MR imaging findings in neuro-Lyme disease.

Poster No.: C-0594
Congress: ECR 2017
Type: Educational Exhibit
Authors: M. D. M. Cordon Holzknecht¹, E. Salvado¹, A. Samitier Pastor¹, L. E. Guerrero Acosta², O. MEZOSI¹, S. Ricart Farre³; ¹Tarragona/ES, ²Tarragona, Ca/ES, ³Tarragona, Sp/ES
Keywords: Parasites, Education and training, Education, MR, Neuroradiology spine, Neuroradiology peripheral nerve, Neuroradiology brain
DOI: 10.1594/ecr2017/C-0594

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR’s endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys’ fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
**Learning objectives**

The main objective of this review is to give an insight into the literature and highlight the epidemiology features, clinical manifestations and diagnosis of the nervous system affection secondary to Lyme disease, putting special emphasis on the diagnostic neuroimaging.
Background

Lyme disease is a tick-transmitted inflammatory disease caused by the spirochete *Borrelia burgdorferi* in North America and by *Borrelia garinii* in Europe. It can affect multiple systems such as the skin, peripheral nervous system, central nervous system, musculo-skeletal system, heart and eyes. The MR imaging findings are usually focal lesions in the white matter of the brain, nerve-root and/or meningeal enhancement.
Lyme neuroborreliosis (LNB) is the neurological involvement resulting from the systemic infection of Lyme disease. Lyme disease is transmitted through the bite of an infected Ixodes species of tick. Its geographical distribution is throughout the forested areas of Asia, North America and north-western, central and eastern Europe (Fig. 1). The incidence of Lyme disease shows a peak during the summer months when the nymphal stage is most active. Transmission of the disease requires at least 24-48 hours of tick attachment.

Lyme disease occurs in three stages:

Stage 1: Incubation varies from three to thirty-two days after which a characteristic target-like rash known as erythema migrans appears along with flu-like symptoms of fever, headache and myalgias.

Stage 2: One to four months after infection neurological and cardiac symptoms may be seen.

Stage 3: Arthritic and chronic neurological symptoms appear up to a few years later. Neurological symptoms are highly variable and include aseptic meningitis, radiculoneuropathies, myelopathies, polyneuropathies, facial nerve palsies, as well as encephalopathy (Fig. 2) \(^1,2,5\).

Diagnosis for Lyme disease is usually based on a characteristic clinical evidence and a positive antibody response because of the limited utility of microbiologic techniques. Most patients with suspected Lyme disease are tested for antibodies against *B. burgdorferi* \(^1,2\).

The sensitivity of microbiologic culture remains low (except in erythema migrans, where it is unnecessary) and probably reflects the small number of spirochetes present in accessible specimens from patients. The polymerase chain reaction (PCR) assay has remained problematic, probably for the same reason.

The European Federation of Neurological Societies (EFNS) has a three point criteria for the diagnosis of LNB. First is evidence of a neurological disorder within the spectrum of those known to be caused by neuroborreliosis without other apparent cause. Second is CSF pleocytosis and third, intrathecal antibody production. LNB is defined as the
presentation of three out of the three indications and possible if two out of the three are present.

The American Academy of Neurology has a different criteria for the diagnosis of LNB. One is the possible exposure to Ixodes ticks in Lyme-endemic areas. Second is one or more of the following symptoms: Erythema migrans, histopathologic, microbiologic or PCR proof of \textit{B. burgdorferi} infection and immunologic evidence of exposure to \textit{B. burgdorferi}. Third is the occurrence of a clinical disorder within the realm of those associated with Lyme disease without other apparent cause (Fig. 3).

Classical clinical LNB manifests by a predominant meningitis and radiculitis and the rare presence of intra-axial parenchymal brain and spinal cord involvement. Borrelia subspecies account for the different clinical presentations of LNB between Europe and North America.

Approximately 10-15% of patients with untreated Lyme disease will develop neurologic manifestations. Neuroimaging may be completely normal even in these patients $^{1,2,5}$.

\textbf{Peripheral Nervous System}

In Europe, up to 85% of the disease presents with Bannwarth Syndrome, a painful lymphocytic meningoradiculitis, which is rare in North-American LNB. Enhancement of cervical, thoracic and lumbar spinal nerve roots and leptomeningeal enhancement on poscontrast T1-weighted sequences, have been described $^2$(Fig. 4).

North American LNB usually presents as a subacute meningitis weeks to months after an Erythema migrans. Third, fifth and seventh cranial nerve enhancements have been described$^2$. The seventh cranial nerve is the most frequently involved and unilateral affectation is more frequent than bilateral $^2$ (Fig.5).

LNB should be included in the differential diagnosis of meningeal and nerve enhancement in endemic populations and patients with a travel history of endemic areas, as they are common findings $^1$.

Frequently there is an absence of a correlation between multiple enhancing cranial or radicular nerves and neurological symptoms $^2$.  

Central Nervous System

Borrelia species can reach the CNS hematogenously or retrogradely via the peripheral nerves. The first via is the predominant in the North-American LNB and the second in the European LNB. The mechanism of central nervous system involvement has multiple possible pathophysiologic explanations such as brain invasion, immunologic mechanisms or vasculitic processes 1,2.

