Did Garin and Bujadoux Actually Report a Case of Lyme Radiculoneuritis?

Gary P. Wormser  
*New York Medical College*

Vanessa Wormser  
*New York Medical College*

Follow this and additional works at: [https://touroscholar.touro.edu/nymc_fac_pubs](https://touroscholar.touro.edu/nymc_fac_pubs)

Part of the *Infectious Disease Commons*

**Recommended Citation**  
Wormser, G. P., & Wormser, V. (2016). Did Garin and Bujadoux actually report a case of lyme radiculoneuritis? Open Forum Infectious Diseases, 3(2), ofw085. doi:10.1093/ofid/ofw085

This Article is brought to you for free and open access by the Faculty at Touro Scholar. It has been accepted for inclusion in NYMC Faculty Publications by an authorized administrator of Touro Scholar. For more information, please contact touro.scholar@touro.edu.
Did Garin and Bujadoux Actually Report a Case of Lyme Radiculoneuritis?

Gary P. Wormser and Vanessa Wormser
Division of Infectious Diseases, New York Medical College, Valhalla

A 1922 report by Garin and Bujadoux is widely regarded as describing the first case of neurologic Lyme borreliosis. Although the patient reported had a tick bite followed by the development of a rash and radiculoneuritis, there were a number of highly atypical features, raising the question of whether the patient, in fact, had neurologic Lyme borreliosis. The paper may not deserve the historic recognition that it has received.

Keywords. Borrelia; Lyme disease; meningitis; radiculitis; syphilis.

Lyme borreliosis is an infectious disease caused by various species of Borrelia. Clinical manifestations may involve the skin, nervous system, heart, and joints. Early neurologic Lyme borreliosis is characterized by meningitis, cranial nerve palsies, or radiculoneuritis that may occur individually or in combination [1–3].

It has been proposed that the first clinical description of Lyme radiculoneuritis was a case report from France that was authored by Garin and Bujadoux [4] in 1922, 60 years before the discovery of the etiologic agent Borrelia burgdorferi sensu lato [5]. In recognition of this seminal publication, the species of Lyme Borrelia most often associated with Lyme neuroborreliosis in Europe was named Borrelia garinii. In addition, the paper was translated into English (except for the abstract) and republished in 1993 in the journal, *Clinical Infectious Diseases*, under the category of publications entitled, "Classic in Infectious Disease" [6].

Over the years, a number of case series of patients with neurologic Lyme borreliosis have been published, allowing a more complete understanding of this clinical entity [7–13]. Information that has emerged about Lyme radiculoneuritis includes the following. (1) When the patient has an erythema migrans skin lesion, it usually precedes development of radicular pain by more than 1 month. (2) The majority of patients do not have a concomitant erythema migrans skin lesion when the neurologic symptoms start. (3) A cerebrospinal fluid pleocytosis is expected, and the vast majority of white cells are lymphocytes, and there may be plasma cells [7,8,10,11,12,14–19]. This is so typical that one of the names for this neurologic condition is lymphocytic radiculoneuritis (Table 1) [2,7,8,11,13–16,19–21]. (4) Cerebrospinal fluid testing for nontreponemal antibody used to diagnose syphilis, for example the Wassermann test, has been uniformly negative in patients with Lyme neuroborreliosis [7]. (5) Meningeal signs are uncommon in neurologic Lyme borreliosis. In a case series of patients from the United States with Lyme meningitis, all of the 38 patients tested had both a negative Kernig’s sign and a negative Brudzinski’s sign [12].

However, the published English translated version of the Garin and Bujadoux paper [6], in conjunction with an independent translation by one of us (V. W.), describes a number of findings that run counter to what would be expected if the patient reported actually had neurologic Lyme borreliosis. Relevant aspects of the case described include the following.

The patient was a 58-year-old married man who was a sheep farmer in France and had previously served in the military in Algeria where he had dysentery and malaria. On June 14, 1922, he was bitten by what the authors called an *Ixodes hexagonus* tick on his left buttock that he found and removed. Three weeks later, he developed left buttock pain as well as radicular pain along the left sciatic nerve. An approximately 3-cm diameter tender erythematous ring lesion was observed on the left buttock with a punctum in the center. Left inguinal lymphadenopathy was also present. Over an undefined period of time, the skin lesion expanded over the entire left buttock. The skin lesion also extended into the right buttock, to the base of the spine, and involved the left thigh all the way down to the knee. In addition, it extended to the hypochondrium. Which hypochondrium was not specified, but even if it only extended to the left hypochondrium, the skin lesion was, by any estimate, enormous (if it was a single lesion).

Radiculitis symptoms became multifocal. By September 16, 1922, additional physical findings included right posterior...
cervical lymphadenopathy (ie, at a site distant from the skin lesion) and paralysis of the right deltoid muscle with atrophy.

