



HAL
open science

Atypical *Borrelia garinii* infection in an immunocompromised patient mimicking high-grade lymphoma

Victor Eiferman, Guillaume Le Guenno, Nathalie Boiret-Dupré, Bertrand Barres, Léa Luciani, Pierre Edouard Fournier

► **To cite this version:**

Victor Eiferman, Guillaume Le Guenno, Nathalie Boiret-Dupré, Bertrand Barres, Léa Luciani, et al.. Atypical *Borrelia garinii* infection in an immunocompromised patient mimicking high-grade lymphoma. *International Journal of Infectious Diseases*, 2022, 121, pp.102-104. 10.1016/j.ijid.2022.04.062 . hal-03678801

HAL Id: hal-03678801

<https://amu.hal.science/hal-03678801v1>

Submitted on 22 Jul 2024

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 - NonCommercial 4.0 International License

1 **Title: Atypical *Borrelia garinii* infection in an immunocompromised patient mimicking**
2 **high grade lymphoma**

3 Author list : Victor Eiferman^{1,2}, Guillaume Le Guenno³, Nathalie Boiret-Dupré⁴, Bertrand

4 Barres⁵, Léa Luciani⁶, Pierre Edouard Fournier^{1,2}

5 Affiliations:

6 ¹ Aix-Marseille Univ, IRD, APHM, SSA, VITROME, IHU-Méditerranée Infection, Marseille,
7 France

8 ² IHU-Méditerranée Infection, Marseille, France

9 ³ Service de médecine interne, CHU Estaing, Clermont-Ferrand, France

10 ⁴ Service d'Hématologie biologique, CHU Estaing, Clermont-Ferrand, France

11 ⁵ Service de radio-nucléaire, Centre Jean Perrin, Clermont-Ferrand

12 ⁶ Laboratoire de microbiologie, IHU-Méditerranée Infection, APHM, Marseille, France

13

14 **Corresponding author:** Victor Eiferman (victor.eiferman@gmail.com), Institut Hospitalo
15 Universitaire Méditerranée Infection, 19-21 Boulevard Jean Moulin, Marseille 13385 Cedex
16 05, France.

17

18 **Keywords:** *Borrelia garinii*; spirochete; immunocompromised; *Borrelia burgdorferi* com-
19 plex; lymphoma; PCR16s

20

21 **Abstract**

22 We report an atypical *Borrelia garinii* infection in an immunocompromised patient. It was
23 first suspected as a transformation of follicular lymphoma into high-grade lymphoma.

24 Spirochetes were directly observed on a peripheral blood smear and the diagnosis was

25 confirmed using molecular methods. The clinical presentation and the diagnosis are unique
26 and contrast with the cases described in the literature in immunocompromised patients.

27

28

29 **Case report**

30 A 67-year-old woman was hospitalized in the internal medicine department of the University
31 Hospital of Clermont-Ferrand (France) for general asthenia for 4 months, associated with a
32 weight loss of 5 kilograms, a fluctuating biological inflammatory syndrome (C-reactive pro-
33 tein oscillating between 50 and 150 mg/L) and progressive bi-cytopenia (hemoglobin from
34 129g/L to 82g/L despite erythropoietin therapy and thrombocytopenia of 200G/l to 80 G/l).

35 Her medical history included a refractory phenotype B follicular lymphoma evolving for four
36 years, at stage IV according to Ann Arbor classification. Diagnosis was initially performed on
37 a cervical lymph node showing a follicular lymphoid proliferation (CD20, BCL2, BCL 6, CD
38 10 positive; cyclin D1 expression negative). The fluorescent in situ hybridization (FISH) for t
39 (14;18) (q32; q21) translocation was positive. She had successively benefited several lines of
40 chemotherapy (6 cycles of R-CHOP, 4 cycles of R-DHAC, 6 cycles of Obinituzumab-
41 Bendamustine, 5 cycles of Revlimid-Rituximab and ultimately Idelalisib) and CAR-T cell
42 therapy was considered.

