

Babesiosis and Lyme Disease in a 68-year-old man

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Case Reports from the Alpert Medical School of Brown University Residency in Emergency Medicine

HARRY VANDUSEN: A 68-year-old man presented to the emergency department from his physician's office with a chief complaint of fatigue, shortness of breath and night sweats. A chest X-ray at the physician's office was normal.

The patient's symptoms started approximately one month earlier and his doctor had diagnosed him with the flu. He initially felt better after a course of oseltamivir but his symptoms returned approximately 4 days prior to coming to the ED. The patient described profound fatigue and shortness of breath with minimal activity in addition to night sweats, chills and nausea. He denied any recent rashes, insect bites, abdominal pain, cough or weight loss. He traveled to Florida approximately 1 month prior, but had not been outside of the U.S. He had no history of smoking but admitted to social alcohol use. The patient lives with a dog and cat, both of which had been fully vaccinated. He had a history of Lyme disease in the early '90s that presented with severe joint pain. Medical history also included osteoarthritis and benign prostatic hypertrophy.

On exam, he had normal vital signs and appeared non-toxic. He had no scleral icterus and his cardiopulmonary and neurological exams were normal. He had mild, left, upper-quadrant (LUQ) tenderness. He had no calf swelling or tenderness, and there were no rashes or insect bites.

DR. ANDREW NATHANSON: The patient appears well but reported new onset fatigue and shortness of breath, as well as night sweats. What were your concerns?

DR. NICHOLAS MUSISCA: The differential diagnosis of fatigue and shortness of breath is large. In the emergency department vague symptoms and a non-focal physical exam are a frequent and difficult presentation requiring a heuristic approach. Our initial strategy was to rapidly rule out immediate life-threatening problems and then gather additional data. Given the patient's age and the frequency of acute coronary syndrome presentations to the ED, a cardiovascular cause was briefly considered, as 'atypical' symptoms such as fatigue, malaise, and dyspnea are common findings in older patients.¹ While the ECG is not a particularly sensitive test for coronary artery disease and acute coronary syndrome

(ACS), it is portable, inexpensive, non-invasive, and can provide significant information quickly. Our patient's ECG was normal.

DR. MARK GREVE: The patient had night sweats. Did you pursue an infectious or hematologic/oncologic cause of the patient's illness?

DR. ALYSSA MIERJESKI: The difficulty in interpreting night sweats is the lack of a standardized definition published on the topic.² However, causes of night sweats are well documented and include autoimmune disorders such as rheumatoid arthritis and giant cell arteritis, as well as cardiovascular, endocrine, neoplastic and infectious causes. Additionally, numerous medications, including selective serotonin reuptake inhibitors (SSRIs) have been associated with night sweats.² As we had no obvious cause of the patient's complaints from his history or physical exam, we obtained a series of labs tests, including a CBC, chem 20, troponin, and a D-dimer.

DR. DAVID LINDQUIST: What were your lab results?

DR. MIERJESKI: The patient had a number of laboratory abnormalities. The WBC count was 2.9×10^9 with 34% segmented neutrophils and 11% bands. The hemoglobin and hematocrit were 10.7 g/dl and 32.4%, respectively, and the platelets were 77,000. The patient had a mild transaminitis (AST 62 IU/L, ALT 59 IU/L), his alkaline phosphatase was mildly elevated at 138 IU/L, and his D-dimer was 2,374 ng/ml (normal < 250). A urinalysis and a troponin were both negative.

DR. ELIZABETH NESTOR: The patient had a number of lab abnormalities, of which the elevation in the D-dimer is particularly striking. Did you pursue the cause of the elevated D-dimer? Furthermore, he was pancytopenic and had a significant percentage of bands.

