Trust the Process: Prolonged Babesia Parasitemia in an Elderly Man with Asplenia from the American Midwest

Corresponding Author: Marko Ivancich, e-mail: mivancich@mcw.edu

Financial support: None declared

Conflict of interest: None declared

Patient: Male, 89-year-old

Final Diagnosis: Babesia microti infection

Symptoms: Falls • fever • general weakness • loss of appetite

Medication: —

Clinical Procedure: —

Specialty: Infectious Diseases • General and Internal Medicine

Objective: Unusual clinical course

Background: Babesia species are intraerythrocytic parasitic protozoa that are endemic to the Northeast and north Midwest of the United States. Babesia microti is the most common cause of babesiosis in North America and causes a malaria-like tick-borne parasitosis. Babesia is commonly transmitted through the bite of Ixodes species ticks, often concomitantly with other tick-borne organisms such as Borrelia burgdorferi, Ehrlichia, Rickettsia rickettsii, and Anaplasma phagocytophilum. In the Midwest, Lyme disease is the most common tick-borne illness, and other organisms can sometimes be overlooked. The risk of tick-borne parasitic or bacterial infection is increased in patients after splenectomy.

Case Report: An 89-year-old man with asplenia and multiple other comorbidities presented to the Emergency Department after a fall at home preceded by 2 to 3 days of fever and loss of appetite and 1 week of generalized weakness. The patient had thrombocytopenia, leukocytosis with neutrophilia, transaminitis, hyperbilirubinemia, and elevated creatine kinase level consistent with tick-borne illness. Laboratory testing revealed Borrelia and Babesia co-infection and other culprits were ruled out via high sensitivity PCR. Owing to the patient’s asplenic status, the babesiosis was slow to resolve with appropriate treatment. After an extended 8-week treatment with azithromycin and atovaquone, the patient demonstrated clinical resolution of babesiosis with a negative blood smear.

Conclusions: First-line treatment with azithromycin and atovaquone is effective in treating babesiosis even in complicated patients, such as this elderly, asplenic patient. However, in cases such as this, an extended course of a first-line treatment regimen is still appropriate.

Keywords: Babesia • Frail Elderly • Ixodes • Parasitemia • Splenectomy

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/936326

© Am J Case Rep, 2022; 23: e936326
DOI: 10.12659/AJCR.936326

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)
Background

*Babesia* species is an intraerythrocytic parasitic protozoa that is endemic to the Northeast and north Midwest of the United States [1,2]. *Babesia microti* is the most common cause of babesiosis in North America and causes a malaria-like tick-borne parasitosis [2]. Babesiosis can be asymptomatic but commonly presents with malaise, fatigue, fever, headache, chills, sweats, weight loss, and myalgia [2]. Laboratory findings typically include low hemoglobin and hematocrit levels, an elevated reticulocyte count, and low platelet count [2]. Physical examination findings often include abdominal tenderness, hepatosplenomegaly, and sometimes jaundice and petechiae, which can be a sign of disseminated intravascular coagulopathy [2]. Babesiosis can be diagnosed using a peripheral blood smear, antibody testing, and species-specific polymerase chain reaction (PCR) testing. Severe fulminant disease can occur and may result in death in immunodeficient patients, such as the elderly, asplenic patients, and those on immunosuppressing medications [1,3]. Most fatal babesiosis infections occur in the setting of a dysfunctional reticuloendothelial system and insufficient innate immune response [2-4]. In this report, we detail the case of an 89-year-old asplenic man with babesiosis and possible *Borrelia burgdorferi* complicated by prolonged parasitemia. Despite having significant risk factors, the patient responded to prolonged treatment and made a full recovery.

Case Report

An 89-year-old asplenic man with a past medical history of coronary artery disease, chronic kidney disease, hypertension, hyperlipidemia, sinoatrial node dysfunction, obstructive sleep apnea, and basal and squamous cell skin cancers, presented to the Emergency Department after a fall at home that was preceded by 2 to 3 days of subjective fever and loss of appetite and 1 week of generalized weakness. Physical examination revealed no obvious abnormalities, other than mild tachycardia. Laboratory testing showed thrombocytopenia, leukocytosis with neutrophilia, transaminitis, hyperbilirubinemia, and an elevated creatine kinase level (Table 1). SARS-CoV-2 infection was ruled out. Further history revealed that the patient lived in rural Wisconsin near a wooded area and had 2 pet cats, one of whom lived outdoors. However, he did not recall any recent tick bite. We suspected tick-borne illness, and the patient was admitted and started empirically on doxycycline and ceftriaxone. Blood and urine cultures were negative throughout the course of treatment.