43 On admission, the body temperature was 38.4°C and blood pressure 108/62 mmHg. She pre-
44 sented with irregular tachycardia at 106 beats per minute and numerous supra-centimetric
45 cervical, supra-clavicular and inguinal enlarged lymph nodes without splenomegaly. At ad-
46 mission, the biological tests showed hyperleukocytosis (white blood cells 13.000/ μ L), an in-
47 flammatory syndrome (CRP 143mg/L), bi-cytopenia (hemoglobin 7.2 g/dL and thrombocyto-
48 penia, 47g/L) and severe hypogammaglobulinemia at 1.5g/dL. Compared to the one per-
49 formed six months before, the 18F fluorodeoxyglucose positron emission tomogra-

50 phy/computed tomography (18F – FDG PET.CT) showed a global regression of the previous-
51 ly known mediastinal and subdiaphragmatic lymph node hypermetabolism but new hyperme-
52 tabolism of right supraclavicular lymph nodes. We suspected a transformation of her lym-
53 phoma into high-grade lymphoma, but histological examination of a cervical lymph node did
54 not reveal any evidence of transformation and a bone marrow biopsy ruled out the presence of
55 lymphomatous cells.

56 Finally, the diagnosis of borreliosis was suspected by the presence of spiral-shaped bacteria
57 on a routine blood smear (Figure 1). However, serology for Lyme disease was negative using
58 the enzyme-linked immunosorbent assay *Borrelia* spp (LIAISON, DiaSorin, Salluggia, Italy)
59 and Western Blot Lymecheck optima assay (Biosynex, Illkirch-Graffenstaden, France). Pol-
60 ymerase chain reaction (PCR) was performed following DNA extraction from the blood using
61 the EZ1 DNA Tissue kit and an EZ1 XL automaton (Qiagen, Courtabeuf, France). The previ-
62 ously described pan-*Borrelia* real-time PCR assay targeting the 16SrRNA gene was positive
63 (Socolovschi et al., 2012). Sequencing of the PCR produced a sequence exhibiting a 99.4%
64 sequence identity with *Borrelia garinii* (deposited in GenBank under Accesion number
65 MZ329768.1). This identification was confirmed by amplifying and sequencing the 16S-23S
66 rRNA spacer (99.8% identity) as previously described (Mediannikov et al., 2013; Prudent et
67 al., 2018). Other PCR for tick-borne pathogens including *Babesia*, *Bartonella*, *Anaplasma*,
68 *Ehrlichia* and, *Rickettsia* were negative. Subsequently, other specimens were tested by qPCR
69 for *Borrelia*. The bone marrow biopsy was weakly positive, and the cervical lymph node bi-
70 opsy was negative.

71 The patient was treated with doxycycline 200 mg once daily for 28 days and dramatically
72 improved. Spirochetes disappeared from blood smears, C-reactive protein level and blood cell
73 count were within the normal range on day 7 of treatment. Nonetheless, lymphadenopathies
74 remained unchanged six monthes after treatment.

75

76

77 **Discussion**

78 *Borrelia garinii* belongs to the group of *Borrelia burgdorferi sensu lato* (Baranton et al.,
79 1992). It is one of the two predominant Lyme disease-causing species in Europe (Strnad et
80 al., 2017). The patient did not report any tick bites but lived in a rural area near a forest in
81 central France where Lyme disease is endemic.

82 This case presents two unusual aspects. First, the patient developed an original clinical
83 presentation mimicking high-grade lymphoma transformation whereas *Borrelia garinii*
84 infection usually presents as a classical Lyme disease with a neurological tropism (Steere et
85 al., 2016; Strle and Stanek, 2009). In literature, immunocompromised patients present more
86 disseminated erythema migrans with multiple lesions or extra-cutaneous manifestation
87 (Maraspin et al., 2019, 2006). Neuroborreliosis is difficult to diagnose in these patients,
88 especially those receiving rituximab; indeed, serology is often negative due to their
89 hypogammaglobulinemia: PCR is then crucial for the diagnosis (Harrer et al., 2007; van Dop
90 et al., 2013; Wagemakers et al., 2018).

