Lyme Disease: What the Neuroradiologist Needs to Know

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ABSTRACT

SUMMARY: Lyme disease is the most common tick-borne disease in Canada and the United States, caused by *Borrelia burgdorferi*, which affects multiple organ systems. Epidemiology, clinical presentation, and neuroimaging findings are reviewed.

What Is Lyme Disease?

Lyme disease, known as Lyme borreliosis, was first described in 1976 by William E. Mast and William M. Burrows in Old Lyme, Connecticut.1 It is the most commonly reported vector-borne disease in North America. In the United States, it is caused by *Borrelia burgdorferi*, a spirochete, closely related clinically to *Treponema pallidum* (syphilis) and transmitted via the bite of an infected *Ixodes* tick.2,3 Lyme disease is predominantly seen in the mid-Atlantic (primarily New England) and upper Midwest regions (Wisconsin, Minnesota, and Great Lakes region) but is also prevalent in parts of the Pacific coast (Oregon and Washington).4 Transmission of this tick-borne zoonosis requires both infected reservoirs in the small mammalian hosts and vector blacklegged ticks. Large mammals like humans are seldom hosts and are mainly affected by nymphal ticks.5 The incidence of Lyme disease is approximately 30,000 or 0.5 per 1000 individuals in endemic areas per the Centers for Disease Control and Prevention.2,6 However, under-reporting and misclassification are the common drawbacks of any surveillance system. The Centers for Disease Control and Prevention report that highly endemic states may have considerably higher prevalence than that recorded.7

What Are the Clinical Manifestations of Lyme Disease?

Lyme disease can be classified in 3 stages: early localized (stage 1), early disseminated (stage 2), and late disseminated (stage 3). In the early localized stage, erythema migrans is the first and most common sign, seen in up to 70%–80% of the individuals with a tick bite. It appears within 3 to 32 days at the tick bite site and may be asymptomatic, pruritic, or, rarely, painful. In untreated individuals, this lesion can expand up to 61 cm in diameter.8-13 Early dissemination begins within weeks to months after the appearance of erythema migrans. It mainly presents as nonspecific flu-like symptoms such as fatigue, malaise, fever, arthralgias, myalgias, and lymphadenopathies.14 In addition, ~15% and ~8% of patients may develop neurologic and cardiac abnormalities, respectively. The most common neurologic manifestations are lymphocytic meningitis, meningoencephalitis, cranial nerve neuritis, and sensorimotor radiculopathies.15 Patients with cardiac involvement mainly have a spectrum of atrioventricular nodal block.16,17 In late dissemination, arthritis mainly affecting the large joints (most commonly the knees) is the most common presentation. Because most patients are treated with antibiotics, <10% develop arthritis.13,18-20 Neurologic deficits such as loss of short-term memory, word amnesia, and progressive loss of multitasking ability with new-onset attention deficit–type symptoms are being increasingly recognized.21

How to Diagnose and Treat Lyme Disease

Lyme disease is diagnosed by combining the clinical examination with serologic testing. The early localized stage of Lyme disease is typically diagnosed with clinical signs and symptoms.22 Many physicians use the Centers for Disease Control and Prevention criteria of a Lyme reflex test, measuring the antibody titers to Lyme, and, if positive, performing a western blot to Lyme.22 The Centers for Disease Control and Prevention recommend a 2-step quantitative assay to detect antibodies against *B burgdorferi*. The first step involves the use of an enzyme immunoassay or an indirect immunofluorescence assay. If the result is negative, no further testing is required, but if the test is positive or equivocal, step 2 is performed. Step 2 uses an immunoblotting technique such as a western blot. The test is deemed positive...
Neuroradiologic Findings in Lyme Disease

| Location       | Neurologic Presentation                                           | Comments                                                                 |
|----------------|-------------------------------------------------------------------|--------------------------------------------------------------------------|
| PNS            | Subacute meningitis*                                               | Most common presentation in North America*                                |
|                | Plexus neuritis or mononeuritis multiplex*                        | 5%-10% cases*                                                            |
|                | Bannwarth syndrome*                                               | Uncommon in North America*                                               |
| Cranial nerve  | Facial nerve neuritis*                                             | Most commonly involved cranial nerve                                    |
|                | CN III and CN*                                                    | Few case reports*                                                        |
|                | Nonspecific bifrontal white matter T2 hyperintensity*             | 50% of cases with CNS involvement*                                       |
| CNS            | Encephalitis-rhombencephalitis pattern likely*                    | Rare*                                                                   |
|                | Vasculitis*                                                       | Rare*                                                                   |
| Spinal cord    | Nonspecific areas of T2 prolongation*                              | Most common pattern in spinal cord involvement*                          |
| Ocular         | Convergentis and episcleritis, early stages*                      | Rare*                                                                   |
|                | Uveitis, orbital myositis, chronic intraocular inflammation*       | Rare*                                                                   |
| Pediatric      | Cranial neuritis and meningitis*                                   | Most common pediatric neurologic presentation*                           |
|                | Peripheral neuritis, myelitis, Bannwarth syndrome*                | Rare*                                                                   |
|                | Prominent Virchow-Robin spaces*                                   | Less common                                                              |

