

# A Case of Optic Neuritis Secondary to Lyme Disease

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## ABSTRACT

**Introduction:** Optic neuritis is a condition associated with various systemic diseases, such as multiple sclerosis, and is also considered a rare complication of Lyme disease.

**Case:** A 46-year-old white woman presented with sudden onset of bilateral vision loss. After extensive workup, she was diagnosed with Lyme optic neuritis based on the clinical presentation and positive serology. She was treated with doxycycline for 2 weeks.

**Discussion:** Lyme disease is caused by infection with the spirochete *Borrelia burgdorferi*. The most commonly affected areas include the skin, joints, heart, and nervous system. Lyme optic neuritis is a challenging diagnosis and therefore often underreported. Doxycycline or ceftriaxone for 2 weeks are recommended for treatment.

**Conclusion:** We report this case to increase awareness among clinicians to include Lyme disease in the differential diagnosis of optic neuritis for unexplained cases of vision loss, particularly in Lyme endemic areas.

## INTRODUCTION

Lyme disease (Lyme borreliosis) is a multisystem zoonotic disease caused by the spirochete *Borrelia burgdorferi*.<sup>1</sup> In the United States, the primary mechanism of transmission of Lyme is through the bite of its vector, the *Ixodes scapularis* tick.<sup>2</sup> Incidence of Lyme disease in the United States is greatest in the Northeast, Mid-Atlantic, and North Central regions.

The clinical presentation of the infection has been well described in the literature.<sup>2</sup> Most patients (60%-90%) present with erythema migrans, more commonly known as the “bull’s-eye” rash, initially in the location of the bite. Flu-like symptoms

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(fever, headache, myalgias) may be present in the first few days after the bite.<sup>3</sup> Individuals may progress to have cardiac (carditis and atrioventricular block) and neurological (meningitis, cranial nerve palsies) symptoms in the early disseminated stage and musculoskeletal (oligoarthritis) symptoms in the later stage without treatment.<sup>1</sup>

Optic neuritis, described as the inflammation of the optic nerve resulting in blurred vision and eye pain, is a rare complication of Lyme disease. Despite a few published cases of Lyme optic neuritis, a causal link between the infection and ophthalmological manifestation has not been well-established.<sup>4,5</sup>

Here we report a case of a patient with recent

Lyme infection complicated by bilateral optic neuritis.

## CASE REPORT

A 46-year-old white woman from northern Wisconsin with a past medical history of hypertension, asthma, Lyme disease (diagnosed and treated with a course of doxycycline 10 years ago), posttraumatic stress disorder, depression, seizure disorder (last seizure at age 21), and alcohol use disorder presented to the emergency department (ED) with progressive blurring of her vision and paresthesias for 3 weeks duration. The patient reported that her blurry vision began after she had upper respiratory tract symptoms. She also reported having nausea, weakness, dizziness, and tingling/numbness of her bilateral lower extremities. Of note, the patient endorsed visual hallucinations.

Thirteen days prior to her presentation, the patient had gone to an outside optometrist who had documented optic head edema and instructed her to go to the ED for evaluation. She did not go to the ED at that time. Her worsening vision finally prompted her to go to the ED. Upon her arrival, she was found to be hypertensive with a blood pressure of 154/124 mmHg. She was afebrile. Physical examination including neurological exam was unremarkable.

**Figure 1.** Color Fundus Photos of Patient's Right and Left Eye



A. Right eye shows obscuration of the nasal border of the optic disc consistent with grade 1 optic nerve head edema. B. Left eye reveals mild blurring of the entire optic disc border along with elevation of the nasal aspect of the optic nerve. Both eyes exhibited retinal vessel tortuosity.

Visual acuity with Snellen Eye Test Charts was 20/400 in both eyes and color vision using the Hardy-Rand-Rittler color plates was 2/6 in the right eye and 0/6 in the left eye. The pupils were equal, round, and reactive bilaterally without afferent pupillary defect, and extraocular movements were full without pain in any direction. A dilated fundus exam demonstrated bilateral optic head edema, hyperemia, and optic nerve elevation concerning for intracranial hypertension (Figure 1).

