Vertical Transmission of Babesia microti, United States

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Babesiosis is usually acquired from a tick bite or through a blood transfusion. We report a case of babesiosis in an infant for whom vertical transmission was suggested by evidence of Babesia spp. antibodies in the heel-stick blood sample and confirmed by detection of Babesia spp. DNA in placenta tissue.

Babesiosis is an emerging infection in the United States, principally caused by Babesia microti (1). The most common route of infection is the bite of an Ixodes scapularis tick; transmission can also occur by transfusion of infected blood products, and vertical transmission in animals has been documented (2, 3) and is a potential route of transmission for humans. We report a case of babesiosis in an infant for whom vertical transmission was suggested by Babesia spp. antibodies in a heel spot blood sample and confirmed by detection of Babesia DNA in placenta tissue.

The Case-Patient

A 6-week-old girl from Yorktown Heights, New York, was admitted to the hospital on September 16, 2002, with a 2-day history of fever, irritability, and decreased oral intake. The mother was asymptomatic during and after her pregnancy. The infant was delivered vaginally and full term at 3,430 g without complications. The infant’s mother had visited parks in Westchester and Dutchess Counties in New York during the pregnancy but was unaware of any tick bites. The infant had no known tick exposure, and neither mother nor infant had a history of blood transfusion.

During examination, the infant was alert but irritable and pale. Axillary temperature was initially 36.8°C but increased to 38.1°C on the same day. Her conjunctivae were icteric, she had a palpable spleen tip, and her liver was palpable 3 cm below the costal margin. Initial laboratory findings included hemoglobin 7.1 g/dL, platelet count 100 × 10^3/μL, and leukocyte count 19.7 × 10^3 cells/μL with a differential of 4% segmented neutrophils, 80% lymphocytes, and 16% monocytes. Reticulocyte count was 5.5%. Total bilirubin concentration was 2 mg/dL with a direct fraction of 0.4 mg/dL; aspartate aminotransferase level was 66 U/L, alanine aminotransferase level was 50 U/L, and alkaline phosphatase level was 339 U/L. Cultures of blood, urine, and cerebrospinal fluid samples yielded negative results. Lyme disease serologic test result was negative.

Routine examination of a peripheral blood smear showed B. microti in 4% of erythrocytes (Figure); a blood sample from the infant was positive by PCR for B. microti DNA. Total B. microti antibody titer was >256 by indirect immunofluorescence assay, with a polyvalent secondary antibody (anti-IgG+IgA+IgM) (4) that was presumed to be principally IgG because test results for IgM were negative (online Technical Appendix, wwwnc.cdc.gov/EID/pdfs/11-0988-Techapp.pdf). The heel-stick blood sample obtained on the infant’s third day of life as part of newborn screening was tested and found to be negative for B. microti by PCR (5) and for IgM but total antibody positive (>128) (online Technical Appendix).

Examination of the placenta showed focal basal decidual inflammation, mild chorangiosis, and villus dysmaturity. Babesia spp. piroplasms were not detected in
maternal or fetal blood by histologic examination of hematoxylin and eosin–stained sections of formalin-fixed, paraffin-embedded tissue of the placenta disk, amnion/chorion, and umbilical cord. *Babesia* DNA was detected by real-time PCR testing of paraffin-embedded placenta tissue (online Technical Appendix) (6). Cycle threshold values were relatively high (37.1–38.2), indicating that the amount of parasite DNA in the sample was close to the limit of detection; results were reproducible on duplicate testing of DNA samples extracted from separate paraffin blocks. The real-time PCR product was of the correct size, and the melting curve demonstrated melting temperatures within 1°C from the placenta, the positive control, and a positive sample from an unrelated patient, confirming that the correct product was amplified. At time of the illness in the infant, the mother was negative for *Babesia* spp. according to PCR and smear but positive for total antibodies (>256).

### Table. Comparison of selected clinical and laboratory data from reported cases of congenital babesiosis in 5 infants*