DR. MUSISCA: The D-dimer is a fibrin degradation product and is generated from cross-linked fibrin. An elevated plasma concentration of D-dimer indicates recent or ongoing intravascular blood coagulation, and consequently it is a nonspecific finding. Taken in conjunction with the patient's

dyspnea, however, we felt it was prudent to obtain a pulmonary embolism (PE) protocol CT scan. The scan was negative for a PE but did demonstrate a prominent liver and spleen.

In regards to the bands, the patient did not meet systemic inflammatory response syndrome (SIRS) criteria, although his pancytopenia was suggestive of a broad hematologic dysfunction.

DR. MATTHEW KOPP: To summarize, the patient appears nontoxic, has pancytopenia with a predominance of bands, a mild elevation in transaminases, and appears to have a large liver and spleen partially visualized on a PE CT. What were your concerns at this point?

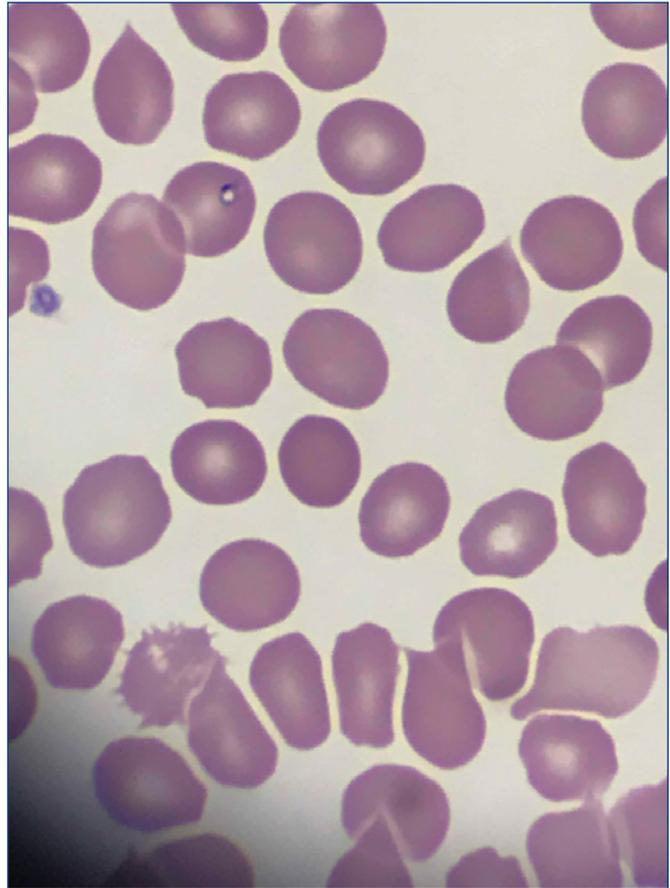
DR. MIERJESKI: The patient's symptoms appeared to develop rapidly and while a neoplastic process such as lymphoma was within the differential, we were concerned about an infectious disease. The patient did not have an upper respiratory infection, and his chest X-ray was normal, making pneumonia unlikely. He did not appear to have a genitourinary infection. Endocarditis was within the differential, although the patient did not have a murmur and did not exhibit any of the Duke criteria for the diagnosis of infective endocarditis.³ Numerous viruses – HIV, CMV, EBV, and others – can cause HSM and pancytopenia. Additionally, and due to the endemicity of tick-borne illness within our region, tick-borne illnesses must be considered.^{4,5} We sent a thin and thick smear for parasites, as well as lyme, ehrlichia, and anaplasma titers. The smear was positive for intraerythrocytic parasites, consistent with babesiosis (See **Figure 1**). He had a parasitemia of 0.26%.

DR. ELIZABETH SUTTON: How common is babesiosis? Is it likely that the patient's initial symptoms over one month ago were consistent with babesiosis?

DR. MUSISCA: Babesiosis is a zoonotic red blood cell parasitic infection transmitted by the tick, *Ixodes scapularis*. It was first identified by Victor Babes in 1888, but was not recognized in humans until 1957, and not noted in an immunocompetent individual until 1969.⁶ During the present century, the prevalence of tick-borne illnesses has escalated, and babesiosis has become an increasingly recognized disease in the northeast and upper Midwest states, and also has a worldwide distribution.^{5,7} While there are over 100 species of babesia, most infections in the US are due to *B. microti*.

