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A 57-year-old woman from Minnesota presented to the emergency department in October with a 4-day history of fever (102° F), alongside progressive fatigue, unsteady gait, confusion, and difficulty speaking. On exam, a diffuse, punctate papular rash was documented on her abdomen and bilaterally on her thighs. The patient was a chronic smoker, but was otherwise healthy. Her family indicated that she had been feeling unwell for approximately one week prior to seeking medical attention. A head CT performed on admission was normal. Cerebrospinal fluid (CSF) was collected and noted to be clear in appearance, with normal glucose (68 mg/dL; normal range is 70-140 mg/dL), elevated protein (75 mg/dL; normal range is 0-35 mg/dL), and a cell count of 153 cells/µL (38% lymphocytes). A CSF Gram stain was negative. The patient was initiated on vancomycin, ceftriaxone and acyclovir for empiric treatment of infectious meningoencephalitis. She was also placed on continuous electroencephalography (EEG) monitoring, which demonstrated evidence of two focal motor seizures. A head MRI performed one day post admission showed leptomeningeal and perivascular enhancement with cerebellitis and basal ganglia involvement. The patient was intubated due to tachypnea and decreasing neurologic function. An extensive diagnostic work-up was undertaken and was ultimately uninformative. A CSF sample was subsequently sent to the State Public Health Laboratory for Powassan and Jamestown Canyon virus serologic testing. The patient was positive for IgM antibodies to Powassan virus in CSF, and confirmatory plaque reduction neutralization testing (PRNT) performed at the CDC demonstrated the presence of neutralizing antibodies to the virus. Upon further discussion with the patient's family, it was revealed that the patient frequently worked outdoors collecting and chopping wood for a wood-burning furnace. The patient expired 3 months following initial presentation.

The vector for Powassan virus can also transmit which of the following infectious agents?

A. *Borrelia burgdorferi*
B. Chikungunya virus
C. Dengue virus
D. Jamestown Canyon virus
E. *Rickettsia rickettsii*

Answer and Explanation

Correct Answer is A: Powassan virus is transmitted by *Ixodes* species ticks, similar to *Borrelia burgdorferi*, the causative agent of Lyme disease.

Powassan virus (POWV) is a single-stranded, positive-sense RNA *Flavivirus* which naturally circulates between *Ixodes* species ticks and small-to-medium-sized rodents such as squirrels, woodchucks, and white-footed mice. Infected humans are regarded as dead-end hosts because they do not develop a high enough viral load to transmit the virus to naïve ticks. Two pathogenic lineages of POWV have been identified. Lineage I is considered the 'prototype' lineage and is associated with *I. cookie* and *I. marxi* ticks, which rarely bite humans. In contrast, linage II, referred to as the deer tick virus, is transmitted by *I.*

scapularis ticks, which are also the primary vectors for numerous other tick-borne agents, including *Borrelia burgdorferi, Babesia microti*, and *Anaplasma phagocytophilum*.

POWV was first identified in 1958 as the causative agent of a fatal case of encephalitis in a 5-year-old boy from Powassan, Ontario. Since then, POWV infections with neurologic involvement have been reported in the Unites States, Canada, and Russia, with an increasing number of cases identified over the past 10 years. This rise in incidence may in part be due to enhanced surveillance efforts, increased clinician awareness, and the availability of diagnostic testing in public health laboratories; however, the full extent and spectrum of disease is still not fully understood. In the United States, the majority of cases occur in New York, Minnesota, and Wisconsin, overlapping with the distribution of *I. scapularis*. In Wisconsin, approximately 1% of *I. scapularis* were shown to carry POWV. Since 2003, over 100 human cases have been reported to the CDC, with 22 cases reported in 2016 alone (USGS Disease Maps https://diseasemaps.usgs.gov/mapviewer/).

The incubation period for POWV ranges from 1 to 5 weeks and while some individuals remain asymptomatic, the prodrome in patients who develop symptoms typically includes fever, headache, fatigue, and confusion. Many patients will also develop a diffuse, maculopapular rash on their trunk and extremities. In cases which progress to significant neurologic disease, patients may present with encephalitis, meningitis, or meningoencephalitis. While specific predisposing factors that may lead to more severe or neuroinvasive disease have not been identified to date, approximately half of reported POWV cases with neurologic involvement occur in patients without underlying comorbidities. There is no targeted antiviral treatment for POWV and the mortality rate for patients with neurologic involvement is ~10%. Among survivors, recovery can take weeks to months, though ~50% of patients will suffer long term neurologic deficits.

The diagnosis of POWV is dependent on clinical suspicion, guided by a detailed clinical evaluation and exposure history, alongside imaging studies and diagnostic testing of CSF. In patients with neurologic involvement, MRI imaging frequently reveals abnormal hyper-intensities in the parenchyma, while CSF studies are generally notable for lymphocytic pleocytosis and elevated protein. Similar to other arboviral infections, molecular testing in serum and CSF is often of low yield due to the short viremic phase (approximately 1 week in duration) and low-level viremia. Therefore, serologic testing for antibodies to POWV in CSF is the preferred diagnostic modality. Serologic assessment includes evaluation for IgM-class antibodies to POWV and plaque reduction neutralization tests (PRNT) for detection of neutralizing, primarily IgG-class antibodies to the virus. IgM antibodies are typically detectable weeks to months following infection, while IgG-class antibodies remain detectable for years following symptom onset. Currently, diagnostic testing for POWV is only available at select public health laboratories and the CDC.

Suggested Reading

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Authors

Elitza S. Theel, Ph.D., D(ABMM); Mayo Clinic

Alexandra Bryson, Ph.D.; Mayo Clinic