

# A 4-year-old boy with ataxia and aphasia

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**A**n otherwise healthy 4-year-old boy was brought to hospital in late December after 3 days of nasal congestion and 2 days of fever, vomiting, malaise, ataxia and aphasia. The patient had a medical history of clubfoot. He had not yet received his immunizations (4–6 yr) or the seasonal influenza vaccine. On arrival, his vital signs were normal, but he had truncal and gait ataxia. The remainder of his neurologic and physical examination was normal. There was no nuchal rigidity, no ankle clonus and the Babinski sign was negative.

## What diagnoses should be ruled out in this patient?

- Central nervous system infection
- Brain neoplasm
- Poisoning
- Cerebrovascular accident
- All of the above.

The answer is (e). Several conditions can cause acute ataxia and aphasia (Table 1). Initial biochemical and toxicologic workup showed a white blood cell count of 20 (normal range 4.7–13.5) × 10<sup>9</sup> cells/L, a neutrophil count of 18 (normal range 1.5–8.50) × 10<sup>9</sup> cells/L and a lymphocyte count of 1.6 (normal range 1.0–

5.5) × 10<sup>9</sup> cells/L. On presentation to hospital, the patient’s high-sensitivity C-reactive protein was 36.2 (normal ≤ 10) nmol/L with an erythrocyte sedimentation rate of 26 (normal 0–20) mm/h.

Acute viral encephalitis can present with fever and neurologic deficits. We started intravenous acyclovir and ceftriaxone to provide empiric coverage for encephalitis caused by herpes simplex virus (HSV) and bacterial meningitis, respectively. Stroke, both hemorrhagic and ischemic, and brain tumours would be visible on imaging and were considered. We planned a magnetic resonance imaging (MRI) of the head, but shortly after admission the patient’s mental status declined. He developed nystagmus, tremor, hyperreflexia with ankle clonus, a positive right-sided Babinski reflex and urinary incontinence. Seizure-like movements were noted, and he was given lorazepam.

## What is your next step?

- Urgent brain computed tomography (CT)
- Lumbar puncture
- Brain MRI
- Electroencephalography
- Observation

The answer is (a). An urgent CT scan was done to rule out intracranial hemorrhage or a space-occupying lesion as a cause of his acute neurologic deterioration. In our case, this was normal. A lumbar puncture is required to make a diagnosis of infectious meningitis or encephalitis, which we performed after the head CT. A sample of cerebrospinal fluid (CSF) was clear and colourless with a lymphocytic pleocytosis (Table 2). A bacterial culture of CSF showed no growth. Results from polymerase chain reaction (PCR) of CSF for HSV1, HSV2 and varicella zoster virus, enterovirus and parechovirus were negative (Table 2). We stopped treatment with acyclovir. His brain MRI showed a non-necrotizing, nonhemorrhagic meningoencephalitis (Figure 1). Further investigations included electroencephalography, electrocardiography, echocardiography and abdominal ultrasonography, which were all normal. After his deterioration, pediatric infectious diseases was consulted. Upon questioning, his parents shared a photograph of a rash that had developed 4 months earlier (Figure 2).

**Table 1: Causes of acute ataxia and aphasia in children**

Condition	Ataxia	Aphasia
Acute cerebellitis	+	
Acute cerebellar ataxia (postinfectious)	+	
Bacterial meningitis	+	±
<i>Mycoplasma pneumoniae</i> pneumonia	+	
<i>Enterovirus</i> encephalitis		
HSV encephalitis	+	
EBV encephalitis	+	
Cerebellar tumour	+	
Lyme disease (neuroborreliosis)	+	±

Note: EBV = Epstein–Barr virus, HSV = herpes simplex virus.

