IDCases 1 (2014) 63–65

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case Report

Spontaneous splenic rupture due to *Babesia microti* infection: Case report and review of the literature

Natalia Usatii [a,*], Aelita Khachatrian [a], John Stratidis [b]

[a] Department of Medicine, Danbury Hospital, Danbury, CT, United States
[b] Infectious Diseases Department, Danbury Hospital, Danbury, CT, United States

ARTICLE INFO

Article history:
Received 8 June 2014
Received in revised form 20 August 2014
Accepted 28 August 2014

Keywords:
Babesia
Polymerase chain reaction
Splenic rupture

ABSTRACT

This article describes the case of spontaneous splenic rupture as a rare complication of infection with Babesia species. We will discuss the symptomatology that this disease could present along with both surgical and non-surgical management approaches. Babesia infection often presents with mild to moderate symptoms, but can rapidly progress to significant injury including splenic rupture. The first case reported in a medical journal was in 2007. Treatment usually involves a two-drug regimen; clindamycin plus quinine, or atovaquone plus azithromycin (as in our patient). If hemodynamic stability is present, a primary non-surgical treatment may be especially beneficial since splenectomy may worsen optimal immunologic function and the infection itself.

Introduction

Babesiosis is an infectious disease caused by protozoa of the genus babesia. The disease is named after Victor Babes, the Hungarian pathologist and microbiologist who identified intraerythrocytic microorganisms as a cause of febrile hemoglobinuria in cattle in 1888. Then in 1893, Theobald Smith and Frederick L. Killborne identified a tick as a vector for transmission of *Babesia bigemina* in Texas cattle. This observation demonstrated the first time that an arthropod could transmit an infectious agent to a vertebrate host. The first documented human case was about half century later in a splenectomized Croatian herdsman by *Babesia divergens*. The first case in an immunocompetent person was in Nantucket Island in Masachusetts, in 1969, by *Babesia microti*; the vector was *Ixodes dammini* tick (now known as *Ixodes scapularis*). The disease became known as "Nantucket fever." *B. microti* is the main etiologic agents in northern and midwestern regions of the United States [1]. Most clinically evident disease occurs primarily in those patients with advanced age or those with underlying immunosuppression [2].

Babesiosis resembles malaria in clinical presentation. Its manifestations range from subclinical illness to fulminant disease and death. Unlike Lyme, there is no characteristic rash and the symptoms are often mild in immunocompetent person. Symptoms include a gradual onset of malaise, fever, fatigue, and headache, along with myalgias, arthralgias, and nausea [2]. *B. microti* can multiply to levels sufficient enough to cause hemolytic anemia, thrombocytopenia, and atypical lymphocytosis. More severe disease can cause organ dysfunction, including mental status change, pulmonary edema, renal failure, hepatosplenomegaly, and jaundice. In the US, 5–6.5% of all patients who develop symptomatic infection with *B. microti* die from the infection. Most common complications are acute respiratory distress syndrome and disseminated intravascular coagulopathy [3].

Other reported complications are splenic enlargement and splenic infarct or rupture. Spontaneous splenic rupture is a rare complication leading to emergent splenectomy in some cases. Asplenia can lead to an overwhelming critical illness. Exacerbation of babesiosis has also been demonstrated experimentally in animals following splenectomy or administration of antisplenic cell serum [4]. Hence splenic preservation is a priority, especially in high risk endemic areas [3,5]. We describe a healthy man, with no history of trauma, presenting with spontaneous splenic rupture on day 1 of hospitalization, later discovered to have babesiosis. Successful non-surgical management is discussed, including using polymerase chain reaction (PCR) DNA, a more sensitive test to make the diagnosis of babesiosis.

Case report

A 54 year old male with no significant past medical history presented to our institution with complaints of dull left upper

* Corresponding author. Tel.: +1 5412062172.
E-mail address: elerlanjlidiakatia@yahoo.ca (N. Usatii).

http://dx.doi.org/10.1016/j.idcr.2014.08.002

quadrant abdominal pain for one week along with abdominal distention and subjective fevers and headache. His appetite had been poor for the past 2 days. He had seen a holistic doctor in Chinatown where who had performed bedside ultrasound and had told him that he had fluid in his stomach. Patient denied nausea, vomiting, diarrhea, chest pain, dyspnea, cough, rash, joint pain, trauma, or any weight loss. He denied using herbal supplements or traditional medicine supplements. The patient describes living in the US for 12 years with no recent travel.

