

Double Crossed: A Case of La Crosse Encephalitis

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ABSTRACT

CASE REPORT: A 10-year-old male with T1DM and recent travel to North Carolina presented to an ED with 1 day of fever, vomiting, and headaches. He was discharged home with the presumptive diagnosis of viral gastroenteritis but returned nine hours later, agitated, and unable to speak.

CSF showed pleocytosis. MRI brain was normal, and EEG showed intermittent seizures. He was started on antiepileptics. Antibiotics were discontinued after negative bacterial work-up. Repeat MRI brain one week later showed enhancement in the left cerebral cortex. IVIG was started due to concern for autoimmune encephalitis. Repeat lumbar puncture was positive for La Crosse virus IgM.

DISCUSSION: This is the first case of La Crosse encephalitis (LACe) reported in Rhode Island.¹

La Crosse virus (LACv) is a ssRNA Bunyavirus transmitted by the eastern tree-hole mosquito typically between July and September. LACv is endemic to the upper Midwestern US and Appalachia. In 2018, 81 of 86 total cases reported by the CDC were pediatric. Children are more likely to present with vomiting, seizures, and focal cortical inflammation or cerebral edema on brain imaging. IgM may be negative early in the disease course. Treatment is antiepileptics and supportive care.

KEYWORDS: Arboviral encephalitis, La Crosse encephalitis, La Crosse virus, Meningoencephalitis

CASE REPORT

Case Presentation

A 10-year-old male with T1DM (diagnosed at 3 years old) presented with 1 day of fever, vomiting, and headaches in August. Vital signs were T99.4, BP 122/68, HR 110, RR 24, and SpO₂ 100%. Physical exam was significant for a normal neurological exam, including complete orientation to person, place, and time; his abdominal exam was notable for mild tenderness to the periumbilical area. Lab work showed Na 134, glucose 113, pH 7.4, UA with 2+ ketones, and beta-hydroxybutyrate of 0.97. The patient was thought to have mild ketosis from viral gastroenteritis and was discharged home, but returned nine hours later with altered

mental status, including agitation, screaming, and aphasia. Vital signs at this time were T99.4, BP 110/64, HR 98, RR20, and SpO₂ 100%. A travel history revealed that the patient recently returned from a trip to a family home in North Carolina, where he was noted to have gone swimming in Lake Lure. He also received numerous mosquito bites, of which he had frequently sent pictures to his mother. The patient's mother reported that a neighbor living on the same street in North Carolina recently presented to a local hospital with similar altered mental status and was diagnosed with La Crosse encephalitis (LACe).

Initial Workup and Hospital Course

In the ED, the patient was given IV fluids for dehydration, as well as IV morphine for his headache with only minimal improvement. A CT brain without contrast was normal. Blood cultures were drawn. A lumbar puncture (LP) was completed under sedation with ketamine. Ceftriaxone, Vancomycin, and Acyclovir were initiated in the ED to provide broad coverage for meningoencephalitides. Initial LP studies were significant for pleocytosis (**Table 1**) and a negative gram stain. The patient was suspected to have viral encephalitis and was admitted to the pediatric hospitalist service. Several hours after admission, the decision was made to transfer the patient to the PICU for closer monitoring of his neurological status. On admission, the patient was continued on Ceftriaxone and Vancomycin, but these were discontinued when CSF cultures returned negative at 48 hours. Acyclovir was discontinued on admission due to low clinical suspicion of HSV encephalitis. Doxycycline was added to cover for Rocky Mountain Spotted Fever and then discontinued when a Rickettsial panel returned negative several days

Table 1. Initial CSF Studies

	Value	Reference Value
Glucose	165	38–85
Protein	55	15–45
RBC	2346	0–5
Nucleated Cells	224	0–7
Polys	60%	0–2%
Lymphs	30%	63–99%
Monocytes	10%	3–37%

