CASE REPORT

Cranial neuropathy and severe pain due to early disseminated *Borrelia burgdorferi* infectionDerek Ebner,¹ Kelsey Smith,² Daniel DeSimone,³ Muhammad Rizwan Sohail³¹Division of General Internal Medicine, Mayo Clinic Minnesota, Rochester, Minnesota, USA²Division of Neurology, Mayo Clinic Minnesota, Rochester, Minnesota, USA³Division of Infectious Disease, Mayo Clinic Minnesota, Rochester, Minnesota, USA**Correspondence to**

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ABSTRACT

A 61-year-old man presented to the emergency department in the summer with a right seventh cranial nerve lower motor neuron palsy and worsening paraesthesias for 6 weeks. He had debilitating pain at the scalp and spine. Prior work up was unrevealing. The patient resided in the upper Midwest region of the USA and worked outdoors, optimising the landscape for white tailed deer. Repeat cerebrospinal fluid testing revealed a lymphocytic pleocytosis and positive IgM Lyme serology. Brain MRI demonstrated enhancement of multiple cranial nerves bilaterally. He was diagnosed with early Lyme neuroborreliosis and treated with 28 days of intravenous ceftriaxone. While the painful meningoradiculitis, also known as Bannwarth syndrome, is more commonly seen in Europe, facial palsy is more frequently encountered in the USA. Clinical manifestations of neuroborreliosis are important to recognise as the classic presentation varies by geography and on occasion repeat serological testing may be necessary.

BACKGROUND

Tick-borne diseases offer a broad spectrum of signs and symptoms. While the classic manifestation of early localised Lyme disease, erythema chronicum migrans, is well known, the signs and symptoms associated with early disseminated or late Lyme disease are more obscure. Unfortunately, the diagnosis of tick-borne diseases remains a challenge as serology can be negative early in the disease process. A provider must be astute and maintain a high clinical suspicion in order to repeat testing if necessary.

The overall incidence of tick-borne diseases is on the rise.¹ As providers in endemic areas will become more likely to see tick-borne disease, an awareness of the disease spectrum and treatment guidelines is imperative. This case demonstrates how Lyme neuroborreliosis can present with non-specific symptoms, with nerve pain being a predominant feature. These findings can be misdiagnosed and attributed to a musculoskeletal aetiology or radiculopathy. However, accurate diagnosis is imperative as while isolated nerve palsy may be amendable to oral antibiotic therapy, other neurological manifestations may require parenteral antibiotics consistent with current recommendations in the USA guidelines.² However, oral doxycycline has been shown to be effective in Europe to treat both central and peripheral nervous system involvement.³

CASE PRESENTATION

A healthy 61-year-old man residing in the upper Midwest region of the USA presented to the emergency department during the summer with a lower motor neuron right sided cranial nerve VII palsy and worsening paraesthesias. Six weeks prior to this presentation, he had been evaluated by his primary care physician and multiple emergency department visits for severe shooting pain over his scalp, neck and back. The degree of discomfort from his hair moving was so extreme he elected to shave his head to provide some relief. While the back pain was non-radiating and had a patchy distribution along the paraspinal regions of the mid-thorax to lumbar spine, his bilateral dorsal arm paraesthesias were radicular and had a C7/C8 distribution. There was no clinical evidence of a myelopathy. He had been up-titrated on gabapentin with minimal response and started on a narcotic for pain control.

The patient reported working outside optimising the landscape for white tailed deer. Further history was notable for an exposure to greater than 30 ticks in 1 day. While he had not noticed any of these ticks burrowing into the skin, he did report three distinct large circular red lesions, one with a central clearing. His initial evaluation, including a lumbar puncture, was conducted within a week of developing the rash. This was approximately 6 weeks prior to his presentation to the emergency department with the lower motor neuron right sided cranial nerve VII palsy and worsening paraesthesias. At the time of initial evaluation, he had undergone basic laboratory studies, Lyme ELISA, tick-borne DNA and cerebrospinal fluid (CSF) cell count which were all within normal limits. He was prescribed only a single dose of oral doxycycline 200 mg. With the development of right sided facial weakness, he presented for re-evaluation.

