CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 19-2025: A 69-Year-Old Man with Headache and Ataxia

Arun Venkatesan, M.D., Ph.D.,[1] Javier M. Romero, M.D.,[2,3]
G. Kyle Harrold, M.D.,[4,5] and Erik H. Klontz, M.D., Ph.D.[6,7]

PRESENTATION OF CASE

Author affiliations are listed at the end of the article.

N Engl J Med 2025;393:176-84.
DOI: 10.1056/NEJMcpc2412528

CME

Dr. Anna K. Bonkhoff (Neurology): A 69-year-old man was admitted to this hospital because of headache and ataxia.

The patient had a history of systemic diffuse large B-cell lymphoma (DLBCL), which had been diagnosed 3 years before the current presentation and had been treated with bendamustine and rituximab. One year after the initial diagnosis, weakness developed in the right hand. Magnetic resonance imaging (MRI) of the head showed an enhancing lesion in the left centrum semiovale; a biopsy of the enhancing brain lesion revealed that the patient had a relapse of DLBCL of the central nervous system (CNS) that was positive for Epstein–Barr virus (EBV). There was no radiographic response to treatment with high-dose methotrexate; treatment with tisagenlecleucel (chimeric antigen receptor [CAR] T-cell therapy) was subsequently initiated, followed by treatment with ibrutinib. Nineteen months before the current presentation, treatment with ibrutinib was stopped after cryptococcal pneumonia developed. DLBCL was thought to be in remission. After treatment, strength in the right arm was 4/5, and reflexes were 3+ in the right brachioradialis, biceps, and triceps.

The patient had been in his usual state of health, active and participating in several water sports, until 2 weeks before the current presentation, when he fell and struck his back while sailing. After the fall, pain developed in the midback and over the right lower ribs posteriorly. Over the course of the next 2 weeks, the patient noted progressive weakness and difficulty with coordination while using his hands, to the point that he was not able to feed himself. He also had headache that felt similar to previous migraines. His wife brought him to the emergency department of this hospital for evaluation.

Other medical history included hypertension, dyslipidemia, nonischemic dilated cardiomyopathy, urinary retention, thrombosis of the superior mesenteric vein, hypogammaglobulinemia, attention deficit–hyperactivity disorder, and mood disorder. Lymphopenia persisted after CAR T-cell therapy. Medications included acyclovir prophylaxis, apixaban, atorvastatin, dextroamphetamine–amphetamine,

empagliflozin, fluconazole, metoprolol succinate, sacubitril–valsartan, sulfamethoxazole–trimethoprim prophylaxis, tamsulosin, and venlafaxine. The patient also received periodic intravenous immune globulin infusions for prevention of infection. There were no known adverse reactions to medications. He was retired from work in real estate. He lived with his wife and dog near a lake in a suburban area of New England and spent time outdoors swimming, paddleboarding, and working in the yard. He had had several recent tick bites but no known mosquito bites. The patient reported that he had not recently consumed any deli meats or unpasteurized dairy products. He was a lifelong nonsmoker, had stopped drinking alcohol 3 years before the current presentation, and did not use illicit drugs.

On evaluation, the temporal temperature was 36.3°C, the blood pressure 107/65 mm Hg, the pulse 86 beats per minute, the respiratory rate 18 breaths per minute, and the oxygen saturation 96% while the patient was breathing ambient air. The body-mass index (the weight in kilograms divided by the square of the height in meters) was 23.1. The patient was awake and alert. He was attentive to conversation, oriented, and able to follow two-step commands. His speech was slow and mildly hypophonic. The neck was supple. There was end-gaze nystagmus on lateral gaze in both eyes. There were fasciculations in the muscles of the legs, and increased tone was noted in the right arm and right leg. Weakness was present on abduction of the fingers of both hands, and finger–nose–finger testing revealed ataxia in both hands. He had weakness and hyperreflexia in the right arm that was similar to findings from previous examinations; strength and reflexes were otherwise normal. Results of tests of sensation were normal.

The blood levels of electrolytes, glucose, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, bilirubin, albumin, total protein, cobalamin, thyrotropin, zinc, and copper were normal, as were the results of tests of kidney function. Screening tests for human immunodeficiency virus infection types 1 and 2, syphilis, and Lyme disease were negative. The white-cell count was 4860 per microliter (reference range, 4500 to 11,000), with a neutrophil count of 3750 per microliter (reference range, 1800 to 7700), a lymphocyte count of 260 per microliter (reference range, 1000 to 4800), a monocyte count of 810 per milliliter (reference range, 200 to 1200), and an eosinophil count of 40 per milliliter (reference range, 0 to 900); the remainder of the complete blood count was normal.