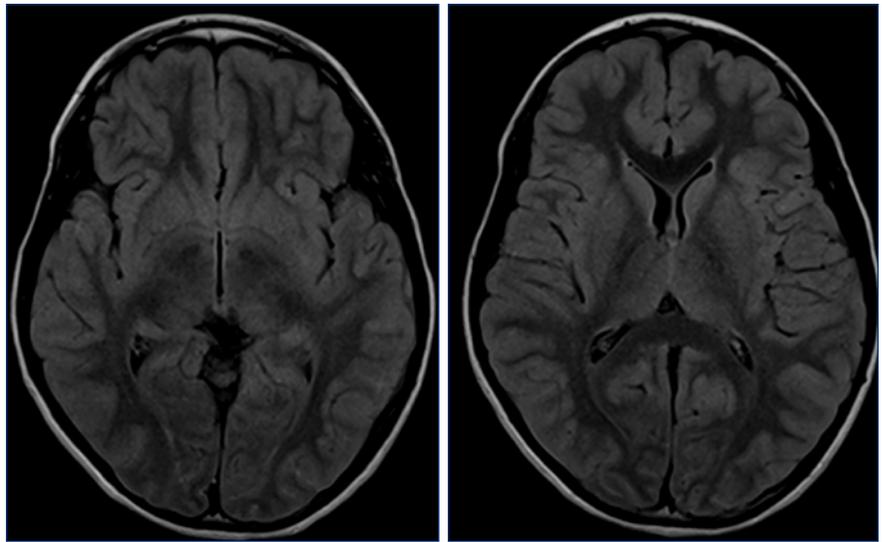
later. While in the PICU, the patient underwent MRI of the brain and spine, as well as an MRV of the brain, all of which were normal. EEG demonstrated bilateral hemispheric slowing, left greater than right, but no epileptiform activity. Ophthalmology was consulted for eye pain and photophobia, which was concerning due to the association of West Nile Virus with various ophthalmological complications, including anterior uveitis, retinal vasculitis, and optic neuritis.² Slit lamp and dilated eye exam showed superficial punctate keratitis but was otherwise normal. He was started on erythromycin ointment and artificial tears for ophthalmological management.

After two days in the PICU, the patient was transferred back to the pediatric hospitalist service due to stable though unchanged mental status. TPN was initiated for nutrition. The initial LP viral workup returned negative for Enterovirus, HSV, West Nile, and Arbovirus panel (which included testing for La Crosse, Western Equine Encephalitis, St. Louis Encephalitis, and Eastern Equine Encephalitis viruses). The patient then developed new-onset episodic right-sided gaze preference and right-beating nystagmus. Repeat EEG showed intermittent epileptiform discharges in the left temporal region associated with a clinical seizure. He was started on antiepileptics fosphenytoin and oxcarbazepine, but his encephalopathy persisted. The patient was transitioned from TPN to nasogastric tube feeds.

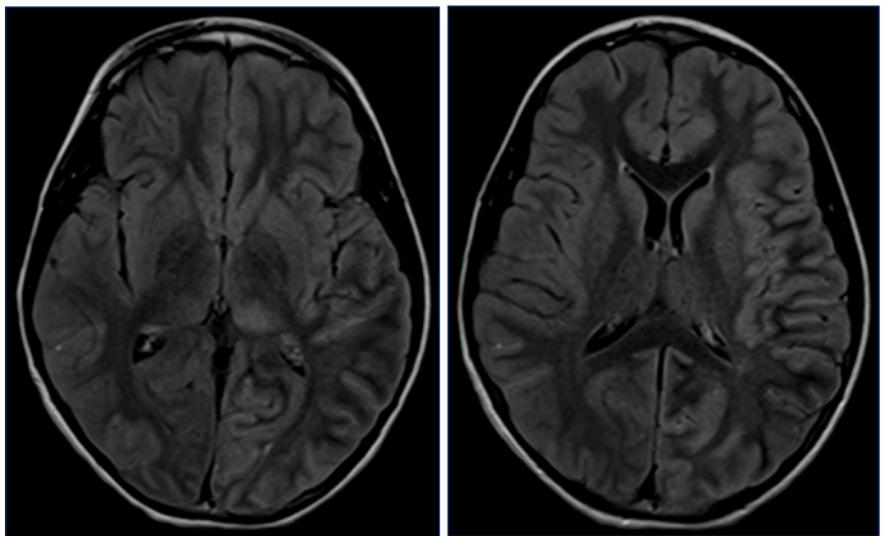
Diagnosis and Management

Autoimmune versus viral encephalitis remained the working diagnoses. Anti-NMDA Ab returned negative, making autoimmune encephalitis less likely. Given his recent travel from North Carolina and known exposure to a sick contact with LACe, the CDC was consulted and favored a viral etiology with supportive management. Repeat CSF studies and brain MRI were performed one week after initial presentation due to persistent altered mental status, recent development of seizures, and the need to send additional CSF studies. CSF studies this time included a repeat Arbovirus panel, Powassan virus testing, and antibodies to GAD65, TPO, and thyroglobulin (to assess for other causes of autoimmune encephalitis, such as Hashimoto's encephalopathy). Rectal Enterovirus cultures were also sent to the CDC

Figures 1 and 2. Initial transverse sections of MRI Brain FLAIR. Normal.