Clinically CNS symptoms can include headache, confusional states and more severe encephalitis. Diagnosis of CNS infection is based on a positive PCR or intratechal production of anti-B burgdorferi antibodies, with lymphocytic meningitis and increased CSF-to-serum antibody ratio in CSF 2.

Approximately 50% of patients demonstrate multiple nonspecific T2 hyperintense lesions in the subcortical and/or periventricular white matter similar to those in multiple sclerosis, which has triggered speculations on an autoimmune mechanism 1,2,5 (Fig. 8).

White matter lesions in middle-age and or elderly patients can be difficult to differentiate from other causes such as small vessel ischemia. In the study by Argwal et al, they found fewer white matter lesions in their affected patients, probably due to the younger mean age and they concluded that Lyme disease should not be considered crucial in the differential diagnosis of foci of T2 prolongation in the cerebral white matter, particularly in middle-aged and elderly patients, except when Lyme disease is clinically suspected 1,2.

White matter involvement often persists on MR imaging despite successful treatment 2.

Encephalomyelitis visualized as tumefactive white matter ring-enhancing lesions is exceptionally rare and may simulate a neoplastic process 1,2.

Another rare manifestation of LNB is vasculitis which may be associated with ischemic stroke, subarachnoid hemorrhage and intracerebral hemorrhage 1,2,5.

Spinal Cord
Spinal cord involvement is very rare and MR imaging findings are diffuse or multifocal T2-weighted cord lesions and nerve-root enhancement on post-contrast T1-weighted images (Fig. 6, 7)².

**Orbits**

Ocular involvement is rare but can be seen at any clinical stage of Lyme disease. Optic neuritis and uveitis are the most common ocular complications and are observed during the second stage. Conjunctivitis and episcleritis are commonly seen during the early stage; keratitis, chronic intraocular inflammation and orbital myositis seen in the third stage of Lyme disease. Lyme disease may closely mimic orbital pseudotumor²,⁵.

**Treatment**

Antimicrobial therapy is highly effective, regardless of disease duration and severity, particularly with doxycycline.

Although most patients with LNB recover fully when treated with antibiotics, some patients who are treated months after the initial infection may still experience ongoing problems with fatigue, cognition, and pain despite receipt of a standard antibiotic treatment. These patients have been described as having chronic Lyme disease⁵.
Fig. 1: Current Ixodes ricinus distribution in Europe (January 2016).
© European Centre for Disease Prevention and Control (ECDC).

Fig. 2: Clinical manifestations of neuro-Lyme disease.
<table>
<thead>
<tr>
<th>European Federation of Neurological Societies (EFNS) criteria for the diagnosis of neuroborreliosis</th>
<th>American Academy of Neurology criteria for the diagnosis of neuroborreliosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Neurologic disorder within the spectrum of those known to be caused by neuroborreliosis without other apparent cause.</td>
<td>1. Possible exposure to Ixodes ticks in Lyme-endemic area.</td>
</tr>
<tr>
<td>2. CSF pleocytosis.</td>
<td>2. One or more of the following: a. Erythema migrans. b. Histopathologic, microbiologic, or PCR proof of B. burgdorferi infection. c. Immunologic evidence of exposure to B. burgdorferi.</td>
</tr>
<tr>
<td>3. Intrathecal antibody production.</td>
<td>3. Occurrence of a clinical disorder within the realm of those associated with Lyme disease, without other apparent cause.</td>
</tr>
</tbody>
</table>

**Fig. 3:** European and North-American diagnosis criteria.

**Fig. 4:** Cervical nerve-root enhancement in a patient with confirmed Lyme disease.

© Hospital Joan XXIII, Hospital Joan XXIII - Tarragona/ES
**Fig. 5:** Cranial nerve enhancement in a suspected Neuro-Lyme disease.


Manifestation of palsy of left seventh cranial nerve in 10-year-old male patient with recent history of camping. **(a)** Transverse T1-weighted postcontrast MR image shows enhancement of left seventh cranial nerve (arrow). **(b)** Coronal T1-weighted postcontrast MR image demonstrates left trigeminal nerve enhancement (arrow).
**Fig. 6:** Myelopathy and leptomeningeal enhancement in the spinal cord secondary to Lyme disease.

© Hospital Joan XXIII, Hospital Joan XXIII - Tarragona/ES

**Fig. 7:** Same patient as in figure 6 with complete resolution of mielopathy and spinal cord leptomeningeal enhancement after treatment.
**Fig. 8:** Nonspecific white matter lesions in a patient with known neuro-Lyme disease.

Conclusion

The diagnosis of Lyme neuroborreliosis (LNB) is difficult and is essentially clinical based on a history of tick exposure, epidemiology, clinical signs and serologic confirmation.

Positive MR findings in patients with neuro-Lyme disease are unusual and non-specific. In the proper clinical setting, Lyme disease should be considered in the differential diagnosis of focal lesions in the white matter of the brain, nerve root and/or meningeal enhancement.
References