# Two tick-borne diseases in one: a case report of concurrent babesiosis and Lyme disease in Ontario

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**Case**

A 59-year-old man presented to The Toronto Hospital on July 27, 1997, because of fever. His travel history included a trip to Nantucket, Mass., 6 weeks before presentation and to Southeast Asia 7 months earlier. There was no history of rural travel on either trip. The past medical history was noncontributory. The patient had not undergone splenectomy, nor had he ever received a blood transfusion.

The patient had been well until June 21, 1997, when he noticed a small "pinhead" lesion on his left biceps, which he removed. He subsequently experienced fever and spreading erythema (to 5 cm in diameter) surrounding the site of the lesion; the erythema subsequently resolved. He was then well until July 21, when the fever returned, along with rigors, extreme fatigue, headache, myalgia, vomiting and drenching night sweats. On July 22 he saw his family physician, who diagnosed a viral infection. On presentation to the hospital 5 days later, the patient was febrile (temperature 38.8°C) and pale and appeared unwell. He had tachycardia (130 beats/minute), splenomegaly and scattered petechiae. Laboratory investigations revealed anemia, marked thrombocytopenia and a bleeding diathesis (Table 1).

His fever and travel to Southeast Asia suggested malaria; smears were ordered, and the results were initially interpreted as positive for *Plasmodium falciparum* (4% parasitemia). However, a senior technologist reviewed the smears a few hours later and correctly identified the organisms as trophozoites of *Babesia*.

Given the severity of his illness and the preceding rash consistent with erythema migrans, there were concerns about coinfection with additional tick-borne agents. Serologic testing for Lyme disease was performed, and the results of both enzyme-linked immunosorbent assay and Western blotting for IgM were positive, which indicated recent infection. Serologic testing for human monocytic ehrlichiosis (*Ehrlichia chaffeensis*) by immunofluoresence assay, performed at the Ontario Provincial Laboratory, was negative at 1:64 dilution. Polymerase chain reaction assays for human granulocytic and monocytic ehrlichiosis were performed in the laboratory of one of the authors (K.C.K.); the results were negative.[1]

The patient was treated with quinine (600 mg three times daily) and clindamycin (600 mg three times daily) for 7 days for the babesiosis and doxycycline (100 mg twice a day) for 21 days for the Lyme disease. The response was prompt, and smear testing yielded negative results by day 4. When seen at follow-up the patient was asymptomatic, and all laboratory measurements had returned to normal.

## Comments

Babesiosis (caused by *Babesia microti*) and Lyme disease (caused by *Borrelia burgdorferi*) are emerging diseases in the northeastern United States. Their frequency is increasing as the deer tick (*Ixodes scapularis*), which transmits both organisms, increases in distribution.[2,3] Because *B. microti* and *B. burgdorferi* have the same rodent reservoir and are transmitted by the same vector, human coinfection may be more common than appreciated. In support of this hypothesis, up to 66% of residents of Long Island, NY, who have Lyme disease also have antibodies to *Babesia* sp.[4] Although coinfections have been infrequently described, recent reports indicate that the severity and duration of illness are greater in coinfected patients.[5-8]

*I. scapularis* ticks have been found in several Canadian provinces, and 205 cases of Lyme disease were reported in this country between 1984 and 1994.[9,10] However, no case of babesiosis has ever been reported in Canada, and there have been no

previous reports of coinfection. We have described a Canadian with a severe illness caused by concurrent babesiosis and Lyme disease.[11]

*Babesia* spp. are intracellular parasites that may be confused with malaria-causing organisms both clinically and morphologically.[12–14] The features of *Babesia* that permit its discrimination from *Plasmodium falciparum* include the presence of paired piriform stages and a tetrad configuration (the "Maltese cross") formed by binary fission of the trophozoite.

