



Neuropsychiatric Disease Associated with Lyme disease & Tickborne Illness

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EDUCATIONAL OBJECTIVES

Understand the epidemic of Lyme disease

Understand basics regarding EM rashes & diagnostic testing

Discuss literature regarding persistent symptoms after Lyme Disease

Contributors to Neuropsychiatric Symptoms from Tickborne Illness

Case vignettes highlighting neuropsychiatric symptoms after Lyme Disease

Learn about other tickborne illnesses such as *Borrelia miyamotoi*

LYME DISEASE
AND TICKBORNE
ILLNESS: AN
EPIDEMIC

Lyme Disease has been found in every state.

LD caused by the etiologic agent *Borrelia burgdorferi*

CDC: 476,000 Americans are diagnosed and treated for Lyme disease each year.

10-20% of those with EM rash develop Post-treatment Lyme Disease Syndrome (PTLDS).

Neurological symptoms are harder to treat and may persist in 50% (Vrethem et al 2002).

Erythema Migrans (EM) rashes

"Classic" Lyme disease rash



Expanding rash with central crust



Red, oval plaque



Multiple rashes, disseminated infection



DIAGNOSTIC TESTS: POOR SENSITIVITY

Sensitivity	Two-tiered test	C6 peptide test
Early Lyme	35.2	66.5
Early neurologic	77.3	88.6
Lyme arthritis	95.6	98.3

• Specificity only slightly decreased for C6 at 98.9 % versus 99.5% for two-tiered (Wormser, 2013).

- Significant inter-laboratory variability among Lyme disease Western blot (Fallon 2014).

POST-TREATMENT LYME DISEASE SYNDROME (PTLDS)

Persistent symptoms develop within 6 months of diagnosis and treatment AND **functional impairment**

Embraced more by academic community as syndrome implies **pathophysiology is unknown**

10-20% of patients who are treated for Lyme disease at the time of the EM rash (Aucott 2013, Marques 2008, Weitzner 2015).

Neurologic Lyme disease: chronic symptoms is higher, **50%** of the 106 patients compared to 16% of controls and questionnaires sent out on average 32 months after illness (Vrethem et al 2002).

PTLDS

Robinson et al

Posttreatment Lyme Disease Syndrome

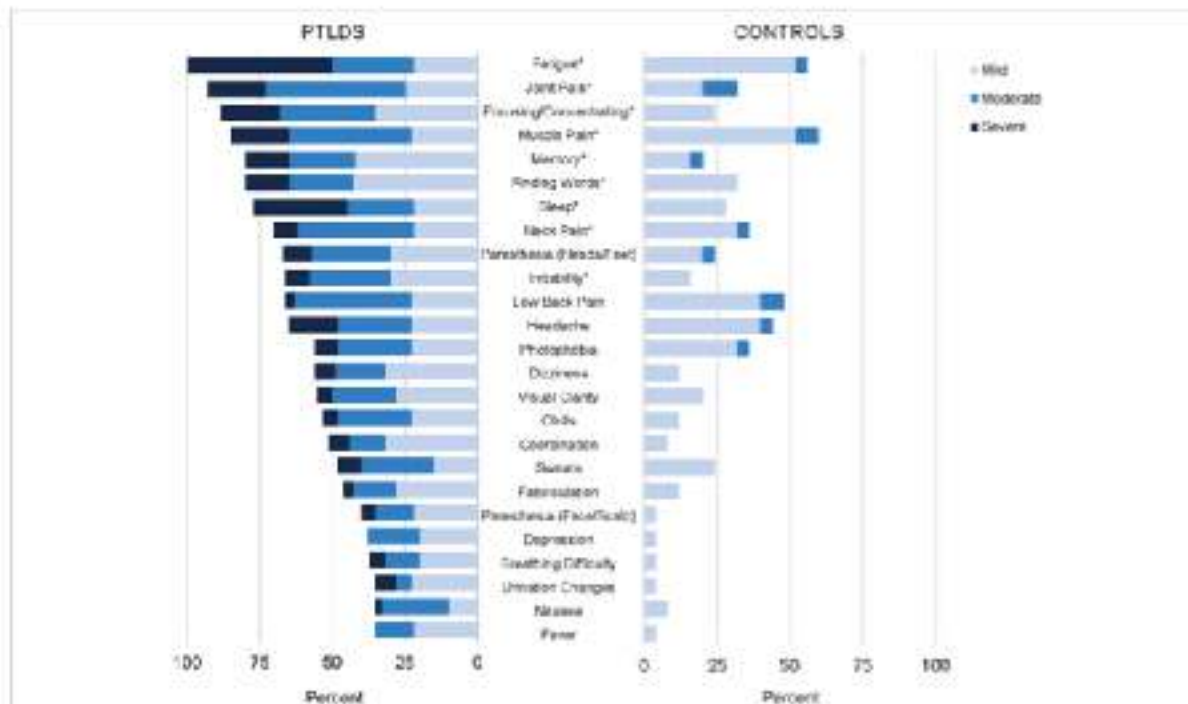


FIGURE 2 | Participants with post-treatment Lyme disease syndrome (PTLDS) and controls were asked about presence and severity of 36 signs/symptoms over the past 2 weeks. Displayed are the 20 signs/symptoms with a statistically significant difference in severity by group ($p < 0.05$), ordered by frequency within the PTLDS group. The nine signs/symptoms with a statistically significant difference ($p < 0.001$ level) are indicated with an asterisk.

