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[Brief Reports]

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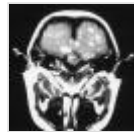
A 7-year-old boy from suburban Baltimore who presented with cerebellar ataxia and headaches was found by magnetic resonance imaging to have multiple cerebellar enhancing lesions. He had no history of tick exposure. He was initially treated with steroids for presumptive postinfectious encephalitis. Lyme disease was diagnosed 10 weeks later after arthritis developed. Testing of the cerebrospinal fluid obtained at the time cerebellar ataxia was diagnosed revealed intrathecal antibody production to *Borrelia burgdorferi*. Treatment with intravenous antibiotics led to rapid resolution of persistent cerebellar findings.

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Children presenting with acute cerebellar ataxia are usually evaluated to identify the most common causes including an immune-mediated postviral infection, labyrinthitis or cerebellar tumor. <sup>1</sup> We recently observed a child with acute cerebellar ataxia associated with Lyme disease, but the diagnosis was not made until several months later when he developed arthritis.

**Case report.** A 7-year-old, previously healthy boy presented on August 31, 1999, with a 6-day history of ataxia and headaches. There was no history of fever, rash, recent immunizations, tick bites or exposures to infectious diseases. Past medical history was unremarkable. The family lives in a semiurban community north of Baltimore with wooded areas near their home. This area is considered to be low-to-moderate risk for Lyme disease. He had never traveled to the Eastern Shore of Maryland or any other area considered to be high risk for Lyme disease. The child was referred to the Johns Hopkins Hospital for evaluation of a possible tumor after a magnetic resonance imaging (MRI) revealed lesions in the cerebellum.

On physical examination he was alert, afebrile and in no acute distress; temperature was 37.4°C, pulse 96/min, respiratory rate 24/min and blood pressure 100/70 mm Hg. There were no meningeal signs, pharyngitis, lymphadenopathy, organomegaly or joint findings. The neurologic examination was normal except for cerebellar signs including ataxia and intention tremor on finger to nose testing. The peripheral white blood cell count was 11 800/mm<sup>3</sup> (4% band forms, 61% neutrophils, 26% lymphocytes, 8% monocytes), hematocrit 37% and platelet count 369 000/mm<sup>3</sup>. The erythrocyte sedimentation rate was 16 mm/h. Cerebrospinal fluid contained 17 white blood cells (100% monocytes) and 34 red blood cells; glucose was 91 mg/dl and protein was 43 mg/dl. Gram-stained smears and bacterial cultures were negative. PCR studies on cerebrospinal fluid (CSF) were negative for Epstein-Barr virus (EBV), enterovirus and varicella zoster virus. Cytopathology was normal, and no oligoclonal bands were observed. Serologic studies were negative for antibodies to EBV IgM-viral capsid antigen and EBV nuclear antigen; and results were positive for IgG antibodies to viral capsid antigen and EBV early antigen. T2-weighted MRI showed 15 to 20, 0.5- to 1.0-cm diameter enhancing lesions throughout the cerebellum with sparing of the deep white matter and the cerebellar peduncles (Fig. 1). The ventricles were of normal size.



[Fig. 1](#)

A presumptive diagnosis of postinfectious encephalitis was made. After treatment with prednisone (2 mg/kg/day), headaches improved and he had marked improvement of cerebellar findings, but his mother noted a slightly unstable gait and a mild alteration in his speech. A repeat MRI 6 weeks after discharge revealed persistence of the cerebellar lesions.

Ten weeks after the initial onset of symptoms, he developed acute pain, swelling and increased warmth of his right knee. A throat culture was positive for group A *Streptococcus*, and he was treated with oral amoxicillin. The arthritis resolved in 1 week. A serologic test for Lyme disease obtained at the time he presented with arthritis became available 10 days later and revealed a positive enzyme-linked immunosorbent assay and Western blot: IgM (bands 23, 31, 39, 41) and IgG (bands 18, 23, 28, 30, 39, 41, 45, 48, 66, 93). A physical examination 10 days after amoxicillin was started revealed mild cerebellar dysfunction including a mild wide-based gait, slight tremor on finger to nose testing, inability to stand on one leg and poor coordination on rapid finger tapping.