| Clinical data | (7) | (8) | (9) | (10) | This study |
|---------------|-----|-----|-----|------|-----------|
| Year of diagnosis/location | Not given/Long Island, New York | Not given/Long Island, New York | Not given/New Jersey | Not given/Long Island, New York | 2002/Westchester County, New York |
| Infant age at time of symptom onset, d | 30 | 32 | 19 | 27 | 41 |
| Clinical findings | Fever, irritability, pallor, hepatosplenomegaly | Fever, lethargy, poor feeding, pallor, scleral icterus, hepatomegaly | Fever, poor feeding, gagging, irritability, pallor, scleral icterus, hepatosplenomegaly | Fever, pallor | Fever, decreased oral intake, irritability, scleral icterus, pallor, hepatosplenomegaly |
| Initial babesia parasitemia level, % | 5 | 4.4 | 15 | 2 | 4 |
| Hospitalization, d | 1 wk before delivery | 7 wk before delivery | 8 | None known | None known |
| Maternal tick bite | 30 d after birth: IgM+/IgG+ (128/128) by IFA; 32 d after birth: IgM+/IgG+ (256/512) by IFA; PCR ND | At illness onset: IgG IFA 160; IgM/IgG immunoblot +; PCR ND | At illness onset: IgM+/IgG+ (40/256) by IFA; PCR ND | NA | Newborn screening (heel stick): IgM– (<16); total antibody + (>128) by IFA; PCR–; 6 wks after birth: IgM– (<16); total antibody + (>256) by IFA; PCR+ |
| Babesia spp. serologic and PCR results for infant | 30 d after birth: IgM+/IgG+ (2,048/1,024); 32 d after birth: IgM+/IgG+ (4,096/1,024); peripheral smear – at time of delivery and at infant illness onset | 7 wk before birth: IgG IFA <40; IgM/IgG immunoblot –; 2 mo after birth: IgG IFA 640; IgM/IgG immunoblot +; peripheral smear negative at time of infant illness onset | At infant illness onset: IgM+/IgG+ (80/>1,024) by IFA; peripheral smear negative at time of infant illness onset | At infant illness onset: PCR+ | Babesia spp. evaluation results for mother |
| Babesia spp. evaluation results for mother | 30 d after birth: IgM+/IgG+ (2,048/1,024); 32 d after birth: IgM+/IgG+ (4,096/1,024); peripheral smear – at time of delivery and at infant illness onset | 7 wk before birth: IgG IFA <40; IgM/IgG immunoblot –; 2 mo after birth: IgG IFA 640; IgM/IgG immunoblot +; peripheral smear negative at time of infant illness onset | At infant illness onset: IgM+/IgG+ (80/>1,024) by IFA; peripheral smear negative at time of infant illness onset | At infant illness onset: PCR+ | Babesia spp. evaluation results for mother |
| HGB, g/dL | 9.3 | 10.8 | 8.8 | NA; HCT 24.3% | 7.1 |
| Platelets, x 10^9/L | 38 | 87 | 34 | 101 | 100 |
| Leukocytes/PMN | 6,500/1,170 | NA | 9,000/1,890 | NA | NA |
| Leukocytes, cells/µL | 894 | NA | 2535 | NA | NA |
| LDH, µL | 3.6 | 5.7 | 5.9 | NA | 1.6 |
| Bilirubin indirect, mg/dL | 3.6 | 9.7 | 9.7 | NA | 5.6 |
| AST, U/L | 90 | NA | 53 | NA | 66 |
| ALT, U/L | 90 | NA | 53 | NA | 50 |
| Treatment | CLI and quinine for 10 d | CLI and quinine with AZT added on day 3 on day 5 changed to AZT plus quinine for additional 7 d | AZT and ATO for 10 d | AZT and ATO, duration not given | AZT and ATO for 9 d |
| Follow-up | Well at 6 mo posttreatment | Improved at 2 wk | NA | NA | 22 mo |
| Blood transfusion for anemia | Yes, for HCT of 18% | Yes, for HGB of 7.3 g/dL | Yes, for HGB of 7.0 g/dL | Yes, for HCT of 17.3% | Yes, for HGB of 5.2 g/dL with HCT of 15.8% |

*No mothers became ill. NA, not available; +, positive; IFA, indirect immunofluorescence assay; ND, not done; −, negative; HGB, hemoglobin; HCT, hematocrit; PMN, polymorphonuclear; LDH, lactate dehydrogenase level; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CLI, clindamycin; AZT, azithromycin; ATO, atovaquone.
The infant was treated with a 9-day course of azithromycin plus atovaquone. A blood transfusion was administered when her hemoglobin concentration fell to 5.2 g/dL. The infant became afebrile by 72 hours and was discharged after a 5-day hospitalization. Repeat blood smears revealed a parasite load of 0.3% at discharge. On final evaluation at 22 months of age, physical examination revealed no abnormalities; hemoglobin level was 11.7 g/dL. *Babesia* antibody level was positive at 128.

**Conclusions**

Congenital babesiosis has been rarely reported (Table) (7–10). This case provided convincing evidence for congenital babesiosis because of prepurpurp infection involving the placenta in the mother. On the basis of experience with congenital malaria, we assume that *Babesia* spp. parasites cross the placenta during pregnancy or at the time of delivery (11,12). In congenital malaria, increasing evidence suggests that the malaria parasites are most often acquired antenatally by transplacental transmission of infected erythrocytes (12).

Reported cases of congenital babesiosis share many similarities, including asymptomatic maternal infection and development of fever, hemolytic anemia, and thrombocytopenia in the infant detected between 19 and 41 days after birth. All of the infants responded to antimicrobial drug therapy; 3 were treated with azithromycin plus atovaquone (9,10), the preferred treatment regimen for mild babesiosis (1). All infants required a blood transfusion because of severe anemia. The clinical signs and symptoms for these cases of congenital babesiosis are similar to those of congenital malaria in non–disease endemic areas (11,13).