Figures 3 and 4. Repeat transverse sections of MRI Brain FLAIR 1 week after initial imaging. Diffuse left cortical swelling and hyperintense signal. Left pulvinar nucleus with hyperintense signal.



to check for Enterovirus D68 (the cause of acute flaccid paralysis syndrome). The repeat MRI brain showed interval new enhancement and swelling of the left cerebral cortex, with particular enhancement noted in the left pulvinar nucleus (**Images 1 through 4**).

Antibodies to GAD65, TPO, and thyroglobulin in the CSF returned elevated, but the significance of the anti-thyroid antibodies was unclear since approximately 25% of patients with T1DM have these antibodies at time of DM diagnosis.³ His thyroid function was normal, but this did not exclude Hashimoto encephalopathy.⁴ The working differential remained autoimmune versus viral encephalitis. While the efficacy of IVIG is uncertain in the management of viral encephalitis, IVIG was given in case of an autoimmune

etiology. After administration of IVIG, the patient was noted to become gradually more responsive and interactive, responding to questions appropriately with simple words. He was transitioned from nasogastric feeds to an oral diet. Due to significant but slowly improving neurodevelopmental deficits, the patient was discharged to a neurorehabilitation facility on antiepileptics. Several days after discharge, the CSF IgM for La Crosse virus (LACv) returned positive, clinching the diagnosis of LACe. Six months after initial presentation, the patient had residual but improved neurodevelopmental deficits, with signs of residual left hemispheric encephalopathy on EEG.

DISCUSSION

The LACv is a ssRNA virus in the genus Bunyavirus that is transmitted most commonly by the eastern tree-hole mosquito, *Aedes triseriatus*. Endemic geographic areas historically included the mid-western US, but recently shifted toward the Appalachian region.⁵ Onset of illness typically occurs July through September.^{5,6}

In 2018, the CDC reported 86 cases of LACe, 81 of which were pediatric.¹ LACv is the leading cause of pediatric arboviral encephalitis in the US with an average of ~70 neuroinvasive cases per year.⁷ The majority of severe clinical cases (>90%) are in children under age 16.⁸ Studies of the mechanism of age-dependent susceptibility to neuroinvasive disease from LACv in mice have shown that the host interferon response and adaptive immunity response have important roles, both of which are underdeveloped in children.⁷ However, LACv should also be considered in adult patients with altered mental status. Clinical disease onset ranges from 5 to 15 days post exposure.⁸ Common presenting symptoms shared in both pediatric and adult patients include headache, fever, and hyponatremia. Children are more likely to present with vomiting, seizures, and focal cortical inflammation or cerebral edema on brain imaging (as with the patient in this case), while adults rarely present with these findings.^{9,10}

Workup includes CSF viral culture, as well as La Crosse IgM in serum or CSF.¹¹ IgM may be negative if the patient presents early in disease course (as this patient was), and it is important to repeat studies if clinical suspicion is high.⁹ The patient in this case had exposure to multiple mosquito bites in the geographic region endemic to LACv and had a sick contact with LACe, which increased clinical suspicion for the diagnosis and prompted the decision to repeat CSF studies. A recent review of 44 articles reporting on risk factors for LACv cited factors that increase exposure to mosquitos, such as rural or wooded areas, time outside, not wearing repellent, and higher numbers of tires or artificial containers near the residence; the review did not note any risk factors of co-morbidities such as T1DM.⁸ The mainstay of LACe management is antiepileptics and supportive care (including speech/physical therapy). Less well-studied interventions

include ribavirin and IVIG, which have been hypothesized as treatments for LACe and other viral encephalitides.¹² Case fatality rates ranging from 1.5 to 3.1%, and up to 8.6% in patients suffering from encephalitis, have been reported.^{13,14}

CONCLUSIONS

In areas non-endemic to arbovirus encephalitides, it is important to obtain a thorough travel history in patients with altered mental status. This case was the first ever reported case of LACe in the state of Rhode Island.¹ LACe more commonly presents in children than adults but should be considered in both populations, especially during July through September. Children are more likely than adults to present with vomiting, seizures, and cerebral edema and inflammation on brain imaging. La Crosse IgM may be negative early in disease course. Consult the CDC and repeat studies if clinical suspicion is high.¹¹

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Disclaimer

The views expressed herein are those of the authors and do not necessarily reflect the views of Brown University, Hasbro Children's Hospital, and Rhode Island Hospital.

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