91 The second characteristic of this case is, unlike Tick-borne Relapsing Fever *Borrelia* species,
92 spirochete visualization on blood smears is very rare for members of the *Borrelia burgdorferi*
93 complex (except for *Borrelia mayonii*), which testifies to the intensity of the bacterial load in
94 this patient, estimated at 4 bacteria per 1000 erythrocytes (Jakab et al., 2022; Pritt et al.,
95 2016). *Borrelia garinii* can nevertheless be isolated in blood culture (in ~1% of cases) and
96 particularly in patients treated with Rituximab (Maraspin et al., 2019). The patient's
97 immunosuppressed status may have favoured a high-grade bacteremia and the spread of the
98 infection. In addition, the identification of the *Borrelia* on a bone marrow biopsy may explain
99 the cytopenias.

100 It is difficult to date the infection, but the role of *B. garinii* in the genesis or as a trigger for
101 the recurrence or aggravation of lymphoma cannot be excluded (Melenotte et al., 2020;
102 Schöllkopf et al., 2008).

103

104 **Declaration of Competing Interest:** The authors declare that they have no conflict of inter-
105 est.

106 **Funding information:** This research did not receive any specific grant from funding agencies
107 in the public, commercial, or not-for-profit sectors.

108 **Ethics:** Written informed consent was obtained from the patient for publication of this case
109 report

110 **Bibliographic references**

- 111 Baranton, G., Postic, D., Saint Girons, I., Boerlin, P., Piffaretti, J.C., Assous, M., Grimont, P.A.,
112 1992. Delineation of *Borrelia burgdorferi* sensu stricto, *Borrelia garinii* sp. nov., and group
113 VS461 associated with Lyme borreliosis. *Int. J. Syst. Bacteriol.* 42, 378–383.
114 <https://doi.org/10.1099/00207713-42-3-378>
- 115 Harrer, T., Geissdörfer, W., Schoerner, C., Lang, E., Helm, G., 2007. Seronegative Lyme neu-
116 roborreliosis in a patient on treatment for chronic lymphatic leukemia. *Infection* 35, 110–
117 113. <https://doi.org/10.1007/s15010-007-6121-0>
- 118 Jakab, Á., Kahlig, P., Kuenzli, E., Neumayr, A., 2022. Tick borne relapsing fever - a systematic
119 review and analysis of the literature. *PLoS Negl. Trop. Dis.* 16, e0010212.
120 <https://doi.org/10.1371/journal.pntd.0010212>
- 121 Maraspin, V., Bogovič, P., Rojko, T., Ružić-Sabljić, E., Strle, F., 2019. Erythema Migrans:
122 Course and Outcome in Patients Treated With Rituximab. *Open Forum Infect. Dis.* 6, ofz292.
123 <https://doi.org/10.1093/ofid/ofz292>
- 124 Maraspin, V., Cimperman, J., Lotric-Furlan, S., Logar, M., Ruzic-Sabljić, E., Strle, F., 2006. Ery-
125 thema Migrans in Solid-Organ Transplant Recipients. *Clin. Infect. Dis.* 42, 1751–1754.
126 <https://doi.org/10.1086/504384>
- 127 Mediannikov, O., Abdissa, A., Socolovschi, C., Diatta, G., Trape, J.-F., Raoult, D., 2013. Detec-
128 tion of a New *Borrelia* Species in Ticks Taken from Cattle in Southwest Ethiopia. *Vector-*
129 *Borne Zoonotic Dis.* 13, 266–269. <https://doi.org/10.1089/vbz.2011.0874>
- 130 Melenotte, C., Mezouar, S., Mège, J.-L., Gorvel, J.-P., Kroemer, G., Raoult, D., 2020. Bacterial
131 infection and non-Hodgkin's lymphoma. *Crit. Rev. Microbiol.* 46, 270–287.
132 <https://doi.org/10.1080/1040841X.2020.1760786>
- 133 Pritt, B.S., Mead, P.S., Johnson, D.K.H., Neitzel, D.F., Respicio-Kingry, L.B., Davis, J.P., Schiff-
134 man, E., Sloan, L.M., Schriefer, M.E., Replogle, A.J., Paskewitz, S.M., Ray, J.A., Bjork, J., Stew-

