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SHORT REPORT

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Babesia microti in a Canadian blood donor and lookback in a red blood cell recipient

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Abstract

Background and Objectives: We describe the third documented case of autochthonous human babesiosis in Canada and the second in a Canadian blood donor.

Materials and Methods: Multiple laboratory investigations were carried out on the donor and the immunocompromised recipient of an associated, potentially infectious red blood cell product.

Results: The donor had not travelled except for outdoor exposure in south-eastern Manitoba, followed by illness and hospital admission. The donor had a notable parasitaemia, positive for *Babesia microti* using whole blood nucleic acid testing (NAT). The recipient was negative for *B. microti* by both serology and NAT.

Conclusion: There was no evidence of transfusion-transmitted babesiosis.

KEYWORDS
Babesia, haemovigilance, protozoal infections, transfusion-transmitted infections

INTRODUCTION

Babesia species are intra-erythrocytic protozoan parasites with *Babesia microti* and *Babesia duncani* being the two main species in North America. Although these parasites are primarily transmitted by bites from *Ixodes* species ticks, transmission via solid organ transplantation or blood transfusion has been reported. Infected donors can be asymptomatic and infectious for weeks to months. In recipients, *Babesia* infection may present with an influenza-like illness weeks to months after transfusion followed by typical manifestations of the disease. Severe disease can include anaemia, organ dysfunction and death. Risk factors for severe outcomes include extremes of age, asplenia, or immunosuppression, and individuals with such conditions may have high parasite burdens that can be detected by examination of blood smears. *B. microti* is endemic in the north-eastern and midwestern United States near the Canadian border [1]. In the United States, over 200 cases of transfusion-transmitted babesiosis (TTB) have been reported since 1980, with a trend of increasing reported incidence, prompting implementation in 2019 of universal, year-round testing in designated states with high reported incidence of babesiosis [1].

Canadian donors are currently indefinitely deferred for known babesiosis, but donor testing is not performed for *Babesia* species (*B. microti*, *B. duncani*, *B. divergens* and *B. venatorum*). In 1998, the only documented case of transfusion-transmitted babesiosis was described in Canada. The donor infection was thought to have been acquired during travel to Cape Cod, Massachusetts, the United States [2]. In 2013, the first documented case of locally acquired tick-borne babesiosis was described in Manitoba, Canada [3]. In the same year, a serological survey of 13,993 donors from across Canada, failed to identify a *Babesia* seropositive donor [4]. Five years later in 2018, 50,752 blood donations from across Canada were screened for *Babesia* species (*B. microti*, *B. duncani*, *B. divergens* and *B. venatorum*) using a nucleic acid test (NAT) and an additional 14,758 NAT-negative donations were screened for *B. microti* antibody [5]. The 2018 survey yielded a single NAT-positive blood donor from Manitoba, while four other Canadian blood donors demonstrated serological evidence of prior *Babesia* species infection.

This manuscript describes a retrospective investigation (formally called a lookback investigation by blood operators) involving a *B. microti* NAT-positive Canadian blood donor from Manitoba, with likely autochthonous *Babesia* infection and a recipient of red blood cells (RBCs) that had been collected during the donor's potential infectious period.

MATERIALS AND METHODS

A lookback investigation was initiated by Canadian Blood Services staff [6], following post-donation notification to the blood operator by

