Lyme Disease Presenting With Persistent Headache

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ABSTRACT. Increased intracranial pressure in patients with Lyme disease is an uncommon but reported finding. We discuss 2 patients from Lyme endemic areas who initially presented with headache, nausea, and vomiting and were eventually found to have increased intracranial pressure, a mild cerebrospinal fluid pleocytosis, and positive Lyme titers. It has been shown that increased intracranial pressure in association with neuroborreliosis can lead to blindness. In endemic areas, it is important for practitioners to consider Lyme disease when patients present with persistent headache, especially in those who have evidence of increased intracranial pressure. Pediatrics 2003;112:477–479. URL: http://www.pediatrics.org/cgi/content/full/112/6/e477; increased intracranial pressure, Lyme disease, persistent headache, neuroborreliosis.

ABBREVIATIONS. CSF, cerebrospinal fluid; PCR, polymerase chain reaction; Ig, immunoglobulin.

Lyme disease was first described by Steere et al1 in 1977. The 3 clinical stages of Lyme—early localized disease, early disseminated disease, and late disseminated disease—are well-documented and described in adult, pediatric, and infectious disease literature.2–5 Neurologic manifestations, which usually present in the latter 2 stages, commonly include motor or sensory radiculopathy, meningitis, and cranial neuropathy6–11 and more rarely can include mononeuritis multiplex,12 cerebellar ataxia,12 cerebrovascular neuroborreliosis,12 encephalopathy,9,13 and myelitis.12 In children, the most common neurologic complications are mild encephalopathy, aseptic meningitis, and facial palsy.14,15 We describe 2 case reports of children with neuroborreliosis who presented with chronic headache, cerebrospinal fluid (CSF) pleocytosis, and increased intracranial pressure. Neuroborreliosis with increased intracranial pressure can cause optic neuropathy and has caused permanent blindness in patients.16 The potential ophthalmologic complications make this an important diagnosis.

CASE 1

A previously healthy 13-year-old female from Massachusetts presented with a 2-week history of headache, nausea, and vomiting in late summer. The headache was frontal and bitemporal in location, constant and throbbing in nature, and severe enough to awaken her at night.

Her primary pediatrician evaluated her and subsequently referred her to an outside hospital, where head computed tomography and abdominal radiograph were normal. A lumbar puncture was unsuccessful. The patient was diagnosed with viral gastroenteritis and sent home after receiving intravenous fluids for dehydration.

Over the ensuing week, the severity of her headache, nausea, and vomiting waxed and waned, and she began to complain of photophobia and phonophobia. She was afebrile throughout her course. She had no history of rash, recent sick contacts, observed insect bites, arthralgias, myalgias, other joint symptoms, or recent changes in her vision.

On initial evaluation at our hospital, she had bilateral blurring of her optic discs. Visual acuity was 20/20 in both eyes. The remainder of her physical examination and repeat head computed tomography were normal. A lumbar puncture demonstrated an opening pressure of 450 mm H2O, leukocytes of 21 cells per mm3 (98% lymphocytes, 1% neutrophils, 1% monocytes), glucose of 49 mg/dL, and protein of 34.2 mg/dL. Gram stain showed no organisms. Complete blood count, electrolytes, and electrocardiogram were normal. CSF culture and enterovirus polymerase chain reaction (PCR) were negative. A serum enzyme-linked immunosorbent assay for polyvalent antibodies to Borrelia burgdorferi antigens were positive, with a positive immunoglobulin (Ig)M Western blot (antibodies to 23- and 41-kDa polypeptides). An IgG Western blot demonstrated antibodies to 23-, 41-, and 58-kDa polypeptides (an insufficient number of bands to be considered positive).

She was diagnosed with neuroborreliosis with increased intracranial pressure. She started on intravenous ceftriaxone and acetzolamide. Her symptoms gradually improved, but 1 week into therapy, she developed rash and pruritis. Her antibiotics were switched and she was treated with intravenous penicillin for 21 days without further complication. Subsequent ophthalmologic examinations showed continued improvement and eventual resolution in bilateral papilledema 13 weeks after her initial presentation. Acetzolamide treatment continued for a total of 11.5 weeks.

CASE 2

A previously healthy 9-year-old female from Massachusetts presented with a 6-day history of head-
ache, nausea, and vomiting 2 months after a trip to Connecticut. The headache was pounding, bilateral and frontal, and radiated to the occiput. She had no history of blurred vision, fevers, head trauma, sick contacts, or tick bites.

In the course of her illness, she was diagnosed with migraines at 2 different hospitals before developing photophobia and neck stiffness. Repeat evaluation at this hospital demonstrated blurring of the optic discs bilaterally as well as nuchal rigidity. Head computed tomography was normal. A lumbar puncture demonstrated an opening pressure of 450 mm H₂O, leukocytes of 31 cells per mm³ (82% lymphocytes, 1% neutrophils, 16% monocytes), glucose of 69 mg/dL, and protein of 18.3 mg/dL. Gram stain showed no organisms. Complete blood count, electrolytes, and liver-function tests were normal. Her headache resolved for 30 minutes after lumbar puncture but then returned with the same characteristics described above.

An enzyme-linked immunosorbent assay for polyvalent antibodies to B. burgdorferi antigens was positive, with a positive Lyme IgM Western blot (antibodies to 23-, 39-, and 41-kDa polypeptides). A Lyme IgG Western blot was also positive with antibodies to 18-, 23-, 39-, 41-, and 45-kDa polypeptides. CSF enterovirus PCR, Lyme PCR, and CSF culture were negative. An electrocardiogram was normal.