*Babesia microti* infection was diagnosed based on a high titer antibody-positive (1: 2048) screening ELISA test, positive direct microscopy for *Babesia* on a peripheral blood smear, and positive *Babesia microti* PCR from the patient’s blood sample. Initial peripheral blood smear revealed a 7.44% *Babesia* parasitemia index (Figure 1). Ehrlichiosis and anaplasmosis were ruled out using a high sensitivity multiplex antibody panel and negative blood PCR studies. Other tick-borne illnesses, such as Colorado tick fever, Rocky Mountain spotted fever, and tick-borne relapsing fever, are not endemic to our region and are not known to be transmitted by the Ixodes tick. Since the patient had no recent travel history, we did not evaluate for these illnesses. Ceftriaxone was stopped and oral azithromycin 1500 mg

| Lab parameter                  | Range          | Day 0 | Day +1 | Week +1 | Week +4 | Week +6 | Week +9 | Week +18 |
|-------------------------------|----------------|------|-------|--------|--------|--------|--------|---------|
| White blood cell count        | 3.4-9.6×10^9/L| 13.9*| 16.3*| 9.1    | 9.5    | 7.6    | 6.5    | 6.6     |
| Hemoglobin                    | 13.2-16.6 g/dL| 12.2*| 9.9*  | 8.4*   | 10.9*  | 11*    | 11.8*  | 11.6*   |
| Hematocrit                    | 38.3-48.6%    | 33.8*| 27.7* | 25.4*  | 34*    | 33.5*  | 36.3*  | 34.4*   |
| Total erythrocyte count       | 4.35-5.65×10^12/L | 3.51* | 2.91* | 2.54*  | 3.1*   | 2.97*  | 3.25*  | 3.25*   |
| Platelet count                | 135-317×10^9/L| 94*  | 99*   | 109*   | 135    | 107*   | 138    | 143     |
| Serum creatinine              | 0.74-1.35 mg/dL | 1.14 | 1.7*  | 0.8    | 0.98   | 0.9    | 0.86   | 0.96    |
| Aspartate aminotransferase    | 8-48 U/L      | 264* | 270*  | 46     | 51     |        | 36     |
| Alanine aminotransferase      | 7-55 U/L      | 67*  | 67*   | 50     | 43     | 34     | 28     | 19      |
| Alkaline phosphatase          | 40-129 U/L    | 92   | 67    | 91     | 92     | 90     | 90     |
| Bilirubin, total              | ≤12 mg/dL     | 2    | 1.4*  | 0.9    |        | 0.5    |
| Bilirubin, direct             | 0.0-0.3 mg/dL | 0.5* | 0.4*  |        | <0.2   |
| C-reactive protein            | ≤8.0 mg/L     | 67.4*| 126.9*| 9.8*   | 4.5    | <3     |

Day 0 – date of first presentation, * values outside normal range for performing laboratory.

Table 1. Laboratory values. Chronological order of relevant laboratory tests performed throughout the patient’s treatment course.
daily and intravenous atovaquone 500 mg daily were started for treatment of babesiosis in consultation with the Infectious Disease Department. Doxycycline was continued for 14 days for the Borrelia co-infection. On day 1 after presentation, the patient had worsening anemia and thrombocytopenia (Table 1). Due to the patient’s asplenia, a prolonged course of treatment was discussed. By day 4, the percent of parasitemia had improved to 6.13% (Figure 1), and most lab abnormalities had resolved (Table 1). However, parasitemia then increased to 7.37% two days later (Figure 1). Although discouraging, this was not completely unexpected. Treatment with atovaquone and azithromycin was continued. The course of parasitemia is demonstrated graphically in Figure 1. The parasitemia index continued to decrease thereafter, but at day 42, a blood smear still showed scant parasitemia of 0.15% (Figure 1). Peripheral blood smears were negative from day 60 onward, and antimicrobial therapy for Babesiosis was discontinued roughly 8 weeks after treatment was initiated.

