A Rare Case of Shock in a Patient with Non-Severe Range Babesiosis

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Abstract
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Keywords
Babesiosis, parasitemia, shock, exchange transfusion

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Conflict of Interest Statement
No conflict of interest

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CASE REPORT

A Rare Case of Shock in a Patient with Non-severe Range Babesiosis

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Abstract

Babesiosis is a tickborne illness caused by microscopic parasites that infect red blood cells. Infections present on a spectrum from asymptomatic to severe, life-threatening presentations. However, life-threatening disease is more typically seen in patients who are asplenic, immunocompromised, or with hepatic/renal disease. We present an unusual case of babesiosis where an immunocompetent patient with age as the only risk factor, became extremely ill with relatively low parasite burden and no co-infection with other tickborne illnesses. A 73-year-old man with essential hypertension and remote prior Lyme disease infection presented to the hospital in late Spring due to acute mental status change after being found acting erratically by police. Upon presentation, he was hypotensive to 70/40 mmHg, tachycardic, and unable to follow commands. Blood parasite smear was positive for Babesia species with 2.2% parasitemia. Ehrlichia, Anaplasma and Lyme IgM species testing was negative. The patient required treatment of septic shock with norepinephrine. Along with azithromycin and atovaquone, he ultimately underwent three exchange transfusions due to significant hemolytic anemia. This led to dramatic improvement in his mental status and he was discharged with 10 additional days of antibiotics. Babesia infections present heterogeneously ranging from asymptomatic to life-threatening presentations with hypotension, hemolysis, thrombocytopenia, DIC, organ failure, and even death, especially in patients with risk factors. Our patient had a critical presentation without an immunocompromised state, no prior splenectomy, lack of liver/renal abnormalities, and relatively low parasitemia. Additionally, exchange transfusion can be considered with hemolysis despite non-severe range parasitemia.

Keywords: Babesiosis, Parasitemia, Shock, Exchange transfusion

1. Background

Babesiosis is primarily a tickborne illness (TBI) caused by microscopic parasites that infect red blood cells (RBCs). In the United States, cases are most concentrated in the northeastern and northern-midwestern territories and are also found throughout the world. It is a disease that presents in a heterogenous manner. Infections present on a spectrum from asymptomatic to severe, life-threatening presentations. However, life-threatening disease is typically seen in patients who are asplenic, immunocompromised with diseases like HIV or cancer, or individuals with liver or renal disease. Common symptoms of Babesia infection are fever, chills, diaphoresis, headache, myalgia, nausea, and fatigue. In severe cases, patients can experience hypotension, hemolysis, thrombocytopenia, disseminated intravascular coagulation (DIC), organ failure, splenic rupture, and even death.

We present an unusual case of babesiosis where a presumed immunocompetent patient, with age as the only risk factor, became extremely ill with a relatively low parasite burden and no co-infection with other TBIs.

2. Case presentation

A 73-year-old man with a medical history of essential hypertension (baseline blood pressure was 140/90 mmHg on combination lisinopril-hydrochlorothiazide) and prior Lyme disease infection several years ago presented to a hospital in
Pennsylvania in late Spring due to acute change in mental status after being found acting erratically by police officers. Initially, due to altered state, history was limited.

When the patient presented to the emergency department, he was noted to have a blood pressure of 70/40 mmHg, heart rate of 120 beats per minute, temperature of 37.9 °C, and he was saturating well without the need for supplemental oxygen. On exam, his skin was warm, and his mucous membranes were dry. There were no rashes or petechiae noted. Cardiopulmonary exam was significant only for tachycardia. Abdominal exam was unremarkable, including nonpalpable spleen. The patient was not following commands but was moving all extremities spontaneously.

3. Investigations

A broad differential diagnosis was considered as the cause for this patient's acute encephalopathy and shock. Initial testing revealed pancytopenia which was concerning for a TBI given the geographic location and time of year. However, since he was not able to provide reliable history early in the hospital course, traditional risk factors like hiking were not able to be elucidated. Laboratory abnormalities included lactic acid 2.3 (normal 0.6–1.4) mmol/L, creatinine 2.21 (normal 0.6–1.3) mg/dL, white blood cells 4.3 (normal 4.8–10.8) 10^3/μL, platelets 71 (130–400) 10^3/μL, and hemoglobin 7.5 (14–17.5) g/dL. Electrolytes had no significant abnormalities. Initial CT brain without contrast and chest x-ray were unremarkable. CT abdomen and pelvis with and without contrast revealed mild splenomegaly but did not reveal bleeding or hematoma. However, since the patient had anemia and thrombocytopenia, further hematologic testing was ordered (Table 1). Direct antiglobulin test (DAT) was negative. His anemia was likely hemolytic with low haptoglobin and elevated lactate dehydrogenase.

