Fatal Disseminated Powassan Virus Infection in Transplant Recipient, Pennsylvania, USA

Derek C. Sung, Robert Colbourn, Niaz Khan, Joseph DiRienzi, Lili Randolph, Federico Valdivieso, Suyash Mohan, H. Isaac Chen, Georgia Ficarra, Brooke Leitgeb, Crystal Gigante, Lillian Orciari, Michael Niezgoda, Pamela Yager, Ryan Wallace, Krystal Mason, Parthasarathy Kesavaramanujam, Hephzibah Tagaram, Betsy Schroeder, Ashley Schafer, Kelly Raum, Sofia Barrios, Kathleen Degnan, Alexa Lustig, Alexandra H. Tatarian, Nicole A. Aqui, Laurel Glaser, Leslie Litzky, Julu Bhatnagar, Julian A. Villalba, MacLean P. Nasrallah

Author affiliations: Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA (D.C. Sung, R. Colbourn, N. Khan, J. DiRienzi, L. Randolph, F. Valdivieso, S. Mohan, H.I. Chen, S. Barrios, K. Degnan, A. Lustig, A.H. Tatarian, N.A. Aqui, L. Glaser, L. Litzky, M.P. Nasrallah); Centers for Disease Control and Prevention, Atlanta, Georgia, USA (G. Ficarra, B. Leitgeb, C. Gigante, L. Orciari, M. Niezgoda, P. Yager, R. Wallace, J. Bhatnagar, J.A. Villalba); Pennsylvania Department of Health, Harrisburg, Pennsylvania, USA (K. Mason, P. Kesavaramanujam, H. Tagaram, B. Schroeder); Chester County Health Department, West Chester, Pennsylvania, USA (A. Schafer, K. Raum)

DOI: https://doi.org/10.3201/eid3212.260193

We describe histopathologic findings from a fatal case of Powassan virus lineage 2 (deer tick virus) in an immunosuppressed liver transplant patient in Pennsylvania, USA. We confirmed infection in postmortem brain, lung, and kidney by immunohistochemistry, in situ hybridization, and reverse transcription PCR, demonstrating infection of pulmonary and renal tissues.

Powassan virus (POWV) is a tickborne flavivirus that causes severe encephalitis. Cases are increasing annually; 60 cases and 9 deaths were confirmed in the United States during 2024 (*1*). Neuroinvasive disease occurs in 94% of confirmed cases and 98% of fatalities (*1*). We describe novel histopathologic findings of disseminated POWV infection with multiorgan involvement in a liver transplant recipient in Pennsylvania, USA.

The patient was a 38-year-old woman in southeastern Pennsylvania, USA, who had alcohol-associated cirrhosis and remote preexposure prophylactic rabies vaccination 16 years earlier. She had undergone orthotopic liver transplant 6 weeks before seeking care at an emergency department for malaise, headache, fever, and leukocytosis. After admission, she had multiple generalized seizures. Magnetic resonance imaging revealed hydrocephalus with rapidly progressive enhancement of the cerebellum, brainstem, white matter, cortex, leptomeninges, and spinal cord (Figure, panels A–E). Cerebrospinal fluid (CSF) studies were consistent with viral encephalitis (Appendix Table 1, https://wwnc.cdc.gov/EID/article/32/12/26-0193-App1.pdf). We ruled out autoimmune and other causes of viral encephalitis. Brain biopsy demonstrated lymphocytic encephalitis without features of a specific infectious etiology. We noted necrotic tissue intraoperatively, and the procedure was complicated by hemorrhage. The patient's neurologic status deteriorated further, and she died after being transitioned to comfort care. CSF reverse transcription PCR testing for POWV was positive for lineage 2 (deer tick virus) the day before her death. POWV serum IgM test result was positive after her death (Table). Of note, CSF metagenomic sequencing on an earlier sample was negative for POWV (Appendix Table 1), which might reflect low viral load or testing detection limits.

Because of the patient's rapid neurologic decline and imaging findings, rabies was initially suspected because other common causes were ruled out. Testing was expeditiously conducted for the safety of other organ recipients. Antemortem serum and CSF indirect immunofluorescent antibody rabies testing detected IgG, but not IgM. A rapid fluorescent focus inhibition test detected high serum rabies antibody titers and low CSF titers. Presence of rabies IgG in the CSF, although atypical, was attributed to previous vaccination and might have resulted from serum antibody spillover secondary to leaky blood–brain barrier from severe meningoencephalitis. Results of additional antemortem and postmortem rabies test results, including immunohistochemistry and PCR of the brain and liver, were negative (Appendix Table 2).

