CASE REPORT

Severe babesiosis in an asplenic patient requiring red cell exchange

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ABSTRACT

Babesiosis is a rare, tick-borne infectious disease, caused mostly by the parasite *Babesia microti* in the United States. It is frequently transmitted through the bite of the *Ixodes scapularis* tick. Babesiosis is characterized by red cell disruption and intravascular hemolysis. Severe cases can be life-threatening and are associated with asplenia, advanced age, and other causes of impaired immune function. Treatment is typically with antibiotics. However, for severe cases, the use of red cell exchange has been reported with debate about its efficacy. Here, we report a complex case of babesiosis with a parasitemia of 22% that required two red cell exchange procedures and multiple antibiotics in a patient with a history of asplenia.

INTRODUCTION

Babesiosis is a rare, tick-borne infectious disease caused by the *Babesia* protozoa family with the *B. microti* parasite as the most common species in the United States. It is frequently transmitted through the bite of the *Ixodes scapularis* tick and rarely through vertical transmission to infants and blood infusions [1]. Babesiosis is characterized by red cell disruption and intravascular hemolysis. Severe cases can be life-threatening and are associated with asplenia, advanced age, and other causes of impaired immune function [1]. Here, we report a severe case of babesiosis that required two red cell exchanges and multiple antibiotics in an asplenic patient.

CASE PRESENTATION

A 62-year-old male with a past medical history significant for asplenia, coronary artery disease, gastroesophageal reflux disease, and iron deficiency anemia presented to his primary care doctor with cyclic fevers and abdominal pain. He was then referred to the emergency department (ED), where he was found to have leukocytosis and elevated liver function tests (LFTs). Computed tomography (CT) showed mid-sigmoid diverticulitis. The patient was discharged on a two-week course of amoxicillin-clavulanate. His symptoms resolved but then recurred soon after stopping the antibiotics. He returned to the ED for worsening symptoms, including

diarrhea with black stools, nausea, lightheadedness, and fatigue. The patient lives in the country in Hatley, Wisconsin. He likes hunting and fishing and has a long history of tick bites with the last known tick exposure about four months ago—for which he presented to his primary care provider who removed the tick and gave one dose of doxycycline. He denies recent long-distance travel. The patient was admitted and started on doxycycline. His peripheral blood smear showed a parasitemia of 22%, which was concerning for severe babesiosis. He received azithromycin and atovaquone and was immediately transferred to the University of Wisconsin Hospital (UWH) for treatment that included urgent red cell exchange.

Upon arrival, the patient complained of worsening diarrhea, as well as dyspnea, fever, chills, fatigue, and decreased urination. Vital signs were stable. Labs revealed a hemoglobin of 7.3g/dl, thrombocytopenia (76K/µl), a white blood cell count of 12.4K/µl, haptoglobin of <8mg/dL, total bilirubin of 6.1mg/dL, a rise in LFTs (alanine aminotransferase [ALT] and aspartate aminotransferase [AST] of 1093 and 2165U/L, respectively), and a creatinine (Cr) of 2.9mg/dL. These findings indicated intravascular hemolysis with declining liver and kidney function. Blood smears for parasites were sent to the UWH lab and Wisconsin State Laboratory of Hygiene (WSLH) in parallel and showed tetrad and ring forms in red cells (Figure 1) with a parasitemia of 15% and 9.6%, respectively, which were consistent with babesiosis. Polymerase chain reaction (PCR) tests confirmed *B. microti* and ruled out a potential coinfection with *Borrelia miyamotoi*. The patient immediately received an automated red cell exchange and was started on clindamycin 600mg IV every 6 hours and quinine 650mg orally every 8 hours. Following the first exchange, his parasitemia decreased to 8%. However, the next day his parasitemia rebounded to 9%, requiring another red cell exchange which reduced it to 3%. In addition, the patient developed an acute kidney injury with a rise in Cr from 2.9 to 5.32mg/dl and in blood urea nitrogen (BUN)—likely due to prolonged diarrhea and poor intake in the setting of intravascular hemolysis. To avoid nephrotoxic drugs, his antimicrobial therapy was changed to azithromycin and atovaquone, which led to an improvement in his renal status. The patient's parasite load was closely monitored and gradually improved with antibiotic therapy. Parasitemia levels were not detected on the fourteenth day of his admission, allowing discontinuation of antimicrobial therapy (Table 1). He was discharged the next day with close nephrology follow-up.