Temperature on presentation was 98.6 F with a blood pressure of 106/64 and oxygen saturation of 98% on room air. His abdomen was mild to moderately distended with tenderness in left upper quadrant. No ecchymosis was seen on his abdomen or flanks. There was no rebound tenderness or guarding. Bowel sounds were present. No visceromegaly was noted.

Laboratory results included total leukocyte count of 4.4 k/cumm, hemoglobin level of 10.6 g/dL, hematocrit of 31.3%, and a platelet count of 123 k/cumm. Total bilirubin of 0.9 mg/dL, aspirate aminotransferase of 67 U/L, alanine aminotransferase 92 U/L, and alkaline phosphatase 107 U/L. CT scan of the abdomen and pelvis showed mildly enlarged spleen with moderate sized hemoperitoneum (perihepatic and perisplenic), extending into the pelvis (Fig. 1). A linear hypodensity was present in the inferomedial aspect of spleen, suspicious for splenic laceration.

The initial clinical impression was Infectious Mononucleosis with spontaneous splenic bleed, and/or spontaneous hemoperitoneum with no clear inciting event with normal coagulation profile. Patient was initially admitted to the surgical services given the CT scan findings. Troponin I, amylase, and lipase were negative.

During day two of his hospitalization he developed high fevers of 101/102. A subacute infectious process was high on the differential. Repeat liver function test was elevated with total bilirubin of 2.1 mg/dL, direct bilirubin of 0.3 mg/dL, alkaline phosphatase level of 168 U/L, aspartate aminotransferase level of 100 U/L, and alanine aminotransferase level of 118 U/L. Urine analysis and chest-X-ray was negative. All blood cultures were without growth. Patient was hydrated for the blood loss, being treated for the pain, and tolerating a surgical liquid diet. Infectious disease consult was called. Panel of tests were ran including: EBV, CMV, Babesia, malaria, LDH, and HIV.

Babesia polymerase chain reaction (PCR) came back positive for *B. microti*. The LDH level was elevated at 1728 U/L. The elevated LDH, indirect bilirubin, along with splenomegaly was suggestive of hemolytic anemia. Treatment was initiated with Zithromax and Atovoquone. CMV DNA PCR, CMV IgG, HIV, mono test, and EBV were all negative.

Patient experienced 2 transient episodes of hypotension where his systolic pressure decreased to 80s; patient was asymptomatic. He was managed conservatively for the splenic rupture; he remained hemodynamically stable with continued intravenous fluids and 2 units of PRBC transfusions. No surgical intervention was necessary. The hemolytic anemia improved. He remained afebrile and the left upper quadrant pain had resolved. He was discharged home on day 12. He was to complete a total of 10 days of antimicrobial therapy and a follow up with the infectious disease specialist as outpatient.

Discussion

Human babesiosis is a malaria-like infection documented since Biblical times in cattle but only recently as a zoonotic pathogen of humans. The first case of human babesiosis was described in 1956. The propagation of babesiosis is currently increasing. This may be due to the increased white-tailed deer population and the white-footed mouse or simply because of increased awareness and reporting. Besides tick transmission, babesiosis can spread transplacentally and through blood transfusions.

Patients typically present with gradual onset of fatigue, malaise, and weakness. Fever is present (intermittent or sustained); less common symptoms include headache, myalgia, arthralgia, and anorexia. Patients experiencing severe babesiosis present with the above along with thrombocytopenia and elevated liver enzymes. The first case reported in a medical journal was in 2007 [7].

Spontaneous splenic rupture is a rare complication as a result of infection with *Babesia* species; and few reports exist in literature. The mechanism is not entirely clear. It may be secondary to phagocytosis of *Babesia*-infected erythrocytes by splenic histiocytes in addition to sequestration of platelets causing thrombocytopenia. This process leads to rapid splenomegaly and eventual spontaneous splenic rupture. The first documented case of splenic rupture from babesiosis was reported in the lay press from 2005, where it described a man in Minnesota who underwent emergent splenectomy for spontaneous rupture secondary to babesiosis. However, this case was never reported in a medical journal [5,7].