At autopsy, the brain contained a 3.2-cm focus of right basal ganglia necrosis and hemorrhage, diffuse edema, and bilateral basal ganglia softening. Histopathologic testing revealed widespread meningoencephalitis involving the cerebrum, pons, and cerebellum, with diffuse lymphoplasmacytic parenchymal and leptomeningeal inflammation, microgliosis, and marked Purkinje cell loss (Figure, panels F–H). Microglial nodules were not prominent, and intranuclear viral inclusions (Negri bodies) were absent. Available viral stain results were

negative. POWV antigens and nucleic acids were detected by immunohistochemistry, in situ hybridization, or reverse transcription PCR (Table) in postmortem brain samples (Figure, panels I–L). Non–central nervous system findings included mild lymphocytic pneumonitis and bronchiolar epithelial apoptosis (Figure, panels M, N), POWV antigen and RNA in bronchiolar epithelial cells (Figure, panel O) and circulating mononuclear cells (Figure, panel P), renal acute tubular necrosis (Figure, panel Q), mononuclear peritubular infiltrates in the kidney (Figure, panels R–T), and mild-to-moderate portal inflammation and sinusoidal congestion with mild ischemic features in the donor liver. Powassan nucleic acids were found by in situ hybridization in rare circulating mononuclear cells in postmortem liver allograft samples.