Dr. Javier M. Romero: Computed tomography (CT) of the head, performed without the administration of intravenous contrast material, showed postsurgical changes related to previous left frontal craniotomy and a hyperdense calcified lesion (measuring 6 mm in diameter) in the left centrum semiovale that had an appearance similar to that seen on previous studies (Fig. 1A). CT angiography of the chest, abdomen, and pelvis, performed after the administration of intravenous contrast material, revealed acute-appearing fractures of the posterior right 11th and 12th ribs. CT of the cervical spine showed moderate endplate degenerative changes involving the fourth through seventh cervical vertebrae but no acute fracture or facet malalignment.

Dr. Bonkhoff: The patient was admitted to this hospital. Treatment with empagliflozin was discontinued, and treatment with apixaban was stopped to facilitate lumbar puncture for the evaluation of cerebrospinal fluid (CSF). Treatment with other home medications was continued.

Dr. Romero: On the second hospital day, MRI of the head showed that the calcified lesion in the left frontal lobe was unchanged, a finding that most likely reflected treated lymphoma (Fig. 1B).

Dr. Bonkhoff: On the third hospital day, electromyography and nerve conduction studies showed electrodiagnostic evidence of a subacute neurogenic process involving multiple nerve roots at the cranial and cervical levels. Such findings are sometimes seen in the context of early chronic polyradiculopathy.

On the fourth hospital day, hypophonia worsened and lethargy developed. Finger–nose–finger testing showed worsening ataxia in the hands, and new truncal ataxia was observed.

On the fifth hospital day, sixth cranial nerve palsy developed in both eyes, and the patient had difficulty with swallowing solids. Treatment with oral acyclovir, which had been administered for prophylaxis, was switched to treatment with intravenous acyclovir. In addition, treatment

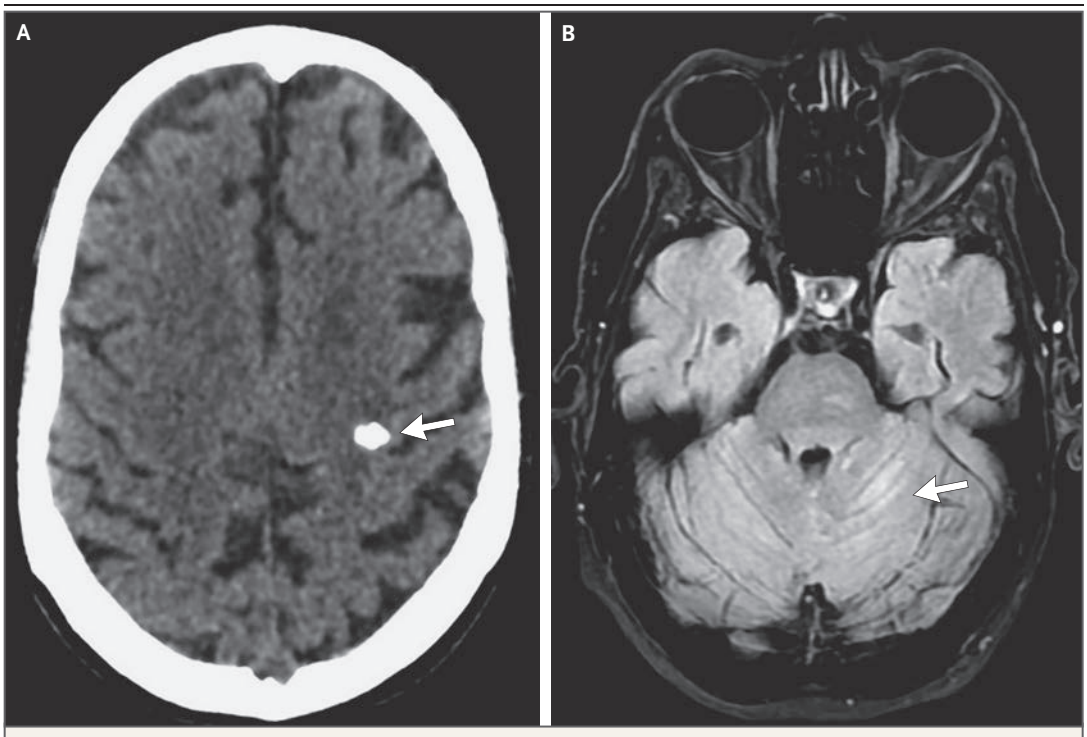

Figure 1. Imaging Studies Obtained on Second Hospital Day.

