

Transfusion-transmitted babesiosis in Ontario: first reported case in Canada

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Abstract

BABESIOSIS HAS ONLY RECENTLY BEEN REPORTED in Canada, but a number of transfusion-transmitted cases of this infection have been reported from the United States. We present a case of transfusion-transmitted babesiosis that occurred in Canada. Canadian physicians must consider babesiosis in the differential diagnosis of patients who experience fever or a hemolytic reaction after blood transfusion. Prompt recognition and treatment are important, because *Babesia* infections can be severe or fatal in certain risk groups. Better strategies to prevent transfusion-transmitted babesiosis are required.

Case report

A 53-year-old immunocompetent, spleen-intact woman presented on Oct. 23, 1998, with a history of dyspepsia and melena stools. Her hemoglobin level was 69 (normally 120–140) g/L, and on Nov. 6, 1998, she received a transfusion of 3 units of packed erythrocytes. After the transfusion, her hemoglobin level rose to 106 g/L. Endoscopy of the upper gastrointestinal tract was performed at that time, and the results were normal. She was readmitted on Feb. 25, 1999, for colonoscopy. At that time, her hemoglobin level was 70 g/L, and she received 2 more units of packed erythrocytes. Her post-transfusion hemoglobin level was 104 g/L. The results of colonoscopy were normal, but a small-bowel follow-through examination revealed an annular tumor of the small intestine, which was laparoscopically resected on Mar. 9, 1999.

The patient was readmitted on Apr. 11, 1999, after 7 days of high fever, chills, diaphoresis, nausea and weakness. Her temperature on admission was 40°C. Laboratory investigations showed that her hemoglobin level was low, at 66 g/L, and that total bilirubin was elevated, at 31 (normally less than 17) $\mu\text{mol/L}$, as was lactate dehydrogenase, at 161 (normally 45–90) U/L, and aspartate aminotransferase, at 63 (normally less than 35) U/L. Examination of peripheral blood smears revealed intraerythrocytic ring forms, which were initially attributed to *Plasmodium falciparum* infection, with a parasitemia of 2.5%. The smears were reviewed at the Centre for Travel and Tropical Medicine, Toronto General Hospital, where at least 400 smear fields (magnification 1000 \times) were examined from Giemsa-stained thick and thin films of whole blood, and babesiosis was diagnosed on the basis of the typical intraerythrocytic forms observed. Polymerase chain reaction (PCR) amplification of whole blood was positive for *Babesia microti*.^{1,2} The patient was treated for 7 days with quinine (600 mg three times daily) and clindamycin (600 mg three times daily). She responded to therapy and was asymptomatic at follow-up 3 months later. Follow-up blood smears were negative for *Babesia*.

In November 1998 the patient had received 3 units of packed erythrocytes from 3 donors. The first donor was a 46-year-old man who had donated blood 9 times previously. He had travelled to Pennsylvania in March 1998 and had camped in rural areas in Ontario. He did not remember any tick bites and remained well during follow-up. He returned for follow-up serologic and PCR testing for babesiosis. The serum specimens were tested by indirect immunofluorescent antibody assay for reactivity to *B. microti* (testing performed at the US Centers for Disease Control

Review

Synthèse

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[Return to June 12, 2001 Table of Contents](#)

and Prevention, Atlanta). The results of blood film examination, serologic testing and PCR testing were all negative. The second donor was a 43-year-old woman who had donated blood products 8 times previously. She had not travelled outside Canada in the previous year and had done no camping or rural travel within Canada. She also remained well. The results of blood film examination, serologic testing and PCR testing were also negative (for both of these donors, at least 400 smear fields were examined from Giemsa-stained thick and thin films of whole blood at the Centre for Travel and Tropical Medicine). The third donor was a 22-year-old first-time male donor who had travelled to Taiwan in January 1998 and to an urban area in the United States (Chicago) in August 1998. He had remained well during and after travel. He did not provide a follow-up blood sample.

During the February 1999 admission, the patient had received 2 units of packed erythrocytes from 2 donors. One was a 48-year-old man who had donated blood 9 times previously. He donated blood on Feb. 6, 1999, and a unit of packed erythrocytes from his donation was transfused into the recipient on Feb. 26, 1999. He had travelled recently to South America but had not travelled in the United States in the previous 3 years. He remained well and submitted a follow-up blood sample. The results of blood film examination, serologic testing and PCR testing were negative (for this donor and the next one, at least 400 smear fields were examined from Giemsa-stained thick and thin films of whole blood at the Centre for Travel and Tropical Medicine). The other donor was a 40-year-old man who had donated blood twice previously. He had been camping in rural and forested areas in Cape Cod, Mass., in August 1998. He did not remember receiving any tick bites and denied any febrile illnesses during or after his return from Cape Cod. He donated a unit of blood on Feb. 6, 1999, and a unit of packed erythrocytes from this donation was transfused into the recipient on Feb. 25, 1999. A follow-up blood sample from this donor was positive for *B. microti* by blood smear and by PCR testing. The results of serologic testing for *Babesia* were also positive, at a titre of 1:1024 by immunofluorescent antibody assay (titres generally become positive 1 to 2 weeks after infection). Serum samples were also tested for human monocytic and human granulocytic ehrlichiosis and Lyme disease by the Ontario Ministry of Health laboratory, but the results were negative. The donor remained well and was treated for 7 days with quinine (600 mg three times daily) and clindamycin (600 mg three times daily). Blood smears obtained 1 month after completion of therapy showed no infection.