We found *Babesia* spp. antibodies on day 3 of life by analyzing the patient’s heel-stick blood sample, which likely represented maternal transfer of IgG. Passive transfer of maternal antibodies is regarded as a protective factor against congenital malaria, and some newborns with malaria who are parasitemic at birth spontaneously clear the infection without ever becoming ill (11,14). The temporary presence of maternal IgG in infants has been suggested as an explanation for the typical 3–6 week incubation period of congenital malaria in non–disease endemic areas (14).

The real-time PCR used to find *B. microti* DNA in placenta tissue is ≈20× more sensitive than microscopic examination of Giemsa-stained blood smears (6). Assuming a blood sample with a parasitemia equivalent to that detected in the placental tissue, a blood smear would contain ≤10 infected cells per slide. Given the low level of *Babesia* DNA in the placenta tissue, it is not surprising that histologic examination did not reveal piroplasms. Nonetheless, limited evidence of placental abnormalities suggests a pathologic process.

In summary, babesiosis is an emerging infectious disease (15) that can rarely cause congenital infection. This diagnosis should be considered in the differential diagnosis of fever and hemolytic anemia in infants from disease-endemic areas.

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**References**

1. Vannier E, Gewurz BE, Krause PJ. Human babesiosis. Infect Dis Clin North Am. 2008;22:469–88. http://dx.doi.org/10.1016/j.idc.2008.03.010
2. de Vos AJ, Imes GD, Cullen JSC. Cerebral babesiosis in a new-born calf. Onderstepoort J Vet Res. 1976;43:75–8.
3. Fukushima S, Suzuki H, Igarashi I, Xuan X. Fatal experimental transplacental *Babesia gibsoni* infections in dogs. Int J Parasitol. 2005;35:1031–5. http://dx.doi.org/10.1016/j.ijpara.2005.03.018
4. Chisholm ES, Ruebush TK II, Sulzer AJ, Healy GR. *Babesia microti* infection in man: evaluation of an indirect immunofluorescent antibody test. Am J Trop Med Hyg. 1978;27:14–9.
5. Persing DH, Mathiesen D, Marshall WF, Telford SR, Spielman A, Thomford JW, et al. Detection of *Babesia microti* by polymerase chain reaction. J Clin Microbiol. 1992;30:2097–103.
6. Teal AE, Habura A, Ennis KE, Keithly J, Madison-Antenucci S. A new real-time PCR assay for improved detection of the parasite *Babesia microti*. J Clin Microbiol. 2012;50:903–8. http://dx.doi.org/10.1128/JCM.05848-11
7. Esenrio-Jenssen D, Sicema PG, Benach JL, Tenenbaum MJ. Transplacental/perinatal babesiosis. J Pediatr. 1987;110:570–2. http://dx.doi.org/10.1016/S0022-3476(87)80552-8
8. New DL, Quinn J, Qureshi MZ, Sigler S. Vertically transmitted babesiosis. J Pediatr. 1997;131:163–4. http://dx.doi.org/10.1016/S0022-3476(97)01434-4
9. Sethi S, Alcid D, Kesarwala H, Tolan RW Jr. Probable congenital babesiosis in infant, New Jersey, USA. Emerg Infect Dis. 2009;15:788–91. http://dx.doi.org/10.3201/eid1505.070808
10. Adenibuyoe O, Syed S. Congenital babesiosis in a four-week old female infant. Pediatr Infect Dis J. 2010;29:188. http://dx.doi.org/10.1097/INF.0b013e3181c3c971
11. Vottier G, Arsac M, Farnoux C, Mariani-Kurkdjian P, Baud O, Ajard Y. Congenital malaria in neonates: two case reports and review of the literature. Acta Paediatr. 2008;97:505–8. http://dx.doi.org/10.1111/j.1651-2227.2008.00690.x
12. Malhotra I, Mungai P, Muchiri E, Kwick JJ, Meshnick SR, King CL. Umbilical cord-blood infections with *Plasmodium falciparum* malaria are acquired antenatally in Kenya. J Infect Dis. 2006;194:176–83. http://dx.doi.org/10.1086/505150
13. Lesko CR, Arguin PM, Newman RD. Congenital malaria in the United States. A review of cases from 1966 to 2005. Arch Pediatr Adolesc Med. 2007;161:1062–7. http://dx.doi.org/10.1001/archpedi.161.11.1062
14. Hagmann S, Khanna K, Niazi M, Purswani M, Robins EB. Congenital malaria, an important differential diagnosis to consider when evaluating febrile infants of immigrant mothers. Pediatr Emerg Care. 2007;23:326–9. http://dx.doi.org/10.1097/01 pec.0000270164.78238.7d

15. Joseph JT, Roy SS, Shams N, Visintainer P, Nadelman RB, Hosur S, et al. Babesiosis in Lower Hudson Valley, New York, USA. Emerg Infect Dis. 2011;17:943–7.

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