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

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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 week. (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).

Radicular pain symptoms became multifocal. By September 16, 1922, additional physical findings included right posterior

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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]

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 neoarsphenamine 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 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 ^a [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.

^a 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, 5–90 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.

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