ard, C.R., Deedon, A., Lee, X., Kingry, L.C., Miller, T.K., Feist, M.A., Theel, E.S., Patel, R., Irish, C.L., Petersen, J.M., 2016. Identification of a novel pathogenic *Borrelia* species causing Lyme borreliosis with unusually high spirochaetaemia: a descriptive study. *Lancet Infect. Dis.* 16, 556–564. [https://doi.org/10.1016/S1473-3099\(15\)00464-8](https://doi.org/10.1016/S1473-3099(15)00464-8)

Prudent, E., La Scola, B., Drancourt, M., Angelakis, E., Raoult, D., 2018. Molecular strategy for the diagnosis of infectious lymphadenitis. *Eur. J. Clin. Microbiol. Infect. Dis. Off. Publ. Eur. Soc. Clin. Microbiol.* 37, 1179–1186. <https://doi.org/10.1007/s10096-018-3238-2>

Schöllkopf, C., Melbye, M., Munksgaard, L., Smedby, K.E., Rostgaard, K., Glimelius, B., Chang, E.T., Roos, G., Hansen, M., Adami, H.-O., Hjalgrim, H., 2008. *Borrelia* infection and risk of non-Hodgkin lymphoma. *Blood* 111, 5524–5529. <https://doi.org/10.1182/blood-2007-08-109611>

Socolovschi, C., Reynaud, P., Kernif, T., Raoult, D., Parola, P., 2012. Rickettsiae of spotted fever group, *Borrelia valaisiana*, and *Coxiella burnetii* in ticks on passerine birds and mammals from the Camargue in the south of France. *Ticks Tick-Borne Dis.* 3, 355–360. <https://doi.org/10.1016/j.ttbdis.2012.10.019>

Steere, A.C., Strle, F., Wormser, G.P., Hu, L.T., Branda, J.A., Hovius, J.W.R., Li, X., Mead, P.S., 2016. Lyme borreliosis. *Nat. Rev. Dis. Primer* 2, 16090. <https://doi.org/10.1038/nrdp.2016.90>

Strle, F., Stanek, G., 2009. Clinical manifestations and diagnosis of lyme borreliosis. *Curr. Probl. Dermatol.* 37, 51–110. <https://doi.org/10.1159/000213070>

Strnad, M., Hönig, V., Růžek, D., Grubhoffer, L., Rego, R.O.M., 2017. Europe-Wide Meta-Analysis of *Borrelia burgdorferi* Sensu Lato Prevalence in Questing *Ixodes ricinus* Ticks. *Appl. Environ. Microbiol.* 83. <https://doi.org/10.1128/AEM.00609-17>

van Dop, W.A., Kersten, M.-J., de Wever, B., Hovius, J.W., 2013. Seronegative lyme neuroborreliosis in a patient using rituximab. *BMJ Case Rep.* 2013. <https://doi.org/10.1136/bcr-2012-007627>

Wagemakers, A., Visser, M.C., de Wever, B., Hovius, J.W., van de Donk, N.W.C.J., Hendriks, E.J., Peferoen, L., Muller, F.F., Ang, C.W., 2018. Case report: persistently seronegative neuroborreliosis in an immunocompromised patient. *BMC Infect. Dis.* 18, 362. <https://doi.org/10.1186/s12879-018-3273-8>

Figure legend

Figure 1: Patient blood smear showing spirochetes

