Babesiosis in Immunocompetent Patients, Europe
Martin Martinot, Mahsa Mohseni Zadeh, Yves Hansmann, Isabelle Grawey, Daniel Christmann, Sarah Aguillon, Maggy Jouglin, Alain Chauvin, Dominique de Briel

To cite this version:
Martin Martinot, Mahsa Mohseni Zadeh, Yves Hansmann, Isabelle Grawey, Daniel Christmann, et al.. Babesiosis in Immunocompetent Patients, Europe. Emerging Infectious Diseases, 2011, 17 (1), pp.114-116. 10.3201/eid1701.100737. hal-02652011

HAL Id: hal-02652011
https://hal.inrae.fr/hal-02652011
Submitted on 29 May 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Distributed under a Creative Commons Attribution 4.0 International License
We report 2 cases of human babesiosis in Colmar, Alsace, a northeastern region of France in which Lyme disease is endemic. The disease was diagnosed in spring 2009 in healthy young persons without history of travel abroad who experienced a marked influenza-like syndrome and recovered. These cases should change the classic description of babesiosis in Europe, in which the disease was thought to affect immunocompromised patients exclusively. Our study indicates that this disease also occurs in Europe among immunocompetent patients.

**Case Reports**

Patient 1, a 37-year-old woman without known medical history, sought treatment on April 29, two weeks after a tick bite. She had a 38.5°C fever with chills, headaches, and arthromyalgia. Results of a physical examination were normal. Laboratory findings included leukopenia (3,300 leukocytes/μL, 45% polymorphonuclear cells, 37% lymphocytes), aspartate aminotransferase and alanine aminotransferase levels of 136 IU/L and 160 IU/L, respectively; γ-glutamyl transpeptidase 135 IU/L; alkaline phosphatase 131 IU/L; and elevated C-reactive protein level (48 mg/L). Serologic results for Lyme disease, tick-borne encephalitis virus, tularemia, *Anaplasma* spp., *Coxiella burnetii*, and *Rickettsia* spp., as well as blood cultures were negative.

A thin peripheral blood smear stained with May-Grünwald-Giemsa did not show any ehrlichial morulae in granulocytes, as suspected, but a retrospective examination of stored slides on May 22 (the same day that case 2 was characterized) showed pear forms and trophozoites of intraerythrocytic parasites (parasitemia level 0.29%), leading to the diagnosis of babesiosis (Figure 1). The patient had initially received doxycycline (200 mg/d) for a suspected bacterial tick-borne infection, and her symptoms rapidly resolved. The first blood sample was discarded, but on June 16 and June 24, additional serum and whole blood samples were collected in sodium citrate vacutainer tubes (Becton-Dickinson, Franklin Lakes, NJ, USA). The blood smears remained positive until July but were negative in August.

Patient 2, a 35-year-old man with an uneventful medical history, was hospitalized on May 21, two weeks after receiving 3 tick bites. He had a 39°C fever, severe headaches, and arthromyalgia. Results of a physical examination were normal. Laboratory findings showed leukopenia (1,860 leukocytes/μL, with 35% polymorphonuclear leukocytes, 49% lymphocytes), marked thrombopenia with 36,000 platelets/mm³, elevated liver enzyme levels (aspartate aminotransferase 70 IU/L, alanine aminotransferase 77 IU/L, γ-glutamyl transferase 161 IU/L, and alkaline phosphatase 86 IU/L), and elevated C-reactive protein (124 mg/L). Tick-transmitted disease serologic results and blood cultures were negative.

We report 2 cases of human babesiosis in Colmar, Alsace, a northeastern region of France in which Lyme disease is endemic. The disease was diagnosed in spring 2009 in healthy young persons without history of travel abroad who experienced a marked influenza-like syndrome and recovered. These cases should change the classic description of babesiosis in Europe, in which the disease was thought to affect immunocompromised patients exclusively. Our study indicates that this disease also occurs in Europe among immunocompetent patients.

**Case Reports**

Patient 1, a 37-year-old woman without known medical history, sought treatment on April 29, two weeks after a tick bite. She had a 38.5°C fever with chills, headaches, and arthromyalgia. Results of a physical examination were normal. Laboratory findings included leukopenia (3,300 leukocytes/μL, 45% polymorphonuclear cells, 37% lymphocytes), aspartate aminotransferase and alanine aminotransferase levels of 136 IU/L and 160 IU/L, respectively; γ-glutamyl transpeptidase 135 IU/L; alkaline phosphatase 131 IU/L; and elevated C-reactive protein level (48 mg/L). Serologic results for Lyme disease, tick-borne encephalitis virus, tularemia, *Anaplasma* spp., *Coxiella burnetii*, and *Rickettsia* spp., as well as blood cultures were negative.

