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Case report

Early Lyme disease-associated Guillain Barre Syndrome: A case report

K. Schrestha[a], K. Kadkhoda[b,*]

[a] Infectious Diseases Division, Akron General, Cleveland Clinic, Cleveland, OH, USA
[b] Immunopathology Laboratory, Robert J. Tomsich Pathology & Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, USA

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ABSTRACT

Lyme disease is the most common tick-borne disease in the United States. Left untreated, it can lead to neuroborreliosis. Here we describe a case of early disseminated Lyme disease-associated Guillain Barre Syndrome in a previously healthy adult that early clinical suspicion and accurate testing led to proper diagnosis and case management. It is important to be aware of Guillain Barre Syndrome as an early consequence of Lyme disease especially during tick activity season. This case report is meant to raise awareness among clinicians and calls for protective measures especially where there is significant outdoor activity.

The case

A 65-year-old gentleman from Northeast Ohio with a past medical history significant for chronic obstructive pulmonary disease and well-controlled diabetes mellitus (HbA1C 6.3%) presented to the local emergency department on July 1, 2021, for acute onset of left-hand numbness and weakness since he woke up in the morning. The symptoms extended to the right arm, followed by lower extremities. There was no radicular pain, significant headache, or neck stiffness. He was well until he experienced an episode of "stomach flu" about a week before the onset of these acute symptoms, however, he did not experience abdominal pain or loose stools. He also noticed erythematous pruritic skin eruptions on his back and chest about a few days before the onset of limb weakness. The eruptions did not have Bull's eye appearance. He was an avid golfer and recently helped his neighbor build a deck before the onset of all signs and symptoms. However, he did not notice any tick bite. The workup for acute stroke was negative.

The laboratory findings were mostly unremarkable for complete blood counts and comprehensive metabolic panel. Lyme serology workup was sent, and Doxycycline (100 mg, q12h) was begun. Given suspected transverse myelitis, he was started on methylprednisolone and transferred to the regional hospital on July 4, 2021. At that time, he was diffusely hyporeflexic with no facial weakness, ataxia, or opthalmoplegia. There were erythematous morbilliform skin eruptions on his trunk. The magnetic resonance imaging of the spine was found unremarkable, and the nerve conduction study (NCS) and electromyography (EMG) of extremities performed, demonstrated findings consistent with an acute demyelinating polyneuropathy. He subsequently developed progressive generalized weakness and respiratory failure requiring intubation. He was treated with intravenous immunoglobulin (IVIG) from July 4 through July 8, 2021. In addition, he received multiple antibiotics to empirically treat pneumonia.

A diagnostic lumbar puncture on July 9, 2021, revealed an elevated opening pressure of 24 cmH_2O, with a clear cerebrospinal fluid (CSF) appearance, red blood cells: 888 cells/μL, glucose: 108 mg/dL (CSF-to-serum glucose ratio: 0.63), total nucleated cell count: 2 cells/μL (reference range: < 5), total protein: 502 mg/dL (reference range: < 45), the latter two highly suggestive of albuminocytologic dissociation which is a hallmark of Guillain Barre Syndrome (GBS). CSF bacterial culture returned negative. CSF also tested negative using the Film array meningitis/encephalitis panel including the following: *Escherichia coli*, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitides*, *Streptococcus agalactiae*, *Streptococcus pneumonia*, Cytomegalovirus, Enterovirus, Herpes simplex virus 1 and 2, human Parechovirus, Varicella Zoster virus, *Cryptococcus neoformans*/*C. gattii*. He tested negative for severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) by nucleic acid test. His elevated white count (22.35 k/μL; ref range: 3.70–11.0) was mostly attributable to the elevated neutrophil count (19.15 k/μL; ref range: 1.45–7.50) which was tested after methylprednisolone administration, however, as is the case with spirochaetal infections, his absolute monocyte count rose from a baseline of 0.29 k/μL on July 4, 2021, to as high as 1.36 (reference range: < 0.87). Despite highly elevated CSF protein, his serum albumin was as low as 2.7 g/dL on July 8, 2021. His liver enzymes and bilirubin were all normal. On the

* Correspondence to: Cleveland Clinic Learner College of Medicine, Case Western Reserve University, LL3-150, 10300 Carnegie Ave., Cleveland, OH 44106, USA.
E-mail address: kadkhok@ccf.org (K. Kadkhoda).

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same day, his C-reactive protein was highly elevated at 31.5 mg/dL (reference range: < 0.9) but his ferritin was only slightly elevated at 595.9 ng/mL (reference range: 30.3–565.7). He had a mild anemia but there was no thrombocytopenia. His coagulation panel was unremarkable.

His CSF's myelin basic protein level was 3.26 ng/mL (normal limits: 0.00–5.50). Antinuclear antibody test also returned negative. Anti-Streptolysin O level was slightly elevated at 346 IU/mL (reference range: < 201). Serology for Hepatitis C virus, Human immunodeficiency virus, and Syphilis as well as *Mycoplasma pneumoniae* IgM, Human herpes virus-7 IgM and IgG, and West Nile virus (WNV) IgM tests were all negative. CSF tested negative for WNV IgM and was non-reactive using Venereal Disease Research Laboratory (VDRL) test. *Legionella* urinary antigen also tested negative. Interestingly, his Lyme serology screen tested positive on July 01, 2021, at a commercial laboratory. The commercial laboratory performed a Lyme IgM enzyme immunoassay screen and since it tested positive, it was reflexed to Lyme IgM and IgG line immunoblots. The results were as follows: for IgM, all three diagnostic bands were detected (p23, p39, p41); for IgG, only two bands out of 10 diagnostic bands that are recommended by the Centers for Disease Control and Prevention (CDC) were present (p23, p41) hence a negative result. Therefore, the overall Lyme serology results was deemed equivocal at the time necessitating follow-up testing. That all 10 diagnostic IgG bands were not present could be attributed to early institution of Doxycycline and methylprednisolone.