He was treated with intravenous ceftriaxone for presumptive Lyme neuroborreliosis. On the ninth day of therapy he developed severe urticaria and angioedema immediately after ceftriaxone was administered. Repeat examination revealed marked improvement in all neurologic findings; two attempts at ceftriaxone desensitization were unsuccessful. After a test dose revealed no sensitization to ampicillin, he received intravenous ampicillin (300 mg/kg/day) for 21 more days because of a nationwide shortage of penicillin. Repeat MRI 3 weeks after completion of therapy was normal, and the neurologic examination revealed complete resolution of all cerebellar findings. Two years after therapy he remains free of neurologic symptoms and any evidence of inflammatory arthritis.

CSF and sera obtained during the initial evaluation (August 31, 1999) that had been stored at -20°C were tested at the Division of Rheumatology/Immunology, New England Medical Center, Tufts University School of Medicine, by antibody capture enzyme immunoassay. <sup>2</sup> Serum and CSF were positive for IgG and IgM antibodies to *Borrelia burgdorferi*, and IgA antibodies to the spirochete were found in CSF. PCR for *B. burgdorferi* DNA in CSF was negative. For all three classes of antibody, optical density values were greater in CSF than in sera, indicating intrathecal antibody production and confirming the diagnosis of neuroborreliosis (Table 1).

Sample	IgG Antibody	IgM Antibody	IgA Antibody	PCR for <i>B. burgdorferi</i> DNA
Sera	Positive	Positive	Negative	Negative
CSF	Positive	Positive	Positive	Negative

[Table 1](#)

**Discussion.** Although cerebellar involvement has been reported with Lyme disease, this manifestation of illness is rare. 3–5 However, children who reside in or travel to Lyme endemic areas and present with acute cerebellar ataxia of unknown etiology should be tested for serum antibodies to Lyme disease as treatment can shorten the duration of acute symptoms and prevent long term sequelae. 3, 4 If serologic testing is positive an MRI should be performed, and testing for CSF antibodies to *B. burgdorferi* should be conducted in parallel with serum to determine whether there is intrathecal antibody production. The absence of a history of a tick bite or the characteristic erythema migrans rash should not deter physicians from testing children with clinical disorders possibly consistent with Lyme disease, given that bites from the nymphal stage of *Ixodes* ticks often go unnoticed, and the rash may be either absent or misdiagnosed. In one study only 27% of children with neurologic manifestations of Lyme disease had a history of erythema migrans or arthritis. 5 Lyme disease can present with other central or peripheral nervous system manifestations including aseptic meningitis, meningoencephalitis, Bell's palsy and other cranial neuropathies, radiculoneuritis or myelitis. 3–5

The child reported here developed neuroborreliosis in late August and arthritis developed 10 weeks later, consistent with the usual timing of these complications after the acute infection. Laboratory testing demonstrated intrathecal production of antibodies to *B. burgdorferi*, establishing the diagnosis of neuroborreliosis. 6 Infection with *B. burgdorferi* typically induces an IgM and IgG antibody response to *B. burgdorferi*, and in patients with meningitis an IgA isotype response may also be seen. Moreover patients with Lyme meningitis often have evidence of intrathecal IgM, IgG and IgA antibody responses to the spirochete. This multiisotype antibody response in the CSF is quite specific and is not seen in control subjects with other neurologic diseases. 6

