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Transfusion-Associated Babesiosis with an Atypical Time Course after Nonmyeloablative Transplantation for Sickle Cell Disease

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Background

Babesiosis is a tick-borne zoonosis that is increasingly recognized as a transfusion-associated infection (1).

Objective

To describe a case of transfusion-associated babesiosis presenting with an atypical time course after nonmyeloablative, peripheral blood stem-cell transplantation.

Case Report

A 21-year-old Puerto Rican woman underwent nonmyeloablative peripheral blood stem-cell transplantation at the National Institutes of Health in October 2005 for hydroxyurea-refractory, severe sickle cell disease. Her peritransplant course was unremarkable, hemoglobin level normalized, and hemoglobin electrophoresis revealed donor type (hemoglobin AS). Her last blood product transfusion was in October 2005. She received long-term *Pneumocystis* prophylaxis with trimethoprim–sulfamethoxazole and underwent periodic therapeutic phlebotomy for iron overload.

In April 2006, she returned for evaluation of daily fever to 39 °C for 1 month. She defervesced during a 2-week course of levofloxacin therapy for presumed sinusitis, yet fever returned after completion of treatment and was accompanied by neck pain, arthralgias, lightheadedness, palpitations, and severe fatigue. On examination, she had marked pallor,

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nuchal rigidity, and a systolic flow murmur. Her hemoglobin level was 6.2 g/dL with an absolute reticulocyte count of 147×10^9 cells/L, a lactate dehydrogenase level of 536 U/L, a total bilirubin level of 1.0 mg/dL (17 μ mol/L), and an undetectable level of haptoglobin. Although sickle cell disease relapse was suspected, the hemoglobin donor type remained, and myeloid cells were all of donor origin. Cerebrospinal fluid was negative for infections, and blood cultures yielded no growth.

A peripheral blood smear contained intraerythrocytic ring-shaped trophozoites, without gametocyte or Maltese cross forms (Figure, *top*). Because of initial suspicion for *Plasmodium falciparum* infection, the patient was given a combination of atovaquone (1000 mg/d) and proguanil (400 mg/d) therapy, which led to rapid defervescence and symptom improvement. Serial peripheral smears, however, revealed persistent parasitemia after 6 days of therapy, and polymerase chain reaction (PCR) testing for *Plasmodium* species was negative. *Babesia* species testing was then performed: *Babesia* indirect fluorescent assay was positive at 1:256 and nested PCR was strongly positive for *B. microti*. Antibiotics were changed to atovaquone (750 mg twice daily) and azithromycin (600 mg/d) (2) to complete a 10-day course of therapy. She has remained well and had no further evidence of parasitemia by blood films or PCR.

Because the patient neither resided in nor had visited an endemic area, a red cell donor inquiry was initiated for possible transfusion-associated babesiosis. One of her 17 peritransplant blood product donors was found to have a very high *Babesia* indirect fluorescent assay (1:1024) but negative PCR. The donor was an avid outdoorsman who had periodically visited babesiosis-endemic areas. The implicated unit was transfused to our patient in October 2005, a week before her transplant.

Discussion

Most of the reported U.S. cases of babesiosis have been caused by *B. microti*, which is transmitted in nature by *Ixodes scapularis* ticks (2). The sporozoites infect erythrocytes and can pose a serious risk to the donated blood supply. More than 50 cases of transfusion-transmitted babesiosis are reported in the literature, although this is the first reported case in a human stem-cell transplant recipient (3). In healthy hosts, naturally occurring babesiosis develops 1 to 6 weeks after inoculation as a mild, self-limited, febrile illness. Asymptomatic parasitemia can persist beyond the clinical illness and therefore escape the symptom screening at blood donation (4–6). Infection in asplenic or otherwise immunocompromised patients follows a more severe course and often results in relapse. Signs and symptoms result from hemolysis and include fevers, chills, myalgias, and malaise. The incubation period of 6 months in this case was far longer than the 1 to 9 weeks reported for most episodes of transfusion-associated babesiosis (1). The extent to which host factors, parasite factors, or medications modulated the clinical course in our patient is unknown. Babesiosis remains an underreported disease. This case illustrates the importance of its consideration in nonendemic areas and highlights the potential for transfusion-associated disease presenting with an atypical time course.

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References

1. Leiby DA. Babesiosis and blood transfusion: flying under the radar. *Vox Sang*. 2006;90:157–65.
2. Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klemperer MS, et al. The clinical assessment, treatment, and prevention of lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*. 2006;43:1089–134.
3. Bronsdon MA, Homer MJ, Magera JM, Harrison C, Andrews RG, Bielitzki JT, et al. Detection of enzootic babesiosis in baboons (*Papio cynocephalus*) and phylogenetic evidence supporting synonymy of the genera *Entopolypoides* and *Babesia*. *J Clin Microbiol*. 1999;37:1548–53.
4. Leiby DA, Chung AP, Gill JE, Houghton RL, Persing DH, Badon S, et al. Demonstrable parasitemia among Connecticut blood donors with antibodies to *Babesia microti*. *Transfusion*. 2005;45:1804–10.
5. Dobroszycki J, Herwaldt BL, Boctor F, Miller JR, Linden J, Eberhard ML, et al. A cluster of transfusion-associated babesiosis cases traced to a single asymptomatic donor. *JAMA*. 1999;281:2927–30.
6. Eberhard ML, Walker EM, Steurer FJ. Survival and infectivity of *Babesia* in blood maintained at 25 C and 2–4 C. *J Parasitol*. 1995;81:790–2.

Figure. Intraerythrocytic ring forms on a Wright–Giemsa-stained smear of peripheral blood from a patient with transfusion-associated babesiosis

Morphologic differentiation of *Babesia microti* and *Plasmodium falciparum* can be difficult, particularly if the parasitemia level is low and only ring forms are found. The presence of vacuolated, pleomorphic rings, without pigment or gametocytes, is characteristic of *Babesia* infection. Tetrad (Maltese cross) forms are pathognomonic but uncommonly seen.