A week later, another specimen was collected on July 8, 2021. This time his Lyme serology using the standard two-tier testing algorithm came back positive as follows: the screening assay using a chemiluminescent immunoassay for *Borrelia burgdorferi* Variable membrane protein [Vmp]-like sequence expressed (VlsE) and Outer surface protein C (OspC) recombinant antigens tested positive with a very strong signal and subsequently was reflexed to separate Lyme IgM and IgG western blot tests. This was done as part of the "Lyme early" panel performed at the immunopathology laboratory at the Cleveland Clinic when specimens are collected within 30 days of the onset of signs and symptoms. The western blot results were as follows: IgM tested positive with all three diagnostic bands (p23, p39, p4) present; IgG tested positive this time with seven (p18, p23, p41, p45, p58, p66, p93) out of ten diagnostic bands present. The combination of the above-mentioned results confirmed the diagnosis of a recent *B. burgdorferi* infection. Amid diagnostic workup, a CSF sample was also sent for Lyme serology to a reference laboratory. It tested weakly positive (index value: 1.46; reference range < 1.2) for *B. burgdorferi* antibodies using an enzyme immunoassay. A comment on the laboratory report stated: "*The CSF specimen shows evidence of blood contamination and is, therefore, likely contaminated with serum antibodies. Antibody testing from this specimen is not recommended as blood may interfere, causing a false-positive result that does not represent intrathecally produced antibodies*". We indeed did concur with this comment given the high-level Lyme antibodies found in serum plus the traumatic lumbar puncture mentioned earlier. So given the latter finding, absence of radicular pain and of CSF pleocytosis, early neuroborreliosis was deemed unlikely. Furthermore, the case was clinically and electromyographically indeed compatible with GBS.

The antibiotics were changed to ceftriaxone. He was successfully extubated and discharged to an inpatient rehabilitation center for over three weeks. He received four weeks of ceftriaxone that he completed on August 10, 2021. His extremity strength slowly improved and he went home from the rehabilitation center able to walk on his feet without support.

Discussion

B. burgdorferi sensu lato includes several genospecies but the only one that causes Lyme disease in North America is *B. burgdorferi sensu stricto*. According to CDC, every year in the United States, there are 30,000–40,000 incident cases of Lyme disease but the estimate is roughly ten times higher due to misdiagnosis or lack of testing [1–3]. Ohio is a low incidence region, however, it is neighbored by high incidence states like Pennsylvania. This is especially the case for rural Ohio. Lyme disease is transmitted by *Ixodes scapularis* ticks in Midwestern and northeastern United States with nymphal tick activity predominating May through June. This makes sense as why our patient did not notice any tick bites as nymphs are very small. His onset of illness in early July also strongly suggests a tick bite sometime in June given the incubation time of 3–32 days. Left untreated, Lyme disease has a variable clinical course with three distinct stages: early localized, early disseminated, and late stage. An early disseminated stage may include neurological signs and symptoms such as Bannwarth syndrome, Lyme meningitis, and Bell's palsy to name a few. Bannwarth syndrome was not clinically justified in this case as GBS was determined the most likely explanation. As also mentioned earlier, EMG and NCS both pointed to a demyelinating neuropathy. Additionally, albuminocytologic dissociation further supported GBS. Last but not least, pleocytosis is a very common feature of early neuroborreliosis which was absent in this case.

GBS is a rare neuroinflammatory disorder involving the peripheral nervous system. Its prevalence varies among different geographical locations and across different races/ethnicities but its incidence is usually around 1–2 per 100,000 person-years [4,5]. There are 3 different subtypes: acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor-sensory axonal neuropathy (AMSAN). The case presented here was consistent with AIDP and clinically compatible with a classic sensorimotor pattern. It is important to have a high level of clinical suspicion as GBS may lead to respiratory failure (such as in this case) and death or disability, whereas neuroborreliosis rarely leads to death or disability. GBS should typically be suspected where any of the following occur: rapidly progressive bilateral extremity weakness and/or sensory deficits, hypo-/areflexia, facial or bulbar palsy, ophthalmoplegia, and ataxia. Our case at least had two of the above. It is also paramount to highlight that early neuroborreliosis is only treated by antibiotics whereas GBS management does not require antibiotics but instead requires IVIG or plasma exchange. However, where there is clinical and serological evidence of early disseminated Lyme disease with neurological signs and symptoms, it is prudent to also treat for early neuroborreliosis per current guidelines [1], therefore, our case was treated for early neuroborreliosis and GBS.

From an immunopathological point of view, molecular mimicry may trigger GBS. Myelin basic protein has been implicated as a target in this context [6]. Although our patient tested negative for myelin basic protein in CSF, it is important to keep in mind that GBS involves the peripheral nervous system and the absence of myelin basic protein in CSF cannot necessarily dismiss the possibility of molecular mimicry in triggering GBS. Not to mention, T cells also play an important role in GBS which was not investigated in this case.

There are not a lot of case reports in the literature on the association of early disseminated Lyme disease with GBS [7–10]. This may point to a lack of awareness and/or misdiagnoses potentially leading to missed opportunities and as a result, disastrous consequences. Raising awareness and prompt management of these cases is highly warranted.

Author statement

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clinical suspicion and accurate testing led to proper diagnosis and case management. It is important to be aware of Guillain Barre Syndrome as an early consequence of Lyme disease especially during tick activity season. This case report is meant to raise awareness among clinicians and calls for protective measures especially where there is significant outdoor activity.

Ethical approval

Exempt for case reports per our institutional IRB policy.

Consent

Obtained.

Conflicts of interest

None declared.

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