In the absence of trauma, splenic rupture can occur in infectious mononucleosis, malaria, typhoid fever, leukemia, CMV, *Plasmodium* species, *Coxiella* species, *Bartonella* species, *Staphylococcus* species, and *Streptococcus* species [3,7].

Diagnosis is generally determined upon microscopic examination of thin blood smears, polymerase chain reaction (PCR), small animal inoculation, and identification of babesia antibody titer [6]. The method used to diagnose babesiosis in our patient was light

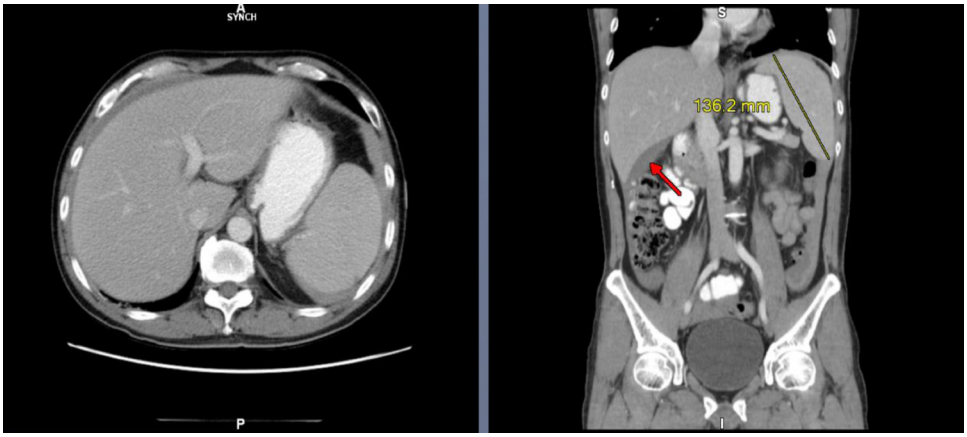

Fig. 1. There is moderate amount dense peritoneal fluid in the abdomen and pelvis, suggestive hemoperitoneum. The fluid is slightly more prominent in the perisplenic area. There is hyperdense clot in the left paracolic gutter. The spleen is borderline enlarged, measuring 13.4 cm × 10.5 cm × 7 cm in craniocaudal × AP × transverse dimensions. There is a subtle linear hypodensity in the inferomedial aspect of spleen. Mild diffuse fatty infiltration of the liver is present.

cycler real time PCR. Detection of *B. microti* was based on the sequence of 252-bp fragment of the highly conserved 16S-like ribosomal RNA gene and was carried out through a light cycler probe utilizing the Roche Light Cycler. To control for substances that may interfere with PCR amplification, all samples were tested with a separate Light Cycler assay for Beta2 microglobulin.

A molecular (PCR-based) screening strategy-either as a stand-alone or as a means to complement serology-would enable detection of acute parasitemia, independent of phase of infection. PCR assay can rapidly detect and quantify genotype of small subunit ribosomal RNA gene (SSUrDNA) of *B. microti*. The genotype-specific pairs of primers targeted on internal transcribed spacer (ITS) 1 or 2 sequences is used and amplicons by pairs of primers displayed the high specificity for homologous genotype DNA. DNA is amplified using the following primers: Bab 2 (5′-GTTATAGTTTATTTGATGTTCGTTT-3′/Bab 3 (5′-AAGCCATGC-GATTCGCTAAT-3′ and Bab1 (5′-GTTAGTATAAGCTTTTATACAGC-3′)/Bab 4 (5′-ATAGGTCAGAAACTTGAATGATACA-3′) to generate 154-bp amplicons. Bab 2 and Bab 3 are *B. microti*-specific fragments from a gene encoding the small subunit R RNA at decreasing inoculum of 445, 44.5 and 4.45 copies/ml, the assay has positive rates of 100, 97.5 and 81%, respectively. A blinded probit analysis demonstrates a detection rate of 95 and 50% at 12.92 and 1.52 parasites/2 ml of whole blood, respectively, which proves that quantitative real-time PCR-based assay for detection of *B. microti* is a highly sensitive and specific test [8–10].

