The Journal of Emergency Medicine, Vol. 57, No. 4, pp. 563–566, 2019

0736-4679/$ - see front matter

Case Presentations of the Harvard Affiliated Emergency Medicine Residencies

ABDOMINAL PAIN AFTER A TICK BITE

Derek L. Monette, MD,*† Emily S. Miller, MD,*‡ Kimon C. Zachary, MD,*‡ Kathleen Wittels, MD,*§ and Susan R. Wilcox, MD*†

*Department of Emergency Medicine, Harvard Medical School, Boston, Massachusetts, †Department of Emergency Medicine, Massachusetts General Hospital, Boston, Massachusetts, ‡Department of Infectious Diseases, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, and §Department of Emergency Medicine, Brigham and Women's Hospital, Boston, Massachusetts
Reprint Address: Susan R. Wilcox, MD, Department of Emergency Medicine, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114

Dr. Derek Monette: Today's case is that of a 46-year-old male with recent diagnoses of Lyme disease and babesiosis who presented to our emergency department (ED) with abdominal pain, nausea, and diarrhea. The patient was previously healthy and had been well until approximately 2 weeks before the day of ED presentation, when he developed headache, fatigue, and myalgias. He also noticed that his right calf "looks sunburned," and was warm to the touch. He was evaluated by his primary care physician (PCP) after 1 week of symptoms. A screening enzyme-linked immunosorbent assay for Lyme, ordered by his PCP, was positive, and he was subsequently started on doxycycline. His follow-up Lyme IgM Western blot was positive, and an IgG Western blot was equivocal. Three days later, he developed fever to 101°F, a dry cough, and worsening myalgias. His PCP obtained a chest x-ray study, which did not show any pathology. Laboratory studies from the second PCP visit revealed hemoglobin and hematocrit of 13.5 g/dL and 39.7%, respectively, in addition to a platelet count of 62,000/μL, alanine aminotransferase (ALT) of 93 U/L, and aspartate aminotransferase (AST) of 75 U/L. A blood smear for babesia was performed and returned with a positive result, at 0.3% parasitemia. The patient was referred to an infectious disease (ID) specialist and was started on atovaquone and azithromycin. He started these medications the night before presenting to the ED for evaluation of his new abdominal pain, nausea, and diarrhea.

In the ED, the patient reported a gradual onset of crampy, constant, bilateral upper quadrant abdominal pain without radiation. This pain was associated with nausea and loose, non-bloody stools. These symptoms began hours after taking his first dose of atovaquone and azithromycin. He reported recent tick exposure while traveling to Nantucket, followed by the development of a mild headache, which had been constant over the past 2 weeks. He denied any focal weakness or neck stiffness. He had been adherent to his doxycycline and other antimicrobials and was avoiding sun exposure as instructed. The review of systems was notable for the absence of any other recent antibiotic exposure or travel.

The patient's medical history was notable for hypertension, hyperlipidemia, and prior alcohol use disorder. He reported recent reduction in his alcohol intake over the previous months. He had no surgical history and simvastatin was his only daily medication prior to his recent illness. He had no known allergies. His social history was only notable for alcohol use, and he denied tobacco or illicit substance use. He lived in Boston with his wife and two young children.

Dr. Emily Miller: How did the patient appear on arrival to the ED? Could you describe his physical examination?

Dr. Derek Monette: The patient was afebrile, with a heart rate of 88 beats/min, blood pressure of 101/66 mm Hg, respiratory rate of 16 breaths/min, and an oxygen saturation of 99% on room air. He appeared uncomfortable, but not acutely ill. He was alert, oriented, and answering questions appropriately in full sentences. He was warm to the touch, but there was no diaphoresis. His mucous membranes were dry. His lungs were clear bilaterally, and his cardiac examination was without murmur. His abdomen was soft, mildly tender to palpation of both the right and left upper quadrants. He had no shake or tap tenderness and no rebound or guarding. There was no joint swelling or pain with range of motion, and his skin was without any lesions.