DISCUSSION

Here, we describe an asplenic patient with a *Babesia* parasitemia level of 22% who required two rounds of therapeutic red cell apheresis and multiple antibiotics to reduce his parasite load. Our patient initially received quinine and clindamycin, the standard treatment for severe symptoms [5]. However, due to acute kidney injury, he was switched to atovaquone and azithromycin, indicated for mild to moderate symptoms [5]. Therapeutic apheresis for babesiosis is recommended for individuals with severe disease (i.e. renal or liver dysfunction or severe hemolysis) and/or high parasitemia levels (>10%), as seen in our patient [5]. It is relatively safe, even in severe babesiosis. One systematic review of twenty-two patients who underwent twenty-nine red blood cell (RBC) exchanges reported no adverse events [6]. Apheresis is thought not only to relieve parasite burden but also to remove RBCs that may cluster and obstruct microcapillaries, as well as cytokines produced by hemolysis that may lead to renal

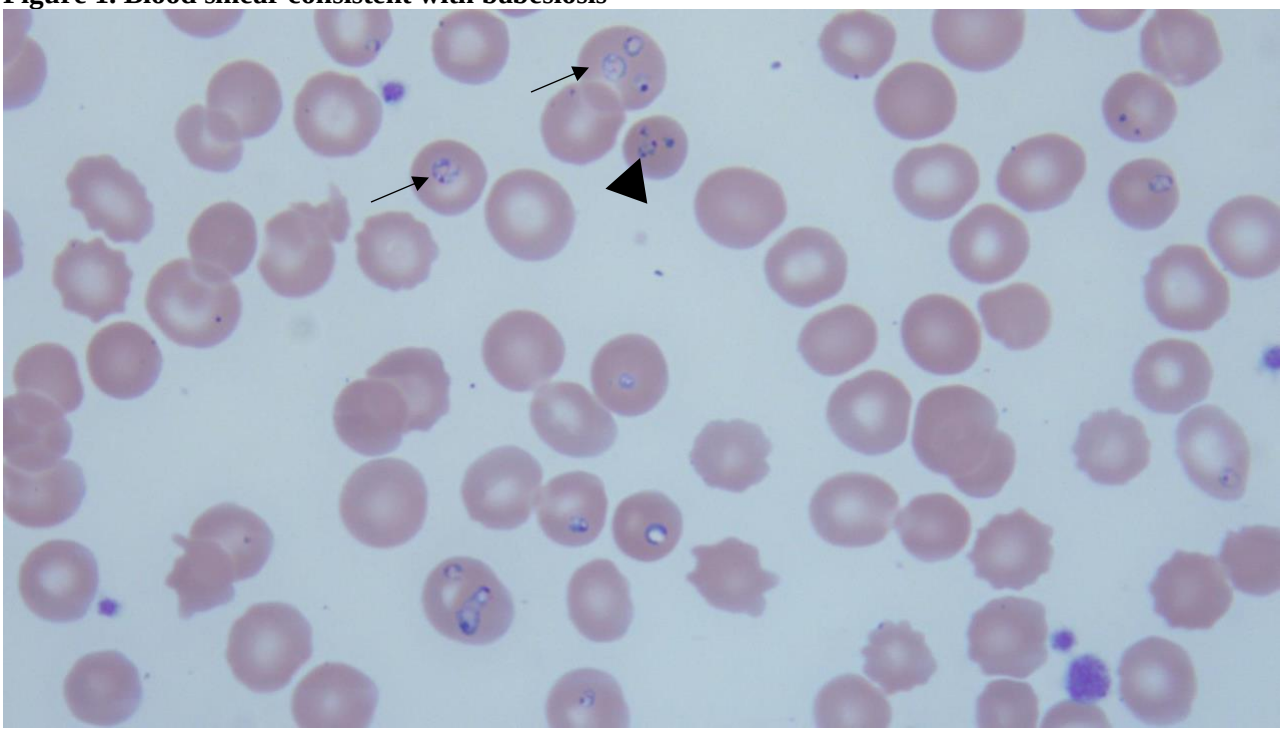
failure and disseminated intravascular coagulation [5]. After the first RBC exchange procedure, our patient experienced a rebound parasitemia from 8% to 9%—complicated by an acute kidney injury which caused a transition of antimicrobials from clindamycin and quinine to azithromycin and atovaquone. Due to his worsening condition, another RBC exchange was conducted to decrease the parasitemia level to less than 5% and allow the new antimicrobials to become effective. Although red cell exchange is usually stopped once parasitemia is <5%—as we did in our patient—the patient's overall clinical condition needs to be considered [5]. This procedure has a Grade 2C recommendation, indicating it is a weak recommendation with low-quality evidence (usually from observational studies, clinical observations, or randomized trials with serious flaws) [5].