An axial image from CT of the head (Panel A), obtained without the administration of intravenous contrast material, shows a focal area of high density (arrow) that most likely corresponds to calcification, a typical finding in patients who have had previous radiation treatment. An axial T2-weighted fluid-attenuated inversion recovery (FLAIR) image of the head (Panel B), obtained at the level of the posterior fossa, shows faint increased signal intensity within the left cerebellar hemisphere (arrow).

with intravenous ceftriaxone, vancomycin, and ampicillin was started.

On the sixth hospital day, lumbar puncture was performed; the opening pressure was 15 cm of water. Analysis of the CSF showed 21 nucleated cells per microliter (reference range, 0 to 5), of which 77% were lymphocytes (reference range, 0 to 100), 14% were monocytes (reference range, 0 to 100), and 9% were unclassified cells (reference value, 0) that were described as enlarged lymphoid cells with prominent nucleoli and abundant cytoplasm. The CSF glucose level was 51 mg per deciliter (2.8 mmol per liter; reference range, 50 to 75 [2.8 to 4.2 mmol per liter]), and the total protein level was 74 mg per deciliter (reference range, 5 to 55). Gram's staining of the CSF revealed moderate mononuclear cells with no bacteria. Cytologic examination of the CSF revealed numerous lymphocytes with rare, atypical forms; flow cytometry did not show evidence of a monoclonal B-cell population.

Dr. Romero: On the ninth hospital day, T2-weighted fluid-attenuated inversion recovery (FLAIR) images from MRI of the head revealed signal hyperintensity in both hemispheres of the cerebellar cortex, in the cerebellar folia, and in the brain stem; no abnormal enhancement was noted (Fig. 2). These findings were similar to those seen on the previous study obtained 1 week earlier (Fig. 1B) but were more conspicuous than the earlier findings. The calcified lesion in the left frontal lobe was unchanged.

Dr. Bonkhoff: A diagnostic test was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Arun Venkatesan: This 69-year-old man with persistent lymphopenia after treatment for systemic and CNS DLBCL presented with multiple neurologic deficits that evolved over the course of several weeks after a sailing accident.

LOCALIZATION AND TEMPO OF DISEASE

The patient described difficulty with coordination of the hands, and ataxia was noted in both hands on examination. These findings, together with end-gaze nystagmus, which I presume to be a deficit in gaze holding, and truncal ataxia, reflect dysfunction of the lateral, inferior, and midline regions of the cerebellum and point to a widespread, bilateral cerebellar process. Although many conditions can lead to progressive cerebellar dysfunction, marked deterioration over days to weeks narrows the categories of disease to cancer, infection, immune-mediated conditions, trauma, metabolic conditions, and exposure to drugs and toxins.

In addition, the patient had headache, sixth cranial nerve palsies, and fasciculations. Electromyography and nerve conduction studies showed evidence of an evolving polyradiculopathy. These signs and symptoms can localize to the subarachnoid space, which is surrounded by pain-sensitive meninges and through which cranial nerves and spinal nerve roots must pass. Involvement of both the cerebellum and the subarachnoid space rules out exposure to drugs and toxins, as well as metabolic conditions. The results of initial neuroimaging studies were normal, which ruled out traumatic causes such as hemorrhage or traumatic CSF leak. Therefore, the list of possible causes of this patient's clinical syndrome can be further narrowed to immune-mediated conditions, cancer, and infection, all of which are supported by the finding of CSF lymphocytic pleocytosis.

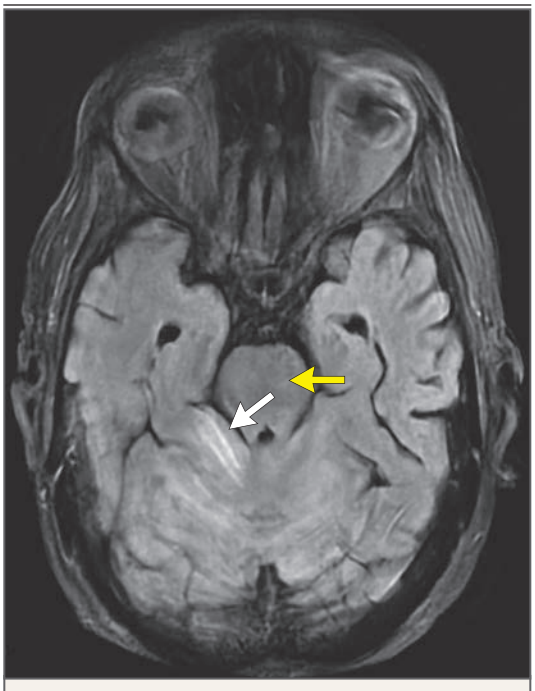

Figure 2. MRI of the Head Obtained on Ninth Hospital Day.

