on both legionella⁴ and mycoplasma⁵ pneumonias being associated with rhabdomyolysis.

Our patient had evidence of influenza A infection. There have also been repeated case reports of rhabdomyolysis associated with this infection over the last 30 years⁶⁻⁹. A recent literature review identified 31 cases of renal failure induced by influenza A. Twenty one of these cases ultimately required renal replacement therapy. When muscle biopsies were performed in these cases they often showed necrosis without significant inflammation, suggesting direct viral myositis¹⁰. In fact, the true rate of muscle inflammation related to influenza is not known. It's possible it may be overlooked in many mild cases of the influenza. Myalgias are a common symptom of influenza infection. Of note, a recent review of hospitalized cases during the 2009 H1N1 influenza epidemic showed 19% of these patients had CK elevations¹¹.

The management of rhabdomyolysis induced renal failure is based mainly on studies done on crush injuries¹². Adequate volume resuscitation is believed important to continue kidney perfusion and replenish intravascular volume extravasations into the inflamed muscles. Serum calcium, potassium and uric acid should be checked frequently as they will often increase as the muscle tissue breaks down. Some have advocated forced alkaline diuresis with bicarbonate in IV fluids, although this needs to be done cautiously as it can aggravate hypocalcemia. The routine use of bicarbonate in resuscitation fluids has been challenged, and many feel normal saline is just as efficient¹³. Often dialysis is needed in the setting of severe acute renal failure. Most cases of rhabdomyolysis induced renal failure will reverse if the patient's overall condition can be improved. The overall mortality, however, for critically ill patients who develop renal failure requiring renal replacement therapy is known to be high¹⁴.

Rhabdomyolysis is a rare but well reported complication of influenza A infection. Prompt recognition and careful fluid and electrolyte management are important to avoid progression to renal failure. Clinicians should be aware of this potential complication associated with this common respiratory infection.

REFERENCES

1. Tomaszewski M, Stępień KM, Tomaszewska J, Czuczwar SJ. Statin-induced myopathies. *Pharmacol Rep.* 2011;63(4):859-66. Review. PubMed PMID: 22001973.

2. **Kashani A, Phillips CO, Foody JM, Wang Y, Mangalmurti S, Ko DT, Krumholz HM.** Risks associated with statin therapy: a systematic overview of randomized clinical trials. *Circulation*. 2006 Dec 19;114(25):2788-97. Epub 2006 Dec 11. Review. PubMed PMID: 17159064.
3. **Alreja G, Inayatullah S, Goel S, Braden G.** Rhabdomyolysis caused by an unusual interaction between azithromycin and simvastatin. *J Cardiovasc Dis Res*. 2012 Oct;3(4):319-22. doi: 10.4103/0975-3583.102720. PubMed PMID: 23233778; PubMed Central PMCID: PMC3516014.
4. **McConkey J, Obeius M, Valentini J, Beeson MS.** Legionella pneumonia presenting with rhabdomyolysis and acute renal failure: a case report. *J Emerg Med*. 2006 May;30(4):389-92. PubMed PMID: 16740446.
5. **Berger RP, Wadowksy RM.** Rhabdomyolysis associated with infection by *Mycoplasma pneumoniae*: a case report. *Pediatrics*. 2000 Feb;105(2):433-6. PubMed PMID: 10654971.
6. **Cunningham E, Kohli R, Venuto RC.** Influenza-associated myoglobinuric renal failure. *JAMA*. 1979 Nov 30;242(22):2428-9. PubMed PMID: 490855.
7. **Berry L, Braude S.** Influenza A infection with rhabdomyolysis and acute renal failure--a potentially fatal complication. *Postgrad Med J*. 1991 Apr;67(786):389-90. PubMed PMID: 2068037; PubMed Central PMCID: PMC2398832.
8. **Wakabayashi Y, Nakano T, Kikuno T, Ohwada T, Kikawada R.** Massive rhabdomyolysis associated with influenza A infection. *Intern Med*. 1994 Jul;33(7):450-3. PubMed PMID: 7949648.
9. **Annerstedt M, Herlitz H, Mölne J, Oldfors A, Westberg G.** Rhabdomyolysis and acute renal failure associated with influenza virus type A. *Scand J Urol Nephrol*. 1999 Aug;33(4):260-4. PubMed PMID: 10515090.
10. **Watanabe T.** Renal complications of seasonal and pandemic influenza A virus infections. *Eur J Pediatr*. 2013 Jan;172(1):15-22. doi: 10.1007/s00431-012-1854-x. Epub 2012 Oct 13. Review. PubMed PMID: 23064728.
11. **Cao B, Li XW, Mao Y, Wang J, Lu HZ, Chen YS, Liang ZA, Liang L, Zhang SJ, Zhang B, Gu L, Lu LH, Wang DY, Wang C;** National Influenza A Pandemic (H1N1) 2009 Clinical Investigation Group of China. Clinical features of the initial cases of 2009 pandemic influenza A (H1N1) virus infection in China. *N Engl J Med*. 2009 Dec 24;361(26):2507-17. doi: 10.1056/NEJMoa0906612. Epub 2009 Dec 9. PubMed PMID: 20007555.
12. **Gunal AI, Celiker H, Dogukan A, Ozalp G, Kirciman E, Simsekli H, Gunay I, Demircin M, Belhan O, Yildirim MA, Sever MS.** Early and vigorous fluid resuscitation prevents acute renal failure in the crush victims of catastrophic earthquakes. *J Am Soc Nephrol*. 2004 Jul;15(7):1862-7. PubMed PMID: 15213274.
13. **Brown CV, Rhee P, Chan L, Evans K, Demetriades D, Velmahos GC.** Preventing renal failure in patients with rhabdomyolysis: do bicarbonate and mannitol make a difference? *J Trauma*. 2004 Jun;56(6):1191-6. PubMed PMID: 15211124.
14. **Lown DJ, Knott J, Rehnitzer T, Maclsaac C.** Predicting short-term and long-term mortality in elderly emergency patients admitted for intensive care. *Crit Care Resusc*. 2013 Mar;15(1):49-55. PubMed PMID: 23432502.