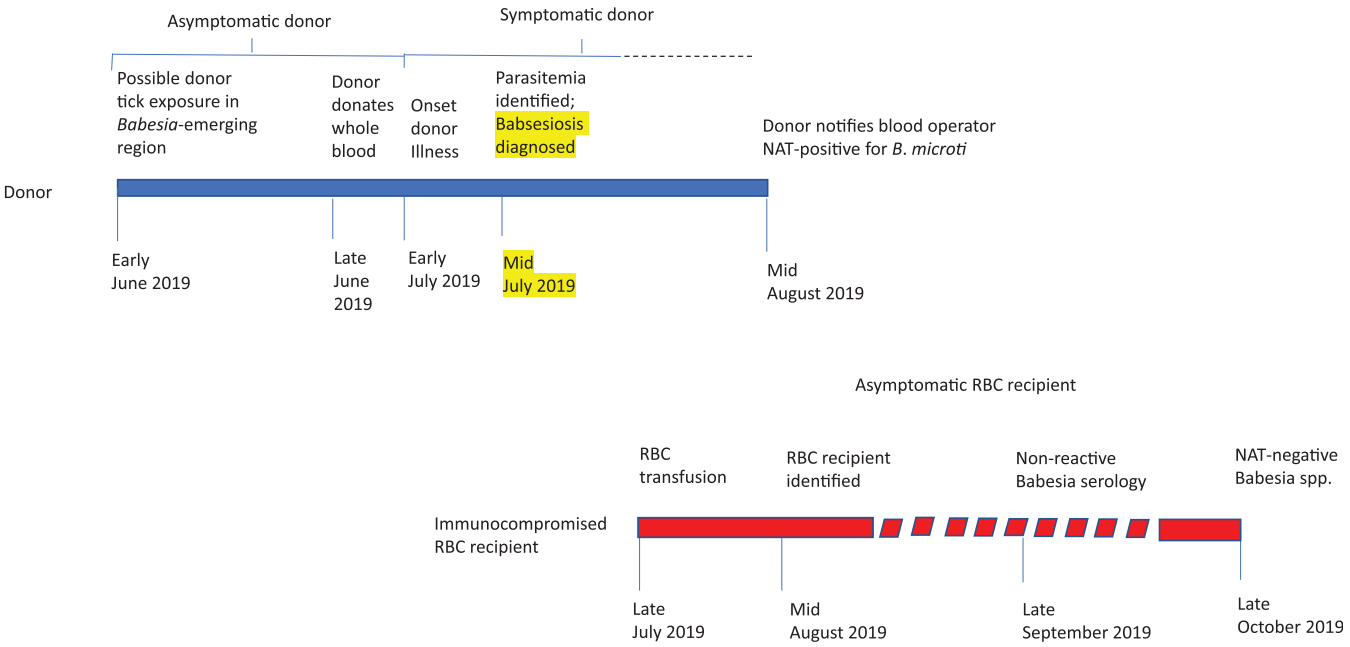

FIGURE 1 Time course for the investigation of a *Babesia microti*–infected blood donor and a recipient of red blood cells (RBCs). Key timings for investigation of the infected donor are in the top half of the figure. Key timings for the investigation of the immunocompromised RBC recipient are in the bottom half of the figure. No transfusion transmission of *B. microti* via donor RBCs was identified in this investigation [Colour figure can be viewed at wileyonlinelibrary.com]

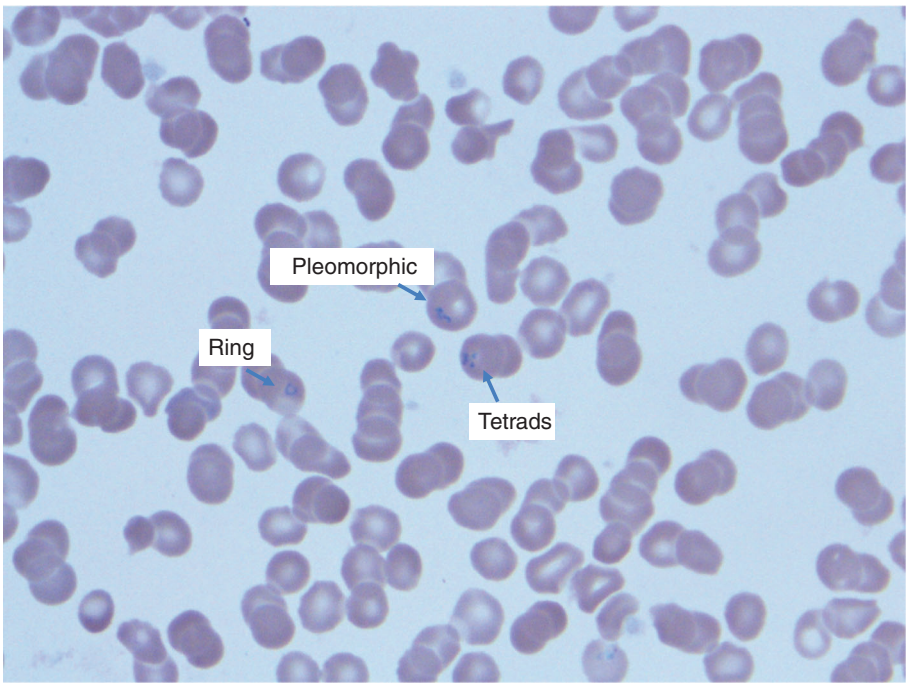

FIGURE 2 Microscopic investigation of donor blood for parasites. This image is of a thin blood smear (oil, ×1000, Giemsa stain). *Babesia* trophozoites and merozoites were identified morphologically. Trophozoites were ring-shaped, pleomorphic and vacuolated. Merozoites were occasionally identified displayed in tetrads [Colour figure can be viewed at wileyonlinelibrary.com]

the donor (Figure 1). During the donor's hospitalization, whole blood specimens were initially analysed by the hospital pathology staff. During the lookback process, details of the donor's clinical and travel history were obtained, and additional microscopy was undertaken on donor whole blood specimens by public health at the Cadham Provincial Laboratory (Winnipeg, Manitoba, Canada). Donor whole blood specimens were also tested by NAT for *B. microti*, *B. divergens* and *B. duncani* (National Microbiology Laboratory [NML], Winnipeg, Canada) [7, 8] (Figure 1).

Anti-*B. microti* immunofluorescence assay serology testing on serum from the RBC recipient was performed by the National Reference Centre for Parasitology (Montreal, Quebec, Canada) [9]. NML performed NAT for *Babesia* on a recipient whole blood specimen.

