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Case Reports

Powassan Virus-Related Encephalitis in the Off-Season: A Case Report

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Abstract

Arboviral infections, increasingly identified due to the effects of climate change, pose significant health risks. We present a case of meningoencephalitis due to Powassan (tick-borne Flavivirus) virus in a middle-aged man from Rhode Island, unexpectedly diagnosed in the winter season. Confirmatory plaque reduction neutralization testing (Centers for Disease Control) revealed elevated titers for Powassan virus >1:20,480. The cerebrospinal fluid analysis demonstrated lymphocytic pleocytosis. The case highlights the expanding seasonal and geographic range of arboviruses, necessitating year-round vigilance. No targeted therapies exist; management remains supportive as 40-60% of patients develop chronic sequelae, including persistent confusion, fatigue, and headache. Arboviral etiologies in patients with altered mentation must be prioritized on the differential, even outside of peak transmission seasons.

BACKGROUND

Arboviral infections are increasingly recognized as significant causes of central nervous system (CNS) infections, particularly as climate change alters the distribution and activity of vector populations.[1] It is essential to include arboviral pathogens in the differential diagnosis in patients presenting with altered mentation. These pathogens, primarily transmitted by mosquitos and ticks, include notable agents such as Powassan virus.[2] Powassan virus, a member of the *Flavivirus* genus, is transmitted by *Ixodes scapularis* ticks and is endemic to the northern, central, and eastern regions of the United States.[2,3] Powassan virus is an emerging cause of viral encephalitis with significant morbidity and mortality.[3,4] The traditional seasonal patterns of arboviral transmission are becoming less predictable due to factors such as climate change, increased travel, intra-seasonal variations, and diverse environmental exposures.

CASE PRESENTATION

A 63-year-old man with a history of migraines, managed with erenumab and sumatriptan, presented with acute confusion. The patient had been in his usual state of health until three days prior to the presentation when he developed worsening pulsatile headaches accompanied by photophobia and phonophobia. His symptoms did not improve with his usual sumatriptan. Upon consulting his neurologist, he was administered a dose of erenumab and started on a prednisone taper, but he continued to deteriorate. He subsequently developed confusion, disorientation to time and place, and ataxia and was referred to the hospital for further evaluation. The patient had a dog that frequently acquired ticks despite routine tick prevention measures. The patient often engaged in outdoor activities such as hiking and hunting in local wooded areas and had recently traveled to the state of Maine for a fishing trip one month prior to the presentation. He denied any recent tick bites or exposure to ticks. His medical history included treatment for Lyme disease 20 years ago with oral doxycycline. He worked as a technical writer and editor and lived with his wife and son.

During hospitalization, the patient presented with a fever of 100.8 F, underwent a lumbar puncture and was initiated on empiric antimicrobial therapy for suspected meningoencephalitis, including acyclovir, ampicillin, ceftriaxone, vancomycin, and dexamethasone. Cerebrospinal fluid (CSF) analysis revealed the following: glucose of 59 mg/dL (42-91mg/dl), protein 90 mg/dL (13-43mg/dl), with CSF erythrocytes 2303 cells/mm3, 34 nucleated cells/mm3 (differential: 10% neutrophils, 86% lymphocytes, 4% monocytes, and 0% blasts). CSF cultures and multiplex PCR testing (BioFire) returned negative results for bacterial and viral pathogens, including Listeria monocytogenes, Neisseria meningitidis, and Streptococcus pneumoniae. Herpes simplex virus (HSV) 1/2 PCR and CSF Borrelia burgdorferi IgG and IgM antibodies were negative. Serum testing demonstrated a Borrelia burgdorferi antibody level of 2.9 (0.0 - 0.8) with a Lyme western blot showing 1/3 IgM bands and 2/10 IgG bands interpreted as non-reactive under our laboratory standards. Serum treponemal IgG and IgM and HIV screening were negative. Serum Powassan virus IgM and Jamestown Canyon virus (JCV) IgM returned positive. Magnetic resonance imaging (MRI) of the brain with and

without gadolinium demonstrated no acute abnormality. The electroencephalogram (EEG) revealed moderate diffuse slowing, with no focal or lateralized findings, consistent with moderate diffuse encephalopathy.

