Photoclinic

Shigellosis Presenting with Myocarditis

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A 31-year-old woman presented to the emergency department with 3 days of nausea, vomiting, and abdominal pain, and 2 days of diarrhea.

History. The vomitus consisted of food particles but did not contain blood. Her abdominal pain was cramping, non-radiating, constant, and without bloating, and would decrease after each episode of vomiting. She had four to five episodes of watery, non-bloody diarrhea for 2 days, which brought her to the hospital.

On the day of admission, she also noticed intermittent sharp left-sided chest pain that radiated to her neck and jaw which resolved within 15 minutes and did not recur. The pain was non-exertional and was unrelated to any physical activity. Upon admission, her vital signs included a temperature of 98.2˚ F, heart rate of 110 beats/min, blood pressure of 100/70 mm hg, respiratory rate of 14 breaths/min, and saturation of 98% on room air.

Her physical examination was within normal limits, including skin turgor and capillary refill. No murmur or collapsed neck vessels were observed. The patient had no significant medical history. There were no similar symptoms in her family members and she had no recent history of travel. She was born in Honduras but had been living in the United States for the past 10 years.

Diagnostic testing. Laboratory investigations showed neutrophil predominant leucocytosis of 17.6 x 10^3/mm^3, a hemoglobin of 13.3 g/dl, and a platelet count of 24 x 10^3/mm^3. Values for partial thromboplastin time, prothrombin time, international normalized ratio, and comprehensive metabolic panel were all within normal limits. Troponin was elevated at 0.730 ng/ml. An electrocardiogram (EKG) showed sinus rhythm within normal range with widespread ST depression, seen in leads I, II, and V5-6 with T wave flattening, and subtle ST elevation in V1 and aVR suggestive of subendocardial ischemia (Figure 1).

