Case Report

Three cases of acute myositis in adults following influenza-like illness during the H1N1 pandemic

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ABSTRACT

Acute viral myositis is a rare condition that occurs during the recovery phase of an illness, most commonly influenza. It is characterized by muscle pain and weakness with an isolated laboratory finding of elevated serum creatine kinase (CK). We describe three previously healthy patients who were hospitalized after developing myositis following influenza-like illness during the 2009 influenza A (H1N1) virus pandemic. All experienced myalgias and weakness in all four extremities, including distal upper extremities, associated with an elevated CK level that resolved along with their myalgias and weakness within one week with supportive care. These cases serve as a reminder that influenza-related myositis may have atypical characteristics depending on the strain of influenza, and clinicians should be open to this possibility when new outbreaks occur.

Key words: H1N1, influenza, muscle weakness, myositis, viral myositis

Introduction

Acute myositis is associated with multiple viruses, with influenza most commonly implicated.[1] Viral studies show that influenza B is more likely than influenza A to cause myositis, likely due to the presence of NB protein in the membrane of influenza B, which is implicated in viral entry and may have myotrophic properties.[2-4] Viral myositis is most commonly characterized as sudden onset of muscle weakness, pain and tenderness during the early recovery phase of the virus.[5] Symptoms are often isolated to the calf muscles, but other muscle groups are involved in one third of cases.[1,5] It is typically self-limiting, with recovery within one week of the onset of symptoms,[1] but there are reports of rhabdomyolysis with renal failure and compartment syndrome.[6-8]

Myositis occurs only in a small percent of those affected with influenza, and is most common in children (mean age eight years), possibly because of virus tropism for immature muscle cells, which has been documented in animal studies.[2,8,9] It has, however, been reported in all age groups.[10,11] Males are more commonly affected than females (2.4:1).[2,8] It is associated with mildly to moderately elevated serum creatine kinase (CK) level. Muscle biopsy typically reveals muscle fiber degeneration and muscle necrosis with infiltration of leukocytes.[8,9] However, it is unclear whether this is due to direct infection of the muscle by the virus, myotoxic cytokines or other immunologic processes, as the viral agent has not been consistently demonstrated in biopsy.[9]

The novel 2009 influenza A (H1N1) virus was first identified in humans in April 2009 in Mexico with the first confirmed case in Utah on May third, 2009.[12,13] The virus rapidly spread throughout the world, and the World Health Organization (WHO) declared it a pandemic on June 11, 2009.[14] Epidemic levels of influenza like illness were reported in Utah from October 2009 to January 2010, and H1N1 was the only influenza in circulation in Utah during this time.[15] The symptoms include fever, cough, sore throat, runny nose, body aches, headache, chills and fatigue. The predicted prevalence of clinical influenza during the 2009 H1N1 epidemic was 12-30% of the population, compared with the typical rate of 5-15% for seasonal influenza.[16] Influenza associated hospitalizations in Utah in 2009-2010 were highest in

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5-24 year-olds followed closely by 25-49 year-olds, with 27.2% and 26.8% respectively.[15] Additionally, myositis has been reported with H1N1 influenza.[6,7,17,18] Here we report three cases of myositis associated with influenza like illness during the pandemic, associated with distal upper extremity involvement.

Case Reports

Case 1

A 37-year old male surgeon presented with three days of progressive muscle pain and weakness. Five days prior he had fever, myalgias and sore throat. His fever and sore throat resolved after two days, but he continued to have muscle pain that evolved into diffuse muscle weakness, greatest in his distal upper extremities. This disabled him from performing surgery. He denied any recent trauma or strenuous exercise. He also denied any medical history or medication use prior to his illness, except for ibuprofen three days prior to his presentation. He reported multiple sick contacts, including sick patients and his four-month old son.

His vital signs and general examination were normal. He had no rashes or joint pain. His forearm muscles and intrinsic muscles of the hand were tight and tender to touch. His neurological examination was notable for 5/5 strength throughout except bilateral wrist flexion and extension (4/5), finger flexion (3/5), finger extension (2/5) and thumb adduction (3/5). His reflexes and sensation were normal.

Laboratory values were generally unremarkable with the exception of CK (1,504 ng/ml). Pertinent negative virologic tests included RSV by PCR, parvovirus B19, EBV, CSF bacterial culture, HIV, Influenza A by PCR, Influenza B by PCR, and CSF Influenza by PCR.

He was given IV fluids and ibuprofen. One day after presentation, the swelling and tenderness improved. Two days later his symptoms had nearly resolved. Examination revealed only subtle 5-/5 weakness in bilateral forearms and hands. CK decreased to 752 ng/ml and serum creatinine remained stable and within normal limits. Nerve conduction and needle EMG (proximal, distal and paraspinal muscles) studies were normal. A few days later he was able to return to work, including performing surgeries.