Chronic Neuropsychiatric Manifestations of Lyme Disease

Table 1. Course of Lyme Disease in the 27 Study Patients.*

Chronic neurologic abnormalities	27	(100)
Median time from erythema migrans to chronic peripheral nervous system involvement — mo (range)	16	(1–156)
Median time from erythema migrans to chronic central nervous system involvement — mo (range)	26	(1–168)
Duration of chronic neurologic involvement at time of evaluation — mo (range)	12	(3–168)
Intravenous antibiotics for arthritis and neurologic abnormalities		
Penicillin	3	(11)
Ceftriaxone	3	(11)

*Unless otherwise noted, values are numbers of patients, with percentages given in parentheses.

Table 2. Signs and Symptoms of Chronic Neurologic Abnormalities.

Signs and Symptoms	No. of Patients (%)
Encephalopathy	24 (79)
Memory loss	22 (81)
Disorientation	20 (77)
Sleep disturbance	8 (30)
Irritability	7 (26)
Difficulty finding words	5 (19)
Polyneuropathy	19 (70)
Spinal or radicular pain	11 (41)
Distal paresthesia	7 (26)
Sensory loss	12 (44)
Lower motor neuron weakness	2 (7)
Acute hyporeflexia	2 (7)
Leukoencephalitis	1 (4)
Upper motor neuron weakness	1 (4)
Myoclonus	1 (4)
Increased muscle tone	1 (4)
Other symptoms	77 (100)
Fatigue	20 (79)
Headache	12 (48)
Hearing loss	4 (15)
Tinnitus	1 (4)
Etiomnesia	4 (15)

Months to years after the initial infection with *B. burgdorferi*, patients with Lyme disease may have chronic encephalopathy, polyneuropathy, or less commonly, leukoencephalitis. Logigian EL, Kaplan RF, Steere AC. N Engl J Med 1990; 323:1438-1444

Contributors to neuropsychiatric symptoms

Biologic mechanisms

- Persistent infection
- Inflammation
- Autoimmune - molecular mimicry
- Altered neurocircuitry (e.g. central sensitization)

Psychological Amplifiers

- Current stressors (pain, economic, interpersonal)
- Invalidiation/Dismissal by health care providers, *medical trauma*
- Uncertainty re diagnostic tests, treatment options

Persistent infection

- *B. burgdorferi* can persist in the animal host: dogs, mice, monkeys (Straubinger 1997, Hodzic 2008, Embers 2012).
- **Borrelia that persistent are living, infectious and stimulate an ongoing immune response** (Hodzic 2014).

HOW?

- Analysis of **human & animal** tissues: Bb spirochetes are found intercalated in extracellular collagen rich matrixes (**immune evasion**).
- **Bb** can modify it's outer surface protein expression depending on pH, temperature, and other factors.
- **Bb** has the ability to **produce proteins** that **bind to** and **inactivate** a key component of the immune system called **complement**.
- Bb can revert to round body forms versus spirochetal forms.
- **Borrelia persisters are not killed by standard antibiotics** (Zhang 2015).

The Lyme Wars:

BETWEEN PATIENTS, DOCTORS,
RESEARCHERS AND INSURANCE
COMPANIES.

Conflict centers around:

- What are the signs and symptoms needed to diagnose the disease?
- How accurate are the blood tests and how do you interpret them?
- Do some patients with persistent symptoms have persistent infection?

Recommended further reading

- “Conquering Lyme Disease” by Brian Fallon, MD and Jennifer Sotsky, MD
- “Cure Unknown” by Pamela Weintraub

Lyme Disease: The New “Great Imitator”

Case #1: “Bicycle Boy” 12 year old with Lyme Arthritis + OCD/Anorexia

2. Behavioral Changes

Between 1982 and 1984, a 12-year-old boy had four attacks of swelling of the right knee; the diagnosis of Lyme arthritis was confirmed serologically. After the last attack, he was treated with doxycycline, 100 mg twice a day for 30 days. Two months later, the patient became withdrawn and depressed. He no longer interacted with his friends, spent most of this time alone, and would no longer do his school work. He ate very little and began to exercise compulsively. His weight dropped 14 kg. On admission to a psychiatric hospital, he was grossly depressed and uncommunicative. He was diagnosed as having anorexia nervosa.