Admission laboratory results were within normal limits except for elevated transaminases with aspartate aminotransferase (AST) 329 unit/L (Normal: 11 – 33 unit/L) and alanine aminotransferase (ALT) 146 unit/L (Normal: 6 – 37 unit/L), which were thought to be related to her chronic alcohol use.

Based on the recommendations from neurology and ophthalmology, she had an extensive workup to rule out other causes for vision loss and paresthesia. Computed tomographic scan of head without contrast was negative, and magnetic resonance imaging of brain with orbits was unremarkable except for nonspecific white matter lesions. An automated perimetry visual field test showed cecocentral visual field defects in both eyes (Figure 2). A lumbar puncture showed normal opening pressure, and glucose, protein, and cell count were within normal limits. There was no cerebrospinal fluid (CSF) pleocytosis. Final CSF cultures, Lyme and West Nile Viral serologies were pending at time of discharge. She had normal results for other tests including Venereal Disease Research Laboratory (VDRL) test; rapid plasma reagin (RPR); C-reactive protein; sedimentation rate; antinuclear antibodies; C3 complement; C4 complement; total complement; CCP antibody; rheumatoid factor; Quantiferon-TB; HIV 1,2 AB; Hepatitis C

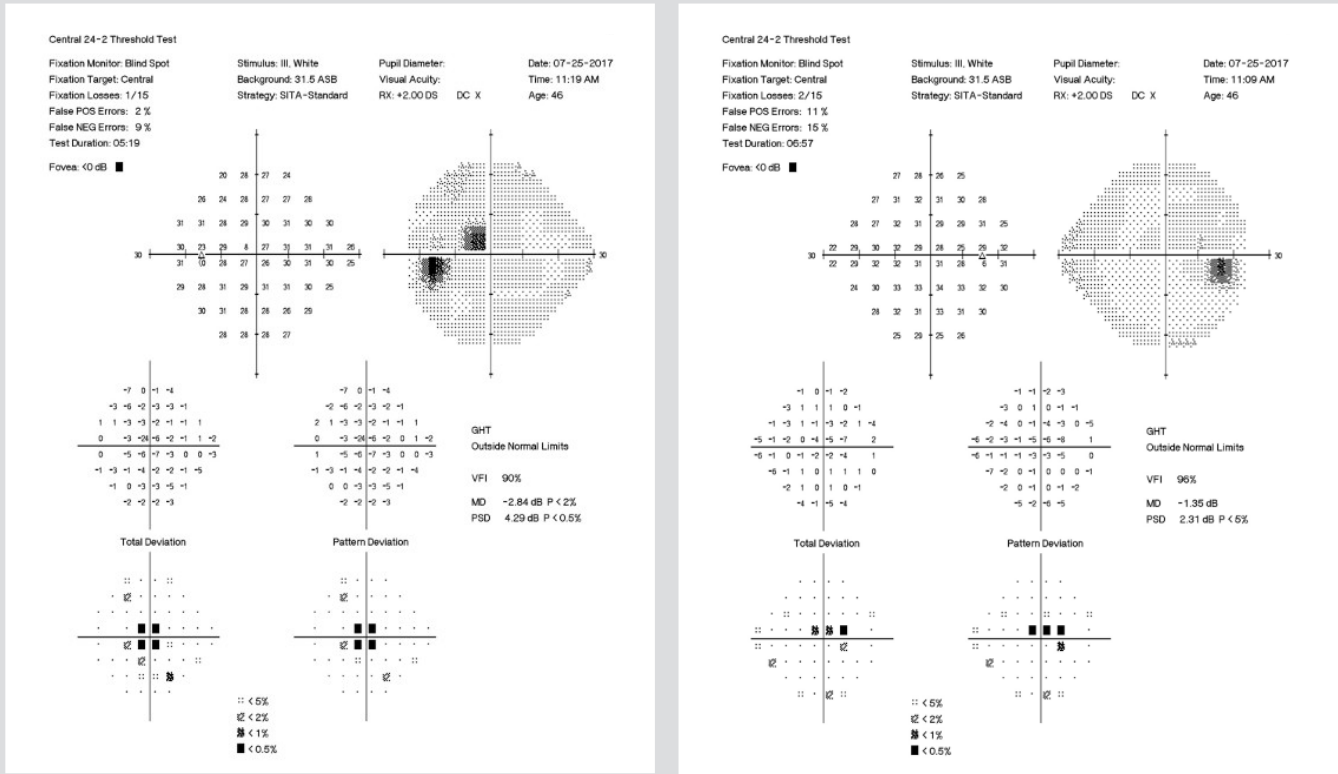
antibody; Hepatitis B surface antigen; Hepatitis B surface antibody; cardiolipin antibodies; beta-2 glycoprotein 1 antibodies IgA/IgM; urine heavy metal screen; and lupus anticoagulant panel.