**Table 2: Results of cerebrospinal fluid investigations in a 4-year-old boy with aphasia and ataxia**

Laboratory test	Result	Reference range
CSF glucose, mmol/L	2.9	3.3–4.4
CSF protein, g/L	0.55	0.15–0.45
CSF appearance	Clear/colourless	Clear/colourless
Red blood cells, $\times 10^6$ cells/L	< 1	0–5
White blood cells, $\times 10^6$ cells/L	39	0–7
CSF neutrophil differential	1%	NA
CSF lymphocyte differential	80%	NA
CSF mono/macro differential	19%	NA
Bacterial culture	Negative	Negative
PCR for HSV/VZV	Negative	Negative
PCR for enterovirus RNA	Negative	Negative
PCR for <i>Borellia</i> species	Negative	Negative

Note: CSF = cerebrospinal fluid, HSV = herpes simplex virus, NA = not applicable, PCR = polymerase chain reaction, VZV = varicella zoster virus.

### Based on the photograph, what is the diagnosis?

- Encephalitis associated with HSV
- Pneumonia associated with *Mycoplasma pneumoniae*
- Lyme neuroborreliosis
- Encephalitis associated with Epstein–Barr virus (EBV)
- Drug reaction

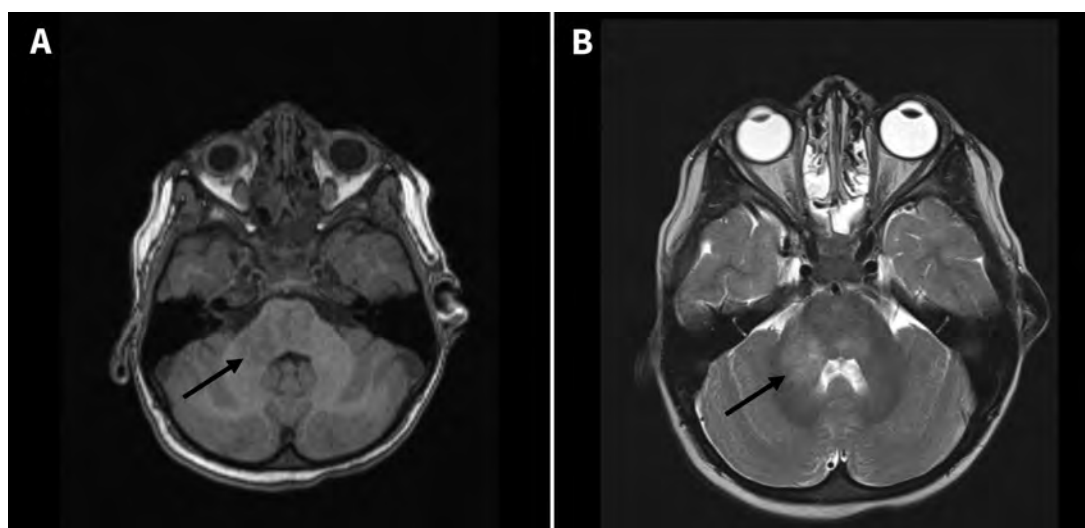
The answer is (c). The patient lived in southeastern Ontario in an area highly endemic for Lyme disease. Four months before presenting to the hospital, the patient was seen in an urgent care clinic for multiple disseminated erythematous patches that had

appeared 5 days earlier. The lesions had appeared after 2 days of fever and vomiting. At the time, there was no history of headache, facial asymmetry, visual changes, weakness, palpitations, shortness of breath with exertion or joint involvement. He had played in a wooded area at a local farm, but there was no recollection of a tick bite. The fever and skin lesions were diagnosed as erythema multiforme, which resolved completely 1 month after they appeared. A drug eruption can cause erythema multiforme; however, our patient had no exposure to medication. Erythema multiforme lesions are usually no more than 1–2 cm in diameter, do not enlarge and often appear on the palms and soles, unlike in our patient. There were no respiratory symptoms to suggest pneumonia associated with *M. pneumoniae*.