An axial T2-weighted FLAIR image of the head, obtained at the level of the posterior fossa, shows increased signal intensity within the right cerebellar hemisphere (white arrow) and in the left pons (yellow arrow), findings that most likely represent cerebellitis and rhombencephalitis.

IMMUNE-MEDIATED CONDITION

Autoimmune disorders account for approximately 6% of all cases of sporadic cerebellar ataxia in adults, the most common of which is associated with the presence of autoantibodies against glutamic acid decarboxylase. In addition, many other antineural antibodies associated with autoimmune cerebellar ataxia have been described.[1] Some autoimmune disorders occur in association with certain cancers but are rare in the context of DLBCL, the main consideration in this patient. The most well-recognized paraneoplastic condition affecting the cerebellum occurs in the context of ovarian or breast cancer in women, in association with antibodies to Purkinje cytoplasmic antibody type 1 (PCA-1, or anti-Yo). In men, several cerebellar syndromes of note include those associated with antibodies to PCA type Tr (PCA-Tr, or DNER), which are found in patients with Hodgkin's lymphoma, and with antibodies to the kelch-like protein 11, which are found in patients with testicular seminomas.[2] Other inflammatory conditions, such as sarcoidosis or demyelinating disorders (e.g., acute disseminated encephalomyelitis), can also affect the cerebellum but are typically accompanied by enhancing lesions on MRI. Overall, immune-mediated conditions of the cerebellum are unlikely in this patient, given his history of impaired humoral and cell-mediated immunity.

CANCER

This patient has a known history of systemic DLBCL with CNS relapse. A CNS recurrence in patients with DLBCL is a strong consideration in any patient with this disease in whom new neurologic signs and symptoms develop. In this

patient, persistent lymphopenia would most likely result in a higher risk of disease recurrence owing to a failure of T-cell control of EBV reactivation, with associated oncogenic effects. Further increasing the possibility of recurrent CNS lymphoma is the presence of atypical lymphocytes in the CSF. However, MRI of the head did not show the typical enhancing, space-occupying lesions usually seen in patients with DLBCL involving the CNS. It is also important to note that flow cytometric analysis of the CSF did not show a monoclonal population of B cells.

In patients with other types of cancer, the posterior fossa can be the primary site of CNS metastases. However, there is no evidence of another systemic cancer in this patient. Moreover, most metastatic cancers manifest as space-occupying lesions, a finding not seen in the imaging studies for this patient. Primary glial tumors can manifest with diffuse infiltration of the CNS and radiologic characteristics that resemble those of infectious or inflammatory conditions; however, symmetric involvement of the cerebellum is uncommon in primary glial tumors, and I would not expect the rapid clinical and radiologic progression seen in this patient.

INFECTION

Infection with a variety of pathogens can lead to progressive cerebellar dysfunction. Some of these infections, such as *Mycoplasma pneumoniae* infection, predominantly affect children and are unlikely in this patient. Prion diseases are also unlikely in this patient because they would progress more gradually than was seen in this case, are not typically associated with CSF pleocytosis, and would be accompanied by restricted diffusion in the cortical and deep gray matter on MRI.[3] Infection with fungal organisms such as *Cryptococcus neoformans*, along with mycobacterial infections such as tuberculosis, should be considered given the patient's immunocompromised state. However, these would be unlikely diagnoses in this patient, since he was receiving long-term suppressive therapy with fluconazole for a previous cryptococcal infection. Furthermore, these infections typically manifest in the context of basilar meningitis or space-occupying lesions in the brain, neither of which were seen in this patient.

Protozoal Infection

This patient participated in several water sports, which prompts consideration of exposure to free-living amebas. Although acanthamoeba species are occasionally found in New England, CNS infection is associated with a less aggressive course than was seen in this patient. *Naegleria fowleri*, a flagellated ameba found in bodies of fresh water, causes a fulminant, necrotizing CNS infection (primary amebic meningoencephalitis).[4] The portal of entry is the nares, with access to the brain thought to be through the cribriform plate. In this patient, imaging findings did not support a necrotic process; moreover, the ameba resides in water with warmer temperatures than those of the bodies of water typically found in New England.