Comments

Human babesiosis is a tick-borne zoonosis caused by protozoa of the genus *Babesia*. Although the genus comprises more than 100 species, most cases of human babesiosis in North America are caused by *B. microti*,^{1,3-5} usually

transmitted by a bite from the deer or black-legged tick, *Ixodes scapularis*.³⁻⁵ Current areas where the disease is endemic include the northeastern (notably New York State [specifically Long Island], Connecticut, Rhode Island and Massachusetts [specifically Cape Cod, Nantucket and Martha's Vineyard]) and upper midwestern (notably Wisconsin) United States. As was the case for the infected donor described here, people with babesiosis may remain asymptomatic but parasitemic for months to years after tick transmission of the infection.⁶ The clinical manifestations of babesiosis range from no symptoms to severe, occasionally fatal disease characterized by fever, intravascular hemolysis and renal failure. Severe disease is more common in asplenic people, elderly patients and those with underlying immunodeficiency, including AIDS.^{5,7,8} Even with treatment, the case fatality rate in a series of 136 patients in New York State was 5%.⁵

Babesia parasites invade the erythrocytes and remain viable under blood bank conditions, making transfusion-transmitted babesiosis a risk of transfusion with blood components such as platelet concentrates, packed erythrocytes, and frozen, thawed and deglycerolized erythrocytes.⁹⁻¹⁴ At least 21 cases of babesiosis acquired by blood transfusion have been recognized in the United States, which makes babesiosis the most commonly reported transfusion-transmitted tick-borne infection.⁹⁻¹⁴ In a study of transfusion recipients in Connecticut, an area where babesiosis is endemic, Gerber and colleagues¹³ reported a risk of 0.17% per unit of packed erythrocytes. The risk of acquiring babesiosis from a blood transfusion in Canada is unknown, but we suspect that it is very low.

This is the first reported case of transfusion-transmitted babesiosis in Canada.¹⁵ Remarkably, the first recognized case of babesiosis in Canada was reported only 2 years ago, in 1999.¹ The present case highlights the rapidity with which newly recognized infectious agents can threaten blood safety.

In Canada, blood banks do not routinely ask donors about travel to *Babesia*-endemic areas, tick bites or history of babesiosis. Because most immunocompetent people who acquire babesiosis do not remember receiving a tick bite and most have either minimal or no symptoms, few infected donors would be identified by such questioning. Most cases of babesiosis in the northeastern United States are acquired during peak tick activity (June to September).⁴ Consequently the risk of transfusion-transmitted babesiosis might be expected to be greatest during the summer.¹³ However, infected people may remain parasitemic for up to several years and packed erythrocytes are stored for up to 42 days, so even seasonal deferral of potentially high-risk donors could not be expected to prevent this problem.

As in previously reported cases of transfusion-transmitted babesiosis in the United States, the recipient of the infected blood product in this case exhibited moderate to severe manifestations of infection,⁹ beginning within the typical period of symptom onset (usually 4 to 9 weeks after transfu-

sion⁹⁻¹⁴). Both the donor and the recipient were treated with a combination of quinine and clindamycin, and both had a satisfactory response. Recent reports have described a number of patients who have not responded optimally to this traditional therapy. These patients generally responded to the combination of azithromycin and atovaquone.^{16,17}

Given the large numbers of Canadians who visit *Babesia*-endemic regions of the United States each year, we must anticipate an increase in the number of cases of imported babesiosis and the potential for transfusion-transmitted disease in this country. As the geographic distribution of animal reservoirs and tick vectors increases, the incidence of babesiosis and subsequent transfusion-transmitted infections can also be expected to increase.^{3,14,18,19} Furthermore, tick-borne and transfusion-transmitted infections with related parasites, including the piroplasm WA1 and MO1, have recently been reported.^{20,21}

Canadian physicians must consider babesiosis in the differential diagnosis of any patient who experiences fever or a hemolytic reaction soon after blood transfusion. Prompt recognition and accurate diagnosis are important, because even though *Babesia* infections usually respond to therapy, they may be severe or fatal in certain risk groups. Better strategies to prevent transfusion-transmitted babesiosis are required.

Competing interests: None declared.

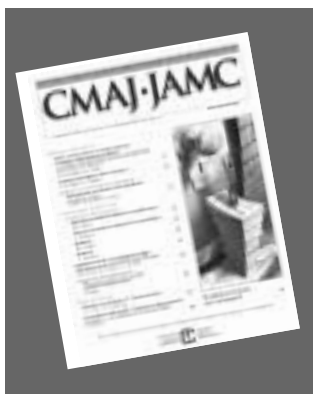
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