Dr. Emily Miller: After examining the patient, what diagnoses were you considering? How did his positive Lyme and babesia testing factor into your initial clinical impression?

Dr. Derek Monette: The patient's abdominal pain, nausea, and loose stools started shortly after initiating treatment for babesia. These symptoms were distinctly different from the headache, fatigue, and myalgias of the past 2 weeks. Both azithromycin and atovaquone are associated with gastrointestinal side effects, including diarrhea, and could have explained the patient's new symptoms. However, a broad differential for his upper abdominal pain, nausea, and diarrhea was considered. Viral gastroenteritis and foodborne disease commonly present with these symptoms, however, the patient had no known sick contacts or exposures. Gastritis, esophagitis, gastroesophageal reflux, and peptic ulcer disease may present with upper abdominal pain and nausea or vomiting, and his previous frequent alcohol use is a risk factor for these etiologies, along with pancreatitis. However, all of these etiologies are less likely to explain the patient's loose stools. His presentation was also less consistent with a bowel obstruction or mesenteric ischemia. He had no risk factors of ischemic colitis, which include dysrhythmia, valvular disease, and impaired cardiac function (1). Infectious colitis was considered, although colitis related to *Clostridium difficile* seemed unlikely. Although he was currently treated with doxycycline, this antibiotic is not classically associated with the development of colitis and he had only been taking the medication for 1 week (2). There was no history of trauma to raise concern for liver or splenic lacerations. Pyelonephritis and renal colic may present with upper abdominal pain and nausea, although the patient did not report any urinary symptoms or flank pain, making these diagnoses less likely. Finally, pulmonary diseases, such as pneumonia, pleural effusion, and pulmonary embolism, may present with upper abdominal pain, however, these are unlikely to cause nausea and diarrhea; additionally, this patient did not endorse any respiratory symptoms. Given the patient's overall appearance on arrival to the ED, including normal vital signs and lack of peritonitis on abdominal examination, life-threatening etiologies of his symptoms seemed lower on the differential, and the initial focus was on treating his symptoms with i.v. fluids, analgesia, and anti-emetics.

Dr. Emily Miller: What did the initial laboratory studies reveal?

Dr. Derek Monette: In the ED, the patient's complete blood count was notable for a drop in the hemoglobin and hematocrit compared to the studies from the previous day—from 13.5 g/dL and 39.7% to 10.9 g/dL and 31.4%, respectively (with a mean corpuscular volume of 87 fL). The platelet count remained low, but stable, at 58,000/μL. The white blood cell count was 4400/μL. The carbon dioxide level was 24 mmol/L and there was no anion gap, with a lactic acid of 2.0 mmol/L. The liver function studies included an ALT of 60 U/L, AST of 56 U/L, and alkaline phosphatase of 92 U/L. The lipase was within normal limits. The urinalysis was negative for red or white blood cells and otherwise unremarkable. During the initial period of his ED course he received 2 L of i.v. normal saline, 4 mg of i.v. morphine, and 4 mg of i.v. ondansetron for his pain, nausea, and presumed dehydration.

Dr. David Brown: What was your impression of the drop in his hemoglobin and hematocrit?

Dr. Derek Monette: The acute drops in hemoglobin and hematocrit were surprising, as we had not anticipated acute blood loss as a likely etiology of his presentation. We had to rethink our differential at this point, however, we were reassured by his presenting vital signs, normal carbon dioxide, and absence of an anion gap. Intra-abdominal hemorrhage and gastrointestinal bleeding are life-threatening sources of acute blood loss, however, hemolysis was another consideration in a patient with recently diagnosed tick-borne illness. Babesiosis causes hemolysis and some degree of anemia is common, depending on the degree of parasitemia. This patient's initial parasitemia was quite low, however. Further, babesiosis can lead to profound anemia and disseminated intravascular coagulopathy (DIC), but these are rare complications (3–5). We broadened our differential to include these, but the patient's normal coagulation studies and indirect bilirubin argued against DIC. Our primary concern was for acute blood loss, and we reassessed the patient with a plan for repeat abdominal examination and to perform a rectal examination. However, we found the patient to have rigors and worsening abdominal pain from presentation. He appeared pale and the abdomen was rigid. The heart rate had increased to116 beats/min and the systolic blood pressure had decreased to 88 mm Hg.