Because of the history of Lyme disease, he was transferred to Yale-New Haven Hospital. Serum and CSF antibody titers to *B. burgdorferi* were elevated, but neurologic evaluation was normal. He was treated with intravenous penicillin, 20 million U a day for 14 days, and within several weeks he began to eat more, gain weight, and communicate. During the following several months, his behavior returned to normal, he went back to school, and has remained asymptomatic for the past 2 years.

Pachner AR. *Borrelia burgdorferi* in the nervous system: the new "great imitator". Ann NY Acad Sci. 1988;539:56-64.

CASE VIGNETTE #2

Patient: SS

Age: 14 year old girl from MO

Onset of Illness: July 2013

Presenting Symptoms: chronic auditory hallucinations, visual problems, pain, headaches, and insomnia



CASE VIGNETTE #3

Patient: MM

Age: 12, houses in NYC & Hudson Valley

Onset of Illness: 2015

Presenting Symptoms: fatigue, headaches, neuropathies, cognitive problems, rage



Narrative from a 12 year old with Lyme Disease

“Many things have happened in my life, and I am only 12. Since I was 7, I have had Lyme-Bartonella. This illness has been very hard for me to live with because the symptoms make it seem like I am a bad person. I have developed head-jerking tics from it, very severe mental health issues, and a lot of headaches, and at one point over the summer, seeing double of everything (some doctors thought I had a brain tumor and I went to the hospital for the 5th time in my life for something Lyme-related). This life event has been very hard for me to deal with, because some of the symptoms you can't see when you look at me. People say that this life event has made my life harder, but to me this life event has made me stronger.”

Case Discussion Points

Depression and OCD emerged in Case 1 after Lyme arthritis and neuropsychiatric symptoms resolved with IV antibiotic.

Psychosis and auditory hallucinations improved with Doxy in Case 2

Case 3 illustrated a mix of neurological and psychiatric symptoms that responded to longer term treatment with antibiotics.

Lyme and PANS: FAMILY IN CRISES

Sick child: physically and mentally.

Parents: “We lost our kid”

Kid: “There’s a monster in me.”

“The original me is gone.”

Unclear diagnosis: often see multiple specialists but no answers or improvement

DX: Psychological stress/anxiety/conversion disorder

Unclear treatment course: often gone down the psychiatric road for many years before getting correct diagnosis



FAMILY: SPIROCHAETACEAE
GENUS: BORRELIA
SPECIES: BORRELIA BURGDORFERI AND BORRELIA MIYAMOTOI



Borrelia miyamotoi and clinical disease

***Borrelia miyamotoi* Serology in a Clinical Population With Persistent Symptoms and Suspected Tick-Borne Illness**

Shannon L. Delaney^{1,2*}, Lily A. Murray^{1,2}, Claire E. Aasen¹, Clair E. Bennett^{1,2}, Ellen Brown^{1,2} and Brian A. Fallon^{1,2}

- **82 patients** seeking consultation with persistent symptoms after suspected tick-borne illness were consecutively tested for *Bm* antibodies.
- **21 of the 82 patients (26%) tested positive** on the GlpQ IgG ELISA.
- **(98%) had no prior *B. miyamotoi* testing.**
- Compared to patients who solely tested positive for Bb antibodies, patients with *B. miyamotoi* antibodies presented with **significantly more sleepiness and pain. No EM rash!**
- A prospective study is needed to ascertain the relationship between the presence of *B. miyamotoi* antibodies and persistent symptoms.

AN ATTACHED TICK

In the NY region, finding an *Ixodes scapularis* tick:
-**57 %** chance of carrying *Borrelia burgdorferi*
-**63 %** chance of carrying ≥ 1 tickborne illness (Tokarz 2019)

Other co-infections transmitted faster than Bb, some within 15 minutes (*Anaplasma*, and *Borrelia miyamotoi* & *Powassan.virus*)

Ticks will be out if it is **45 degrees** or warmer

Submit the tick for analysis! Tickreport.com



Clinical Considerations & Summary

New onset psychiatric problem: consider doing tickborne illness work-up, **especially** if presenting with medical symptoms and/or exposures to Lyme endemic areas (summer camp, hiking, gardening, wooded backyard)

Lyme disease: **ELISA (Lyme C6 peptide offered at MDL) AND Western blot (s).**

Borrelia miyamotoi antibodies (only available through Quest)

Consider other tickborne illness testing as well: **antibody testing** for RMSF, Ehrlichia, Anaplasma, *Babesia microti* and *Babesia duncani* and Bartonella.

Submit your tick for analysis! (Tick-report.com)

Future research study: Lyme & PANS

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Questions?