The inpatient workup ruled out posterior reversible encephalopathy syndrome, idiopathic intracranial hypertension, multiple sclerosis, meningitis (viral, fungal, tuberculosis, syphilis, and other bacterial), autoimmune process and cerebrovascular disease. She was discharged home in stable condition with outpatient neuro-ophthalmology follow-up.

A week later, the serum immunoassay for Lyme disease resulted in elevated IgG/IgM antibodies of 1.39 (reference 0.00-0.90 in situ hybridization), and the Western blot was positive for serum IgM Lyme antibodies but negative for IgG antibodies. More specifically, 2 bands (P41 IgM, P23[Osp C] IgM) were positive in addition to the positive Western blot, which fulfilled the Centers for Disease Control and Prevention (CDC) recommendation for a positive Lyme test.<sup>6</sup> The CSF Lyme study only was positive for 3 IgG antibody bands (P39, P41, P45) with a negative Western blot. Based on the clinical presentation and the positive serologies, the patient was diagnosed with optic neuritis and peripheral neuropathy secondary to Lyme disease.

On further questioning, she did not recall any recent tick bite. She was evaluated by neuro-ophthalmology and infectious disease as outpatient and was started on doxycycline 100 mg twice daily for 2 weeks. The patient was again admitted a week later with alcohol intoxication. Upon questioning, she endorsed some improvement in vision after initiation of antibiotic. However, the patient left against medical advice and was not adherent with her follow-up appointments. Whether her symptoms resolved completely thereafter is unknown.

**Figure 2.** Humphrey Visual Fields of Patient's Right and Left Eye



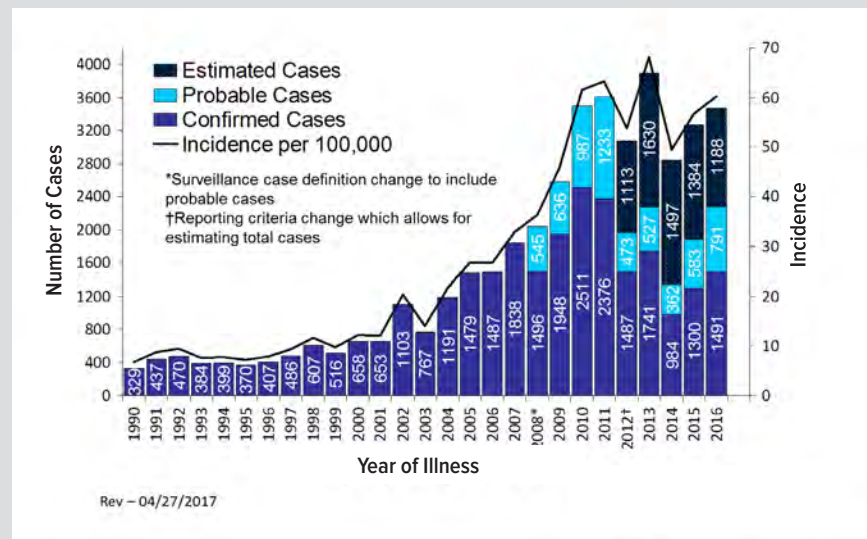
Humphrey Visual Fields shows cecentral defects in both eyes, with greater prominence in the left eye.