Case 2

A 25-year-old male presented with four days of progressive weakness and muscle pain. Initially he noticed myalgias in his chest and biceps. Two days prior to presentation he noticed forearm pain and hand weakness. One day prior to presentation he noticed lower extremity weakness and pain, limiting his ability to ambulate. Two weeks prior to presentation he had been prescribed amoxicillin for a sore throat and fever, however he was not tested for streptococcus or influenza at that time. He denied prior medical problems, trauma, routine medication use or recent strenuous exercise.

Vital signs and general examination were normal. He had no rashes or joint pain. Bilateral arm and forearm muscles were tight and tender. Strength was decreased bilaterally in upper and lower extremities, including wrist extension and flexion (4/5), grip strength (4-/5), hip flexion (3/5), hip extension (5-/5), knee flexion (4-/5) and knee extension (5-/5). His reflexes and sensation were normal.

Laboratory values were generally unremarkable with the exception of a CK of 3,575 ng/ml. Pertinent negative virologic tests included CSF bacterial culture, HIV, Influenza A by DFA, Influenza B by DFA, and CSF Influenza by PCR. An MRI of the cervical spine was normal.

He was given IV fluids and ibuprofen. The day following presentation his weakness continued to progress and involved truncal weakness. Needle EMG study (distal, proximal and paraspinal muscles) showed only one run of positive waves in the thoracic paraspinal muscles. Two days after presentation he had dramatic improvement. His strength returned to 5/5 except in his left upper extremity strength, which improved to 4+/5 in wrist flexion, wrist extension and finger extension. The swelling and tenderness also improved. His CK decreased to 975 ng/ml and serum creatinine remained stable and within normal limits.

Case 3

A 45-year-old male presented with four days of progressive weakness and pain. He first noticed trouble manipulating small objects with his fingers. The weakness in his hand progressed to the point that he was no longer able to perform his job as a cable installer. He reported his forearms were tender to the touch. The patient's wife had confirmed H1N1 influenza four weeks prior, requiring hospitalization. He also had a fever, cough and sore throat shortly after his wife was sick, but did not seek medical attention. He had otherwise been in his usual state of good health with no medication use or recent trauma.

Vital signs and general examination were normal. There was no evidence of skin rash. His muscles were tender to the touch. His neurological examination was notable

for decreased strength to grade 4+/5 in bilateral upper extremities, hip flexors and hip extenders. Reflexes and sensory examination were normal.

Laboratory values were generally unremarkable with the exception of a CK of 600 ng/ml. Pertinent negative virologic tests included CSF bacterial culture, Influenza A by PCR, Influenza B by PCR, and CSF Influenza by PCR.

The day following admission his strength had returned to 5/5 and the muscle soreness had resolved. His CK declined to 410 ng/ml and serum creatinine remained stable and within normal limits. He had been given IV fluids and ibuprofen.

Discussion

These cases have many of the classic features of influenza myositis, including; acute onset of muscle weakness, pain and tenderness during the recovery phase of the virus, laboratory abnormality of mildly to moderately elevated CK, and complete resolution occurring within one week. However these cases of viral myositis also have several unique characteristics that may be unique to H1N1; influenza-related myositis more commonly affects a younger population and typically has isolated bilateral calf involvement, while all of our patients had four extremity involvement, with more distal than proximal upper extremity involvement. While these cases only represent a small portion of those with myositis related to H1N1, the presentation pattern is stereotyped and notably benign.

Acute myositis is associated with a large number of viruses, including H1N1.[7,16-18] The cases described in this report were not virologically-confirmed influenza, but all met the World Health Organization (WHO) definition for possible H1N1 influenza-like illness[19] and occurred when H1N1 influenza was highly prevalent in Utah during the fall and winter of 2009. Additionally, H1N1 disproportionately affects younger and healthier patients when compared to typical influenza, which is consistent with the cases described here.[20] The median duration of viral shedding by PCR is 5-9 days for H1N1, and given that PCR on serum for influenza was preformed 5-21 days after symptom onset, a false negative PCR is not unexpected.[21-23] According to the CDC, the sensitivity of rapid influenza testing for detecting H1N1 infection is as low as 10%.[20] Therefore, a negative rapid influenza result, as in case number two, does not exclude H1N1 infection. Additionally, influenza by PCR on CSF is insensitive, even in cases of influenza-related encephalopathy or myositis.[24-26] For these reasons, H1N1 diagnosis during the pandemic was generally based on CDC clinical criteria in geographic regions with a heavy disease burden. According to Monto *et al*., the positive predictive value of typical viral symptoms (as demonstrated in all of our cases) during an influenza epidemic is about 80%.[27] Muscle biopsy is not routinely recommended in the workup of viral myositis as a negative muscle biopsy does not exclude viral myositis[9,18] and was not performed due to the improvement of symptoms in all three cases. Given the patient profiles, symptoms, and timing during the peak of the H1N1 pandemic, we postulate that these cases were H1N1-associated viral myositis.

Recognition of this benign pattern of H1N1 myositis in adults may aid in the cost-effective and appropriate evaluation and management of future patients. These cases also serve as a reminder that influenza-related myositis may have atypical characteristics depending on the strain of influenza, which should be kept in mind in when new outbreaks occur.

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