Patients with active babesiosis require treatment, which includes those with viral infection-like symptoms and identification of babesial parasites in blood smear by PCR. Symptomatic patients with positive antibody to *Babesia* but absent babesial parasites on smear or babesial DNA by PCR should not receive treatment. Treatment is also not suggested for asymptomatic patients regardless of the results of the serologic tests, blood smears, or PCR. If parasitemia persists after repeat testing in a 3 month period, then treatment should be considered [2].

Treatment usually involves a two-drug regimen; clindamycin plus quinine, or atovaquone plus azithromycin (as in the case of our patient) for 7–10 days. Either treatment is acceptable for non-life-threatening babesiosis. Clindamycin and quinine should be given with severe babesiosis. If patients are persistently symptomatic, longer duration of antimicrobial therapy may be employed. Partial or complete red blood cell exchange transfusion is indicated for those with severe babesiosis with high grade parasitemia (>10%), significant hemolysis (hemoglobin <10), or renal, hepatic, or pulmonary compromise [2].

Our patient developed a rare complication of babesiosis infection-spontaneous splenic rupture. However, it was not severe enough to be treated surgically. Frequently splenic rupture develops into an extensive intraperitoneal hemorrhage leading to hemodynamic instability requiring urgent splenectomy to prevent death. Conservative management is an option for more stable patients.

Interventional radiology is another option for patients who continue to require blood transfusion while maintaining hemodynamic stability. In case of sudden deterioration, splenectomy is appropriate. Splenic artery angiography and embolization can successfully stop hemorrhage. Patients who are asplenic are vulnerable because of their inability to clear parasitemia. However, to best optimize patient outcomes, there should be low threshold for urgent laparatomy and splenectomy.

References

[1] Vannier E, Krause PJ. Human babesiosis. N Engl J Med 2012;366(June 21 (25)):2397–407. http://dx.doi.org/10.1056/NEJMra1202018.

[2] Kavanaugh MJ, Decker CF. Babesiosis. Dis Mon 2012;58(June (6)):355–60. http://dx.doi.org/10.1016/j.disamonth.2012.03.007.

[3] Kuwayama DP, Briones RJ. Clin Infect Dis 2008;46(May 1 (9)):e92–5. http://dx.doi.org/10.1086/587175.

[4] Wormser GP, Lombardo G, Silverblatt F, El Khory MY, Prasad A, Yelon JA, et al. Babesiosis as a cause of fever in patients undergoing a splenectomy. Am Surg 2011;77(March (3)):345–7.

[5] Tobler Jr WD, Cotton D, Lepore T, Agarwal S, Mahoney EJ. Case report: successful non-operative management of spontaneous splenic rupture in a patient with babesiosis. World J Emerg Surg 2011;6(January 20):4. http://dx.doi.org/10.1186/1749-7922-6-4.

[6] Krause PJ. Babesiosis diagnosis and treatment. Vector Borne Zoonotic Dis 2003;3(Spring (1)):45–51.

[7] Abbas HM, Brenes RA, Ajemian MS, Scholand SJ. Successful conservative treatment of spontaneous splenic rupture secondary to babesiosis: a case report and literature review. Conn Med 2011;75(March (3)):143–6.

[8] Bloch EM, Lee TH, Krause PJ, Telford 3rd SR, Montalvo L, Chafets D, et al. Development of a real-time polymerase chain reaction assay for sensitive detection and quantification of *Babesia microti* infection. Transfusion 2013;53(October (10)):2299–306. http://dx.doi.org/10.1111/trf.12098 [Epub 2013 January 30].

[9] Thill C, Blackenson PB, Prusinski MA, Kogut SJ, Lee JH, Coleman JL. Detection of *Babesia microti* DNA in *Ixodes scapularis* (Acari: Ixodidea) by use of Chelex 100 resin and polymerase chain reaction. J Med Entomol 2005;42(July (4)):694–6.

[10] Ohmori S, Kawai A, Takada N, Saito-Ito A. Development of real-time PCR assay for differential detection and quantification for multiple *Babesia microti*-genotypes. Parasitol Int 2011;60(December (4)):403–9. http://dx.doi.org/10.1016/j.parint.2011.06.021 [Epub 2011 June 25].