From September 20, 1922 to October 11, 1922, the patient received 4 injections of neosarsphenamine and 3 injections of mercury cyanide. Coincident with this treatment, the “excruciating” pains subsided.

On October 3, 1922, the Kernig’s sign was elicited, and the patient underwent a lumbar puncture that day. Cerebrospinal fluid testing showed an increased protein level of >1.3 g/L and 75 white cells, the majority of which were neutrophils (of note, the published English translation of the Garin and Bujadoux [6] paper erroneously stated that there were 75 lymphocytes). The Wassermann reaction was weakly positive.

Garin and Bujadoux [4, 6] thought that their patient had tick paralysis. However, this diagnosis was clearly incorrect, because the paralysis in this condition is painless, occurs while the tick is attached, and is often dramatically relieved by removing the tick [22]. However, at the same time, these authors did believe that their patient was infected with a microorganism that had invaded the nervous system, and without giving any explanation as to why, they specifically mentioned that a spirochete was the most likely cause. Although these physicians ordered syphilis testing on the cerebrospinal fluid (of note, for a period of time in the history of syphilis, the etiological agent was not believed to be a spirochete, which is the reason why the name was changed to Treponema pallidum from the original name Spirochaeta pallida [23]) and obtained a positive result for the Wassermann test, and although they treated the patient with medications often used to treat syphilis in the pre-antibiotic era and he improved, the authors did not feel that he had clinical signs of syphilis. They regarded the positive Wassermann test in the cerebrospinal fluid sample as falsely positive, which, although rare [24], does occur [25–28]. Nevertheless, and of potential relevance to at least considering the diagnosis of neurosyphilis for this patient is that a neutrophil predominance in cerebrospinal fluid was observed in 69 (40.1%) of the 172 patients with neurosyphilis who had a pleocytosis of at least 5 white cells/mL in a large case series antedating the acquired immune deficiency syndrome epidemic [29].

Numerous publications have since concluded that the patient had Lyme borreliosis, without mentioning the atypical features [6, 7, 11, 13]. Table 2 compares certain of the findings found in this patient with what has been reported in patients diagnosed with neurologic Lyme borreliosis [4, 6, 7, 8, 10–13]. (Personal communication D. Tveitnes 12/17/15). The differences seem substantive enough to raise concerns over whether the patient described by Garin and Bujadoux [4], in fact, had neurologic Lyme borreliosis. However, the apparent beneficial effect of arsenic treatment in the reported patient may not diminish the likelihood that he might have had Lyme borreliosis, because anecdotal data in patients who presumably had erythema migrans do suggest that this treatment might be beneficial [30].

In addition, it is of interest to note that the patient was apparently not bitten by an Ixodes ricinus tick (the tick that most commonly transmits Lyme borreliosis in Europe) but instead by the I hexagonus tick. Ixodes hexagonus ticks do sometimes bite humans and have been established experimentally to be a competent vector for Lyme borreliosis and for tick-borne encephalitis virus [31–36]. In addition, I hexagonus ticks in nature may be infected with Lyme Borrelia, tick-borne encephalitis virus, and other infectious agents [35, 37–39]. However, to our knowledge, there has never been a well-documented case

Table 1. Some of the Terms Used for Lyme Neuroborreliosis Involving Nerve Roots (Additional Names for This Entity Can be Found in [19])

| Name | Illustrative Reference |
|------|------------------------|
| Painful, lymphocytic meningoradiculitis | [7] |
| Bannwarth’s syndrome | [7] |
| Bannwarth’s meningopolyneuritis | [8] |
| Meningopolyneuritis Garin-Bujadoux-Bannwarth | [9] |
| Garin-Bujadoux-Bannwarth syndrome | [14] |
| Lymphocytic meningoradiculitis | [15] |
| Meningoradiculoneuritis | [20] |
| Lyme meningoradiculitis | [16] |
| Painful meningoradiculitis | [21] |
| Painful spinal meningoradiculitis | [13] |
| Meningoradiculitis spinalis | [13] |
| Tick-borne meningopolyneuritis | [11] |

Table 2. Comparison of the Case Reported by Garin and Bujadoux With Reported Case Series of NLB

| Characteristic | Garin and Bujadoux [4, 6] | NLB [Reference] |
|---------------|---------------------------|-----------------|
| EM and radiculitis begin simultaneously | Yes | Not typical* [7, 11, 13] |
| CSF pleocytosis with neutrophil predominance | Yes | A neutrophil predominant CSF pleocytosis was not explicitly mentioned for any of 187 consecutive patients in one European study [7], or in any of 100 patients in a separate European study [11]. In another report, at least 40 of 41 patients had a mononuclear CSF pleocytosis [8]. In a European study of 139 children with Lyme meningitis, a neutrophil predominance in CSF was found only once [10]. (Personal communication D. Tveitnes 12/17/15). |
| CSF with a positive Wassermann test | Yes | 0 of 187 [7] |
| Positive Kernig’s sign | Yes | 0 of 38 in a study from the United States [12] |

Abbreviations: CSF, cerebrospinal fluid; EM, erythema migrans; NLB, neurologic Lyme borreliosis.

