



Case Reports

A Fatal Case of Powassan Virus Encephalitis

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Abstract

The Powassan virus (POWV) is part of the Flaviviridae family. It is mainly transmitted via tickbite but can rarely be spread person-to-person through blood transfusions. Initial symptoms include fever, headache, and vomiting. It can cause severe symptoms, including confusion, aphasia, and seizures. Approximately 1 out of 10 people with severe disease die. From 2010 to 2020, 194 Powassan virus cases have been reported to the Center for Disease Control (CDC), with 22 of them resulting in death. In this case report, we discuss a 39-year-old female who presented with fever, myalgia, and confusion. During her hospitalization, she developed tonic-clonic seizures, which required sedation and intubation. A central venous catheter was inserted due to poor intravenous access, and in the process of placing it, the provider sustained a needle stick injury. The patient was eventually diagnosed with POWV encephalitis and transferred to a higher level of care, where a brain perfusion study showed an absence of brain flow consistent with brain death. After a discussion with the family, the decision was made to extubate the patient terminally. The provider who sustained the needle stick injury reported no concerning symptoms two years after the event.

BACKGROUND

The Powassan virus (POWV) is part of the Flaviviridae family and is the only North American member of the tick-borne encephalitis serogroup of flaviviruses.¹ POWV can be found in parts of Canada, the United States, and Russia. It can be further distinguished between two lineages. Lineage I is transmitted by *Ixodes cookei*, which is endemic primarily in the Great Lakes region, and lineage II is transmitted by *Ixodes scapularis*, which is endemic mainly in Northeast United States.² According to the Centers for Disease Control (CDC), the Powassan virus can rarely be spread person-to-person through blood transfusions.^{3,4} Initial symptoms include fever, headache, and vomiting. It can also cause severe disease, including confusion, loss of coordination, difficulty speaking, and seizures. Approximately 1 out of 10 people with severe disease die.⁵ Fifty percent of survivors display long-term sequelae such as hemiplegia, muscle wasting, recurrent headaches, ocular abnormalities, and impaired memory.¹ From 2010-2020, 194 Powassan virus neuroinvasive and non-neuroinvasive cases have been reported to the CDC. These have occurred mainly in Minnesota, Wisconsin, and New York. Of the 194 cases, 22 of them led to death.⁶

CASE PRESENTATION

In late Fall, a 39-year-old female with a past medical history of COVID-19 one month prior to admission and a recent tick bite that occurred in upstate New York about ten days earlier presented to the hospital because of fever, nausea, myalgias, vomiting, diarrhea, and confusion present for four days. She was in the emergency department (ED) two days prior for similar symptoms but was discharged home after her symptoms improved. She was initially afebrile in the ED, but her temperature later increased to 103.0 Fahrenheit (F). She also became tachycardic, hypertensive, and tachypneic. The ED physician noted that the patient was restless, disoriented, and had possible right cranial nerve VI palsy. Her laboratory analysis was unremarkable except for slight transaminitis with ALT 47 IU/L [7-40] but a normal AST of 38 IU/L [15-41]. A computed tomography (CT) scan of the abdomen, pelvis, and head and a CT angiogram showed no acute abnormalities.

The patient received a liter of normal saline and intravenous doses of acyclovir, ceftriaxone, doxycycline, vancomycin, and ondansetron. The patient was agitated and restless and, therefore, required sedation to perform a lumbar puncture. Her cerebrospinal fluid (CSF) was clear in color, with an elevated protein of 162 mg/dl

[12-60], normal glucose of 74 mg/dl [40-80], elevated white blood cell count (WBC) 55 cells/mcL [0-10], and red blood cell count 11 cells/mcL [0-10]. At this point, viral meningitis was high on our differential, and the CSF WBC count made a bacterial etiology less likely. Various serologic and CSF tests were ordered. Serologic tests included Lyme antibody (Ab) screen with a reflex blot, *Babesia microti* DNA polymerase chain reaction (PCR), *Anaplasmosis phagocytophilum* reverse transcription (RT)-PCR, blood parasite smear, Herpes simplex I and II DNA PCR, SARS-CoV2 immunoglobulin (Ig)-G, *Naegleria fowleri* PCR, blood cultures, Human Immunodeficiency Virus (HIV) testing, and Syphilis screen. These labs were later found to be negative or non-reactive. CSF tests included Lyme CSF Serum Index, Lyme Western Blot CSF, West Nile Ab CSF, COVID-19 PCR CSF, Powassan virus RNA PCR CSF, Herpes simplex PCR CSF, *Mycobacteria* CSF culture, Fungal CSF culture, CSF culture with gram stain, and CSF cell count. The patient was admitted to the intensive care unit (ICU) for closer monitoring and management of possible meningoencephalitis.

The patient was started on ceftriaxone 2 grams (g) IV every 12 hours (q12hr), vancomycin 1 g IV q12hr, and acyclovir 10 mg/kg q8hr for empiric meningoencephalitis coverage. She was also placed on continuous electroencephalogram (EEG) monitoring. The following day, the patient continued to be febrile and had multiple bouts of vomiting. Later that night, she developed tonic-clonic seizures and had fevers ranging between 101.8 F-103.8 F. The patient received multiple doses of lorazepam 2 mg intravenously, with no improvement. She then received a 1000 mg dose of levetiracetam and a loading dose of fosphenytoin 20 mg/kg. Due to poor IV access, a central line was ordered. A provider placed a triple-lumen catheter in the right internal jugular vein; however, in the process of inserting it, he sustained a needle stick injury that caused a small break superficially to his skin. The provider was wearing sterile gloves during the procedure. The patient continued to have seizures and was eventually intubated and placed on a ventilator the following morning to protect her airway and suppress seizure activity. She was started on midazolam and propofol, which controlled the seizures. EEG monitoring showed burst suppression with mixed delta and theta slow wave activity bursts consistent with an encephalopathic process and pharmacological suppression. The patient was hemodynamically stable on the ventilator, and the decision was made to transfer her from our community hospital to a tertiary care center where she could receive a magnetic resonance imaging (MRI) of her brain while maintaining ventilatory support. At discharge, the patient's completed labs included blood cultures, blood parasite smear, CSF Gram stain, HIV testing, Syphilis screen, and Lyme IgG and IgM, which were all negative.

