Atypical presentation of Lyme neuroborreliosis related meningitis and radiculitis

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Abstract

Lyme disease related central and peripheral nervous system manifestations can occur in isolation or together. Radiculitis or inflammation of the nerve root can be seen 3-5% of the time in acute neuroborreliosis affecting the PNS with a typical presentation and meningitis affecting the CNS is usually seen 1% of the time. The appropriate diagnosis and management of neuroborelliosis can be challenging and require meticulous medical approaches. Herein we present a unique case of Lyme disease with neurologic manifestations including both radiculitis and meningitis due to its atypical and challenging clinical presentation and management with updated literature review.

Introduction

Lyme disease (LD) and its known pathogen *Borrelia burgdorferi* is an arthropod-born disease transmitted by the *Ixodes* species of ticks commonly seen in the northern hemisphere. Neurological manifestations of LD, first described by Garin and Bujadoux in 1922, have been seen to occur isolated in 12% of acute Lyme cases and may present as early as 2-18 weeks after exposure.[1,2] Central nervous system (CNS) as well as peripheral nervous system (PNS) manifestations can occur in isolation or together.[1-6] PNS involvement of cranial or peripheral nerves is the more common neurological findings and occurs in roughly 10% of infected untreated patients.[1,3,5,6] Radiculitis or inflammation of the nerve root can be seen 3-5% of the time in acute neuroborreliosis affecting the PNS with a typical presentation involving intractable pain, as well as muscle denervation and areflexia over one or a few adjacent dermatomes.[1] Meningitis affecting the CNS is usually seen 1% of the time, these cases may present variable symptoms and patients may rarely develop brain parenchyma or spinal cord inflammation.[1-4] There have been 262,481 confirmed cases of LD in the United States (U.S.) between 2007-2016 though it is believed these numbers are significantly underreported and there may actually be up to 300,000 people diagnosed with LD per year in the U.S.[7-9] Herein, we will discuss a case of LD with CNS and PNS manifestations including radiculitis and meningitis.

Case Report

A 43-year-old man with a past medical history of gout presented to our hospital with one-month history of progressive lower extremity weakness, gait instability, and acute back pain. The patient reported he was subjectively diagnosed with viral meningitis one month prior to presentation to the emergency department (ED) with symptoms at the time including cough, fever, anorexia, malaise, fatigue, myalgias, cervicalgia/neck stiffness with flexion and extension, mild photophobia, headache and two-week history of scaly erythematous macular rash on his proximal medial upper and lower extremities. The patient refused to undergo lumbar puncture at the initial onset of his symptoms and thus a diagnosis of any infectious intracerebral/intrathecal process was never confirmed. At the onset of the patient's symptoms, he had tried over-the-counter analgesics with some relief of his headaches though his generalized pain persisted. He initially underwent extensive laboratory studies at the onset of his symptoms ordered by his primary care physician one month prior to his presentation including rheumatologic evaluation and screening tests for tick-borne infections including Lyme serologies, however they were unremarkable, except for mildly elevated AST 79 and ALT 79, elevated CRP 4.95 mg/dL, and complement C3 227 mg/dL. His symptoms persisted and changed requiring hospital evaluation.

At presentation to our hospital, the patient reported progressive weakness and severe radicular lancinating pain going from his lower back to his heels worse on the right side that is worsened with sitting and supine, emotional lability along with depression and anxiety. He had also noticed occasional action tremor in hands interfering with fine motor tasks, and mentioned feeling tremor in his legs causing imbalance and instability though with no falls. He denied any bowel and bladder dysfunction, although he reported an episode of premature ejaculation a couple weeks prior to presentation.

His neurological exam was normal including strength, sensory, and reflex testing except for an unsteady wide based gait. We obtained a magnetic resonance imaging of lumbar spine with and without contrast that showed slightly thickened enhancement along the surface of the conus medullaris as well as enhancement of the nerve roots of the cauda equina, pronounced degenerative disc disease at L4-L5 with a broad-based disc-osteophyte complex, and mild bilateral facet arthropathy at L4-L5 results in mild-moderate bilateral neural foraminal stenosis as shown in Figure 1. The nerve conduction studies and electromyography of his bilateral lower extremities were normal. A lumbar puncture was performed and the patient's cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis with white blood cell count of 225 and elevated protein of 77 and decreased glucose 38. Ultimately his serum LD Western Blot came back reactive with three IgG proteins and two IgM proteins, and one LD IgM band in CSF also came back positive.

The patient was started on oral doxycycline 100mg BID for 5 days prior to placement of a PICC line for starting the patient on IV ceftriaxone 2g daily for 4 weeks in treatment of Lyme radiculitis and meningitis. On follow up in clinic two and a half weeks after starting medical therapy the patient noted his symptoms were significantly improved including resolution of the pain, weakness, constitutional and affective

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symptoms, while he still had some ambulatory difficulties.

