

candidemia detection, and their clonal transmission was not detected by routine hospital surveillance, partly because more than half of the patient hospitalizations did not overlap. These findings indicate that clonal Y132F isolates may be dormant over long periods and can survive and persist outside their host on hospital environmental surfaces, which may be similar to the behavior of *C. auris* (10). Although our study was limited by the relatively low number of isolates, our data suggest that *C. parapsilosis* Y132F isolates should be identified in clinical microbiology laboratories to prevent further clonal transmission of BSI caused by Y132F isolates.

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Reference

- Pfaller MA, Jones RN, Doern GV, Sader HS, Messer SA, Houston A, et al.; The SENTRY Participant Group. Bloodstream infections due to *Candida* species: SENTRY antimicrobial surveillance program in North America and Latin America, 1997–1998. *Antimicrob Agents Chemother*. 2000;44:747–51. <http://dx.doi.org/10.1128/AAC.44.3.747-751.2000>
- Sandven P. Epidemiology of candidemia. *Rev Iberoam Micol*. 2000;17:73–81.
- Souza AC, Fuchs BB, Pinhati HM, Siqueira RA, Hagen F, Meis JF, et al. *Candida parapsilosis* resistance to fluconazole: molecular mechanisms and in vivo impact in infected *Galleria mellonella* larvae. *Antimicrob Agents Chemother*. 2015;59:6581–7. <http://dx.doi.org/10.1128/AAC.01177-15>
- Grossman NT, Pham CD, Cleveland AA, Lockhart SR. Molecular mechanisms of fluconazole resistance in *Candida parapsilosis* isolates from a U.S. surveillance system. *Antimicrob Agents Chemother*. 2015;59:1030–7. <http://dx.doi.org/10.1128/AAC.04613-14>
- Berkow EL, Manigaba K, Parker JE, Barker KS, Kelly SL, Rogers PD. Multidrug transporters and alterations in sterol biosynthesis contribute to azole antifungal resistance in *Candida parapsilosis*. *Antimicrob Agents Chemother*. 2015;59:5942–50. <http://dx.doi.org/10.1128/AAC.01358-15>
- Asadzadeh M, Ahmad S, Al-Sweih N, Khan Z. Epidemiology and molecular basis of resistance to fluconazole among clinical *Candida parapsilosis* isolates in Kuwait. *Microb Drug Resist*. 2017;23:966–72. <http://dx.doi.org/10.1089/mdr.2016.0336>
- Clinical and Laboratory Standards Institute. Reference method for broth dilution antifungal susceptibility testing of yeasts—third edition: approved standard (M27–A3). Wayne (PA): The Institute; 2008.
- Clinical and Laboratory Standards Institute. Reference method for broth dilution antifungal susceptibility testing of yeasts: fourth informational supplement (M27–S4). Wayne (PA): The Institute; 2012.
- Lockhart SR, Etienne KA, Vallabhaneni S, Farooqi J, Chowdhary A, Govender NP, et al. Simultaneous emergence of multidrug-resistant *Candida auris* on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. *Clin Infect Dis*. 2017;64:134–40. <http://dx.doi.org/10.1093/cid/ciw691>
- Welsh RM, Bentz ML, Shams A, Houston H, Lyons A, Rose LJ, et al. Survival, persistence, and isolation of the emerging multidrug-resistant pathogenic yeast *Candida auris* on a plastic health care surface. *J Clin Microbiol*. 2017;55:2996–3005. <http://dx.doi.org/10.1128/JCM.00921-17>

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***Borrelia miyamotoi* Disease in an Immunocompetent Patient, Western Europe**

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Borrelia miyamotoi disease is a hard tick-borne relapsing fever illness that occurs across the temperate climate zone. Human *B. miyamotoi* disease in immunocompetent patients has been described in Russia, North America, and Japan. We describe a case of *B. miyamotoi* disease in an immunocompetent patient in western Europe.

A 72-year-old woman in the Netherlands sought treatment in her third day of fever ($\leq 38.6^{\circ}\text{C}$) and reported myalgia, arthralgia, headache, and a 2.5-kg weight loss. Three weeks earlier she had noticed a tick bite after gardening. Several days later, an erythematous lesion appeared, increasing to palm size within 1.5 weeks and dissolving in a similar period. Full medical history was not

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suggestive of other causes of fever. Her previous medical history included cervical carcinoma and breast cancer, curatively treated.

