Coinfection With *Babesia microti* and *Borrelia burgdorferi* in a Western Wisconsin Resident

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A 68-year-old woman, who had not traveled outside of western Wisconsin, was hospitalized after 4 weeks of chills, fevers, myalgias, neuralgias in her right arm, and pain in the right upper quadrant of her abdomen. Physical examination revealed hepatosplenomegaly, and laboratory studies showed anemia, thrombocytopenia, increased aspartate transaminase level, and microscopic hematuria. Wright's stain of a blood smear revealed intraerythrocytic organisms consistent with *Babesia* species. A polymerase chain reaction of whole blood specimens along with an increased serologic titer confirmed the diagnosis of *Babesia microti*. Indirect immunofluorescent antibody serology and Western blot analysis revealed a simultaneous infection with *Borrelia burgdorferi*. Coinfection with *B. microti* and *B. burgdorferi* may occur in endemic areas where both organisms are carried by the same tick vector, *Ixodes scapularis*. The intensity and duration of illness seem to be greatest in patients with concurrent infection.

Less than 30 years ago, Lyme disease, now known to be caused by the spirochete *Borrelia burgdorferi*, was found to be endemic in the northeastern seaboard states, northwestern Wisconsin, and contiguous northeastern Minnesota. The reservoir host for Lyme disease is primarily the deer mouse, and its vector is the tick *Ixodes scapularis* (formerly *I. dammini*). The immature ticks, both larval and nymph stages, feed on deer mice (*Peromyscus* species), whereas the adult ticks primarily feed on deer (*Odocoileus virginianus*). *B. burgdorferi* is maintained in nature by horizontal transmission from infected nymphal *I. scapularis* to deer mice to larval *I. scapularis*, which mature and become nymphs infected with the spirochete. Probably because of the increasing abundance of deer, the endemic areas of Lyme disease seem to be spreading. In addition, increasing human habitation in rural wooded areas is producing more deer tick-human contact. As a result, Lyme disease has become the most frequently identified arthropod-borne disease in the United States.

*I. scapularis* is also the vector for two other potentially serious but rarely fatal diseases. These are babesiosis, caused by the piroplasmid protozoan *Babesia microti*, and the recently described human granulocytic ehrlichiosis (HGE), caused by granulocytic *Ehrlichia* species that are closely related to or identical with *Ehrlichia phagocytophila* or its relative *E. equi*. Therefore, mixed infections with two, and maybe three, of these agents are possible and may cause a confusing clinical picture.

**REPORT OF CASE**

A 68-year-old woman from western Wisconsin noted an unidentified arthropod bite on her right thigh in August 1996. One week later, fevers (temperature between 39 and 40°C) and malaise developed. During the first week of illness, the patient had muscle spasms of her legs, which resolved spontaneously. After 2 weeks of fever, she had development of right anterior chest and upper abdominal pain associated with a poor appetite and abdominal bloating, as well as concurrent persistent numbness down the inner aspect of her right arm.

The patient was assessed as an outpatient, and no localizing abnormalities were found on examination. Laboratory tests yielded a normal aspartate transaminase level, and a complete blood cell count revealed only mild thrombocytopenia, platelet count of 144 X 10^9/L (normal, 150 to 400).

Four days later, the patient was hospitalized because of a temperature of 38.7°C, pulse rate of 110 beats/min, blood pressure of 127/48 mm Hg, and respiratory rate of 24/min. A few petechiae were noted on the extensor aspect of her
lower extremities, and a moist erythematous lesion (0.5 by 0.5 cm) was evident at the site of the arthropod bite. On palpation, pronounced tenderness over the right anterior lower chest wall was present along with modest hepatosplenomegaly. Laboratory studies yielded an aspartate transaminase level of 95 IU/L (normal, 0 to 36), lactate dehydrogenase of 296 IU/L (normal, 0 to 237), total bilirubin of 1.2 mg/dL (normal, 0.1 to 1.0), normal leukocyte count, hemoglobin of 12 g/dL, and a low platelet count of 53 x 10^9/L; urinalysis revealed 10 erythrocytes per high-power field. A Wright’s stain of her blood disclosed normal leukocyte morphology, including the absence of morula, but intraerythrocytic parasites consistent with Babesia were identified (Fig. 1). Polymerase chain reaction (PCR) and a serologic titer of 1:1,046 for B. microti were confirmatory. In addition, Lyme disease was diagnosed on the basis of the clinical findings, indirect immunofluorescent antibody (IFA) testing with an IgM titer of 1:512, and an increasing IgG titer (1:128 to 1:512 over a 1-week period). Western blot analysis confirmed the IgG and IgM seropositivity for Babesia burgdorferi. PCR of serum was negative for Borrelia DNA. Serology for Leptospira and HGE was negative, as was the PCR for HGE.

On the basis of the clinical picture and laboratory evaluation, coinfection with B. burgdorferi and B. microti was suspected. The patient was treated with clindamycin, 600 mg orally every 8 hours, and quinine sulfate, 650 mg orally every 8 hours, for 14 days and doxycycline, 100 mg orally every 12 hours, for 2 weeks. On the second day of hospitalization, her platelet count decreased to 36 x 10^9/L, and on the third day, her hemoglobin concentration decreased to 8.4 g/dL because of hemolysis; both subsequently normalized. Three weeks after treatment, the patient was experiencing mild fatigue, but her level of function was almost normal. The arm numbness had resolved.