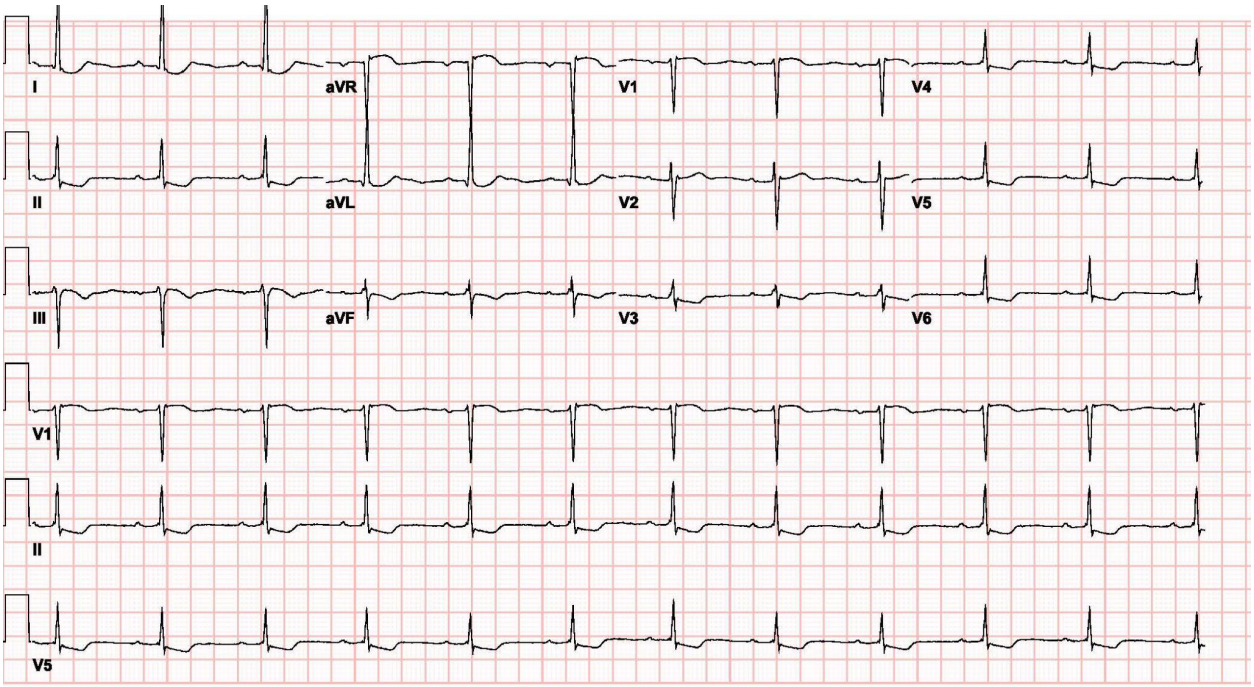

Figure 1. *Electrocardiogram with sinus rhythm within normal limits; ST depression in I, II, and V5-6 with T wave flattening; ST elevation in V1 and aVR.*

Chest X-ray and computed tomography (CT) scans of the abdomen and pelvis did not reveal any abnormalities. Stool studies were obtained and were pending. The patient was treated with fluid resuscitation for systemic inflammatory response with intravenous lactated ringers and

symptomatically for nausea with intravenous ondansetron 4 mg. Despite the resolution of the chest pain prior to admission, troponins trended upwards from 0.730 ng/ml to 2.620 ng/ml. A repeat EKG was unchanged from the one taken on admission. At that point, the elevated troponins were considered to be secondary to demand ischemia and not due to an acute coronary syndrome. An echocardiogram was within normal limits with an ejection fraction of 65%.

To evaluate the etiology of thrombocytopenia, HIV antigen, hepatitis C viral antibody, antinuclear antibody, and a peripheral smear were collected, all of which were negative. The patient was treated with oral prednisone 60 mg daily for thrombocytopenia and consideration of viral myocarditis, and her platelet count was monitored.

On day 2 of hospitalization, the patient's diarrhea and other symptoms improved and her chest pain did not recur. Her platelet count improved from 24 to 50 x $10^3/mm^3$ and troponins trended down from 2.620 to 1.070 ng/ml. The results of the stool enteric panel was positive for *Shigella sonnei* on a polymerase chain reaction (PCR) test. Two serial blood cultures were negative for *Shigella.*

Differential diagnoses. Adenovirus and parvovirus were on the differential since they can cause a diarrheal illness. Human herpesvirus 6 was low on the differential since it does not predominantly cause diarrhea. However, we did not test for these infections following receipt of the results of the patient's stool culture.

Treatment and management. Treatment was initiated with oral ciprofloxacin 500 mg daily for the next 3 days. At that point, the patient's chest pain was attributed to myocarditis occurring secondary to the *Shigella* infection and thrombocytopenia secondary to sepsis from shigellosis. The patient's diarrhea resolved. She was discharged with instructions to complete a total of 3 days of antibiotics and a tapering regimen of prednisone (60 mg, 40 mg, 20 mg, 10 mg). A cardiologist was consulted, and he advised against any additional immediate measures in favor of an outpatient follow-up.

Outcome and follow-up. During outpatient follow-up, the patient's symptoms had completely resolved. Her platelet count was 166 x $10^3/mm^3$. A follow-up EKG (Figure 2) was obtained 1 week after discharge which showed sinus rhythm within normal limits and no ST-T wave abnormalities.