Physical examination showed a moderately ill patient with a temperature of 36.7°C, heart rate of 59 bpm, blood pressure of 100/72 mmHg, an erythematous skin lesion (1.5 cm in diameter) on the thigh, and mild generalized lymphadenopathy. Initial laboratory tests revealed increased C-reactive protein (22.7 mg/L), leukopenia (2.1×10^9 cells/L), elevated monocytes (11%), and thrombocytopenia (144×10^9 platelets/L) (reference ranges in online Technical Appendix Table 1, <https://wwwnc.cdc.gov/EID/article/24/9/18-0806-Techapp1.pdf>). All other test results, including urinalysis, were unremarkable. Molecular tests of blood and skin biopsy and serologic testing for *Borrelia burgdorferi* sensu lato and syphilis were repeatedly negative, except for a C6 EIA IgM/IgG seroconversion (Immunitics, Boston, MA, USA) in convalescent-phase serum samples that was positive but could not be confirmed by either IgM or IgG immunoblot (Mikrogen, Neuried, Germany) (online Technical Appendix Table 2). We did not admit the patient to the hospital, and we did not initiate antimicrobial drug treatment because her symptoms had largely resolved. At a 2-month follow-up visit, the patient had fully recovered, and laboratory test results were normal.

On the basis of the patient's description, we suspect that she was bitten by an *Ixodes ricinus* tick, the most prevalent tick species in western Europe (1), which can potentially

carry several tickborne pathogens: *Borrelia burgdorferi* s.l., *B. miyamotoi*, *Rickettsia helvetica* and *R. monacensis*, *Anaplasma phagocytophilum*, *Babesia divergens* and *B. microti*, *Neoehrlichia mikurencis*, and tick-borne encephalitis virus (2). Specific molecular and serologic diagnostic tests for all of these pathogens were negative, except for 1 (false-positive) tick-borne encephalitis virus IgM ELISA result in convalescent-phase serum samples (online Technical Appendix Table 2).

B. miyamotoi, a relapsing fever *Borrelia* species uniquely found in *Ixodes* spp. ticks in Eurasia and North America, is the causative agent of *Borrelia miyamotoi* disease (BMD), a tickborne febrile disease (3,4). Diagnosis of BMD relies on detection of spirochetes by quantitative PCR of blood and experimental serology based on glycerophosphodiester phosphodiesterase (GlpQ) antigen detection (3,5). GlpQ is present in relapsing fever *Borrelia* but not in *B. burgdorferi* s.l. and therefore can discriminate between the 2 types (4). In a well-described cohort of PCR-positive patients in Russia, characteristic clinical symptoms were fever, myalgia, nausea, and headaches; laboratory findings showed thrombocytopenia and diffuse organ damage (3).

In this patient, results of pan-relapsing fever *Borrelia* PCR and *B. miyamotoi*-specific PCR (6) of blood drawn at the day of clinical visit were negative. However, the fever and symptoms had subsided, which probably impeded these direct diagnostic tests. We tested for anti-GlpQ and anti-variable major proteins (Vmps) IgM and IgG using ELISA