The focus shifted towards suspected septic shock from a TBI, and a comprehensive workup was done to exclude other infectious etiologies. Thin and thick smears were prepared using Giemsa stain and found to be positive for Babesia species (Fig. 1). Percent parasitemia was calculated by identifying the number of parasitized RBCs and dividing it by the total RBCs counted and multiplying it by 100. The percent parasitemia was 2.2. Babesia serology and PCR testing was not available at our center. Malaria was unlikely because the patient did not travel outside of the Northeast United States, and it was not visualized on Giemsa stain. Serology testing for Ehrlichia chaffeensis and Anaplasma phagocytophilum IgM and IgG were both negative (normal level for both species' IgM <1:20 and IgG <1:64). Patient tested positive for IgG antibody for Lyme disease but tested negative for IgM antibodies. Rocky Mountain Spotted Fever is not endemic to the region. The patient's respiratory status with lack of oxygen requirement along with unremarkable chest x-ray made a pulmonary source less likely. Meningitis was a concern because of his altered mentation, leukopenia, and his borderline body temperature, so lumbar puncture was obtained. The sample was not significantly abnormal, including negative CSF culture with Gram stain, negative Lyme by PCR, and negative meningitis encephalitis panel by PCR. This was not consistent with CNS infection. Additionally, MRI brain without contrast did not reveal any significant abnormalities. Blood cultures remained negative. HIV testing was negative.

Toxicities, stroke, and metabolic derangements were initially contemplated but lower on the differential diagnosis after initial lab work and imaging studies. Other additional causes of hemolytic anemia were considered including hereditary, acquired, and immune. Upon chart review, he had no prior significantly abnormal complete blood counts, and his peripheral smear did not reveal many abnormal cells except for the babesia species seen, making a hereditary cause less likely. Besides infection, other acquired causes that can be considered are liver disease, hypersplenism, toxins, oxidant agents, and microangiopathic hemolytic anemia (MAHA). Aside from a mildly enlarged spleen, which was most likely related to his infection, the patient's presentation was not consistent with the other acquired causes. Prior lab work demonstrated normal liver function and his acute presentation yielded only mild transaminase elevations. His family denied any known exposure to toxins or oxidant agents. MAHA was less likely given his lack of schistocytes along with normal fibrinogen and normal fibrin split

Table 1. Laboratory investigations.

<table>
<thead>
<tr>
<th>Lab values</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reticulocyte count</td>
<td>2.4</td>
<td>0.5–2%</td>
</tr>
<tr>
<td>PT</td>
<td>17.2</td>
<td>11.7–14.5 s</td>
</tr>
<tr>
<td>INR</td>
<td>1.4</td>
<td>0.9–1.1</td>
</tr>
<tr>
<td>aPTT</td>
<td>35.7</td>
<td>22.8–34.2 s</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>410</td>
<td>191–524 mg/dL</td>
</tr>
<tr>
<td>D-dimer</td>
<td>2.25</td>
<td>&lt;0.5 μg/mL</td>
</tr>
<tr>
<td>Fibrin split products</td>
<td>&lt;10</td>
<td>&lt;10 μg/mL</td>
</tr>
<tr>
<td>Haptoglobin</td>
<td>&lt;30</td>
<td>40–215 mg/dL</td>
</tr>
<tr>
<td>Lactate dehydrogenase</td>
<td>467</td>
<td>140–271 IU/L</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>1.0</td>
<td>0.3–1.0 mg/dL</td>
</tr>
</tbody>
</table>
products. Immune causes were less likely because of his negative DAT. There was initially high suspicion for another tickborne coinfection given the severity of his condition with only 2.2% Babesia parasitemia. After testing for other TBIs was negative, it was solidified that babesiosis was the sole infection to result in his septic shock.

4. Treatment

Despite 2 L of initial volume resuscitation with crystalloid fluids, the patient remained hypotensive requiring placement of central venous catheter for administration of norepinephrine. The patient was admitted to the intensive care unit for treatment of septic shock caused by parasitemia from babesiosis infection. Antimicrobial therapy was initiated with azithromycin 500 mg IV daily and atovaquone 750 mg by mouth twice daily. Patient underwent exchange transfusion considering the significant hemolytic anemia.

Following exchange transfusion and initiation of antibiotics, the patient’s mental status improved dramatically, and IV vasopressors were discontinued 24 h after admission. It was discovered that patient is an avid hiker and has had multiple tick bites in the past. During the hospital course, patient underwent a second exchange transfusion due to ongoing hemolytic anemia with hemoglobin dropping to 4.4 g/dL. On hospitalization day two, parasitemia was 0.46%. On hospitalization day four, parasitemia was 0.1% and on the sixth day of hospitalization there were no parasites identified on blood smear (Fig. 2). Patient was discharged from the hospital in stable condition with plans for 10 additional days of oral antibiotics following clearance of parasite from the bloodstream.