## Discussion

We present a case of Babesia parasitemia lasting more than 6 weeks and requiring almost 8 weeks of parasite specific therapy in a patient with asplenia. The duration was likely due to the lack of a functioning reticuloendothelial system. Babesia exclusively infects erythrocytes, and pathogenesis of this infection is primarily mediated by the innate immune system [2]. Macrophages, primarily those found in the spleen, phagocytize infected reticulocytes and secrete TNF and IL-12 [4]. The role of B and T lymphocytes in the human immune response is not fully elucidated, but animal studies suggest that clearance of parasitemia is dependent on an interplay between the clearance of infected cells by an intact spleen as well as innate immune response [5,6].

Recommended treatment of patients with a positive Babesia smear or PCR test consists of atovaquone and azithromycin, with the treatment duration being dependent on the severity of infection and parasitemia [7]. Patients with mild symptoms are typically treated for 7 to 10 days. In immunocompromised
patients, providers should expect to treat *Babesia* infections for a minimum of 6 weeks [8]. Some commonly used alternatives include atovaquone-proguanil, clindamycin, quinine, and artemisinin [7,9].

Cases of prolonged parasitemia, such as in the case presented, have been known to relapse, sometimes even 2 years later [3]. Therefore, we suggest that providers consider follow-up examination after the apparent clearance of babesiosis. It is also important to note that co-infection with Lyme disease, transmitted by a common vector, can complicate therapy. Animal models have shown that infection with *B. microti* can cause functional immunosuppression and worsen *B. burgdorferi* co-infection [10]. Timely and appropriate pharmacotherapy for both pathogens is essential in co-infected individuals, especially in immunocompromised patients. We suggest prompt consultation with infectious diseases specialists in these cases.

### References:

1. Rosner F, Zarrabi MH, Benach JL, Habicht G. Babesiosis in splenectomized adults. Review of 22 reported cases. Am J Med. 1984;76(4):696-701
2. Vannier E, Gewurz BE, Krause PJ. Human babesiosis. Infect Dis Clin North Am. 2008;22(3):469-88, vili-ix
3. Bloch EM, Kumar S, Krause PJ. Persistence of Babesia microti infection in humans. Pathogens. 2019; 8(3):102
4. Terkawi MA, Cao S, Herbas MS, et al. Macrophages are the determinant of resistance to and outcome of nonlethal Babesia microti infection in mice. Infect Immun. 2015;83(1):8-16
5. Djokic V, Akoolo L, Parveen N. Babesia microti infection changes host spleen architecture and is cleared by a Th1 immune response. Front Microbiol. 2018;9:85
6. Jeong YI, Hong SH, Cho SH, Lee WJ, Lee SE. Induction of IL-10-producing CD1d^high^CD5^+^ regulatory B cells following Babesia microti-infection. PLoS One. 2012;7(10):e46553
7. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: Clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2006;43(9):1089-134
8. Krause PJ, Gewurz BE, Hill D, et al. Persistent and relapsing babesiosis in immunocompromised patients. Clin Infect Dis. 2008;46(3):370-76
9. Sanchez E, Vannier E, Wormser GP, Hu LT. Diagnosis, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: A review. JAMA. 2016;315(16):1767-77
10. Djokic V, Akoolo L, Primus S, et al. Protozoan parasite Babesia microti subverts adaptive immunity and enhances Lyme disease severity. Front Microbiol. 2019;10:1596

### Conclusions

In complicated cases of babesiosis with prolonged parasitosis, first-line therapy atovaquone and azithromycin should be sufficient if maintained for an adequate duration. In cases in which the parasitemia is slow to resolve, such as in our asplenic patient, a clinician may be tempted to alter treatment due to concern for treatment failure; however, first-line therapy is still recommended. Additionally, providers should have a low threshold for *Babesia* testing in patients with suspected or known *Ixodes* tick-borne infection, especially when treating immunocompromised or immunosuppressed patients.

### Declaration of Figures’ Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.