Discussion

Herein we present a unique case of LD with neurologic manifestations including both radiculitis and meningitis due to its atypical and challenging clinical presentation. Classically, this combination of painful radiculoneuritis and lymphocytic pleocytosis in the CSF, often associated with cranial nerve involvement and peripheral paresis is referred to as Bannwarth Syndrome.[10,11] When neuroborreliosis affects the peripheral nervous system, it is believed to be a variant form of a mononeuropathy multiplex syndrome.[1,3]

Consideration of neuroborreliosis in an individual with neurologic complaints requires an understanding of the complex seasonality and transmission of *B burgdoferi* to humans. The nymphal stage of the *Ixodes* tick is when *B burgdoferi* is most likely to be transmitted to humans.[12]A key reason for this is due to the small size of the nymphal ticks (<2mm), which permits the nymphal tick to avoid detection and remain attached to the host, as the minimal period for transmission of an infectious dose of *B burgdoferi* is 2 days.[12] Nymphal ticks become active in early summer starting in mid-May, their activity peaks in activity in June, and then declines during late July. The incubation period between the tick bite and development of LD takes approximately two weeks, thus the onset of LD typically occurs mainly during the summer months of June, July, and August.[13,14] Interestingly, in our case, he was seen at the hospital in July and he developed his initial symptoms in June.

Diagnosis of LD is made using a two-tiered approach to serologic testing for antibodies to *B burgdoferi*. This two-tiered approach entails an initial Enzyme-Linked Immunosorbent Assay (ELISA) followed by a Western Blot test and is highly sensitive and specific for diagnosis of LD. It typically takes 4-6 weeks of infection with *B Burgdoferi* for the immune system to develop antibodies detectable on serologic testing. This was recognized in our case, when anti-Borrelia antibodies were not initially present in the serum when tested at the time the patient first developed symptoms one month prior to presentation to the hospital, however were observed on serologic testing during his hospital admission. Typically, CSF analysis shows a lymphocytic predominant pleocytosis, though monocytes may be present as well. The pleocytosis will have a median white blood cell count of 160cells/microL.[15] Additionally, there is moderately elevated protein with an upper limit of 200-300 mg/dL, and usually the glucose is normal. Neuroborreliosis much like neurosyphilis can elicit a prominent B cell response so patients can have increased IgG synthesis within the CNS and even oligoclonal bands seen in their CSF. This was observed in our patient. Patients with increased IgG production in the CNS will have production of anti-B Burgdorferi antibodies. Measurement of this is determined by comparing the ratio of CSF IgG specific to the organism to the corresponding in serum.[4]

In patients with strong suggestive features of Lyme neuroborreliosis, treatment remains straightforward with use of antibiotics. Treatment duration as evident by various randomized controlled trials (RCT's) is of 7-14 days for early Lyme neuroborreliosis, extending it to 2-3 weeks for Late (chronic) Lyme neuroborreliosis.[16,17] In a meta-analysis after reviewing 5779 records including eight RCT's and eight non randomized studies (NRS), no statistically significant difference was found between the use of oral doxycycline versus intravenous beta-lactam antibiotics, thus confirming doxycycline has sufficient CNS penetration.[18] The choice of antibiotic depends on patient demographics such as age, allergies, pregnancy, route and frequency of drug administration. Patients with early Lyme neuroborreliosis and were given proper treatment saw marked neurological improvement within a few weeks-months, with 90% symptom free rate after one year. These positive resulted dropped in chronic LD patients as 60-80% of patients had residual neurologic symptoms despite adequate treatment.[10,19,20] In our case, oral doxycycline was started after Lyme serology came out to be positive but given concerns for meningitis, IV Ceftriaxone was added to the regimen as well for a total duration of 4 weeks. This showed adequate neurological improvement in our case when seen in follow up after two weeks.

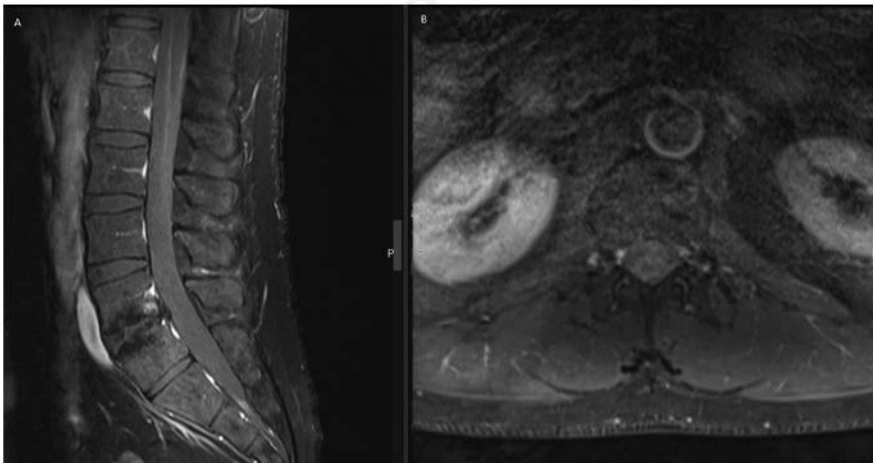

Figure 1. A) T1 Post-Contrast Saggital view showing slightly thickened enhancement along the surface of the conus medullaris as well as enhancement of the nerve roots of the cauda equina. B) T1-Post-Contrast Axial view showing slightly thickened enhancement along the surface of the conus medullaris as well as enhancement of the nerve roots of the cauda equina.