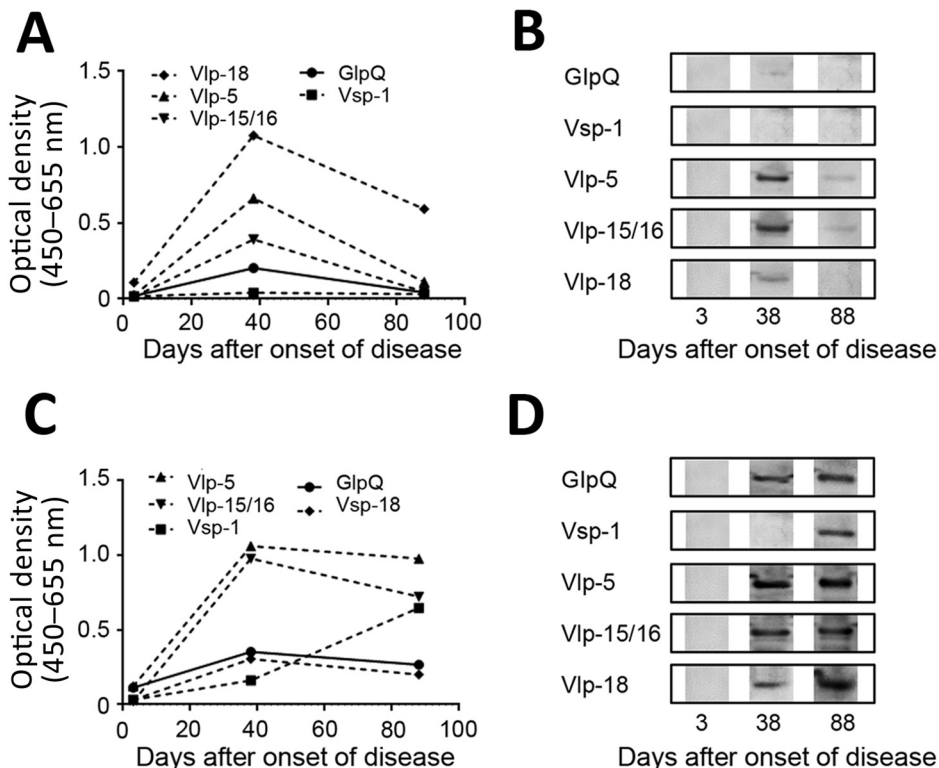


Figure. Results of GlpQ and variable major proteins (Vmps) IgM and IgG ELISA and confirmatory Western blot tests in testing of a 72-year-old woman in the Netherlands who showed evidence of *Borrelia miyamotoi* disease.

A) Anti-GlpQ and anti-Vmps IgM ELISA results representative of 3 individual ELISAs.

B) Confirmatory IgM Western blot results of samples taken at 3 different time points with recombinant proteins.

C) Anti-GlpQ and anti-Vmps IgG ELISA results representative of 3 individual ELISAs.

D) Confirmatory IgG Western blot results of samples taken at 3 different time points with recombinant proteins. GlpQ, glycerophosphodiester phosphodiesterase; Vlp, variable large protein; Vsp, variable small protein.

and Western blot in serum samples taken on the day of the hospital visit (3 days after disease onset), after 5 weeks (38 days), and after 3 months (88 days). Results demonstrated a clear seroconversion for predominantly IgG against GlpQ (Figure). We had previously shown that Vmps are highly immunogenic in patients with BMD (7) and that the presence of antibodies against GlpQ combined with antibodies against Vmps had 100% specificity for IgM and 98.3% for IgG (8). In this case, we could demonstrate antibodies against multiple Vmps over time (Figure). Finally, our findings were further confirmed by preferential IgM and IgG reactivity to lysates of the *B. miyamotoi* strain HT31 (tick isolate, Japan) and Izh-16 (clinical isolate, Russia) compared with reactivity to the *B. afzelii* strain PKo (skin isolate, Germany) and *B. hermsii* HS-1 (tick isolate, United States) control lysates (online Technical Appendix Figure).

These findings, combined with the established presence of *B. miyamotoi* in *I. ricinus* ticks throughout Europe, clinical presentation, and laboratory findings, strongly suggest that *B. miyamotoi* was the causative agent of the patient's symptoms. That the patient recovered even without antimicrobial treatment is consistent with a recent BMD case described in the United States (9). Because of the initial skin rash, we did not completely rule out *B. burgdorferi* s.l. co-infection; however, prior evaluation by an independent dermatologist, a negative *B. burgdorferi* s.l. immunoblot despite high C6 reactivity, and a negative PCR on DNA obtained from the skin biopsy argue against co-infection. Regardless, the clinical picture of fever and mild leukopenia and thrombocytopenia is compatible with BMD and not with Lyme borreliosis. Of interest, C6 reactivity in combination with a negative *B. burgdorferi* s.l. immunoblot has been described in BMD patients in the United States (10).

This case identifies *B. miyamotoi* as an emerging tickborne pathogen in western Europe. Because of the widespread presence of multiple other tickborne pathogens across Europe, more attention and awareness for other tickborne diseases is warranted.

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Dr. Hoornstra and Dr. Koetsveld are PhD students at the University of Amsterdam at the Department of Infectious Diseases in Professor Joppe W. Hovius's laboratory. They focus on tickborne pathogens, and their work has been key in research on *B. miyamotoi* disease.