* The time period between the onset of EM and the development of radiculitis has been estimated to vary from the following: a median of 8 days (range, 0–95 days) [13], a median of 19 days (range, 0–95 days) [7]; a mean of at least 3½ weeks [11].
in which a patient developed an erythema migrans lesion due to Lyme borreliosis after the bite of an I hexagonus tick. Thus, if the case reported by Garin and Bujadoux [4, 6] represents the first patient with neurologic Lyme borreliosis, it may also be the first (and perhaps only) established case of Lyme borreliosis to have been transmitted by the bite of an I hexagonus tick.

CONCLUSIONS

In conclusion, if the patient described by Garin and Bujadoux [4] did have neurologic Lyme borreliosis, it was far from a typical case. Whether the paper deserves the historic recognition that it has received may be questionable.

Acknowledgments

We thank Dr. Edouard Vannier, Dr. Sam Telford, Dr. Nancy Joy, Julia Singer, Sophia Less, and Lisa Giarratano for assistance.

Potential conflicts of interest. G. W. reports receiving research grants from Immunetics, Inc., Institute for Systems Biology, Rarecyte, Inc., and Quidel Corporation. G. W. owns equity in Abbott and has been an expert witness in malpractice cases involving Lyme disease. G. W. is also an unpaid board member of the American Lyme Disease Foundation. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2006; 43:1089–134.
2. Hansen K, Crane C, Kristoferitsch W. Lyme neuroborreliosis. Handb Clin Neurol 2013; 115:559–75.
3. Mygland A, Ljostrand U, Fingerle V, et al. EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis. Eur J Neurol 2010; 17:8–16.
4. Garin Ch, Bujadoux. [Paralyse par les tiques]. J Med Lyon 1922; 71:655–7.
5. Burgdorfer W, Barbour AG, Hayes SF, et al. Lyme disease - a tick-borne spirochetosis? Science 1982; 216:1317–9.
6. Garin Ch, Bujadoux A. Paralyse by ticks. 1922. Clin Infect Dis 1993; 16:168–9.
7. Hansen K, Lebecch AM. The clinical and epidemiological profile of Lyme neuroborreliosis in Denmark 1985-1990. A prospective study of 187 patients with Borrelia burgdorferi specific intrathelial antibody production. Brain 1992; 115 (Pt 2):399–423.
8. Kohler J, Thoden U. [Pain syndromes in tick-borne neuroborreliosis. Clinical as aspects and differential diagnosis]. Schmerz 1987; 1:107–13.
9. Kristoferitsch W, Baumhackl U, Sluga E, et al. High-dose penicillin therapy in meningopolyneuritis Garin-Bujadoux-Bannwarth. Clinical and cerebrospinal fluid data. Zentralbl Bakteriol Mikrobiol Hyg A 1987; 263:357–64.
10. Tevittes D, Oymar K. Gender differences in childhood Lyme neuroborreliosis. Behav Neurol 2015;790762.
11. Ackermann R, Horstrup P, Schmidt R. Tick-borne meningopolyneuritis (Garin-Bujadoux-Bannwarth). Yale J Biol Med 1984; 57:484–90.
12. Pachner AR, Steree AC. The trial of neurologic manifestations of Lyme disease: meningitis, cranial neuritis, and radiculoneuritis. Neurology 1985; 35:47–53.
13. Ochssmann P, Dornhoff W, Hornig C, et al. Stages and syndromes of neuroborreliosis. J Neurol 1998; 245:262–72.
14. Stanek G, Fingerle V, Humfeld KP, et al. Lyme borreliosis: clinical case definitions for diagnosis and management in Europe. Clin Microbiol Infect 2011; 17:69–79.
15. Razavi-Encha F, Fleury-Feith J, Gherardi R, Bernaudin JF. Cytologic features of cerebrospinal fluid in Lyme disease. Acta Cytol 1987; 31:439–40.
16. Sinderen E, Malin JP. Phenotypic analysis of cerebrospinal fluid cells over the course of Lyme meningoradiculitis. Acta Cytol 1995; 39:73–5.
17. Jacobsen M, Zhou D, Cepok S, et al. Clonal accumulation of activated CD8+ T-cells in the central nervous system during the early phase of neuroborreliosis. J Infect Dis 2003; 187:963–73.