Although acute neuroborreliosis may resolve without antibiotic treatment, the duration of neurologic manifestations is longer and the risk of sequelae is greater. Steere et al. 7 reported on the treatment of acute neuroborreliosis with oral prednisone alone vs. intravenous penicillin for 10 days. Among 12 patients treated with intravenous penicillin, headache, stiff neck and radicular pain usually began to subside by the second day of therapy and were often resolved by 7 to 10 days; no one relapsed after the completion of treatment. In contrast the duration from treatment to resolution of symptoms was 29 + 11 weeks among 15 patients treated with 15- to 60-mg/day doses of prednisone only. Oral amoxicillin therapy failed to treat neuroborreliosis in our patient, similar to previous experience with a limited number of children with arthritis who were incubating neuroborreliosis when treated for arthritis. 8 Intravenous ceftriaxone or penicillin is recommended for treatment of early and late neuroborreliosis, except for patients with isolated facial palsy who may be treated successfully with oral amoxicillin or doxycycline.

The rapid clinical response to high dose ceftriaxone therapy and complete resolution of cerebellar lesions on MRI are consistent with a response to treatment of persistent viable *B. burgdorferi* in brain tissue for several months after disease onset. The negative PCR for *B. burgdorferi* in the CSF of the patient presented here is not unusual; in one series only 25% of patients with acute neuroborreliosis had a positive CSF PCR. [9](#)

Cerebellar ataxia has been recognized as a complication of several viral infections including varicella, enteroviruses and EBV. [1](#) The child reported here had serum IgG antibody to viral capsid antigen and no antibody to EBV nuclear antigen. Although this antibody pattern suggests recent EBV infection, testing for viral capsid antigen IgM antibody was negative, and PCR (sensitivity, 6 to 60 copies of EBV DNA) testing for EBV in the CSF was negative. Thus we do not think that his cerebellar findings were caused by infection with EBV.

The clinical manifestations of neuroborreliosis are thought to result from the presence of *B. burgdorferi* in the affected tissues and from the host inflammatory response. However, the pathogenesis of the reversible tissue damage is not well-understood. Neurologic injury could be the result of the direct action of the spirochetes on neurons. There is *in vitro* evidence for the adherence of spirochetes to neurons, glia and Schwann cells. [10](#) Another mechanism of injury could be through amplification of the inflammatory response in response to the organisms. There is experimental and clinical evidence for production of interleukin 6, tumor necrosis factor alpha and nitric oxide by neural cells exposed to *B. burgdorferi*. [10](#) Autoimmune mechanisms have been hypothesized to explain some manifestations of neuroborreliosis, but this hypothesis is unproved.

Multiple focal areas of increased signal intensity in white matter have been reported in children with acute neuroborreliosis, but multiple cerebellar lesions, as seen in our patient, have not been previously described. [11](#), [12](#) In adults with chronic neuroborreliosis, MRI scans suggestive of demyelination [13](#) and punctate hyperresonant areas were seen in the white matter of the cerebral hemispheres and the brainstem. [14–16](#) The number of lesions ranged from 1 to 27; although multiple areas of the brain were affected, the cerebellum was spared. There was no correlation between the duration of disease and the number of lesions.

1. Cherry JD, Shields WD. Encephalitis and meningoencephalitis. In: Feigin RD, Cherry JD, eds. Textbook of pediatric infectious diseases. Philadelphia: Saunders, 1998: 457–68. [\[Context Link\]](#)

2. Steere AC, Berardi VP, Weeks KE, Logigian EL, Ackermann R. Evaluation of the intrathecal antibody response to *Borrelia burgdorferi* as a diagnostic test for Lyme neuroborreliosis. J Infect Dis 1990; 161: 1203–9. [Article Linker](#) | [Full Text](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

3. Reik L, Steere AC, Bartenhagen NH, Shope RE, Malawista SE. Neurologic abnormalities of Lyme disease. *Medicine* 1979; 58: 281–94.

[Article Linker](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

4. Pachner AR, Steere AC. The triad of neurologic manifestations of Lyme disease: meningitis, cranial neuritis, and radiculoneuritis.