**DISCUSSION**

*I. scapularis* is the vector for *B. microti* and *B. burgdorferi.* The former is caused by a piroplasmid protozoan morphologically similar to but not closely related to malaria. Investigators believe that the *I. scapularis* nymph form is the likely vector of *B. microti* to humans, usually between May and August. Asexual reproduction occurs within the erythrocytes of the host, and two to four daughter cells are formed. After rupture of the infected erythrocytes, other erythrocytes are infected, and the cycle is repeated.

In the United States, the incidence of babesiosis is highest during the summer months and is most common along the coastal areas and islands of Massachusetts, Connecticut, Rhode Island, and New York. The infection, however, has been reported in Wisconsin, Minnesota, California, Maryland, Virginia, and Georgia. Babesiosis has been reported in Europe, although rarely. Seroprevalence in humans has been reported to be as high as 9% in some endemic areas of the United States. The incubation period is 1 to 4 weeks. In the United States, babesiosis is caused most often by *B. microti* and less often by *B. divergens* and a third species, currently termed “WA1,” which has been described in the western United States. Babesiosis usually results in a subclinical or mild illness; however, the infection occasionally causes a severe illness in immunocompetent patients. The highest incidence of babesiosis occurs in adults older than 70 years of age, but clinically apparent disease is also common in patients 40 to 70 years of age. Frequent clinical findings include irregular fevers and chills, muscle pain, and fatigue. Less commonly, mild hepatosplenomegaly, hemolytic anemia, thrombocytopenia, proteinuria, and increased liver enzymes may be noted. Infection in patients who have undergone splenectomy causes a more severe and sometimes fatal illness. Rarer infection with *B. divergens* causes a more severe illness with jaundice, hemoglobinemia, and renal failure.

Diagnosis is usually made by Giemsa or Wright’s stain of thick and thin blood film smears in which intraerythrocytic parasites are sought. Parasitemia may exceed 10% of the erythrocytes. Differentiation of Babesia from Plasmodium-infected erythrocytes is made by observing the larger size of ring forms and absence of pigment, schizonts, or gametocytes of Babesia. IFA tests are useful but do not replace blood smears. The sensitivities and specificities of the antibody tests are 88 to 96% and 90 to 100%, respectively. The titers increase 2 to 4 weeks after the infection and wane over 6 to 12 months. A PCR test...
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<th>Common clinical findings</th>
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<th>Babesia microti</th>
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*Parentheses indicate possible association.*

Table 1.—A Guide to Identifying Infections and Coinfections for Which *Ixodes scapularis* Is the Vector*

that uses amplification of a portion of the 16S-like gene is currently available and is thought to provide an adjunct to the conventional methods. In fact, this test is more sensitive than blood smear evaluation or hamster inoculation and thus is useful when the blood smear is negative.

The diagnosis of Lyme disease depends on an appropriate exposure and clinical picture in conjunction with the detection of specific antibodies against *B. burgdorferi*. These antibodies are usually detectable by enzyme-linked immunosorbent assay or IFA. IgM is found 2 to 4 weeks after the onset of the erythema chronicum migrans, peaks at 6 to 8 weeks, and declines to undetectable levels over 4 to 6 months. IgG is increased at 6 to 8 weeks after the onset of the illness and peaks at 4 to 6 months. If the enzyme-linked immunosorbent assay or IFA results are equivocal or concerns exist about the presence of many other possible infections that can give cross-reacting antibodies, Western blot testing should be used to confirm the presence of IgM or IgG antibodies (or both) directed against *B. burgdorferi* antigens.

PCR with use of DNA sequences encoding the flagellin, OspA, or unassigned portions of the spirochetal chromosome has been successful for diagnosing Lyme disease in the evaluation of cutaneous, cerebrospinal fluid, urine, and synovial fluid specimens. This test is less sensitive for blood and serum samples (as in our patient). Mixed infections with *B. microti* and *B. burgdorferi* are well documented. About 10% of patients with Lyme disease from Connecticut and Rhode Island, areas where both diseases are zoonotic, are coinfected with babesiosis. Moreover, one study found that as many as 66% of randomly selected patients with Lyme disease from Long Island had antibabesial antibody. Immunoassays of residents of Wisconsin and Minnesota has also detailed the occurrence of coinfections in the geographic region of our patient’s residence. Of 96 patients with Lyme disease, 9.4% were seropositive for *B. microti* or the agent of HGE (or both). Of note, symptoms and duration of illness in patients with concurrent infections can be greater than in those with either infection alone. The clinical features and protracted course of our patient clearly exemplify this point. Specifically, the finding of *Babesia* on the peripheral smear in conjunction with the numbness in her arm suggested coinfection with Lyme disease. Such coinfections can produce various overlapping clinical findings, as summarized in Table 1. Recommended treatment for mild to moderate disease caused by *B. microti* is clindamycin, 300 to 600 mg orally every 8 hours (20 mg/kg per day in three divided doses in the pediatric population), and quinine, 650 mg orally every 6 hours (25 mg/kg per day in four divided doses in the pediatric population). More severe infections can be treated with intravenous administration of clindamycin and quinidine (with appropriate electrocardiographic monitoring). Exchange transfusions are also indicated in severely ill patients with hemolysis.

Because of the human-induced changes in the ecosystem, a 50-year progressive reforestation has occurred in a substantial part of Wisconsin and Minnesota. With this change, the white-tailed deer population has dramatically increased, an outcome accompanied by dissemination of the *I. scapularis* ticks. Simultaneous HGE and Lyme disease have recently been described in New York, and clinicians should remember that, by treating acute Lyme disease with doxycycline, the HGE will also be treated effectively. Physicians may observe an increasing incidence of *Ixodes*-borne diseases in their patients, occasionally occurring as coinfections with overlapping clinical findings (Table 1).

REFERENCES