References

1. Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JW, et al. Lyme borreliosis. *Nat Rev Dis Primers*. 2016;2:16090. <http://dx.doi.org/10.1038/nrdp.2016.90>.
2. Michelet L, Delannoy S, Devillers E, Umhang G, Aspan A, Juremalm M, et al. High-throughput screening of tick-borne pathogens in Europe. *Front Cell Infect Microbiol*. 2014;4:103. <http://dx.doi.org/10.3389/fcimb.2014.00103>
3. Platonov AE, Karan LS, Kolyasnikova NM, Makhneva NA, Toporkova MG, Maleev VV, et al. Humans infected with relapsing fever spirochete *Borrelia miyamotoi*, Russia. *Emerg Infect Dis*. 2011;17:1816–23. [10.3201/eid1710.101474](https://doi.org/10.3201/eid1710.101474) <http://dx.doi.org/10.3201/eid1710.101474>
4. Molloy PJ, Telford SR III, Chowdri HR, Lepore TJ, Gugliotta JL, Weeks KE, et al. *Borrelia miyamotoi* disease in the northeastern United States: a case series. *Ann Intern Med*. 2015;163:91–8. <http://dx.doi.org/10.7326/M15-0333>
5. Krause PJ, Narasimhan S, Wormser GP, Rollend L, Fikrig E, Lepore T, et al. Human *Borrelia miyamotoi* infection in the United States. *N Engl J Med*. 2013;368:291–3. <http://dx.doi.org/10.1056/NEJMc1215469>
6. Hovius JW, de Wever B, Sohne M, Brouwer MC, Coumou J, Wagemakers A, et al. A case of meningoencephalitis by the relapsing fever spirochaete *Borrelia miyamotoi* in Europe. *Lancet*. 2013;382:658. [http://dx.doi.org/10.1016/S0140-6736\(13\)61644-X](http://dx.doi.org/10.1016/S0140-6736(13)61644-X)
7. Wagemakers A, Koetsveld J, Narasimhan S, Wickel M, Deponte K, Bleijlevens B, et al. Variable major proteins as targets for specific antibodies against *Borrelia miyamotoi*. *J Immunol*. 2016;196:4185–95. <https://dx.doi.org/10.4049/jimmunol.1600014>
8. Koetsveld J, Kolyasnikova NM, Wagemakers A, Stukolova OA, Hoornstra D, Sarkysyan DS, et al. Serodiagnosis of *Borrelia miyamotoi* disease by measuring antibodies against GlpQ and variable major proteins. *Clin Microbiol Infect*. 2018; S1198-743X(18)30215-5.
9. Sudhinda P, Wang G, Schriefer ME, McKenna D, Zhuge J, Krause PJ, et al. Insights into *Borrelia miyamotoi* infection from an untreated case demonstrating relapsing fever, monocytosis and a positive C6 Lyme serology. *Diagn Microbiol Infect Dis*. 2016;86:93–6. <http://dx.doi.org/10.1016/j.diagmicrobio.2016.06.015>
10. Molloy PJ, Weeks KE, Todd B, Wormser GP. Seroreactivity to the C6 peptide in *Borrelia miyamotoi* infections occurring in the northeastern United States. *Clin Infect Dis*. 2018;66:1407–10. <http://dx.doi.org/10.1093/cid/cix1023>. <http://dx.doi.org/10.1093/cid/cix1023>

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Borrelia miyamotoi Disease in an Immunocompetent Patient, Western Europe

Technical Appendix

Technical Appendix Table 1. Laboratory results for patient with *Borrelia miyamotoi* disease*

Test	Result	Normal range
Chemistry		
C-reactive protein, mg/L	22.7	0–5
Creatinine, umol/L	78	65–95
AST, U/L	34	0–40
ALT, U/L	23	0–34
γ-GT, U/L	16	0–40
Alkaline phosphatase, U/L	56	40–120
LDH, U/L	228	0–247
Total bilirubin, umol/L	6	0–17
Creatine phosphate kinase, U/L	77	0–145
Hematology		
Erythrocyte sedimentation rate, mm/h	2	0–30
Leukocyte, /L	2.1 × 10⁹	4–10.5 × 10 ⁹
Monocytes, %	11	2–9
Hemoglobin, mmol/L	8.2	7.5–10
Platelet count, /L	144 × 10⁹	150–400 × 10 ⁹

*Laboratory findings at initial visit. Bold indicates values outside the normal range. AST, aspartate transaminase; ALT, alanine transaminase; γ-GT, gamma-glutamyl transferase; LDH, lactate dehydrogenase.