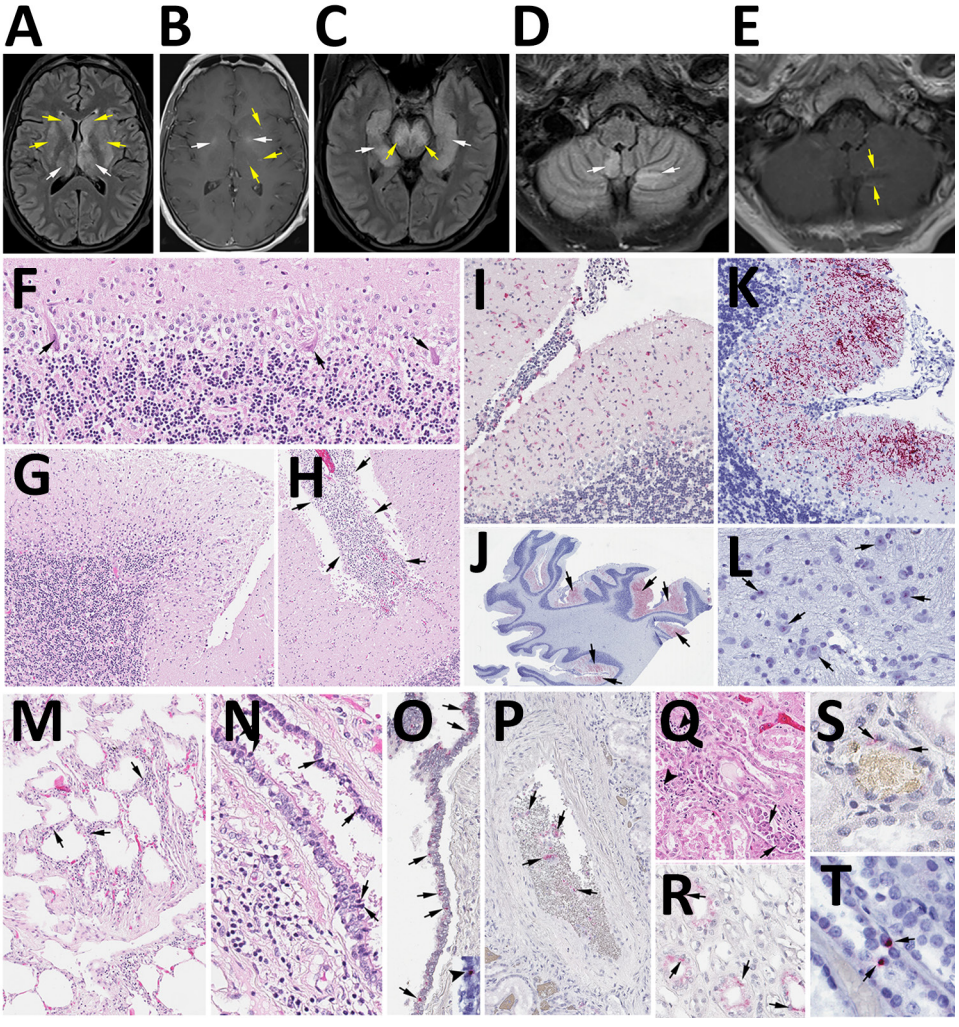


Figure. Magnetic resonance imaging and microphotographs for detection of POWV lineage 2 (deer tick virus) in postmortem tissues from a liver transplant patient with fatal infection and histopathological features of formalin-fixed, paraffin-embedded tissues collected at autopsy, Pennsylvania, USA. A) Axial T2-FLAIR image revealing T2 hyperintensity in (left worse than right) bilateral deep gray nuclei (caudate nucleus and putamen, yellow arrows) and thalami (white arrows). B) Axial postcontrast T1-weighted image demonstrating faint areas of perivascular enhancement (yellow arrows) in the deep gray nuclei. T1 hyperintensity of bilateral globus pallidi from manganese deposition in this patient with history of chronic liver dysfunction. C, D) Axial T2-FLAIR images demonstrating near symmetric involvement of bilateral hippocampi (white arrows), brain stem (yellow arrows, substantia nigra) and bilateral cerebellar hemispheres (white arrows). E) Axial postcontrast T1-weighted image demonstrating faint areas of leptomeningeal enhancement (yellow arrows) along left cerebellum. F–L) Cerebellum: widespread meningoencephalitis with extensive cerebellar involvement associated marked Purkinje cell necrosis (F, arrows) diffuse lymphoplasmacytic parenchymal (G), and leptomeningeal inflammation and microgliosis (H). Abundant POWV antigen (I) and RNA (J–K) were detected, which was more abundant in the molecular cell layer (J) (arrows), but present in multiple cell types of all layers. We identified histopathologic evidence of meningoencephalitis and POWV antigen and RNA detection in other regions of the central nervous system including neurons in the pons (L) (arrows) and cerebrum. M–P) Lungs: features of mild lymphocytic pneumonitis (M) (arrows, infiltrates in alveolar septa), and bronchiolar epithelial denudation (N) with epithelial cell apoptosis (arrows). We detected POWV antigen (O) and RNA (O, inset) in bronchiolar epithelial cells (arrows), and other cell types such as pneumocytes and endothelial cells. We detected POWV antigens (arrows) and RNA (not shown) in circulating mononuclear cells in various organs, including the kidneys (P), lungs, and liver. Q–T) Kidney: multifocal, interstitial, and predominantly mononuclear peritubular infiltrates (Q) (arrowheads) associated with features of acute tubular injury, including epithelial denudation (arrows), attenuation with loss of apical cytoplasm, and pigmented casts (S) (pigmented intratubular brown material). POWV antigen (R and S) and RNA (T) were detected in renal tubular epithelial cells. Panels F–H, M, N, and Q, hematoxylin and eosin stain; panels I, O, P, R, and S, POWV immunohistochemistry; panels J–L, O inset, and T, POWV in situ hybridization. Original magnifications: F and R, ×128; G, I, M, and P, ×84; H, ×65; J, ×15; K, ×104; L, ×212; N and T, ×176; O ×152; S, ×216; O inset, ×284; Q, ×124.

Table. Summary of antemortem and postmortem testing for Powassan virus in a transplant recipient, Pennsylvania, USA*

Specimen	Test	Result	Cellular tropism
Antemortem			
CSF†	Powassan virus RT-PCR	Lineage 1 (POWV), negative; Lineage 2 (DTV), positive	NA
Serum†	Powassan virus IgM	IgM ELISA positive	NA
Donor liver, time zero biopsy	Powassan IHC, RT-PCR	IHC negative; RT-PCR negative	NA
Postmortem FFPE tissues‡			
Hippocampal formation	Powassan IHC, ISH, RT-PCR	IHC negative; ISH positive; RT-PCR positive	Neurons (dentate gyrus), glia, ependymal cells, endothelial cells, mononuclear inflammatory cells (parenchyma)
Frontal cortex, right	Powassan IHC, ISH, RT-PCR	IHC immunoreactive (positive); ISH positive; RT-PCR positive	Neurons, glia, endothelial cells, mononuclear inflammatory cells (parenchyma and leptomeninges)
Cerebellum	Powassan IHC, ISH, RT-PCR	IHC immunoreactive (positive); ISH positive; RT-PCR positive	Neurons and glia in molecular layer, Purkinje cell layer, granule cell, mononuclear inflammatory cells
Pons	Powassan IHC, ISH, RT-PCR	IHC negative; ISH positive; RT-PCR positive	Neurons, glia, endothelial cells, mononuclear inflammatory cells
Lung, left lower lobe	Powassan IHC, ISH, RT-PCR	IHC immunoreactive (positive); ISH positive; RT-PCR positive	Bronchiolar epithelial cells, endothelial cells, circulating mononuclear cells, pneumocytes
Kidney, left	Powassan IHC, ISH, RT-PCR	IHC immunoreactive (positive); ISH positive; RT-PCR negative	Tubular epithelial cells, endothelial cells, circulating mononuclear cells
Donor liver allograft, right and left lobes	Powassan IHC, ISH, RT-PCR	IHC negative; ISH positive; RT-PCR negative	Rare circulating mononuclear cells in liver sinusoids and portal tracts

*CSF, cerebrospinal fluid; DTV, deer tick virus, lineage II; FFPE, formalin-fixed paraffin-embedded; IHC, immunohistochemistry; ISH, in situ hybridization; POWV, Powassan virus; RT-PCR, reverse transcription PCR.
†Testing performed at Mayo Clinic Laboratories, Rochester, Minnesota, USA.
‡Testing performed at the Centers for Disease Control and Prevention, Atlanta, Georgia, USA as previously published (*5*).