The patient developed left lid ptosis and was diagnosed with neuroborreliosis with increased intracranial pressure. She was started on 4 weeks of intravenous ceftriaxone. Nine days after discharge, she developed rash and pruritis and was changed to intravenous penicillin for 21 days of treatment without complication. She continued to have papilledema and was started on acetazolamide. Acetazolamide treatment continued for 6 weeks with eventual resolution of bilateral papilledema 10 weeks after her initial presentation.

**DISCUSSION**

Lyme disease is the most commonly reported tick-borne illness in the United States. It is endemic to 3 main geographic locations in the United States including the northeast (from Maryland to Maine), 2 north central states (Wisconsin and Minnesota), and the Pacific Coast region. Most cases occur from June through August with the majority of cases presenting in the 6-month span from May to October. In pediatrics, cases are most common among children 5 to 9 years old. In 1998, the number of reported cases of Lyme disease increased by 70% compared with 1992. This increase likely represents the increase in incidence. With increasing incidence of Lyme disease, rarer and more subtle presentations may become more common.

Lyme disease has been called “the latest great imitator” and often can be difficult to diagnose. Both of our patients demonstrate how Lyme disease can present without the classically described manifestations. The etiology of both of our patients’ complaints early in the course of the illness was not clear and both were misdiagnosed initially. Neither of our patients at the time of diagnosis had erythema migrans, fever, arthralgias, or myalgias. They both, however, presented complaining of persistent headache, nausea, vomiting, and photophobia and later developed papilledema.

Another difficult distinction to make is that of Lyme meningitis and viral meningitis. Both patients had lumbar punctures with increased opening pressures and a mild pleocytosis with a lymphocytic predominance. A study examining 22 children found Lyme meningitis and viral meningitis to be equally prevalent in an area endemic for Lyme disease. This same study demonstrated slight differences in clinical symptoms and laboratory values that may help distinguish Lyme meningitis from viral meningitis. Although the clinical symptoms of headache, neck pain, and malaise were present in both situations, children with Lyme meningitis were more likely to be afebrile and have a longer duration of symptoms. Papilledema, present in both of our patients, and cranial neuropathies, present in one of the above patients, were found only in the patients with Lyme meningitis. In cases of Lyme meningitis, the CSF profile demonstrated a lower white blood cell count and glucose level than with viral meningitis.

CSF testing for Lyme disease is controversial because of the low sensitivity of the available tests. Antibody titers and Western blots were not performed on the CSF in either patient. To demonstrate intrathecal production of antibodies, an index of CSF to serum levels of specific antibodies has to be elevated. Picha et al demonstrated only a 54% sensitivity of the antibody index in cases of neuroborreliosis. Lyme PCR was obtained on patient 2 and was negative. Nocton et al demonstrated a sensitivity of 38% of Lyme PCR in acute neuroborreliosis, which further decreased to 25% in patients with chronic neuroborreliosis. Though these tests can be useful when positive, the low sensitivity clearly limits their practicality in clinical terms.

The association of Lyme disease and increased intracranial pressure was first described by Raucher et al in 1985 and termed pseudotumor cerebri. Since then, there have been 23 cases of increased intracranial pressure described in children. For the majority of cases in the literature, there was a mild CSF pleocytosis (as in our 2 patients) as well as increased CSF protein.

The terminology used to describe the increased intracranial pressure in neuroborreliosis has caused much debate in the literature. It has been described as pseudotumor cerebri, pseudotumor cerebri-like syndrome, as well as benign intracranial hypertension, but all these terms have shortcomings. Pseudotumor cerebri and its other terms by definition should be idiopathic and have normal CSF findings except for elevated pressure. In addition to having elevated CSF pressure, both of our patients had increased CSF white blood cells and a diagnosis. We therefore think our patients are best described as having subacute meningitis with increased intracranial pressure.

The pathophysiology of the increased intracranial
pressure present in Lyme disease remains unclear. It has been postulated that it could result from an immune-mediated process similar to cases of pseudotumor cerebri in the setting of systemic lupus erythematosus where the function of arachnoid villi is disrupted.15 In support of this theory, B. burgdorferi-specific immune complexes have been found in the CSF in neuroborreliosis-associated neurologic disease.34 Another theory is that the mild pleocytosis and increased intracranial pressure in Lyme disease is most likely a result of direct infection and low-grade inflammation causing CSF absorption/production disequilibrium.28

There is no standard of care for patients with neuroborreliosis and increased intracranial pressure. One patient with papilledema and increased intracranial pressure secondary to Lyme disease16 was treated with antibiotics and corticosteroids and still had progression of visual impairment, eventually causing bilateral blindness. In cases of increased intracranial pressure secondary to Lyme disease16 was treated with antibiotics and corticosteroids and still had progression of visual impairment, eventually causing bilateral blindness. In cases of increased intracranial pressure and neuroborreliosis, antibiotics and acetazolamide have been shown to be effective.29,31 Corticosteroids have not been shown to have a significant effect.25 Serial taps, used in pseudotumor cerebri in the setting of systemic lupus erythematosus where the function of arachnoid villi has occurred.16 In this scenario, consideration should be given to empiric treatment with antibiotics and acetazolamide pending results of Lyme titer.

A high index of suspicion is frequently needed to diagnose Lyme disease,35 and practitioners should consider the diagnosis when patients present in an endemic area between the late spring and early fall with severe persistent headache, especially if they have evidence of increased intracranial pressure. Patients who present with the aforementioned constellation of symptoms and have a CSF pleocytosis and/or increased intracranial pressure may need aggressive clinical management given that blindness has occurred.16 In this scenario, consideration should be given to empiric treatment with antibiotics and possibly acetazolamide pending results of Lyme titers.

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