Note: CN indicates cranial nerve; PNS, peripheral nervous system.

when both steps are positive. Doxycycline, amoxicillin, or cefuroxime axetil is the first-line treatment, and results in complete resolution of a patient’s symptoms. Cases resistant to these antibiotics are treated with macrolides.18

What Are the Neuroradiologic Findings in Patients with Lyme Disease?
There are several neurologic manifestations of Lyme disease. Imaging can be helpful in the assessment of peripheral Lyme disease. A clinical presentation of radiculitis in an endemic region should raise suspicion for the disease. The summary of these neurologic findings is in the Table.

Peripheral Nervous System. In the North American population, the peripheral manifestations are likely an extension of subacute meningitis, such as plexus neuritis or mononeuritis multiplex seen in 5%-10% of cases.24,25 Bannwarth syndrome, another complication of Lyme disease less frequently seen in North America, would be indicative of meningoradiculitis. On MR imaging, meningoradiculitis presents as an increased T2 signal of the affected nerve roots, which enhances with gadolinium contrast medium.15

Cranial Nerves. Facial nerve involvement is seen in approximately 80% of the cases, presenting as cranial neuritis. Of these, approximately 25% of cases show bilaterality. On MR imaging, enhancement of the affected nerve can be seen.26,27 Cranial nerve III and V involvement has also been reported.28,29 There still remains a lack of specificity to diagnose Lyme disease on imaging alone. In the clinical setting, attention should be paid to asymmetry or marked intensity of enhancement in the course of facial nerve geniculate ganglion and beyond. Enhancement of the typically nonenhancing facial nerve segments proximal to geniculate ganglion should also raise the suspicion.25

Central Nervous System. Half of the affected patients with CNS involvement show nonspecific abnormal signal in the frontal lobe white matter. This signal may persist even after clinical resolution post-antibiotic treatment.15 On a molecular level, the immune response to Lyme disease and MS has been found to be relatively similar, yet T-cell lines demonstrate only weak cross-reactivity between myelin basic protein and B burgdorferi.30 On magnetization transfer and DTI sequences, the presence of occult brain and cervical cord pathology in otherwise normal white matter would be more indicative of MS.31 Progression of CNS involvement can lead to encephalitis. Although there is no specific pattern of involvement, there have been a few cases showing a rhombencephalitis pattern of involvement affecting the brain stem and cerebellum, though this pattern of involvement can also be seen in tubercular or Listeria infection.25 There have been a few case reports of Lyme-related vasculitis and subsequent stroke-like symptoms. Lyme disease rarely affects the spinal cord.15 In affected patients, it is characterized by diffuse or multifocal areas of T2 prolongation. In contrast to MS, there are no occult lesions on magnetization-transfer images. Postcontrast images are helpful to demonstrate any associated nerve root enhancement.31,32

Ocular. The most common orbital/ocular manifestations of Lyme disease in the early stages are conjunctivitis, episcleritis, and subtle keratitis. Later stages may present as uveitis, orbital myositis, or chronic intraocular inflammation presenting with floaters and photophobia. Later stages of chronic intraocular inflammation can mimic orbital pseudotumor (due to raised intracranial pressure) or lymphoma.33,34 The clinical and imaging manifestations of orbital myositis in Lyme disease closely mimics those orbital pseudotumors; lymphoma and thyroid dysorbitopathy are possible differential diagnoses.15,33

Pediatric Patients. Facial neuritis and meningitis are the most common neurologic presentations in the pediatric population.35,36 Peripheral neuritis, myelitis, and Bannwarth syndrome are rare in children. The overall clinical course is milder and shorter compared with adults. Affected pediatric patients may show prominent Virchow-Robin spaces and T2 hyperintense lesions.37,38

CONCLUSIONS
This Clinical Vignette reviews the most common tickborne disease in Canada and the United States and important neuroradiologic
findings. Heightened interpretive sensitivity to the myriad nonspecific imaging findings may provide critical clinical information to diagnose and monitor *Borrelia burgdorferi* infection.

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