Dr. Jim Gordon: What were your initial steps in resuscitating this patient?

Dr. Derek Monette: This clinical change, in combination with the acute drop in hemoglobin and hematocrit, suggested acute intra-abdominal hemorrhage. We pursued several steps in parallel. We placed 2 large-bore i.v. catheters to facilitate rapid volume resuscitation, requested an emergent surgical consultation, and performed a bedside focused abdominal sonography in trauma examination. We repeated the patient's laboratory studies. The bedside ultrasound revealed free fluid in both the right and left upper quadrants and pelvis. We obtained emergency release blood products and initiated a transfusion with packed red blood cells. The repeat hemoglobin and hematocrit later returned at 6.7 g/dL and 19.5%, respectively, consistent with hemorrhagic peritonitis. Our surgical colleagues expeditiously evaluated him.

Dr. Emily Miller: Describe your differential for this patient's free fluid and peritonitis in the absence of trauma?

Dr. Derek Monette: Potential etiologies for this patient's acute atraumatic hemorrhagic peritonitis included liver or splenic rupture, leaking aortic dissection or aneurysm, or a perforated gastric or duodenal ulcer. At this time, we were most concerned for splenic rupture, given his known babesia, and its association with splenomegaly. Though rare, splenic rupture has been reported in cases of babesiosis, and concurrent Lyme disease may increase the overall severity of disease manifestation (6–10). Although the most common etiology of atraumatic splenic rupture is a malignancy, this seemed less likely, given the history of present illness. Infectious causes are the next most common cause of atraumatic splenic rupture, including mononucleosis and malaria. The patient's presentation was less consistent with these infections, and babesia was the likely culprit (11).

Dr. David Brown: Please tell us what happened next with your patient.

Dr. Derek Monette: The patient went directly from the ED to the operating room (OR) where General Surgery performed an exploratory laparotomy. In the OR, the patient's spleen was noted to have a normal-sized spleen with an obvious laceration of the inferior pole. The abdomen was full of old blood and clots. General Surgery completed a splenectomy, during which the patient received 3 units of packed red blood cells, 2 units of fresh frozen plasma, and one 6-pack of platelets. The patient had an unremarkable postoperative course; he was monitored in the surgical intensive care unit for < 24 h and discharged from the hospital on postoperative day 4. Over the course of his hospitalization, he received therapies for his concomitant Lyme and babesia infections, later completing a 2-week course. He also received a vaccination series for adults with asplenia (HiB, MCV4, MenB, and PCV13). These protect against infection from encapsulated organisms, including *Haemophilus influenzae* type b and various meningococcal and pneumococcal bacteria. One week after his surgery, he was evaluated at ID follow-up clinic, where he reported he was tolerating his medications and had full resolution of all symptoms.

Dr. Emily Miller: What are the key learning points from this case?

Dr. Derek Monette: The key learning points from this case include recognition of the acute abdomen, knowledge of zoonotic infections and their association with splenic rupture, and the importance of patient reassessments.

First, this case underscores the importance of recognizing an acute abdomen. Patients with peritonitis often have time-sensitive illnesses that require emergent therapy, often operative, and delays in diagnosis and treatment increase morbidity and mortality. Remembering to consider life-threatening etiologies of acute abdominal pain for all patients presenting with abdominal pain is key.