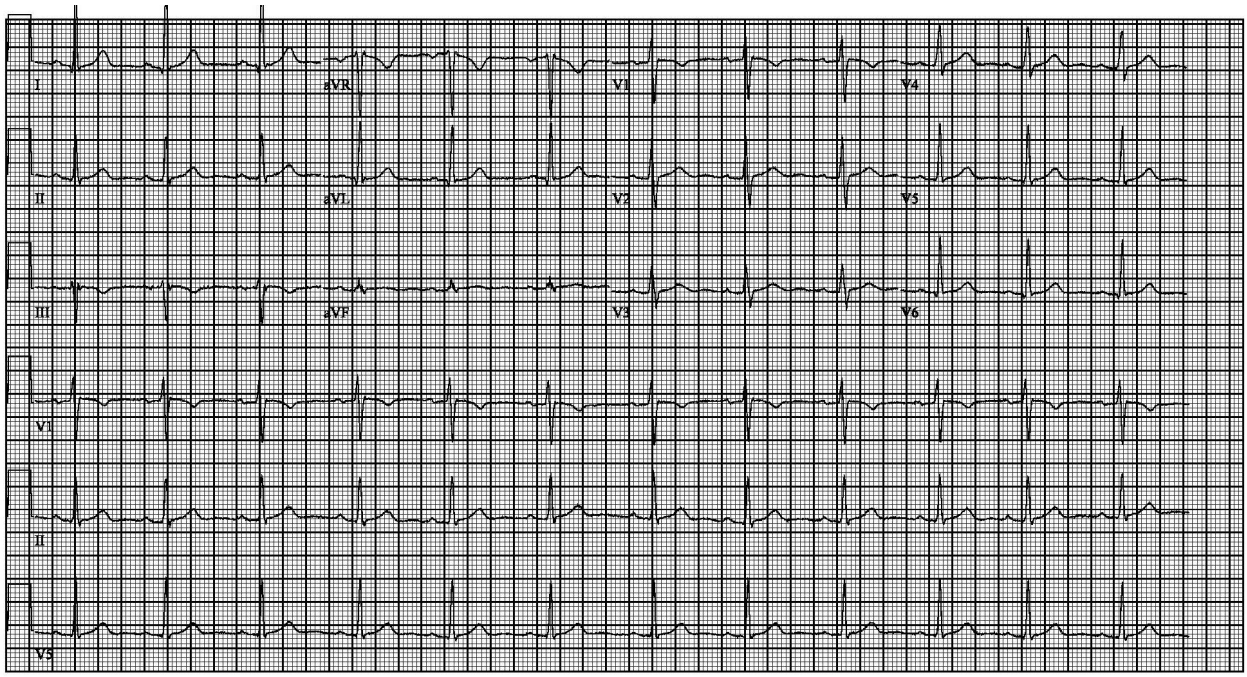

Figure 2. *Electrocardiogram with sinus rhythm in normal limits.*

Discussion. *Shigella* is one of the most common bacterial infections worldwide. It is prominent in developing countries with around 165 million cases reported yearly.[1] *Shigella* is transmitted via the fecal-oral route including person-to-person contact and contaminated food and water. It is predominate in developing rural and urban communities that are affected by poor hygiene. In developed countries, many cases of *Shigella* present in travelers returning from endemic regions such as sub-Saharan Africa and South Asia. According to the CDC, developed countries such as Canada and Australia reported that 40% to 50% of locally diagnosed cases of shigellosis were associated with international travel. Moreover, in the United States, there was a large *Shigella* outbreak in 2014-2015 that occurred in travelers returning from India, Haiti, the Dominican Republic, and other countries with ciprofloxacin-resistant shigellosis.[1] *Shigella* has four species that can affect humans (*S. dysenteriae, S. flexneri, S. boydii,* and *S. sonnei*), which can manifest with some differences.[2]

The presentation of *Shigella* mainly includes inflammatory colitis that can range from short-term watery stools to dysentery involving cytotoxic megacolon and gastrointestinal bleeding. Other extraintestinal symptoms include fever, vomiting, alterations in consciousness, neurologic manifestations, severe hyponatremia, leukemoid reaction, and hemolytic uremic syndrome (HUS). Both leukemoid reaction and HUS are thought to be related to Shiga-toxin production, which presents as a white blood count of less than 50 K/uL and evidence of hemolysis or acute kidney injury on laboratory findings,[3] neither of which were present in our case patient.