*Neurology* 1985; 35: 47–53. [Article Linker](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

5. Bingham PM, Galetta SL, Athreya B, Sladky J. Neurologic manifestations in children with Lyme disease. *Pediatrics* 1995; 96: 1053–6.

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6. Reik L. Lyme disease and the nervous system. New York: Thieme, 1991. [\[Context Link\]](#)

7. Steere AC, Pachner AR, Malawista SE. Neurologic abnormalities of Lyme disease: successful treatment with high-dose intravenous penicillin. *Ann Intern Med* 1983; 99: 767–72.

[Article Linker](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

8. Steere AC, Levin RE, Molloy PJ, et al. Treatment of Lyme arthritis.

*Arthritis Rheum* 1994; 37: 878–88. [Article Linker](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

9. Nocton JJ, Bloom BJ, Rutledge BJ, et al. Detection of *Borrelia burgdorferi* DNA by polymerase chain reaction in cerebrospinal fluid in Lyme neuroborreliosis. *J Infect Dis* 1996; 174: 623–7.

[Article Linker](#) | [Full Text](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

10. Garcia-Monco JC, Benach JL. Mechanisms of injury in Lyme neuroborreliosis. *Semin Neurol* 1997; 17: 57–62. [\[Context Link\]](#)

11. Demaerel P, Wilms G, Casteels K, Casaer P, Silberstein J, Baert AL. Childhood neuroborreliosis: clinicoradiological correlation.

*Neuroradiology* 1995; 37: 578–81. [Article Linker](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

12. Belman AL, Coyle PK, Roque C, Cantos E. MRI findings in children infected by *Borrelia burgdorferi*. *Pediatr Neurol* 1992; 8: 428–31. [Article Linker](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

13. Pachner AR, Duray P, Steere AC. Central nervous system manifestations of Lyme disease. *Arch Neurol* 1989; 46: 790–5. [Article Linker](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

14. Logigian EL, Kaplan RF, Steere AC. Chronic neurologic manifestations of Lyme disease. *N Engl J Med* 1990; 323: 1438–44.

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15. Halperin JJ, Pass HL, Anand AK, Luft BJ, Volkman DJ, Dattwyler RJ. Nervous system abnormalities in Lyme disease. *Ann NY Acad Sci* 1988; 539: 24–34. [Article Linker](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

16. Fernandez RE, Rothberg M, Ferencz G, Wujack D. Lyme disease of the CNS: MR imaging findings in 14 cases. *AJNR Am J Neuroradiol* 1990; 11: 479–81. [Article Linker](#) | [Bibliographic Links](#) | [\[Context Link\]](#)

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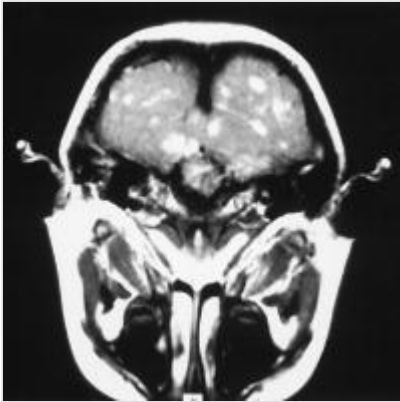


Fig. 1

**TABLE I.** Optical density values from antibody capture enzyme immunoassay measurement of antibody to *Borrelia burgdorferi* in CSF and sera

	OD*			CSF: Serum Ratio
	Control serum cutoff value†	Serum	CSF	
IgM	0.168	0.182	0.344	1.8
IgG	0.058	0.370	0.534	1.4
IgA	0.094	0.049	0.145	3.0

\* Each value is the OD of the well containing serum or CSF with antigen divided by the OD of the well containing serum or CSF without antigen.  
 † These values are 3 SD above the mean values of serum samples from five representative normal subjects whose samples were included on the same plate.  
 ‡ OD values greater in CSF than in serum are defined as evidence of local production of specific antibody in CSF. The details of this assay have been previously published.

Table 1

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