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Case report

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Severe babesiosis and *Borrelia burgdorferi* co-infection

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Case report

A 73-year-old man from upstate New York visited his primary care physician with a bull's eye rash in his right arm and fatigue. He traveled to the state of Massachusetts in the week before the lesion's appearance, where he spent most of his time outdoors and had a tick bite in that same arm. He was initially diagnosed with Lyme disease and was given a prescription for amoxicillin. The fatigue persisted, and 3 weeks later, he presented to our hospital with intermittent fever (38.8°C), chills and night sweats. His medical history was remarkable for coronary heart disease and coronary artery bypass graft surgery.

On physical examination, the patient was febrile and tachycardic with a normal respiratory rate. The rest of the examination was otherwise unremarkable. No distinctive rashes, jaundice, lymphadenopathy, swollen joints or hepatosplenomegaly were appreciated. Initial laboratory studies revealed thrombocytopenia (60×10^9/l) with normal white and red blood cell counts; they also showed undetectably low levels of haptoglobin, unconjugated hyperbilirubinemia, increased fraction of reticulocytes (6.1%) and elevated lactate dehydrogenase levels (726 U/l), all consistent with early hemolysis. A radiography of the chest yielded normal findings. Lyme disease was confirmed by elevated indirect immunofluorescent antibodies, immunoglobulin (Ig)M and IgG fractions, against *Borrelia burgdorferi*. A peripheral blood smear was examined under light microscopy and showed numerous intraerythrocytic trophozoites consistent with *Babesia* spp. (Figure 1).

The patient had an initial estimated parasitemia of 11% and was admitted to the intensive care unit to receive further medical care. In view of the severe parasitic load, treatment with intravenous clindamycin and oral quinine was initiated, followed by a 2% decrease of the parasitemia in 1 day. However, the patient developed acute respiratory distress syndrome (ARDS) in a matter of 48 h and required intubation. Electrocardiogram (ECG) did not show any acute changes, and echocardiography showed a normal ejection fraction without new akinetic areas. A third infection with *Ehrlichia chaffeensis* causing superimposed human monocytotropic ehrlichiosis was ruled out by negative serology. Paralytic ileus and intestinal malabsorption were suspected at this point, and quinidine was substituted for quinine. After 3 days, the parasitemia reached a level of 3%, and the patient required multiple blood transfusions; he also had new severe hypotension demanding four intravenous pressors at maximum doses. Anuria and renal failure were present as well. After 8 days, the patient was requiring high-frequency oscillatory ventilation in the

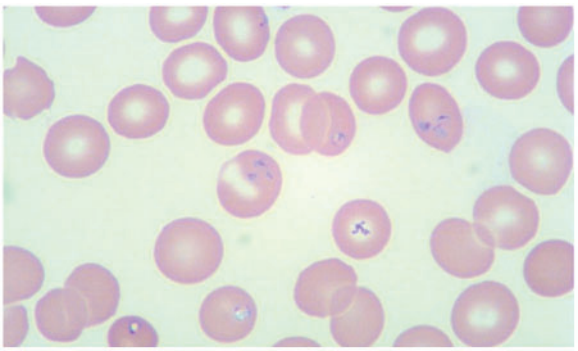

Figure 1. Thin blood smear stained with Wright's stain showing multiple intraerythrocytic trophozoites, consistent with *Babesia* spp.

setting of multiple organ failure. The measured parasitemia during the last 4 days was consistently ~2%. Ultimately, the patient's family decided to withhold life-sustaining measures, and the patient died.

Discussion

The clinical features along with the serologic and smear findings confirmed a co-infection with *B. burgdorferi* and *Babesia* spp. in our patient, causing Lyme disease and babesiosis, respectively. Human babesiosis is most commonly caused by *Babesia microti,* and it is endemic to some areas of the Northeast and northern Midwest USA, with cases reported in the states of Connecticut, Massachusetts, New Jersey, New York, Rhode Island, Minnesota and Wisconsin.[1,2] *B. microti* is a very uncommon but rising cause of human disease in Europe, where *Babesia divergens* is the agent causing the few cases of babesiosis reported. However, autochthonous presence of *B. microti* infecting the *Ixodes ricinus* ticks in Switzerland has been proven to exist, with 1.5% of the local population having positive serology for the parasite.[3] Other cases have been reported in Japan and Taiwan as well. Lyme disease caused by *B. burgdorferi* is a much more established disease in the rest of the world, however, less extensively than other *Borrelia* genospecies.

In the USA, both diseases have an overlapping geographic distribution[1,2,4] that can be explained by the fact that they share the *Ixodes scapularis* tick as their common vector.[5] Subclinical co-infections are frequent, and, in Massachusetts in particular, 66% of patients with documented Lyme disease had positive antibodies against *B. microti*.[5,6]

Co-infections of *B. microti* and *B. burgdorferi* seem to be associated with a longer duration of disease and persistent symptoms. Approximately half of these patients are symptomatic for 3 months or longer against 4% of patients with Lyme disease alone.[7] They are also twice as likely to experience fever, chills, headache, diaphoresis, nausea and fatigue.[8] Of note, fatigue seems to be the most common persistent symptom reported for co-infection, and our case is a clear example of this fact.[7] Any patient with Lyme disease who remains symptomatic despite adequate antibiotic treatment should be tested early for the presence of other microorganisms causing concurrent disease.

It is unclear whether co-infection is associated with worse clinical outcomes. The small sample size of the studies limits their power to detect differences, and most *Babesia* spp. infections are subclinical, confounding the results. Currently, neither an increased mortality nor an elevated rate of long-term complications has been proven to occur in co-infected individuals.[8]

Predictive factors for severe babesiosis include immunosuppression, age > 50 years, parasitemia > 4%, male gender, splenectomy, leukocytosis and alkaline phosphatase > 125 U/l.[9,10] The recommended treatment consists of oral quinine and intravenous clindamycin; if absorption of oral medications is a concern, intravenous quinidine is an alternative to quinine (with ECG monitoring for QTc prolongation).[11] The degree of hemolysis and parasitemia should be monitored everyday, and the goal is to decrease the parasitic load to <5%. Exchange transfusion is an adjuvant intervention for patients with severe presentations, and the frequency of treatments is dictated by the same parasitemic target.[11]

There are no current recommendations for antibiotic prophylaxis of babesiosis in patients with Lyme disease. The patients should be monitored closely for persistence of symptoms and development of hemolysis and thrombocytopenia. This is important as neither amoxicillin nor doxycycline has coverage against *Babesia* spp; of note, doxycycline is the preferred drug in areas where ticks have a high rate of *Anaplasma phagocytophilum* carriage.[5,11] Any suspicion of concurrent babesiosis should prompt testing, as early detection followed by administration of antibiotics decreases the parasitemia and the severity of the disease.[11] Finally, our case demonstrates the importance of knowing the types of microorganisms that ticks carry based on their geographic distribution; the clinician should be vigilant and prepared to treat multiple and potentially severe infections that can present with subtle initial findings.

Conflict of interest: None declared.

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