5. Discussion

Babesiosis is a parasitic infection that is primarily tickborne. Most often, Babesia infections occur among healthy individuals and manifest as an asymptomatic or self-limited condition. Rarely, patients can have severe babesiosis which is defined as the presence of severe range parasitemia (≥4%).

![Fig. 1. Peripheral blood smear identifying parasite infiltration of red blood cells.](image1.jpg)

![Fig. 2. Percent parasitemia throughout hospital course.](image2.jpg)
and/or severe symptoms including hypotension, hemolysis, thrombocytopenia, DIC, organ failure such as acute respiratory distress syndrome, and even death. However, patients typically have an immunocompromised state predisposing them to more severe infections. Our patient had an initial parasite load of 2.2%. He was presumed to be immunocompetent given that he had no significant comorbidities (including normal liver and renal function at baseline), HIV negative status, and that he was up to date with all age-appropriate cancer screenings. The severe clinical presentation in our patient was unexpected because of his presumed immunocompetence, lack of major comorbidities, no history of splenectomy, and lack of high parasite burden. There have been multiple case reports of patients without comorbidities becoming significantly ill from babesiosis, however in previously reported cases, these patients had severe range parasitemia. Nevertheless, few reports in the literature indicate that B. microti infection can manifest as severe disease in older individuals (>60 years old). Given that our patient was >60 years old, his age may have played a role in his severe presentation.

Hematologic manifestations of Babesia are common, particularly thrombocytopenia. This is usually caused by hypersplenism but can also occur because of DIC. Anemia is a result of the parasites directly lysing the RBCs. This occurs because the parasites reproduce in the RBCs and when they mature, they disrupt the cell membrane, resulting in non-immune-mediated hemolysis. It can affect the bone marrow, but likely did not in our patient's case because his reticulocyte count was elevated. Mechanisms for leukopenia are not fully understood.

Shock is a known complication of B. microti infections. Some reports have noted that the severity of shock is directly proportional to the parasite burden. With the climate changing, it is possible that the geographic area for babesiosis infectivity will expand. This should probe clinicians to add it to their differential diagnosis for undifferentiated shock. Overall prevalence in the USA in 2020 was 1827 cases in 24 out of 40 states. Dual infection, meaning more than one TBI, among I. scapularis species in the USA ranged from 1.0 to 28.2%. In fact, a previous study confirmed dual infections in 71/192 individuals (37%) (predominantly Lyme disease and babesiosis) and triple infections in 4/192 (2%) (Lyme disease, babesiosis, and anaplasmosis). When TBI is suspected, screening for coinfections should be considered as this can guide how to appropriately manage patients. We must particularly be mindful about screening when one of the existing infections is Lyme, babesiosis, or anaplasmosis.

Doxycycline is the mainstay of treatment for anaplasmosis, ehrlichiosis, and Lyme disease, however, it is not effective against Babesia. Recommended treatment for babesiosis includes IV quinine and oral or IV clindamycin. The addition of red cell exchange transfusion therapy is recommended in high parasite burden (>10%), severe anemia, and pulmonary, renal, or hepatic compromise. In the case of our patient who presented with shock, renal failure, and hemolytic anemia despite a low parasite load, a multidisciplinary team including hematology, nephrology and critical care made the decision to perform red cell exchange transfusion. This led to dramatic improvement in his mental status and discontinuation of vasopressor support. He underwent a second transfusion due to ongoing hemolysis. His parasitic load improved to 0.1% and was eventually undetected. The aim of this therapy is to remove the infected erythrocytes, proinflammatory cytokines, and vasoactive compounds derived from the intraerythrocytic infection and the immune host response. Among hospitalized immunocompetent patients, the fatality rates range between 6% and 9%. Thus, prompt initiation of exchange transfusion when indicated along with antimicrobial therapy could be lifesaving. There is questionable benefit with respect to morbidity and mortality, however in severe cases such as ours, the benefits may outweigh the risks of the procedure, mainly exposure to multiple RBC transfusions.

Practitioners need to be aware of the risk of life-threatening illness in known endemic regions, particularly during the spring and summer months. Treatment of severe cases requires prompt evaluation in the hospital setting for initiation of antimicrobials and supportive care for complications such as shock. Prevention should be reinforced with patients including risk factor mitigation for tick exposure. Some precautions hikers can take are wearing clothing that covers the arms and legs in addition to closed-toe shoes, as well as using insect repellents that contain at least 20% DEET. Additionally, hikers should check for ticks and remove them immediately when found.

In conclusion, this case is particularly interesting because of the presentation of florid septic shock requiring vasopressor support and exchange transfusion therapy in an otherwise healthy 74-year-old gentleman with a rather low parasite burden.
Learning points

1. Severe babesiosis can occur even with parasitemia in non-severe range in the absence of coinfection and immunocompromised state.
2. Exchange transfusion can be considered in patients with hemolysis and shock despite non-severe range parasitemia.

Conflicts of interest

No conflict of interest.

References