This case also highlights the importance of knowing some of the complications of zoonotic infections. In addition to splenic rupture, life-threatening complications associated with babesia include acute respiratory distress syndrome and DIC. Interestingly, nausea, vomiting, and diarrhea are predictive of severe babesia infection (10). However, other predictive factors include male sex, alkaline phosphatase values > 125 U/L, and white blood cell counts > 5.0 K/μL (12). This patient had only one of these three objective risk factors. Patients with concomitant Lyme and babesia infections may, in fact, experience a greater number of acute symptoms and a longer duration than patients with isolated Lyme disease (10,13). Our patient required surgical management of his splenic rupture, however, non-operative management has become the treatment of choice to preserve splenic immune function. Mortality in atraumatic splenic rupture is associated with splenomegaly, age older than 40 years, and neoplastic etiologies (14). A palpable spleen may be the only early finding on examination, but a spleen must increase in size by approximately 40% before it becomes palpable (14). If diagnosed early, a hemodynamically stable patient may be managed with splenic artery embolization (15).

Lastly, a key learning point from this case is the value of serial patient assessments. This patient's initial ED presentation did not suggest acute intra-abdominal hemorrhage from splenic rupture; although he had tenderness on abdominal examination, he had normal vital signs and there was no peritonitis. Recognizing that the patient's initial laboratory results were not consistent with providers' initial expectations and promptly reassessing the patient were critical in arriving at the correct diagnosis.

REFERENCES

1. McKinsey JF, Gewertz BL. Acute mesenteric ischemia. Surg Clin North Am 1997;77:307–18.
2. Doernberg SB, Winston LG, Deck DH, et al. Does doxycycline protect against development of *Clostridium difficile* infection? Clin Infect Dis 2012;55:615–20.
3. Vannier EG, Diuk-Wasser MA, Ben Mamoun C, et al. Babesiosis. Infect Dis Clin North Am 2015;29:357–70.
4. Vannier E, Krause PJ. Human babesiosis. N Engl J Med 2012;366: 2397–407.
5. Hatcher JC, Greenberg PD, Antique J, et al. Severe babesiosis in Long Island: review of 34 cases and their complications. Clin Infect Dis 2001;32:1117–25.
6. Sanchez E, Vannier E, Wormser GP, et al. Diagnosis, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: a review. JAMA 2016;315:1767–77.
7. Florescu D, Sordillo PP, Glyptis A, et al. Splenic infarction in human babesiosis: two cases and discussion. Clin Infect Dis 2008; 46:e8–11.
8. Froberg MK, Dannen D, Bernier N, et al. Case report: spontaneous splenic rupture during acute parasitemia of *Babesia microti*. Ann Clin Lab Sci 2008;38:390–2.
9. Kuwayama DP, Briones RJ. Spontaneous splenic rupture caused by *Babesia microti* infection. Clin Infect Dis 2008;46:e92–5.
10. Mareedu N, Schotthoefer AM, Tompkins J, et al. Risk factors for severe infection, hospitalization, and prolonged antimicrobial therapy in patients with babesiosis. Am J Trop Med Hyg 2017;97:1218.
11. Renzulli P, Hostettler A, Schoepfer AM, et al. Systematic review of atraumatic splenic rupture. Br J Surg 2009;96:1114–21.
12. White DJ, Talarico J, Chang HG, et al. Human babesiosis in New York State: review of 139 hospitalized cases and analysis of prognostic factors. Arch Intern Med 1998;158:2149–54.
13. Krause PJ, Telford SR 3rd, Spielman A, et al. Concurrent Lyme disease and babesiosis. Evidence for increased severity and duration of illness. JAMA 1996;275:1657–60.
14. Blackburn CR. On the clinical detection of enlargement of the spleen. Australas Ann Med 1953;2:78–80.
15. Skattum J, Naess PA, Gaarder C. Non-operative management and immune function after splenic injury. Br J Surg 2012;99(suppl 1): 59–65.