Influenza A Infection as the Catalyst for Appendicitis and Rhabdomyolysis in a Pediatric Patient

Jessica Budiselic MD, Kent Nelson MD, F.A.A.P
Department of Pediatrics - Advocate Children's Hospital - Oak Lawn

Abstract:
Respiratory viruses such as influenza have the potential to affect not only the respiratory system but consequently other systems of the body as well. Although knowing the true viral source of infection will not generally change management other than supportive care, there are cases in which knowing the cause can help in dictating whether further investigation of symptoms is warranted, or if symptoms can be attributed to the virus alone. Our patient initially presented with upper respiratory infection (URI) symptoms in the setting of right lower quadrant pain which was suspicious for appendicitis. He concurrently reported myalgias and dark-red urine which was concerning for rhabdomyolysis and which lab work confirmed. The diagnosis of rhabdomyolysis was especially important as it dictated his course of treatment for appendicitis. There are several reported cases of influenza infection causing appendicitis and rhabdomyolysis. This case is unique as there are no reported cases of influenza A infection causing both appendicitis and rhabdomyolysis simultaneously.

Objective:
• Present the case of a patient presenting with right lower quadrant pain and dysuria in the setting of a viral upper respiratory infection (URI)
• Discuss the mechanism for how viruses can cause appendicitis and rhabdomyolysis
• Describe the necessity of diagnosing rhabdomyolysis in patients requiring surgery

Introduction:
Cough, sore throat, congestion, and rhinorrhea are symptoms typically indicative of an upper respiratory infection (URI) usually caused by a virus. Respiratory viruses such as Influenza have the ability to affect not only the respiratory system but consequently other systems of the body as well. Although knowing the true viral source of infection will not generally change management other than supportive care, there are cases in which knowing can help dictate whether further investigation of symptoms is warranted, or if symptoms can be attributed to the virus alone. Our patient presented with URI symptoms in the setting of right lower quadrant pain, dysuria, nausea, vomiting, and initially suspicious for appendicitis. Differential diagnoses include constipation, gastroenteritis, lactose intolerance, testicular torsion, urinary tract infection, and mesenteric adenitis. Further work up to differentiate included ultrasound, CT imaging, and lab work.

Case Description:
MB is a 12-year-old previously healthy male who presented from an outside hospital with persistent right lower quadrant pain, nausea and vomiting, dysuria, and decreased urinary output for 4 days prior to admission. His urine was dark red-colored and he also had symptoms of a URI during this time.

Physical exam:
Abdominal exam was significant for a firm distended abdomen, tympanic on percussion in all four quadrants, tenderness in RLQ, no guarding, and no rebound. Tenderness was present on the right anterior thigh and he was refusing to move the right lower extremity due to abdominal pain.

Imaging:
CT abdomen and pelvis with contrast revealed a thickened appendix with several calcified appendicoliths and an indistinct distal appendiceal wall. There were several bubbles of extraluminal gas anterior to the appendix and medial to the cecal tip with extensive inflammatory infiltration of the surrounding fat planes compatible with perforated appendicitis. Ultrasound of the abdomen showed an aperistaltic heterogeneous peri-appendiceal region comparable with a phlegmon, a small amount of free fluid, and significant edema. Findings were further compatible with perforated appendicitis.

Lab work:
A viral quad screen was positive for Influenza A. Dark urine was concerning for rhabdomyolysis. Urinalysis was significant for large blood, 3 to 5 erythrocytes, and trace leukocyte esterase. Creatine phosphokinase (CPK) was elevated at 25,409 U/L. CPK continued to fluctuate during the 10-day hospital stay. Liver enzymes were initially elevated at an AST 110 U/L and an ALT 39 U/L. They remained elevated until down-trending after day 5 of admission.

Management:
The patient was started on IV fluids and placed on antibiotics. He received ceftriaxone 2000 mg and metronidazole 1500 mg daily for 10 days. Tamiflu 75 mg BID was started for 5 days in total. The patient was not a surgical candidate for an appendectomy at the time due to the rise in CPK levels.

<table>
<thead>
<tr>
<th>Pertinent labs day of admission</th>
<th>Pertinent labs day of discharge</th>
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<tbody>
<tr>
<td>CPK 25,409 Units/L</td>
<td>3,926 Units/L</td>
</tr>
<tr>
<td>AST 110 Units/L</td>
<td>394 Units/L</td>
</tr>
<tr>
<td>ALT 39 Units/L</td>
<td>309 Units/L</td>
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Discussion:
Appendicitis in children is most common between the ages of 5 to 12 years old. It is typically the result of obstruction of the appendix by mucus, impacted fecalith, or by viral inflammation. One of the mechanisms for viral infections preceding appendicitis is their potential to cause mucosal ulcerations potentially resulting in bacterial infection of the appendix. [1,2] Abdominal pain and vomiting are commonly present and the classic migration of periumbilical pain to the right lower quadrant may not be present. Atypical symptoms include dysuria due to abdominal pain with voiding and not urethral pain, constipation, or diarrhea. In this case, the patient did have pain with voiding but did not report urethral, perineal, or testicular pain. Appendicitis occurring in the setting of influenza A infection was determined as the most likely source of initial infection. A handful of cases have reported an increased incidence of acute appendicitis during influenza infection, but the magnitude of the true incidence is still unknown. [3-5]

Rhabdomyolysis is the result of muscle necrosis releasing myoglobin, a heme-containing protein into the circulation. Common findings include elevated CPK, darkened urine, muscle weakness, and myalgias. A urinalysis is required to differentiate between myoglobinuria and hematuria. Viral infections have been associated with a vast spectrum of muscle disorders, ranging from acute non-specific myalgia to severe myositis and rhabdomyolysis. [6] Fadila et al. reported that the proposed mechanism for rhabdomyolysis-induced influenza A infection is thought to be multifactorial for several reasons: (1) the direct invasion of skeletal muscles by the virus, (2) the release of cytokines resulting in direct muscle damage, and (3) the viral toxin itself causing myonecrosis. [7] Several studies since the 2009 Influenza A “Swine” flu pandemic declared by the World Health Organization (WHO) have documented cases of rhabdomyolysis caused by the virus. [6-9] The influenza positive tests reported for the 2023 season to the Center for Disease Control (CDC) by Public Health in Illinois determined the majority of positive tests were due to Influenza A (H3). [10] Our test only confirmed the presence of influenza A infection and further lab work would be required to determine the strain.

Conclusion:
The diagnosis of rhabdomyolysis was crucial in this case in order to dictate the proper management of appendicitis. Given the perforated appendix, this patient required surgical management, yet due to the rhabdomyolysis, the recommendation was to be medically managed with antibiotics until 8 to 10 weeks after resolution to have surgical intervention. Thus, a case of rare causing influenza appendicitis and rhabdomyolysis. There have been no documented case reports of influenza infection causing appendicitis and rhabdomyolysis simultaneously.

References:
3. Cunha BA, Dhaffar IA, Dennis M. Influenza influenza (H1N1) and appendicitis. Heart Lung 2010;39:544-6.
9. Cunha BA, Dhaffar IA, Dennis M. Influenza influenza (H1N1) and appendicitis. Heart Lung 2010;39:544-6