In addition, apheresis as a treatment for babesiosis has unclear efficacy, especially when used in conjunction with antibiotics. As of 2020, there have been about fifty cases of babesiosis treated with RBC exchange [2-4]. Some cases have demonstrated rebound parasitemia or required multiple exchanges, similar to our case [2, 4, 7]. One case in an asplenic 56-year-old male demonstrated doubling of the parasitemia from 15% to 30% twelve hours after a two-volume RBC exchange, requiring a second RBC exchange and subsequent antibiotic therapy for forty-eight days after the initial presentation [7]. Another case reported an asplenic 47-year-old female who underwent a whole-volume RBC exchange requiring another half-volume exchange, following a rebound parasitemia from 5% to 11.4% [4]. However the authors felt her immunotherapy-treated rheumatoid arthritis contributed to the need for long-term antibiotics, unlike our patient [4]. The history of asplenia in these two patients, as well as in our patient, contributed to the severity of the babesiosis presentation and prolonged the clinical course. In contrast to these two cases, PCR testing was conducted in our patient, confirming *B. microti* and ruling out other types of *Babesia*—further elucidating his clinical presentation. One retrospective study of nineteen patients who underwent RBC exchange revealed that there was no significant association between both length of stay and mortality and post-procedural parasitemia or a percent parasitemia reduction [2]. The authors posit that patients can be observed for an antimicrobial response for at least one to three days before undergoing RBC exchange, since there was no difference in clinical outcome if the procedure had been done on admission or one to three days later [2]. These authors also indicate that a repeat exchange should be based on the patient's clinical status compared to a fixed level of parasitemia [2].

There is also the question of how to accurately measure parasitemia. Parasitemia is determined by the percentage of parasitized RBCs divided by the total RBCs. This percentage is usually recorded by a lab technician after visualization of morphology and manual counts, which can be subject to error. Not only can there be variability within an institution's laboratory but also between institutions, as seen in our case between UWH and WSLH (Table 1).

Future studies should include randomized trials of therapeutic apheresis for babesiosis, as there have been no studies demonstrating its efficacy thus far [8].

Figure 1. Blood smear consistent with babesiosis



Ring (arrow) and tetrad forms (arrow head) of *B. microti* in red cells, 1000x.

Table 1: Percentage of parasitemia during hospital admission.

Admission Day	1	2	3	4	5	6	7	9	10	11	12
WSLH	9.6	4.2	2.467	2.267	1.785	0.489	0.425	N/A	0.117	N/A	Ring forms seen on thick smear only. Parasitemia below the limit of detection
UWH	15	9	3	N/A	N/A	2	2	1	1	<1	No blood parasites seen

Notes
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