One of the very rare manifestations of *Shigella* is myocarditis. Myocarditis causes inflammation of the cardiac muscles due to infection. The infection can be caused by protozoa, fungi, spirochetes, bacteria, or cardiotoxins. The most common cause of myocarditis worldwide is

Chagas disease which is caused by the parasitic protozoan *Trypanosoma cruzi*. In developed countries, viruses such as Coxsackie B, adenovirus, herpesvirus 6, and parvovirus B19 have been linked to myocarditis. Bacterial infections causing myocarditis have been rarely reported in immunocompetent hosts.[4]

Shigellosis presenting with myocarditis was reported in three prior cases. The first case reported in 1987 described myocarditis related to shigellosis in a 19-year-old man presenting with abdominal pain, fever, and diarrhea who was found to have abnormal electrocardiogram (ECG) findings, revealing diffuse ST-T changes. This was attributed to myocarditis induced by *Shigella*.[5] The other two were reported in 1993 in children who presented with fevers and gastrointestinal symptoms such as nausea, vomiting, and loose stools. Both were found to have a significant cardiovascular impairment which was attributed to myocarditis.[6]

Myocarditis can present with a variety of symptoms, including fever, leukocytosis, acute chest pain, difficulty breathing, dysphagia, nausea, vomiting, lethargy, arthralgias, myalgias, rash, and new or worsening dyspnea at rest or during activity. In addition to fatigue and weakness that may be associated with symptoms of right or left heart failure, sinus tachycardia, unexplained arrhythmias, fainting, and sudden cardiac death have also been linked to myocarditis.[6]

The mechanisms of *Shigella*-induced myocarditis are still under investigation. Suggested mechanisms include the theory that *Shigella sonnei* toxin may induce cardiac tissue damage by a mechanism similar to that of diphtheria toxin, which works by slowing protein synthesis.[7] Other possible mechanisms include direct cardiac tissue invasion or immunologically mediated myocardial injury. This mechanism is similar to how *Shigella* can cause acute inflammatory arthritis and reactive arthritis.[7]

Investigations for the diagnosis of patients presenting with gastrointestinal symptoms should include checking for the presence of white blood cells and red blood cells on direct microscopic examination. However, stool culture is the preferred method for the diagnosis of *Shigella*. PCR testing of the stool sample can be done as it can help identify multiple enteric bacterial pathogens.[8]

When myocarditis symptoms are present, patients should have their cardiac troponin levels checked. According to research, only 7.5% of patients with histopathology myocarditis had high creatinine kinase, but myocardial troponin T or I is raised in at least 50% of the patients having biopsy-proven myocarditis. Other laboratory values that can also be beneficial include red blood cell count, subacute phase reactants, blood viral antibody titers, and anti-cardiac antibody titers.[9]

Preventative measures to reduce *Shigella* infections mainly include better hand hygiene. Waterless hand sanitizers may be a helpful solution when access to soap or clean water is limited. Food also remains a source for pathogen transmission, especially raw meat, poultry, fruits, and vegetables. It's recommended to practice proper hygiene during food preparations

and separate raw from cooked food to prevent cross contamination.[10] According to a systemic review with random effect meta-analysis examining the impact of hand washing with soap on developing the risk of diarrheal disease, it was found that hand washing with soap decreased the risk of intestinal infections by 48% and decreased the risk of shigellosis specifically by 59%.[11] Additional safe practices include avoidance of food preparation by diaper-changing employees in childcare facilities, barring children who have diarrhea from attending childcare centers, and placing children who recently recovered from shigellosis together in one classroom to reduce spreading infection to other kids.[12]

The CDC recommends shigellosis be treated with appropriate antibiotics whenever possible based on clinical characteristics and reported susceptibility.[1] *Shigella* dysentery is treated with penicillin, amoxicillin, ciprofloxacin, or third generation cephalosporins. Azithromycin along with sulfonamides can also be used.[13] A formal paraphrase Zinc supplement (20 mg essential zinc for 14 days) has been found in malnourished children to shorten the length of diarrhea, enhance body weight through recovery, and decrease the amount of diarrhea.[14]

The management of myocarditis centers on the etiology and associated complications. Many patients recover completely from myocarditis on their own or with therapy. Depending on the associated complications, management can include medication therapy, lifestyle modification, and procedural interventions.[9]

Conclusion. *Shigella* is one of the most common bacterial infections worldwide. It's commonly transmitted via the fecal-oral route and causes a range of inflammatory colitis. One of the rarely reported complications of *Shigella* is myocarditis, as presented in this case. *Shigella*-induced myocarditis may cause several severe complications, so prompt diagnosis and management is necessary for positive outcomes.

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