The nymph stages of *I. scapularis* are small (less than 3 mm) and are primarily responsible for transmission of both babesiosis and Lyme disease.[15] It is possible that the lesion removed by our patient was a nymphal-stage tick. Nymphs typically feed in May and June, which results in a peak of clinical illness in July. As in this case, the symptoms of babesiosis usually begin 1 to 4 weeks later.[15] The clinical spectrum ranges from mild to life-threatening infection, the latter characterized by severe hemolytic anemia, thrombocytopenia and renal failure.[15] Mortality rates are higher in elderly people, those who have undergone splenectomy and those with HIV infection.[15,16]

Coinfection with other tick-borne agents is an important determinant of outcome. The illness associated with concurrent babesiosis and Lyme disease is more severe than either infection alone.[5–8] Krause and colleagues[8] reported that 11% of patients with Lyme disease were coinfected with *B. microti*.[8] Overall, patients with coinfections reported a greater number, severity and duration of symptoms. Coinfected patients had significantly more fatigue, headache, sweats, chills, nausea, conjunctivitis and splenomegaly than those with Lyme disease alone. Furthermore, 50% of these patients were ill for 3 months or more, whereas only 7% of those with Lyme disease alone were ill for that period.

The mechanism by which human babesiosis and Lyme disease each potentiate the severity of the other remains unknown. Animal experiments indicate that *Babesia* infections may impair host defence mechanisms.[8,17] These immunosuppressive effects may explain why it is possible to detect DNA from *Borrelia* spirochetes in people with coinfections more frequently and for longer periods than in patients with Lyme disease alone.[18] *Babesia* infections enhance the manifestations of Lyme disease in mice, which suggests that coinfection might also potentiate the pathogenicity of *B. burgdorferi* infections in humans.[17] Finally, a synergistic inflammatory reaction has also been suggested as a putative cause for the increased severity of disease in patients with coinfections.[8]

**Table 1: Laboratory measurements for a 59-year-old man with fever and drenching night sweats**

| Test | Result | Normal range |
|---|---|---|
| Hemoglobin, g/dL | 10.6 | 13.5–17.5 |
| Leukocytes, x $10^9$/L | 4.2 | 4.5–11.0 |
| Platelets, x $10^9$/L | 14 | 150–400 |
| Lactate dehydrogenase, U/L | 799 | 45–90 |
| Bilirubin, μmol/L | 26 | 2–17 |
| Aspartate aminotransferase, U/L | 151 | 8–20 |
| Haptoglobin, g/dL | < 0.012 | 0.06–0.29 |
| D-dimers, ng/mL | < 250 | 500–1000 |
| Fibrinogen, μmol/L* | 12.4 | 4.4–10.3 |
| FDP, μg/mL | > 10 | < 2.5 |
| International normalized ratio | 4.89 | 1 |

Note: FDP = fibrinogen degradation product.
*The SI unit for fibrinogen is micromoles per litre, where 1 g/dL = 29.41 μmol/L.

Recently, evidence of coinfection with a third tick-transmitted zoonotic parasite, *Ehrlichia*, has been reported.[14,19,20] These studies indicate that tick-borne diseases are widespread and prevalent in some regions of the United States. Canadians will be at risk when they visit these areas during tick season (generally from May to September). *I. scapularis* and *I. pacificus* ticks have been identified in about 250 locations in Canada, although established populations are focal and are at present limited to Ontario and British Columbia.[9,10] Prolonged parasitemia accompanying coinfection involving babesiosis may facilitate transmission of the organism to ticks in areas of Canada where established *Ixodes* populations exist, such as Long Point peninsula in Point Pelee National Park.[8–10] Finally, blood products are not screened for *Babesia* spp. or *B. burgdorferi*, both of which can be transmitted by blood transfusion.[21,22]

In summary, given the current levels of travel between Canada and the US and the emergence of Lyme disease, babesiosis and ehrlichiosis, we must anticipate an increase in the number of imported cases of these pathogens in Canadians. Patients with a tick-transmitted infection should be assessed for coinfection with other known agents, particularly if the symptoms are severe or persist after therapy.

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