Clinical manifestations of babesiosis can range from a subclinical disease to severe and fulminant illness. While most patients are symptomatic within 1–6 weeks of a nymph tick feeding, parasitemia can exist silently for months to years.^{8,9} More commonly patients report symptoms similar to our patient – gradual, nonspecific flu-like complaints including chills, sweats, headaches, nausea, myalgias, anorexia, and occasionally a non-productive cough about 1–6 weeks after

Figure 1. Trophozoites noted on giemsa stain smear. This patient had a low (0.26%) parasitemia.



a nymph tick feeding.¹⁰ Transmission from a tick is usually in the spring or summer months when the nymphs quest for a blood meal. Many patients do not recall a tick bite. Additional avenues of infection include blood transfusion, and rarely transplacental transmission from a mother to the neonate.¹¹ Laboratory abnormalities can reveal pancytopenia, elevated transaminases, and an increased total bilirubin due to hemolysis.⁹

DR. JESSIE WERNER: How is the diagnosis made?

DR. WILLIAM BINDER: Diagnosis of an acute infection is made through detection of *Babesia* parasites on Giemsa or Wright stained thin and thick blood smears. The trophozoites can appear as pleomorphic ring forms, and rarely tetrads of merozoites can arrange to form a Maltese cross pattern. PCR can be used to detect low-grade *Babesia microti* infection and is more sensitive than light microscopy. Serology can also be utilized to detect antibodies and confirm the diagnosis.⁴ A travel history is important in patients with findings of intraerythrocytic parasites as the ring forms can resemble those of *Plasmodium falciparum*. As autochthonous malaria

is rare in the U.S., and has not been detected in New England in over 70 years, we felt confident that the trophozoites were consistent with Babesia.¹²

DR. VICTORIA LEYTIN: How was the patient treated?

DR. MIERJESKI: Our patient was symptomatic but not unstable, and fell into the category of mild to moderate disease. Mild to moderate disease is treated with atovaquone and azithromycin for 7 to 10 days. Alternatively, patients can be treated with intravenous clindamycin and quinine for 7 to 10 days, although this regimen tends to have more adverse side effects.

Immunocompromised individuals – patients with HIV, on immunomodulators, a history of hematologic malignancies, and those with splenectomies – are at higher risk in developing severe and fulminant disease. While the treatment regimen for severe disease is also clindamycin and quinine, the treatment duration is often increased to 6 weeks due to increased chance of persistent disease. There are also several alternative regimens including atovaquone-proguanil; atovaquone, clindamycin and doxycycline; and atovaquone, azithromycin and doxycycline. In patients with severe disease who have greater than 10% parasitemia, exchange transfusion is an important therapeutic adjunct.¹¹

DR. ANGELA JARMAN: What was the patient's outcome?

DR. MIERJESKI: Although this patient had several laboratory abnormalities, overall he appeared very well with no overt contraindications to outpatient treatment. Antibiotics were initiated in the emergency department, and he was eventually discharged home on oral antibiotics with outpatient follow-up scheduled in 48 hours. The following day, the patient's Lyme titer also came back positive, and doxycycline was added to his treatment regimen. The patient has done well and after several months was back to his baseline.

DR. OTIS WARREN: How frequently do multiple organisms occur in an *Ixodes scapularis* tick?

DR. MUSISCA: Concentrated cases of babesiosis are seen in Lyme-endemic parts of the country. While Lyme disease is much more commonly seen as an isolated infection, dual infection is not uncommon. The organisms responsible for either Lyme disease, babesiosis, or human anaplasma may occur in over 20% of *Ixodes scapularis* ticks, although it is rare to find all 3 of these organisms present together.^{10,13}

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