A thin peripheral blood smear stained with May-Grünwald-Giemsa did not show any ehrlichial morulae in granulocytes, as suspected, but a retrospective examination of stored slides on May 22 (the same day that case 2 was characterized) showed pear forms and trophozoites of intraerythrocytic parasites (parasitemia level 0.29%), leading to the diagnosis of babesiosis (Figure 1). The patient had initially received doxycycline (200 mg/d) for a suspected bacterial tick-borne infection, and her symptoms rapidly resolved. The first blood sample was discarded, but on June 16 and June 24, additional serum and whole blood samples were collected in sodium citrate vacutainer tubes (Becton-Dickinson, Franklin Lakes, NJ, USA). The blood smears remained positive until July but were negative in August.

Patient 2, a 35-year-old man with an uneventful medical history, was hospitalized on May 21, two weeks after receiving 3 tick bites. He had a 39°C fever, severe headaches, and arthromyalgia. Results of a physical examination were normal. Laboratory findings showed leukopenia (1,860 leukocytes/μL, with 35% polymorphonuclear leukocytes, 49% lymphocytes), marked thrombopenia with 36,000 platelets/mm³, elevated liver enzyme levels (aspartate aminotransferase 70 IU/L, alanine aminotransferase 77 IU/L, γ-glutamyl transpeptidase 161 IU/L, and alkaline phosphatase 86 IU/L), and elevated C-reactive protein (124 mg/L). Tick-transmitted disease serologic results and blood cultures were negative.
Babesiosis in Immunocompetent Patients

A thin peripheral blood smear stained with May-Grünwald-Giemsa showed intraerythrocytic Babesia spp. (parasitemia level 0.23%) (Figure 2). The patient received azithromycin 500 mg on day 1 then 250 mg/day plus atovaquone, and his illness rapidly resolved. Two samples of serum and whole blood were collected in sodium citrate vacutainer tubes on June 16 and July 21 and sent to the veterinary laboratory of Nantes for B. divergens serologic analysis (indirect immunofluorescent assay by using gerbil-derived strain B. divergens Rouen F5 antigen), erythrocyte cultures, and DNA extraction (Wizard genomic DNA Purification kit; Promega, Madison, WI, USA) for PCR Babesia spp. (9).

Serologic results and cultures remained negative for both patients. However, serologic analysis is neither sensitive nor specific (7,10), and cultures probably were inhibited because blood samples were collected after doxycycline or azithromycin proguanil treatments. The PCR for Babesia spp. is specific for an 18S rDNA 540-base long region of a variable part of the gene with Bab primers GF2 and GR2, was performed (9,11). Results were positive for patient 1. The sequencing of PCR products showed 100% homology with B. divergens human strains GenBank accession nos. FJ944822 and FJ944823 (9). PCR results were negative for patient 2. Samples from patient 2 were collected 1 month after treatment with atovaquone-proguanil, and the blood smear was negative. However, the clinical and biological data and the observation of trophozoites (especially 2 trophozoites in 1 erythrocyte) in the blood smear from patient 2 confirmed by a reference laboratory led us to strongly suspect babesiosis (Figure 2). In this case, the Babesia species remains unknown, and a non-B. divergens species cannot be ruled out, although it is rarer.

Conclusions

Our cases highlight that, in Europe, babesiosis can occur in healthy persons and manifest as moderate illness. The rarity of other reported cases in nonimmunocompromised patients in Europe may be related to the difficulty of diagnosing babesiosis. A stained thin blood smear is rarely performed in Europe after tick bite in healthy patients. The difficulty of detecting intra-erythrocytic forms of babesia coupled with frequent low levels of parasitemia, may result in accurate diagnoses, although acridine orange and fluorescent microscopy may assist in the detection of parasites (1). Other diagnostic tests, such as PCR and serologic analysis, are not routinely performed in France and require a reference laboratory (8).

Babesiosis, although difficult to diagnose, needs to be diagnosed for various reasons: 1) without treatment, babesiosis can lead to severe illness; 2) the disease can persist for a long period without symptoms, which could lead to posttransfusion cases (12); and 3) effective specific treatments are available (atovaquone plus azithromycin, or for severe cases, clindamycin and quinine) (2). These drugs are not usually prescribed in febrile tick-bite cases; doxycycline is the usual drug used to treat tick-borne bacterial diseases. Moreover, patients with moderate infection could benefit from an atovaquone plus azithromycin regimen, which is better tolerated (13).