Samples were sent to the Centers for Disease Control and Prevention (CDC) for confirmatory plaque reduction neutralization testing (PRNT), with results available post-discharge. Serum PRNT titers for JCV were positive at 1:160, with none on CSF testing. Serum PRNT titers were markedly elevated for Powassan virus >1:20,480, and CSF PRNT titers were 1:4, strongly supporting acute Powassan infection with a past JCV infection. During hospitalization, the patient's mental status gradually improved, although it did not return to baseline. He was discharged to a rehabilitation facility with instructions to complete a 21-day course of doxycycline. At a one-month outpatient infectious diseases follow-up, he reported persistent symptoms, including fatigue, forgetfulness, neck pain, and headaches, though these were slowly improving. The patient has continued to follow up with physical therapy and neurology clinics for ongoing management of his symptoms.

DISCUSSION

Viral etiologies, particularly arboviral pathogens, are critical considerations in patients presenting with acute altered mentation. Reported cases of arboviral infections have steadily increased from 2015 to 2024, though the true incidence is likely higher due to underreporting from mild or subclinical cases that go unrecognized. Powassan virus has a case fatality rate of 10-15% with focal neurologic deficits occurring in over 50% of patients.[3] In ArboNet in 2024, 54 Powassan virus cases were reported in the United States.[2]This case highlights an infection with confirmed Powassan virus with a past JCV infection. We hypothesized that the patient had a past JCV infection that was improved and had acute neurological decline following the Powassan virus infection.

Powassan virus transmission occurs within 15 minutes of tick attachment—a stark contrast to other tick-borne pathogens (*Borrelia, Babesia, Anaplasma*), which require 48-72 hours of feeding and have incubation periods of 1-5 weeks.[1] Powassan virus's neurotropism drives a biphasic clinical course.[1] The initial febrile phase involves nonspecific symptoms (fever, malaise, headache, nausea, and vomiting), which may transiently resolve within 2-8 days.[1,3] Severe cases progress to a second phase marked by high fever, recurrent headache, vomiting, or paresthesia. This phase manifests as meningoencephalitis, poliomyelitis-like flaccid paralysis, or polyradiculoneuritis resembling Guillain-Barre syndrome.[1,3,5]

Serum and CSF IgM and IgG antibodies with a fourfold increase in acute and convalescent paired sera confirm the diagnosis.[3,4] RT-PCR can be used to detect viremia, and for flaviviruses have a high degree of sensitivity and specificity.[3] IgM may appear early in the CSF in the course of infection; however, caution is required in interpretation as there is a great deal of cross-reactivity between other flaviviruses and non-flaviviruses, which may lead to false positives.[3,4] Confirmation testing is the PRNT, which takes several weeks to result. In a compatible clinical presentation and patient, a fourfold change in serum antibody titers, or virus-specific IgM in the CSF, which reflects intrathecal immune response, can help establish the diagnosis.[3] Typically, presentation and hospitalization occur during the encephalitis phase of the illness, where the viral RNA has cleared, and the viral-specific antibodies are formed. The cornerstone of diagnosing CNS infections is the lumbar puncture. CSF studies can reveal a moderate lymphocytic pleocytosis with normal or elevated CSF protein levels.[3] MRI of the brain can show a variety of signal abnormalities in the thalamus and basal ganglia, such as T2/FLAIR hyperintensities or none at all.[3,6] Electroencephalogram can show diffuse slowing in 90% of patients with encephalitis with or without neurological examination abnormalities in Powassan virus, while in JCV infection, two-thirds of patients may have a periodic lateralizing epileptiform discharges that mimicking herpes simplex encephalitis.[3,4]

This patient developed symptoms and was diagnosed during the winter season in Rhode Island, an atypical presentation given that arboviral infections typically peak in the summer months (May-September) when tick and mosquito activity is highest. This case underscores the importance of maintaining clinical vigilance for arboviral etiologies—even outside traditional transmission seasons—in patients presenting with altered mentation or suspected CNS infections. No specific antiviral therapies exist for Powassan virus infections; management is supportive. Clinical priorities include optimizing nutritional support, addressing neurological sequelae, and excluding alternative causes of encephalopathy. Long-term sequelae occur in 40-60% of survivors, commonly manifesting as asthenia, chronic headaches, memory deficits, impaired concentration, anxiety, and emotional lability.[1,5]

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