INVESTIGATIONS

Repeat laboratory studies revealed normal inflammatory markers, including erythrocyte sedimentation rate and C reactive protein. Haematological studies revealed a very slight normocytic anaemia and metabolic studies were within normal limits. Repeat CSF analysis revealed an elevated nucleated cell count to 77 with 86% lymphocytes, protein elevation to 158 mg/dL (normal: 0–35 mg/dL) and six oligoclonal bands. Repeat Lyme ELISA was positive and Lyme serology in the CSF was positive and revealed IgM and IgG immunoblot. PCR for *Borrelia burgdorferi*, *B. mayonii*, *B. garinii*/B. *afzelii*

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Figure 1 Enhancement of the right cranial nerve VII.

Figure 2 Bilateral enhancement of cranial nerves X.

in the CSF were negative. Intrathecal antibody production and CXCL13 were not assessed.

MRI of the head revealed patchy linear enhancement of multiple cranial nerves including bilateral cranial nerve III, right greater than left cranial nerve V, right greater than left intracranial cranial nerves VII and VIII and bilateral cranial nerve X (figures 1 and 2). MRI of the cervical spine revealed faint oedema and expansion of the right hemicord from C3 to C5 and faint focal enhancement of C4–C5 and C5–C6 disc spaces with mild linear enhancement of multiple exiting dorsal and ventral nerve roots.

DIFFERENTIAL DIAGNOSIS

The most common manifestation of Lyme neuroborreliosis in the USA is facial palsy which can be misdiagnosed as Bell's palsy. While multiple cranial neuropathies can be seen in neurosarcoidosis or tuberculosis, the clinical context and course help with differentiation as these would not respond to the treatment for neuroborreliosis.

The radiculoneuritis associated with neuroborreliosis can be misdiagnosed as mechanical injury or musculoskeletal pain. However, severe pain that worsens at night in a patient from a Lyme-endemic area during peak season should alert the clinicians to consider a diagnosis other than musculoskeletal pain, especially without a preceding injury.

TREATMENT

The patient received intravenous ceftriaxone 2 g every 24 hours for 28 days. Artificial tears and an eyepatch were prescribed to prevent corneal scarring of the right eye. Gabapentin dose was increased to treat the painful radiculoneuritis.

OUTCOME AND FOLLOW-UP

After completion of antibiotic therapy, the patient reported feeling significantly improved. He continued to have minimal weakness of the right side of the face in a lower motor neuron pattern. He had discontinued the use of the eyepatch because he was able to keep his eye closed. He had some additional intermittent back pain that responded to gabapentin.

DISCUSSION

Lyme disease encompasses a broad spectrum of signs and symptoms and may present with atypical or non-specific manifestations. Due to non-specific clinical features (arthralgia, fatigue, malaise, and so on), clinicians must maintain a high index of suspicion in patients presenting from Lyme-endemic areas. Challenges in making the diagnosis include the latency period of the available serological tests and recognising the initial symptoms. While the early localised stage of Lyme disease, erythema migrans, is well known, early recognition of Lyme neuroborreliosis can be more elusive.

The exact pathogenesis of neuroborreliosis has yet to be determined. It has been proposed that spirochaetes migrate along the peripheral nerves from the region of erythema migrans to invade the nervous system.⁴ However, this theory is unsubstantiated and there is no consensus on the mechanism of nervous system damage. As the neurological sequelae are often rapidly reversed with antibiotic therapy, it is presumed that a spirochaete mediated inflammatory response is responsible.⁴

Neuroborreliosis can be clinically characterised as early or late depending on the duration of symptoms lasting longer than 6 months.⁵ Peripheral nervous system involvement can include cranial neuropathies and radiculoneuritis, while central nervous

system manifestations include encephalitis, lymphocytic meningitis and myelitis.⁴ It is the combination of clinical features and subsequent laboratory evaluation that makes the diagnosis of Lyme neuroborreliosis.