As we were preparing to transfer the patient, the lab called to report the Powassan virus RNA PCR CSF result, which returned positive. The remaining CSF and serologic tests were later found to be negative. The Intensivist team at the tertiary care center continued antiepileptic medication and continued sedation with midazolam and propofol while on full ventilator support. The following morning, the patient had fixed, dilated pupils on physical exam. In addition, she had no gag reflex, no response to noxious stimuli, and no corneal reflex. An emergent CT scan of the head showed diffuse cerebral edema with evidence of herniation. The patient subsequently received steroids, mannitol, and 3% saline. The respiratory rate and tidal volume on the ventilator were also increased. Neurosurgery attempted a ventriculostomy and placed an external ventricular drain with very high pressures over 40 cm H₂O. Repeat CT head showed worsening persistent edema. Prior to completing the mannitol bolus, the patient's sodium level ranged between 140 to 150 mmol/L, which was likely due to diabetes insipidus. The patient received desmopressin (DDAVP) and free water boluses to correct her sodium levels. Three percent saline and mannitol infusions were stopped.

Her prognosis was guarded with clinical examination consistent with brain death. A nuclear cerebral perfusion study showed the absence of brain flow consistent with brain death. After a discussion with her family, a Do Not Resuscitate order was entered. Severe hypernatremia needed to be corrected prior to initiating the brain death protocol. The patient was treated aggressively with free water and DDAVP to correct hypernatremia. An insulin drip and insulin glargine were started for persistent hyperglycemia. The patient became hypotensive, and pressors were used to maintain systolic blood pressures between 100 and 140 mmHg. At this point, all antibiotics were discontinued. After a discussion with the family, the decision was made to withdraw care and terminally extubate the patient. She died soon after.

DISCUSSION

Since the mid-1990s, the average number of POWV cases increased drastically from 0.7 cases/year (1958-1998) to 1.3 cases/year (1995-2005) and then 9 cases/year (2006-2016).⁷ *I. scapularis* has more aggressive feeding and transmission properties than does *I. cookie*, thus may pose a more significant public health threat and may account for the increasing prevalence of the disease.¹ Small to medium-sized mammals serve as zoonotic reservoirs for POWV, including white-footed mice, red squirrels, and chipmunks.⁷

To diagnose POWV, a patient must fulfill the clinical criteria, either neuroinvasive or non-neuroinvasive symptoms, and laboratory criteria, such as positive CSF studies.⁸ CSF findings usually include lymphocytic pleocyto-

sis, predominantly neutrophils early in the disease, mildly elevated or normal protein, and normal glucose concentration.⁹ In New York State, testing for POWV is conducted via the state health department laboratory. Based on our index of suspicion for vector-borne neurologic infection in our patient, we sent a sample of the patient's CSF to our state laboratory to evaluate for vector-borne illnesses. The state lab performed a PCR test to detect viral RNA in the patient's CSF. PCR testing allows for rapid diagnosis of arboviral illness, particularly in settings where there is active viral replication. It can provide more timely results than serologic testing for virus-specific antibodies.¹⁰

Currently, there are no vaccines or treatments to prevent or cure POWV infections. However, recent mRNA and DNA vector-based vaccine candidates have shown promising results in animal protection tests.^{11,12} For now, avoiding tick exposure is the most effective method for prevention. Options for preventing tick bites include using Environmental Protection Agency (EPA) registered insect repellents, wearing light-colored clothing, tucking pants into socks, and checking your clothing and body for ticks after being outdoors.⁴ Management is supportive, and in severe cases, respiratory support, pressors, intravenous fluids, and management of seizures and cerebral edema are usually required, as we saw in our case. Case reports mentioned the use of high-dose steroids and intravenous immune globulin (IVIG), but their roles remain unclear.¹³

In this case report, there was a needle stick injury when a central line was being inserted. There is a documented case of POWV infection being transmitted through blood transfusion.¹³ In addition, a small number of West Nile Virus infections, another member of the family Flaviviridae, have been reported from blood transfusions.¹⁴ Thus, in theory, a needle stick injury can spread the infection. The provider who sustained this injury reported no concerning symptoms more than two years after the event. At the time of the injury, the provider followed the needlestick protocol implemented at our hospital, which primarily concerns itself with Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and HIV. The U.S. blood supply currently screens for two flaviviruses, West Nile and Zika. Given the low incidence of POWV disease, even in endemic areas, the cost-benefit ratio of screening for it would likely be high. Currently, there are no U.S. Food and Drug Administration-licensed

tests to screen the blood supply for POWV.¹³ It should be noted that in the limited cases of hematological spread, immunocompromised patients were at higher risk of being infected. Therefore, it is important to keep POWV in the differential when an immunocompromised patient presents with febrile illness, aseptic meningitis, or encephalitis in both endemic and non-endemic areas.

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Author Contributions

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- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosures/Conflicts of Interest

The authors declare they have no conflicts of interest.

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