Influenza A(H1N1) Infection with Rhabdomyolysis and Acute Renal Failure-A Case Report

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Abstract

Pandemic 2009 influenza A (H1N1) is an emerging disease first reported in April, 2009. Previous studies have pointed out that patients with pneumonia and respiratory failure arising from pandemic H1N1 may have abnormal laboratory examination results, including elevated creatine kinase (CK) levels. We report a patient with pandemic H1N1 infection who developed mild rhabdomyolysis and acute kidney injury (AKI). Rhabdomyolysis is uncommon but potentially life-threatening. We present a 33-year-old patient who developed rhabdomyolysis following pandemic influenza A (H1N1/09) infection. Although pneumonia and acute respiratory distress syndrome are the most common severe complications of H1N1/09 infection, clinicians should be aware that H1N1/09 infection may be complicated by rhabdomyolysis. (J Intern Med Taiwan 2011; 22: 138-141)

Key words: Rhabdomyolysis, Acute renal failure, Influenza

Introduction

Rhabdomyolysis has multiple aetiologies, among them, trauma, intense exercise, infection, drugs or toxins, genetic defects, and metabolic or neuromuscular diseases have been described¹. Viral aetiology, mostly influenza, has been reported to be the predominant cause of infection-induced rhabdomyolysis. The mechanisms of rhabdomyolysis caused by influenza virus remain unclear. Certain hypothetical mechanisms, including muscle damage due to direct viral invasion or induction by an immune-mediated action, have been proposed. Recent reports showed that >40% of pandemic influenza A (H1N1/09) admissions had abnormal muscle enzyme values, implying that pandemic influenza A (H1N1/09) virus might cause muscle damage or inflammation.

Case report

A previously fit 33-year-old man presented with productive cough, generalized myalgia for five days. For 24 hours prior to admission he had become aware of marked oligouria, passing very small volumes of dark brown urine. His vital signs included a blood pressure:140/90mmHg, body
temperature of 36.5°C, pulse rate of 110 beats/min, respiratory rate of 28 breaths/min. There was a coarse crackle over bilateral lower lung fields on chest auscultation. The results of laboratory tests were as follows: white blood cell count of $7.6 \times 10^3/\mu L$ (89% neutrophils, 2% lymphocytes); serum urea nitrogen, 46 mg/dL, serum creatinine, 7.0 mg/dL; potassium, 4.7 mEq/L; aspartate aminotransferase, 198 U/L (normal, <40 U/L); and CK level, 1141 U/L (normal, 38-174/L). A urine dipstick test for occult blood had positive findings in the absence of red blood cells. An in-house real-time reverse transcriptase-polymerase chain reaction (RT-PCR) from a nasopharyngeal swab sample was positive for pandemic H1N1. The chest radiography showed mild infiltration over both lower lung fields. Therapy with oseltamivir (75mg q12h) was initiated. He was treated with intense hydration and urine alkalization for rhabdomyolysis and acute kidney injury (AKI). Acute lung edema developed 12 hours later. He received hemodialysis therapy. Ten days after admission, he regained urine output with subsequent falls in serum urea and creatinine (BUN/Cr: 19/1.8mg/dL). He received 6 sessions of hemodialysis.

**Discussion**

Serious and potentially fatal complications of acute influenza infection include pneumonia (occasionally with superimposed staphylococcal infection), myocarditis or pericarditis, and a variety of neurological disorders including encephalitis, myelitis and Guillain-Barre syndrome. No study has examined prospectively the incidence of myoglobinuria and acute renal insufficiency in influenza epidemics. It is conceivable that less serious forms of this syndrome are more common than formerly appreciated, as their presentation may be asymptomatic and recovery in renal function spontaneously.

The classic triad of rhabdomyolysis includes myalgia, red-to-brown or dark urine and muscle weakness. However, less than 10% of patients with rhabdomyolysis show all three classic features and 3.6% have dark urine, implicating a potentially insidious onset. The diagnosis of rhabdomyolysis is confirmed by laboratory studies.