Postmortem rabies test results were negative. Testing of the transplanted donor liver at time zero (time of transplant) showed a negative test result for Powassan (Table) and rabies (Appendix Table 2).

The Philadelphia, Chester County, and Pennsylvania departments of health and the Centers for Disease Control and Prevention conducted an investigation into possible mechanisms of POWV transmission that indicated the most likely route of infection was tick exposure. The patient had multiple opportunities for tick exposures, including a public garden visit, multiple local campground visits before and after the transplant, and dog walks in nature; however, no definitive tick bites were noted (Pennsylvania Department of Health, pers. comm., email, 2026 Apr 20). Since 2011, Pennsylvania has reported 25 neuroinvasive Powassan cases from 16 different counties (*1*), and evidence of POWV transmission from cases, surveillance, and testing of *Ixodes scapularis* ticks has been documented in every Pennsylvania district.

We describe a case of systemic POWV associated with lung and kidney injury. Flaviviruses such as yellow fever and West Nile can infect renal tubular cells, causing kidney damage (*2*), and disrupt pulmonary function through endothelial hyperpermeability (*3*,*4*). The rarity of POWV has limited investigation into possible shared viral tropisms similar to other flaviviruses. We show evidence of viral tropism in non–central nervous system cell types and organ-specific damage. Another documented systemic POWV case involved testicular infection in an immunosuppressed patient on rituximab (*5*–*7*). Severe systemic and neuroinvasive flavivirus disease has been reported among immunosuppressed persons and transplant recipients, often resulting in multiorgan failure and high incidence of death (*7*–*9*). Our report adds to growing literature of severe arboviral disease manifestations in immunosuppressed patients. Although meningoencephalitis is the primary clinical manifestation, multiorgan dysfunction by direct POWV infection is possible.

About the Author

Dr. Sung is an anatomic and clinical pathology resident at the Hospital of the University of Pennsylvania. His primary clinical interests are in medical pathology and hematopathology.

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Address for correspondence: MacLean Nasrallah, Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, 3400 Spruce St, Philadelphia, PA 19104, USA; email: Maclean.Nasrallah@pennmedicine.upenn.edu

Neoehrlichia mikurensis Infection in Immunocompromised Patient, the Netherlands, 2024

Martijn J.H. Tjan,[1,2] William J. Boogers,[1,3] Jaco J. Verweij, Marvin A.H. Berrevoets, Joppe W. Hovius

Author affiliations: Elisabeth-TweeSteden Hospital, Tilburg, the Netherlands (M.J.H. Tjan, W.J. Boogers, J.J. Verweij, M.A.H. Berrevoets); Amsterdam University Medical Center, Amsterdam, the Netherlands (J.W. Hovius)

DOI: https://doi.org/10.3201/eid3212.261316

We report a case of *Neoehrlichia mikurensis* infection from a tick bite in a 69-year-old immunocompromised man with non-Hodgkin lymphoma in the Netherlands. Because of increasing use of immunosuppressive therapies and frequent tick bites, *N. mikurensis* should be recognized as a potential cause of recurrent fever in immunocompromised patients.

Neoehrlichia mikurensis is a gram-negative tick-borne bacterium increasingly identified in Europe and Asia (*1*). Clinical manifestations of infection are fever, chills, night sweats, and systemic inflammatory responses, particularly in immunocompromised patients. We describe the case of *N. mikurensis* infection in a man who had recurrent, cyclical fever over a 1-year period.

A 69-year-old man with indolent non-Hodgkin lymphoma was undergoing immunochemotherapy consisting of rituximab, a CD20 monoclonal antibody that depletes B lymphocytes, along with cyclophosphamide, vincristine, and prednisolone (R-CVP regimen); treatment began in April 2024. He was admitted to Elisabeth-TweeSteden Hospital, Tilburg, the Netherlands, on July 23, 2024, with nonneutropenic fever, chills, night sweats, and mild bilateral edema of the legs. Apart from hiking in a national park in the Netherlands, he reported no other risk factors for infectious diseases (e.g., tick bite, travel abroad). Standard investigations,

[1]These first authors contributed equally to this article.

[2]Current affiliation: Radboud University Medical Centre, Nijmegen, the Netherlands.

[3]Current affiliation: Erasmus University Medical Centre, Rotterdam, the Netherlands.