RESULTS

In mid-August 2019, Canadian Blood Services was contacted post-donation by a 75-year-old male donor from Manitoba who reported being recently diagnosed and treated for babesiosis. The donor had camped in south-eastern Manitoba (early June 2019) and suspected at least one tick bite before donating whole blood in late June 2019 (Figure 1). There was no recent travel history to a reported *Babesia*-endemic region outside of Canada. The donor reported becoming very ill less than 1 week after donation and was hospitalized in early August 2019. Blood parasites were noted in whole blood specimens collected during hospitalization, and further microscopic examination identified 'malaria-like' parasites (Figure 2). Both hospital and public health laboratories estimated a parasitaemia ranging from 0.2% to 1%. Whole blood NAT testing was subsequently positive for *B. microti* (Figure 1).

Three components were produced from the original donation: one fresh product, RBCs, and two subsequently frozen products, cryosupernatant plasma (CSP) and cryoprecipitate (CRYO). The CSP was transfused the second week of July 2019, while the CRYO was transfused the third week of July 2019. No lookback was undertaken on frozen products [10].

A lookback determined that the associated leukoreduced RBC unit was transfused after 27 days of storage in the fourth week of July 2019, to a 74-year-old male recipient with relapsed, diffuse large B cell lymphoma status post-RCEPP (rituximab, cyclophosphamide, etoposide, prednisone and procarbazine) (Figure 1). *Babesia microti* serologic testing on a recipient serum specimen collected in late September 2019 was non-reactive (immunofluorescence assay titre < 1/64). NAT testing for *B. microti*, *B. divergens* and *B. duncani* on a whole blood specimen collected in late October 2019 was negative. There was no clinical evidence of transfusion-transmitted babesiosis in the recipient (Figure 1).

DISCUSSION

Even in low babesiosis prevalent settings such as Canada, blood operators must remain vigilant for transfusion-transmitted babesiosis. In the absence of a complete blood donor travel history, *Babesia* may be mistaken for malaria, if diagnosis relies on microscopy and *Babesia*-specific NAT is not undertaken [11]. Cross-reactivity on *Plasmodium* genus-specific 18S assays may also cloud the microbiological

picture in such scenarios [11]. In the case described herein, babesiosis was diagnosed during a hospital admission based on a history of outdoor activities (and possible tick exposure) in a region with prior, reported autochthonous transmission, along with corroborative laboratory evidence. The impetus for the subsequent blood product lookback investigation was a donor-reported history of recent babesiosis infection shortly after a whole blood donation. Of note, Manitoba is also one of few provinces in Canada (including Quebec) where babesiosis is a specifically designated reportable infection to public health. The lookback investigation was a multi-team process that involved the blood operator, hospital clinical and laboratory staff, and reference laboratory experts from two provincial laboratories and the national public health laboratory.

The recipient of the RBCs was immunocompromised and hence at higher risk of more serious transfusion-transmitted babesiosis. RBC concentrate is the most likely blood product associated with transfusion-transmitted *Babesia* infection. Longer RBC storage times may not prevent parasite transmission as transfusion-transmitted babesiosis implicating RBC units 42 days old have been identified [12, 13]. Thus, in this case, the RBC recipient remained clinically well without signs of babesiosis and was non-reactive for *Babesia* spp. using NAT and serology months after RBC transfusion. Given the immunocompromised nature of the recipient and the possibility of a blunted or negative serologic response, the final specimen collected from the recipient was tested using NAT. During this investigation, the CSP and CRYO units were not investigated as *Babesia* is rapidly killed by freezing [10]. We do note that *Babesia* survives freezing in glycerolized red cells, which have been implication in transfusion cases [14].

This is the third documented case of autochthonous babesiosis in Canada and the second in a Canadian blood donor. Of note, all cases thus far spent time in forested areas in the very southernmost areas of Manitoba, close to the US border. Although there was no evidence of transfusion-transmitted babesiosis in the immunocompromised RBC recipient, we are using this information and results from a 2018 Canadian blood donor surveillance study to undertake a risk-based decision-making (RBDM) assessment. On completion of the RBDM, Canadian Blood Services will determine if further *Babesia*-related blood safety measures, especially in a region of potential *Babesia* emergence, are warranted.

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S.J.D. led the investigation from the blood operator perspective, analysed the data and wrote the first draft of the manuscript; P.V.C., J.B. and L.R.L. coordinated specimen testing on the donor, reviewed the laboratory data and reviewed and edited the manuscript; T.G. and M.P.Z. assisted with the recipient investigations, helped coordinate further testing on the recipient and reviewed and edited the manuscript; D.L. worked with D.M., C.M. and M.A. to initially investigate the donor, undertake and interpret laboratory testing and also reviewed and edited the manuscript; M.N., V.G.A. and A.K.B coordinated the recipient work-up and also reviewed and edited the manuscript; S.F.O. provided epidemiological context for the findings and also reviewed and edited the manuscript and M.B. assisted on both the donor and recipient investigations and reviewed and edited the first and following drafts of the manuscript.

CONFLICT OF INTEREST

Steven J. Drews has acted as a content expert on respiratory viruses for Johnson and Johnson (Janssen). He also acted as a content expert to Roche on Arboviruses. All other authors have no other conflicts of interest.

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