Myoglobinuria can produce pigmenturia thus aiding in the diagnosis of rhabdomyolysis. Although myoglobinuria is usually detected in cases of rhabdomyolysis which does not necessarily result in visible myoglobinuria.

Myoglobin has a short half-life (2-3 hours) and could be rapidly and unpredictably eliminated by hepatic metabolism and renal excretion. The test for myoglobin in plasma or urine would be negative before any medical attention is sought; thus, the diagnosis of rhabdomyolysis cannot be completely ruled out. The classic laboratory finding as the diagnostic criteria for rhabdomyolysis is an elevated serum CK of $\geq 5$ times the normal value, in which the CK is almost entirely of skeletal muscle fraction.

The complications of rhabdomyolysis include hyperkalaemia, hypocalcemia, cardiac dysrhythmias, cardiac arrest, acute renal failure, disseminated intravascular coagulation and compartment syndrome. Acute renal failure is the most common among them and has been reported in 13 to 50% of patients with rhabdomyolysis. The mechanisms of renal damage include tubular obstruction, the toxic effect of free chelatable iron on tubules, and vasoconstriction.

Hypovolaemia or dehydration and aciduria (urine pH <6.5) have been suggested as crucial factors in the development of renal failure from rhabdomyolysis; therefore, early and aggressive fluid repletion and bicarbonate therapy, if necessary, are the standard treatment to prevent acute renal failure.

Although myalgic symptoms are almost invariable in influenza illnesses, myositis
and myoglobinuria appear to be extremely rare and have been documented only in influenza A infection. Myalgia is usually prominent early in the illness, contrasting with available descriptions of influenza-associated myositis where onset is after or during resolution of respiratory symptoms. More commonly reported in children, myositis associated with influenza A and B has been well documented and appears to occur most often during the convalescent phase of illness.

Influenza-associated rhabdomyolysis with myoglobinuria has been shown to complicate 3% of cases of myositis in children, which is more likely to be associated with influenza A infection, and has been associated with renal insufficiency requiring renal replacement therapy.

The frequency of myositis or rhabdomyolysis among adults with pandemic (H1N1) 2009 infection is unclear, but a recently published case series of 18 severely ill patients in Mexico showed that mild to moderate CK elevation (1,000~5,000 U/L) occurred in >60% of tested patients. Clinicians should consider a pandemic influenza A (H1N1/09) infection in any person with cold-like symptoms and suspected contact history in the worldwide pandemic surroundings. Physicians should also be aware that pandemic influenza A (H1N1/09) infection may be complicated by rhabdomyolysis. Rhabdomyolysis should be considered in the evaluation of muscle symptoms associated with pandemic (H1N1) 2009 virus infection, especially among critically ill patients.

Martin-Loeches et al reported a prospective, observational, multi-center study conducted in 148 Spanish intensive care units about H1N1 associated with AKI. It showed that 17.7% of patients developed AKI injury, and 75.5% of them required continuous renal replacement therapy.

Acute renal failure is a complex disorder that occurs in a variety of setting, with clinical manifestations ranging from a minimal elevation in serum creatinine to anuric renal failure. It is often under-recognized and is associated with severe consequence. Acute renal failure has been reported worldwide during the last pandemic with very different incidence. Well-recognized influenza complications in these seriously ill with pandemic 2009 influenza A (H1N1) virus infection have included renal failure, however, the exact impact has not been extensively investigated. Direct muscle invasion by the virus is one of the possibilities suggested for the virus-related rhabdomyolysis, but not all the patients who developed acute renal failure showed high level of CK.

References
A 型流感併發橫紋肌溶解症急性腎衰竭 - 病例報告

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摘 要

首例 A 型流感於 2009 年 4 月發現。以前的研究顯示 A 型流感病患併發肺炎及呼吸衰竭常會有異常上升的肌酸激酶。我們報告一例 33 歲 A 型流感病患，併發橫紋肌溶解症及急性腎衰竭。( 太短，要詳細些 ) 橫紋肌溶解症並不常見，但可能會有生命危險。A 型流感最常見的併發症仍是肺炎及急性呼吸衰竭。臨床醫師仍應該留心 A 型流感可能併發橫紋肌溶解症。