Nervous System Lyme Disease

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KEYWORDS

• Lyme disease • *Borrelia burgdorferi* • Neuroborreliosis
• Garin-Bujadoux Bannwarth syndrome • Nervous system
• Peripheral nervous system • Central nervous system • Intrathecal antibody

KEY POINTS

- The nervous system is involved in 10% to 15% of patients with untreated *Borrelia burgdorferi* infection. This proportion is similar in Eurasian and North American patients.
- Nervous system infection causes either meningitis or multifocal inflammatory changes in the peripheral nervous system (frequent) or central nervous system (CNS; rare), as shown by objective changes on neurologic examination or other objective tests.
- As in many other systemic infectious and inflammatory states, patients may experience cognitive and memory difficulty; these symptoms do not indicate CNS infection and alone are not diagnostic of Lyme disease.
- Treatment with standard courses of oral antimicrobials cures approximately 95% of patients with neuroborreliosis. Parenteral treatment may be needed in those rare patients with parenchymal CNS involvement but some evidence supports the use of oral therapy in these individuals as well.

INTRODUCTION

"It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity…" These famous opening words of Dickens' *A Tale of Two Cities* aptly describe a great deal of what is currently said about Lyme disease and its effects on the nervous system. Numerous factors contribute to this[1,2]; probably the single most important is that patients, the public in general, and even many physicians struggle with the concept

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of what does and does not constitute nervous system disease. Although nervous system function is essential for all behavior, many things affect behavior in the absence of damage to the nervous system, which is the defining requirement of neurologic disorders. Conditions as diverse as sleep deprivation, sepsis, depression, uremia, psychosis, and learned behaviors can profoundly alter how people function, but none of these necessarily implies the presence of neurologic disease. Because the possibility of neurologic diseases (eg, stroke, Alzheimer, Parkinson) is terrifying to most people, it could be argued that these misconceptions about nervous system Lyme disease, or neuroborreliosis, contribute substantially to the widespread fear of this tick-borne infection, and some patients' and physicians' willingness to use highly unconventional therapies to try to eradicate what is, in reality, a straightforward infection.

HISTORICAL BACKGROUND

Although the term Lyme disease was coined in the 1970s, with the initial reports of nervous system involvement appearing shortly thereafter,[3,4] the first description of neuroborreliosis was published in 1922 in a case report[5] that both was brilliant in its insights and foreshadowed how misunderstandings about the specifics of neurologic diagnosis can result in confusion.

Three weeks following the bite of an *Ixodes* tick on his left buttock, a French sheep farmer developed severe pain at the site of the bite and an erythroderm that expanded to cover the entire buttock, much of the thigh, and the lower abdomen. The distribution of the pain expanded; he developed bilateral sciatica and severe and intractable pain in the trunk and right arm. When evaluated, his examination was normal except for marked right deltoid atrophy and weakness. He had a neutrophilic cerebrospinal fluid (CSF) pleocytosis with increased protein and normal glucose levels. In light of a slightly positive Wasserman test the investigators concluded this was a spirochetosis, but went to great pains to explain why this could not possibly have been syphilis, and treated him with neoarsphenamine (state-of-the-art syphilis treatment in 1922) with rapid resolution of his pain.

Although this case succinctly captured most of the key elements of neuroborreliosis, the investigators' discussion also revealed several logical flaws. In attributing the infection to a spirochetosis, they considered spirochetes to be a type of virus, reflecting the limitations of medical knowledge at that time. They went on to equate this patient's problem with tick bite paralysis; a disorder that occurs while a tick is still attached, not weeks later; is associated with *Dermacentor* ticks, not *Ixodes*; and is not associated with a rash, pain, or a CSF pleocytosis. Such inappropriate linking of superficially similar disorders continues to this day.

As European clinical experience with this illness grew, these misunderstandings were increasingly unimportant. The disorder became known as Garin-Bujadoux (and subsequently Bannwarth) syndrome and by the 1950s was routinely recognized by European neurologists, and treated with penicillin.[6] In the 1970s and 1980s, the essentially identical neurologic syndrome was described in US patients in association with Lyme disease, and similarly found to be responsive to penicillin.[3]

It would be reasonable to assume that there could be little controversy surrounding an illness that has been well characterized for nearly a century and is caused by a known, antibiotic-sensitive microorganism. The more than 10,000 book citations on the subject of Lyme disease at Amazon.com (a number similar to the total published scientific articles listed in Medline in a search on the same day [August 17, 2014]) suggests otherwise.

In summarizing what is known about neuroborreliosis, the goal of this article is to address 4 key fallacies (**Box 1**): (1) that nervous system infection with *Borrelia*