Peripheral Lyme serology testing was reactive and included immunoglobulin G (IgG) and immunoglobulin M (IgM) immunoblots (Table 3). Polymerase chain reaction of CSF for *Borrelia species* was negative; however, this test has very low sensitivity, and therefore this result did not change our diagnosis. Unfortunately, there was not enough CSF to test for intrathecal anti-*Borrelia* antibody production. Serum serology testing was also reactive for *Bartonella henselae* IgG by immunofluorescence assay (titre of 1:256) and EBV IgM but nonreactive for EBV IgG. Ongoing exposure to cats at home and the tendency for Lyme disease to cause falsely reactive serology for other infections, such as EBV, explained this. Our patient's clinical picture was not consistent with meningoencephalitis associated with *B. henselae*. He was improving by the fifth day of ceftriaxone administered intravenously and back to baseline by the seventh day. Our patient completed his intravenous ceftriaxone course as an outpatient.

### Discussion

Lyme disease is a tick-borne infection caused by *Borrelia burgdorferi* and transmitted in North America primarily by the deer tick *Ixodes scapularis*. *Ixodes scapularis* is well established in the Kingston, Frontenac, Lennox and Addington region in Ontario and at least



**Figure 1:** Magnetization-prepared rapid gradient-echo ( $T_1$ -weighted; left view) and turbo spin-echo ( $T_2$ -weighted; right view) magnetic resonance images showing multifocal asymmetric edema of the cortical, deep grey matter and white matter tracts, with no cranial nerve involvement (black arrows).



**Figure 2:** Disseminated erythema migrans initially misdiagnosed as erythema multiforme. Published with permission of the patient's parents.

30% of this tick population carries *Borrelia burgdorferi* (Figure 3). In 2017, this region reported an incidence of 96.3 cases of Lyme disease per 100 000 population, whereas the overall incidence in the province of Ontario was 7.2 cases per 100 000 population.<sup>1</sup>

Lyme disease manifests in 3 stages: early localized ( $\leq 30$  d), early disseminated (1–3 mo) and late disseminated disease ( $\geq 3$  mo).<sup>2</sup> Early localized disease is recognized by the presence of erythema migrans, a relatively asymptomatic, expanding, erythematous patch with or without central clearing. In North America, a minority of erythema migrans appear as the classical “bull’s-eye” lesion. Erythema migrans may be confused with other skin lesions, such as erythema multiforme, as seen in our patient.<sup>2</sup>

Early disseminated Lyme disease can present with multiple areas of erythema migrans, carditis and neuroborreliosis alone or in combination.<sup>2</sup> Nonspecific symptoms such as fever, lymphadenopathy, headache, myalgia and arthralgias may also be present but are more common in the early localized and early disseminated stages. Late disseminated Lyme disease mainly manifests as arthritis.<sup>2,3</sup> Neuroborreliosis may involve the peripheral nervous

**Table 3: Results of microbiologic investigations in a 4-year-old boy with aphasia and ataxia**

Laboratory test	Result
EBV EA IgG	Nonreactive
EBV VCA IgG	Nonreactive
EBV EBNA IgG	Nonreactive
EBV VCA IgM	Reactive
Measles IgG	Reactive
Measles IgM	Nonreactive
Mumps IgG	Nonreactive
Mumps IgM	Nonreactive
Urine RNA for mumps	Negative
CMV IgG	Nonreactive
CMV IgM	Nonreactive
<i>Bartonella</i> IgG titre	1:256
Lymphocytic choriomeningitis IgG	Nonreactive
Lymphocytic choriomeningitis IgM	Nonreactive
Lyme IgG/IgM EIA	Reactive
Lyme IgM Western blot	Reactive
Lyme IgG Western blot	Reactive
Nasopharyngeal swab	
Influenza A/B PCR	Negative
Viral culture	Negative
Stool culture	
Bacterial culture	No growth
Norovirus PCR	Positive
Rotavirus ICT	Negative

Note: CMV = cytomegalovirus, EA = enzyme assay, EBNA = Epstein–Barr virus nuclear antigen, EBV = Epstein–Barr virus, EIA = enzyme immunoassay, ICT = indirect Coombs test, IgG = immunoglobulin G, IgM = immunoglobulin M, PCR = polymerase chain reaction, VCA = viral capsid antigen.