Conclusions

LD can cause a wide variety of CNS and PNS manifestations. CNS as well as PNS manifestations can occur in isolation or together. The diagnosis and serological-confirmation of LD can be challenging and difficult due to unusual serological staging of *B burgdoferi.* Clinicians should reconsider to repeat the laboratory tests of LD in cases with atypical presentations with unclear etiology. The treatment of LD is much easier than the diagnosis. Oral and intravenous forms are antibiotics may have similar efficiency and the therapy plan can be decided based on the severity of manifestations and condition of patients. The appropriate diagnosis and management of neuroborelliosis require meticulous medical approaches.

References

1. Halperin JJ. Nervous system Lyme dis-

ease. Handb Clin Neurol 2014;121: 1473-83.
2. Halperin JJ. Neurologic manifestations of lyme disease. Curr Infect Dis Rep 2011;13:360-6.
3. Halperin JJ. Diagnosis and management of Lyme neuroborreliosis. Expert Rev Anti Infect Ther 2018;16:5-11.
4. Halperin JJ. Nervous system lyme disease: diagnosis and treatment. Curr Treat Options Neurol 2013;15:454-64.
5. Burakgazi AZ. Lyme disease -induced polyradiculopathy mimicking amyotrophic lateral sclerosis. Int J Neurosci 2014;124:859-62.
6. Burakgazi AZ, Henderson CS. Unusual Presentation of Unilateral Isolated Probable Lyme Optic Neuritis. Case Rep Neurol Med 2016;2016:7471842.
7. Logigian EL, Kaplan RF, Steere AC. Chronic neurologic manifestations of Lyme disease. N Engl J Med 1990;323: 1438-44.
8. Hinckley AF, Connally NP, Meek JI, et al. Lyme disease testing by large commercial laboratories in the United States. Clin Infect Dis 2014;59:676-81.
9. Nelson CA, Saha S, Kugeler KJ, et al. Incidence of Clinician-Diagnosed Lyme Disease, United States, 2005-2010. Emerg Infect Dis 2015;21:1625-31.
10. Ogrinc K, Lusa L, Lotric-Furlan S, et al. Course and Outcome of Early European Lyme Neuroborreliosis (Bannwarth Syndrome): Clinical and Laboratory Findings. Clin Infect Dis 2016;63:346-53.
11. Shah A, O'Horo JC, Wilson JW, et al. An Unusual Cluster of Neuroinvasive Lyme Disease Cases Presenting With Bannwarth Syndrome in the Midwest United States. Open Forum Infect Dis. 2018;5:ofx276.
12. Diuk-Wasser MA, Hoen AG, Cislo P, et al. Human risk of infection with Borrelia burgdorferi, the Lyme disease agent, in eastern United States. Am J Trop Med Hyg 2012;86:320-7.
13. Daniels TJ, Fish D, Falco RC. Seasonal activity and survival of adult Ixodes dammini (Acari: Ixodidae) in southern New York State. J Med Entomol 1989;26:610-4.
14. Falco RC, Fish D, Piesman J. Duration of tick bites in a Lyme disease-endemic area. Am J Epidemiol 1996;143:187-92.
15. Lakos A. CSF findings in Lyme meningitis. J Infect 1992;25:155-61.
16. Oksi J, Nikoskelainen J, Hiekkanen H, et al. Duration of antibiotic treatment in disseminated Lyme borreliosis: a double-blind, randomized, placebo-controlled, multicenter clinical study. Eur J Clin Microbiol Infect Dis 2007;26:571-81.
17. Dersch R, Freitag MH, Schmidt S, et al. Efficacy and safety of pharmacological treatments for acute Lyme neuroborreliosis - a systematic review. Eur J Neurol 2015;22:1249-59.
18. Borg R, Dotevall L, Hagberg L, et al. Intravenous ceftriaxone compared with oral doxycycline for the treatment of Lyme neuroborreliosis. Scand J Infect Dis 2005;37:449-54.
19. Kaiser R. [Clinical courses of acute and chronic neuroborreliosis following treatment with ceftriaxone]. Nervenarzt. 2004;75:553-7.
20. Berglund J, Stjernberg L, Ornstein K, Tykesson-Joelsson K, Walter H. 5-y Follow-up study of patients with neuroborreliosis. Scand J Infect Dis 2002;34:421-5.