Previous serosurveys from tick-exposed patients or healthy blood donors in France (7), Germany (14), and Switzerland (15) have demonstrated antibodies against Babesia spp. antigens ranging from 1.0% to 11.5%. These data suggest that Babesia spp. infections probably occur more frequently in Europe than previously believed and may affect healthy patients. Although most patients may be asymptomatic, our 2 cases demonstrate that babesiosis can result in a serious influenza-like syndrome in previously healthy...
patients. In Europe, babesiosis is probably underdiagnosed; thus, we suggest that when patients have influenza-like or malaria-like syndromes after confirmed or suspected tick bites, a blood smear be performed regardless of whether the patient is immunocompromised. Blood smear can identify not only Babesia spp. infection but also Anaplasma spp. infection, another emerging and underdiagnosed tick-borne illness. In cases of new European Babesia spp. infections, a deeper characterization of the strains by erythrocytes cultures and standardized PCR, as well as a systematic study of the patients’ immune systems, should be undertaken to enable a better understanding of this disease.

Dr Martinot is a physician at the Department of Internal Medicine and Rheumatology, Hospital Pasteur, Colmar, France. His specialty is infectious diseases and primary research interests are tick-borne diseases, procalcitonin, and infections in immunocompromised patients (HIV).

References

1. Homer MJ, Persing DH. Human babesiosis. In: Goodman JL, Dennis DT, Sonenshine DE, editors. Tick-borne diseases of humans. Washington: ASM Press; 2005. p. 343–60.
2. Vannier E, Krause PJ. Update on babesiosis. Interdiscip Perspect Infect Dis. 2009;9:45–68.
3. Gelfand JA, Vannier E. Babesia species. In: Mandell GL, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases, 7th ed. Philadelphia: Elsevier; 2010. p. 3539–45.
4. L’Hostis M, Dumon H, Dorchies B, Boisdron F, Gorenflo A. Large scale survey of bovine babesiosis due to Babesia divergens in France. Vet Rec. 1995;136:36–8. DOI: 10.1136/vr.136.2.36
5. Hunfeld KP, Hildebrandt A, Gray JS. Babesiosis: recent insights into an ancient disease. Int J Parasitol. 2008;38:1219–37. DOI: 10.1016/j.ijpara.2008.03.001
6. Zintl S, Mulcahy G, Skerret SM, Taylor SM, Gray JS. Babesia divergens, a bovine blood parasite of veterinary and zoonotic importance. Clin Microbiol Rev. 2003;16:622–36. DOI: 10.1128/CMR.16.4.622-636.2003
7. Gorenflo A, Moubri K, Precigout E, Carcy B, Schetters TP. Human babesiosis. Ann Trop Med Parasitol. 1998;92:489–501.
8. Meliani P, Khiti S, Randazzo S, Gorenflo A, Marchou B. Human babesiosis. Med Mal Infect. 2006;36:499–504. DOI: 10.1016/j.medmal.2006.07.002
9. Malandrin L, Jouglin M, Sun Y, Brisseau N, Chauvin A. Redescription of Babesia capreoli (Enigk and Friedhoff, 1962) from roe deer (Capreolus capreolus): isolation, cultivation, host specificity, molecular characterization and differentiation from Babesia divergens. Int J Parasitol. 2010;40:277–84. DOI: 10.1016/j.ijpara.2009.08.008
10. Rosenblatt JE. Laboratory diagnosis of infections due to blood and tissue parasites. Clin Infect Dis. 2009;49:1103–8. DOI: 10.1086/605574
11. Bonnet S, Jouglin M, L’hostis M, Chauvin A. Babesia sp. EUI from roe deer and transmission within Ixodes ricinus. Emerg Infect Dis. 2007;13:1208–10.
12. Gunther DM, Lucey CT, Lee KC, Conley GB, Holness LG, Wise RP. Babesia infection through blood transfusions: reports received by the US Food and Drug Administration. Clin Infect Dis. 2009;48:25–30. DOI: 10.1086/595010
13. Krause PJ, Lepore T, Sikand VK, Gadhaw J Jr, Burke G, Telford SR III, et al. Atovaquone and azithromycin for the treatment of babesiosis. N Engl J Med. 2000;343:1454–8. DOI: 10.1056/NEJM200011163432004
14. Hunfeld KP, Lambert A, Kampen H, Albert S, Epe C, Brade V, et al. Seroprevalence of Babesia infections in humans exposed to ticks in midwest Germany. J Clin Microbiol. 2002;40:2431–6. DOI: 10.1128/JCM.40.7.2431-2436.2002
15. Foppa IM, Krause PJ, Spielmann A, Goethert H, Gern L, Brand B, et al. Entomologic and serologic evidence of zoonotic transmission of Babesia microti, eastern Switzerland. Emerg Infect Dis. 2002;8:722–6.

Address for correspondence: Martin Martinot, Service de Médecine Interne et Rhumatologie, Hôpitaux Civils de Colmar, 39 Ave de la Liberté, 68024, Colmar, France; email: martin.martinot@ch-colmar.fr

GovDelivery

Manage your email alerts so you only receive content of interest to you.

Sign up for an Online Subscription:

www.cdc.gov/ncidod/eid/subscribe.htm