system (facial nerve palsy), the central nervous system (CNS) as a lymphocytic meningitis or, uncommonly, both.<sup>4</sup> Usually, brain parenchyma are not directly involved in CNS infection,<sup>5</sup> and findings from MRI are usually in keeping with rhomboencephalitis.<sup>6</sup> Late neuroborreliosis, particularly when it manifests as meningoencephalitis several months after initial infection, is uncommon.<sup>5</sup> Acute cerebellar ataxia has been reported in childhood Lyme disease;<sup>7</sup> however, ataxia in children is more likely caused by viral infections or *M. pneumoniae*.<sup>8</sup>

A review of childhood neuroborreliosis in Sweden reported that the most common presenting features were headache (61%), fatigue (60%) and cranial nerve palsy (59%).<sup>9</sup> Most patients presented between July and September, whereas only 10% of patients presented in December.<sup>9</sup> In a similar study in Denmark, less than 20% of children with Lyme disease who lived in an endemic area had presented in November or December.<sup>4</sup> The most common signs and symptoms included radicular pain (66%), cranial nerve palsy (43%) and headache (28%). Meningitis (2%–4.9%) and

## Ontario Lyme Disease Map 2019 Estimated Risk Areas

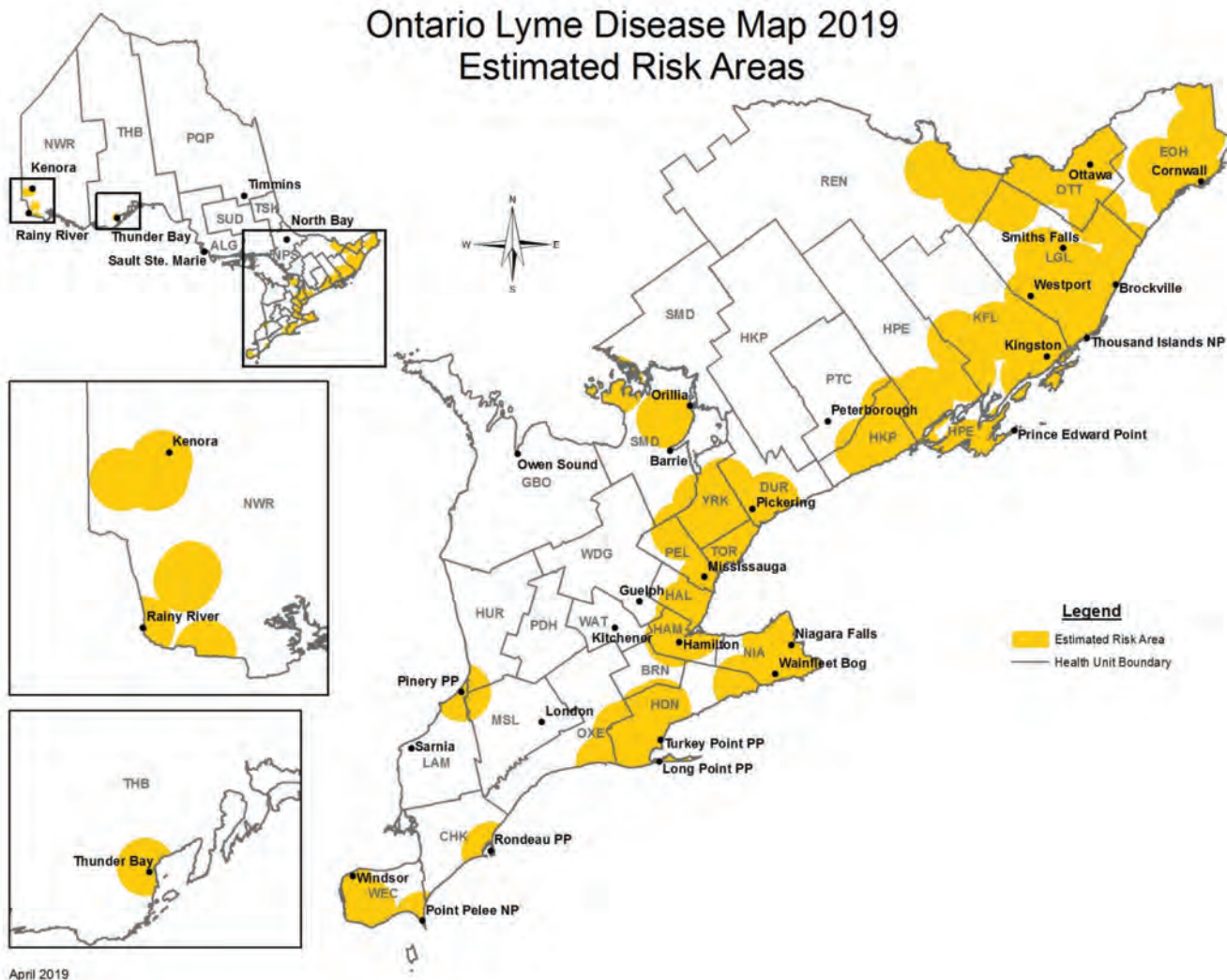


Figure 3: Risk map for Lyme disease. Estimated risk areas in Ontario (2019) ([www.publichealthontario.ca/-/media/documents/lyme-disease-risk-area-map-2019](http://www.publichealthontario.ca/-/media/documents/lyme-disease-risk-area-map-2019)). Published with permission of the Government of Ontario (Public Health Ontario).

encephalitis (3.7%) were both uncommon.<sup>4</sup> In a Norwegian study, neuroborreliosis more commonly presented with headache or meningismus than with cranial neuropathy.<sup>10</sup> A review of clinical manifestations of Lyme disease in Ontario confirmed the unusual nature of this case. Late disseminated Lyme disease was most likely to present in May through September (81%) and less than 3% of all cases of Lyme disease (erythema migrans, early disseminated or late disseminated) presented in December.<sup>11</sup>