At the time of her diagnosis, we had asked the patient to elaborate on her past exposure to Lyme disease. About 10 years prior she had presented to her primary care doctor complaining of fever, rash, and arthralgia. At the time, she was treated successfully with doxycycline based on the clinical presentation and positive Lyme serology. Since she had acquired this care elsewhere, documentation of this encounter was not available in our system. Therefore, limited details were provided by the patient and her daughter, both of whom were poor historians.

**DISCUSSION**

Lyme disease was first recognized in the United States in 1975 at Lyme, Connecticut. It mostly occurs in the Northeast, Mid-Atlantic, and the North Central regions of the United States.<sup>2</sup> According to Wisconsin Division of Public Health Bureau of Communicable Diseases, the highest number of cases in Wisconsin is seen in the western and northern regions and cases have increased in the central region and eastern region in the recent years. With more than 38,000 cases

**Figure 3.** Reported Cases of Lyme Disease in Wisconsin, 1990-2016 (n = 41,864)



Source: Wisconsin Department of Health Services website: [www.dhs.wisconsin.gov/tickborne/lyme/index.htm](http://www.dhs.wisconsin.gov/tickborne/lyme/index.htm). Accessed June, 2018.

reported between 1980 and 2015, it is the highest reported tick-borne disease in the state. In 2016, about 1,491 confirmed cases of Lyme disease (*Borrelia burgdorferi*) were reported to Wisconsin Department of Public Health (Figure 3).

The most commonly affected areas include the skin, joints, heart,

**Box.** Sibony's Criteria for Strong Evidence of Optic Neuritis Associated With Active Lyme Disease Diagnosis<sup>5</sup>

Strong evidence requires the following core elements:

1. Optic neuritis.\*
2. Endemic exposure.\*
3. Negative Venereal Disease Research Laboratory test or Rapid Plasma Reagin.\*
4. Exclusion of multiple sclerosis.\*
5. Positive Lyme titer (enzyme-linked immunosorbent assay [ELISA] or Indirect Fluorescent Antibody).\*

One of the following must be associated as well:

- Encephalitis/Meningitis with CSF pleocytosis, intrathecal antibody production, or CSF polymerase chain reaction positive *B. burgdorferi* DNA and positive Western blot.
- Recent Lyme disease signs (such as facial nerve palsy, arthritis or radiculoneuritis) with positive serum ELISA confirmed by Western blot.
- Recent diagnosis of erythema migrans by a physician, usually with flu-like symptoms.

\* Elements the reported case fulfilled.

Abbreviation: CSF, cerebrospinal fluid.

and nervous system. Fever, headache, malaise, arthralgia, myalgia, and erythema migrans may be the initial presentation. Weeks to months after the initial infection, patients with untreated Lyme disease may develop early disseminated disease that can include migratory musculoskeletal pain, carditis, facial nerve palsy, ocular manifestations, meningitis, or radiculopathies. Approximately 10% to 15% of patients with untreated Lyme disease will develop neurologic manifestations.<sup>7</sup>

Optic neuritis is a common manifestation of central nervous system disease in various autoimmune, inflammatory, and infectious processes.<sup>8</sup> While Lyme disease has been known to involve both the central and peripheral nervous systems, its association with optic neuritis is poorly understood.<sup>9</sup> Lyme optic neuritis is a challenging diagnosis and, therefore, it is underrecognized and underreported. Few cases of Lyme optic neuritis have been published in the literature. While rare, Lyme optic neuritis should be considered in the differential diagnosis when managing patients with visual symptoms in Lyme-endemic regions. Other possible etiologies of optic neuritis should be ruled out before this diagnosis is made.