Technical Appendix Table 2. Specific testing for tickborne infectious diseases*

Test	Result	Time point, d†
<i>Borrelia burgdorferi</i> s.l.		
Serology (C6-EIA IgM/IgG)‡	Neg/ Pos/Pos	3 + 38 + 88
Lyme-index	NA/11.33/4.14	3 + 38 + 88
Western blot IgM and IgG§	Neg/Neg/Neg	3 + 38 + 88
<i>Rickettsia</i> spp.		
Serology (IFA IgM/IgG)	Neg/Neg	3 + 38
<i>R. conorii</i>	Neg/Neg	3 + 38
<i>R. typhi</i>	Neg/Neg	3 + 38
PCR	Neg	3
<i>Neoehrlichia mikurensis</i>		
PCR	Neg	3
<i>Anaplasma phagocytophilum</i>		
Serology (IFA IgM/IgG)	Neg/Neg	3 + 38
PCR	Neg	3
Tick-borne encephalitis virus		
Serology (IgM)	Neg/Weak Pos/Weak Pos¶	3 + 38 + 88
(IgG)	Neg/Neg/Neg	3 + 38 + 88
PCR	Neg	3
<i>Babesia</i> spp.		
Serology (IFA IgM/IgG)#		
<i>B. microti</i>	Neg/Neg	3 + 38
PCR <i>B. microti</i>	Neg	3

*Results of conventional diagnostic tests for tick-borne infectious diseases. Bold indicates positive result. Serologic diagnostic tests for other tickborne pathogens routinely used for clinical purpose in the Netherlands were performed at either the Dutch National Institute for Public Health and the Environment (RIVM) or Erasmus Medical Center in Rotterdam. EIA, enzyme immunoassay; IFA, immunofluorescence assay.

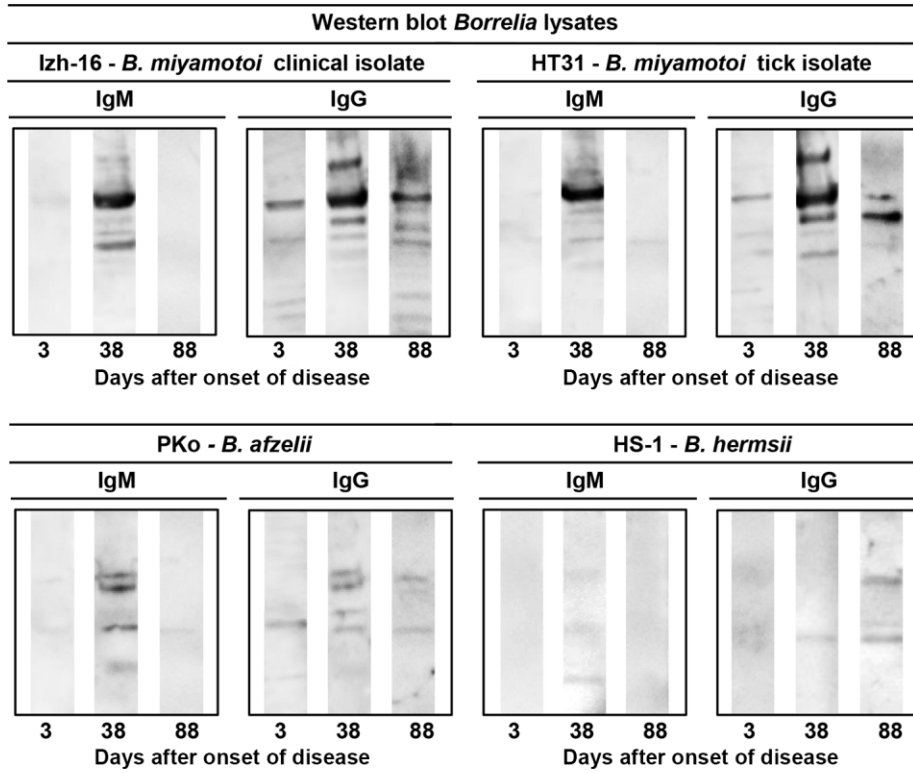
†No. of days after onset of disease.

‡Immunetics (www.immunetics.com)

§Mikrogen (www.mikrogen.de)

¶This was interpreted as a false-positive result because of the lack of dynamics and specific IgG antibodies.

#Fluorescence microscopy.



Technical Appendix Figure. Western blot results of IgM and IgG reactivity for *Borrelia* lysates. Depicted is reactivity against the clinical isolate of Izh-16 strain of *Borrelia miyamotoi*, tick isolate of HT31 strain of *B. miyamotoi*, skin isolate of PKo strain of *B. afzelii*, and tick isolate of HS-1 strain of *B. hermsii*.