18. Bannwarth A. Chronische lymphocytare meningitis, entzündliche polynieuritis und rheumatismus. Arch Psychiatr Nervenkr 1941; 113:284–376.
19. Meyer-Rienecker HJ, Hitzscheke B. Lymphocytic meningoradiculitis (Bannwarth’s syndrome). In: Vinken Pj, Bruyn GW, eds. Handbook of Clinical Neurology. Vol 34. Amsterdam, Holland: North Holland Publishing Co; 1978: pp 571–86.
20. Weber K, Pfister HW. Clinical management of Lyme borreliosis. Lancet 1994; 343:1017–20.
21. Rupprecht TA, Koedel U, Fingerle V, Pfister HW. The pathogenesis of Lyme neuroborreliosis: from infection to inflammation. Mol Med 2008; 14:205–12.
22. Felz MW, Smith CD, Swift TR. A six-year-old girl with tick paralysis. N Engl J Med 2000; 342:90–4.
23. White B, Avery OT. The Treponema pallidum: observations on its occurrence and demonstration in syphilitic lesions. Arch Intern Med 1909; 3:411–21.
24. Jaffe HW, Kabins SA. Examination of cerebrospinal fluid in patients with syphilis. Rev Infect Dis 1982; 4:5842–7.
25. Madiedo G, Ho KC, Walsh P. False-positive VDRL and FTA in cerebrospinal fluid. JAMA 1980; 244:688–9.
26. Scott V, Reynolds FW, Mohr CF. Biologic false positive spinal fluid Wassermann reactions associated with meningitis: report of eight cases. Am J Syphilis Gonorrhea Vener Dis 1944; 28:431–42.
27. Quafle RA, Gostling JV. False positive Wassermann reaction associated with evidence of enterovirus infection. J Clin Path 1971; 24:120–1.
28. McLean AJ, Munger IC Jr. False-positive Wassermanns in cerebrospinal fluid. Western J Surgery Obstetrics Gynecol 1938; 46:455–62.
29. Hooshmand H, Escober MR, Kopf SW. Neurosyphilis a study of 241 patients. JAMA 1972; 219:726–9.
30. Hellerstrom S. Erythema chronicum migrans afebris with meningitis. Acta Dermato-Venereolog 1951; 31:237–44.
31. Gern L, Toutouni LN, Min Hu C, Aeschlimann A. Ixodes (Phoeolixodes) hexagonus, an efficient vector of Borrelia burgdorferi in the laboratory. Med Vet Entomol 1993; 1 Decreasing neuroborreliosis. Acta Cytol 1999; 43:1451–5.
32. Gern L, Rouvinez E, Toutouni LN, Godfroid E. Transmission cycles of Borrelia burgdorferi sensu lato involving Ixodes ricinus and/or I. hexagonus ticks and the European hedgehog, Erinaceus europaeus, in suburban and urban areas in Switzerland, Folia Parasitologica (Praga) 1997; 44:309–14.
33. Estrada-Pena A, Jongejan F. Ticks feeding on humans: a review of records on human-biting Ixodidea with special reference to pathogen transmission. Exp Appl Acarol 1999; 23:685–715.
34. Pichot J, Gilot B, Aimire N, et al. Ixodes populations (Ixodes ricinus Linne, 1758; Ixodes hexagonus, Leach, 1815) in the city of Lyon (France) and its outskirts: preliminary results. Parasite 1997; 4:167–71.
35. Faulde MK, Rentenfraz M, Hepke J, et al. Human tick infestation pattern, tick bite rate, and associated Borrelia burgdorferi s.l. infection risk during occupational tick exposure at the Seedorf military training area, Northwestern Germany. Ticks Tick Borne Dis 2014; 5:594–9.
36. Obsomer V, Wirtgen M, Linden A, et al. Spatial disaggregation of tick occurrence and ecology at a local scale as a preliminary step for spatial surveillance of tick-borne diseases: general framework and health implications in Belgium. Parasit Vectors 2013; 6:190.
37. Strube C, Montenegro VM, Epe C, et al. Establishment of a minor groove binder-probe based quantitative real time PCR to detect Borrelia burgdorferi sensu lato and differentiation of Borrelia spielmani by OspA-specific conventional PCR. Parasit Vector 2010; 3:69.
38. Schreiber C, Krucken J, Beck S, et al. Pathogens in ticks collected from dogs in Berlin/Brandenburg, Germany. Parasit Vectors 2014; 7:535.
39. Krawczyk AV, van Leeuwen AD, Jacobs-Reitsma W, et al. Presence of zoonotic agents in engorged ticks and hedgehog faeces from Erinaceus europaeus in (sub) urban areas. Parasit Vectors 2015; 8:210.