Our patient fulfilled the criteria for acute Lyme infection following the 2-tiered serology test (positive immunoassay followed by a positive Western blot) recommended by the CDC.<sup>6</sup> Our case also fulfilled the criteria for acute Lyme disease with strong evidence of a causal link with optic neuritis, as described by Sibony (Box).<sup>5</sup> It is unclear why our patient's CSF only showed the presence of 3 IgG bands (P45, P41, P39) of 5 required for a positive CSF Western blot. Additionally, no IgM bands were present in the CSF despite the patient's neurological symptoms. Intrathecal antibody production is not observed in all patients with Lyme disease, and is common in some ethnic groups more than others (more in Europeans than Americans).<sup>9</sup> A negative test for Lyme antibody in CSF cannot exclude central nervous system (CNS) disease. Nevertheless, pleocytosis, which was not seen in our patient, is a finding that is more likely to be seen with CNS involvement.<sup>9,10</sup>

Despite the unique laboratory results, our patient's neurological symptoms improved after treatment was initiated, which continues to support the association of her Lyme disease with optic neuritis. Unfortunately, due to the patient's nonadherence to follow-up, we were not able to acquire more details on her recovery. Nevertheless, there continues to be lack of data and guidelines surrounding Lyme-related optic neuritis, a field in which future study is warranted.

Our case is unique due to not only the patient's prior exposure to Lyme disease, but also the lack of traditional Lyme presentation (tickbite, fever, rash, arthralgia) during the most recent infection. The

onset and symptomatology were not consistent with those of post treatment Lyme disease syndrome (PTLDS), which manifests as persistent symptoms even after antibiotic treatment rather than a reestablishment of symptoms as seen with our patient.<sup>11</sup> Additionally, optic neuritis is not included in the clinical spectrum of PTLDS. It is not likely that our patient's neurological changes are due to a relapse of her initial infection, as there is no scientific evidence revealing the persistence of *Borrelia* after treatment with antibiotics.<sup>12</sup> Rather, taking into account her exposure risk, it is more likely that she acquired a second Lyme infection. However, there is a paucity of literature on the use of serological testing for the diagnosis of reinfection,<sup>13</sup> and it is uncertain whether her previous history of Lyme disease affected her current serologies and complicated establishing a strong association between Lyme disease and her optic neuritis.

In summary, the diagnosis of Lyme optic neuritis involves a history with possible tick exposure, optic nerve edema or elevation, and a workup to rule out other systemic illness and positive Lyme serologies in blood or CSF.

Ceftriaxone, cefotaxime, penicillin G, and doxycycline are indicated in the treatment of most neurological Lyme cases.<sup>8</sup> Oral doxycycline achieves spirochetocidal concentration in the CNS and is highly effective in Lyme meningitis, cranial neuritis, and radiculoneuritis. Two weeks of antibiotic treatment is recommended for neuroborreliosis. The cases available in the literature have been treated with both parenteral and oral antibiotics, and no consensus exists on definite recommendations for the treatment.

Lyme optic neuritis is a diagnosis of exclusion. Therefore, early recognition and treatment is crucial to prevent permanent vision loss.

## CONCLUSION

Lyme disease is an uncommon cause for optic neuritis, but it should be considered in the differential diagnosis of unexplained vision loss and optic nerve edema, particularly in Lyme-endemic

areas. Detailed examination and investigation are important to make the diagnosis of Lyme optic neuritis. We report this case to increase awareness among clinicians to include Lyme disease in differential diagnosis of optic neuritis. More reporting of the cases is essential to draw enough attention from the clinicians and researchers to help devise evidence-based guidelines on the approach to diagnose and manage this condition.

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