Lyme disease is diagnosed based on clinical findings and supporting laboratory investigations. Erythema migrans, the earliest manifestation of Lyme disease, requires no laboratory confirmation and should be treated immediately with oral antibiotics. Early disseminated and late disseminated Lyme disease should be considered in endemic areas when patients present with compatible symptoms. Laboratory confirmation by 2-tiered Lyme serology is required.<sup>2</sup> If results from serology testing are nonreactive and Lyme disease is still clinically suspected, then serology testing must be repeated 4–6 weeks later. Nonstandard testing is highly discouraged because of the high rate of false-positive results.

Oral doxycycline, amoxicillin or cefuroxime axetil are the antibiotics of choice for children with Lyme disease of almost any stage. Doxycycline can be used in all age groups for courses up to 10 days.<sup>11</sup> For the treatment of Lyme meningitis, meningoen- cephalitis and carditis, intravenous ceftriaxone is recommended at presentation, but, after the patient improves, the antibiotic course may be completed orally.<sup>2,3</sup>

The keys to the diagnosis of neuroborreliosis in our case were the patient lived in an area endemic for Lyme disease, the preceding febrile illness and the photographic evidence of multiple regions of erythema migrans. The untreated, early disseminated Lyme disease progressed to late neuroborreliosis.

*Ixodes scapularis* is migrating northward and physicians should be familiar with the presentation of Lyme disease across all stages. In particular, recognition and treatment of early disease prevents progression to late disease. In addition, infection by other tick-borne pathogens, including Powassan virus, *Anaplasma phagocytophilum* and *Babesia* species, should be considered in the appropriate clinical contexts. These infections are

also likely to increase in incidence with the changing habitat of *I. scapularis*. Preventive measures must be stressed in all areas at risk of transmission of Lyme disease to decrease the human burden of disease and help protect patients.

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