Early Lyme neuroborreliosis, as reflected in this case, occurs in up to 15% of patients with untreated erythema migrans and on average takes 4 weeks to manifest from the time of developing early localised Lyme disease.⁵ Cranial nerve palsy (particularly facial), painful radiculitis, encephalitis, myelitis and meningitis/headache have been described.⁶ The painful meningoradiculitis, also known as Bannwarth syndrome, displays a curious geographical trend as this is the most common presentation in Europe whereas facial palsy is more frequently encountered in the USA.⁵

While there are differences between the European and American guidelines for diagnosing and treating Lyme neuroborreliosis, there are a few unifying themes. The symptoms should be consistent with Lyme neuroborreliosis and not better explained by another aetiology. Furthermore, there must be evidence of exposure to *B. burgdorferi*. However, the guidelines diverge significantly in what classifies exposure. For example, while serological evidence of exposure suffices in the American guidelines and CSF analysis is not required, the European criteria mandate intrathecal *B. burgdorferi* antibody production.⁵

At present the European Federation of Neurological Societies suggests a possible diagnosis of neuroborreliosis if two of three criteria are met whereas a definite diagnosis can be made if all three criteria are fulfilled.⁷ The criteria are (1) neurological symptoms suggestive of Lyme neuroborreliosis, (2) CSF pleocytosis and (3) intrathecal *B. burgdorferi* antibody production.⁷ Definite nervous system Lyme disease by the American Academy of Neurology guidelines requires (1) possible exposure to ticks in a Lyme-endemic region, (2) a neurological disorder associated with Lyme disease after exclusion of other potential aetiologies and (3) one or more of the following: (a) erythema migrans, (b) immunological evidence of exposure to *B. burgdorferi*, (c) culture, histological or PCR proof of the presence of *B. burgdorferi*.⁸

CSF pleocytosis, a criterion of the European definition of neuroborreliosis, has lent itself to controversy. In retrospective analysis, elevated levels of *Borrelia*-specific antibodies were found in the CSF; however, there was an absence of CSF pleocytosis (defined as >5 mononuclear cells/ μ L).⁹ In this investigation, the lack of CSF pleocytosis was only observed among those patients with a prolonged duration of symptoms. While CSF pleocytosis is expected in virtually all patients with acute neuroborreliosis, pleocytosis may subside over time, especially with successful treatment.¹⁰ In our case, the patient had two lumbar punctures. CSF pleocytosis was absent at the time of initial procedure performed within a week of symptom onset but was present on repeat analysis several weeks later.

Lyme disease can be effectively treated by oral and parenteral antibiotics. While the available evidence to determine the duration of antibiotic therapy is imperfect, a 28-day course is preferred in USA for Lyme neuroborreliosis. In the absence of brain or spinal cord involvement, oral therapy is considered adequate.² While the established antibiotics are effective, the field continues to study novel adjuvant therapeutic strategies to abort the presumed inflammatory mediated cascade responsible for severe manifestations of neuroborreliosis.

Data regarding prognosis of patients presenting with neuroborreliosis is limited but several important trends have been identified. In a prospective study of 77 patients, an unfavourable outcome was predicted if the neurological symptoms persisted

for 14 days into treatment.¹¹ Although most of the patients will have resolution of their symptoms with appropriate antibiotic treatment, some may experience residual neurological symptoms with reported prevalence of up to 28%.¹²

Patient's perspective

This was quite the experience as the actual diagnosis was not immediately determined. A lumbar puncture (LP) was done which turned up negative for Lyme disease. A few weeks later another LP was performed which showed a positive result for Lyme. Treatment was behind obviously and then the infusions for 28 days began. The infusions themselves were not difficult, but not knowing if the symptoms of numbness and paralysis would depart or dissipate was quite worrisome. Lots of doctors, lots of nurses and great care is what got me back on track! Perhaps some divine intervention as well!

Learning points

- Lyme serology testing can be negative early in the disease course and should be repeated if clinical suspicion remains elevated. Lyme PCR in the cerebrospinal fluid has low diagnostic sensitivity.
- Neuroborreliosis can cause multiple cranial neuropathies.
- Pain from Lyme radiculoneuritis can be severe, unresponsive to classical treatments and worsen at night.
- Both oral and parenteral antibiotics may be used to treat nervous system Lyme disease. However, the preferred agent and route are dependent on the clinical syndrome and disease severity.

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