Bacterial Infection

The tempo of disease, CSF profile, and absence of systemic manifestations make pyogenic bacterial infection an unlikely diagnosis. On the other hand, CNS listeriosis, which most often occurs in older adults and persons with immunocompromise, is a consideration. Patients with *Listeria monocytogenes* infection can present with less acute features and more subtle CSF abnormalities than those observed in patients with pyogenic bacterial infections. Infection with *L. monocytogenes* typically results in meningitis; however, involvement of the posterior fossa can occur, which leads to brain-stem encephalitis (rhombencephalitis) and accompanying cranial nerve and cerebellar signs. Typically, single or multiple brain-stem abscesses would be seen on MRI, which is inconsistent with the diffuse parenchymal involvement observed in this patient. Listeria rhombencephalitis, although well-recognized, is reported to occur less commonly than previously thought.[5]

The patient's tick exposure introduces the possibility of infection with *Borrelia burgdorferi*, the causative agent of Lyme disease. Early neurologic manifestations include aseptic meningitis, cranial nerve dysfunction, and radiculitis, although some cases of cerebellar involvement have been reported. Testing for Lyme antibodies, which is usually positive in the context of CNS disease, was negative in this patient. However, antibody testing may not be reliable in a pro-

foundly immunocompromised host. Infection with another borrelia species, *B. miyamotoi*, is recognized as an emerging cause of meningoencephalitis in persons with immunocompromise, but this pathogen is not known to have a predilection for the cerebellum. Rickettsial infections with CNS involvement, such as Rocky Mountain spotted fever, are rare in the absence of rash and fever. Other tickborne bacterial infections, including anaplasmosis and ehrlichiosis, rarely affect the CNS.

Viral Infection

Several aspects of this patient's presentation are strongly suggestive of a viral infection. CSF analysis showed a lymphocytic pleocytosis, rather than a neutrophilic pleocytosis, with modestly elevated protein levels and normal glucose levels. MRI showed symmetric involvement without mass effect, a finding that is also suggestive of a viral process. Lastly, the lack of response to multiple antimicrobial agents is consistent with a viral infection.

Although many viral infections can cause encephalitis, relatively few result in predominance in the cerebellum. Reactivation of the JC virus in the context of impaired cell-mediated immunity leads to infection of glial cells and progressive multifocal leukoencephalopathy. This syndrome typically involves the subcortical white matter but can, on occasion, first develop in the cerebellar white matter or cerebellar peduncles before involving other regions of the brain.[6] A viral mutation that shifts tropism to neurons can result in JC virus granule cell neuronopathy, a distinct syndrome that causes an isolated cerebellopathy.[7] In both syndromes, neurologic signs typically evolve more slowly than those seen in this patient.

Mosquito-borne arboviruses are important to consider owing to the patient's substantial outdoor exposures, and infection from an occult mosquito bite cannot be ruled out. West Nile virus infection can cause cerebellitis, but involvement of the deep cerebral gray matter is more typical in such cases.

Viruses of the human herpesvirus family establish lifelong latent infection after the primary infection and can subsequently undergo reactivation to cause disease, particularly in the context of impaired cell-mediated immunity. Of these, varicella–zoster virus (VZV) and EBV are associated with acute cerebellitis and can also cause polyradiculitis, either through direct infection or through a parainfectious immune-mediated process. VZV reactivation can occur without rash and despite prophylaxis with acyclovir.

The patient had had recent tick bites, followed by rapid, progressive neurologic deterioration. Taken together, these features are highly suggestive of Powassan virus encephalitis. Powassan virus is an arthropod-borne flavivirus that is closely related to tickborne encephalitis virus, a major cause of infectious encephalitis throughout central and eastern Europe. Increasing numbers of cases of Powassan virus encephalitis have been reported in the United States in recent years, mainly in the regions of the upper Midwest and New England, which is consistent with the distribution of the main vector, *Ixodes scapularis* (deer tick). The cerebellum is commonly involved, and cranial nerve palsies can occur. Initial imaging of the head can be unremarkable or show subtle abnormalities with subsequent development of symmetric abnormalities on T2-weighted FLAIR imaging. In addition, CSF analysis typically shows a modest lymphocytic pleocytosis.[8] All these features were observed in this patient. Previous tick bites are reported in about half of cases of Powassan virus encephalitis. Moreover, the presence of atypical lymphocytes in the CSF is not incompatible with this diagnosis, since this finding can simply reflect lymphocytic activation in the context of infection.

The known tick exposure, clinical presentation, and findings on neuroimaging make Powassan virus encephalitis the most likely diagnosis in this patient. To establish the diagnosis, I would perform a CSF polymerase-chain-reaction (PCR) assay for Powassan virus, the test of choice in an immunocompromised host.[9]

DR. ARUN VENKATESAN'S DIAGNOSIS

Powassan virus encephalitis.

DIAGNOSTIC TESTING

Dr. Erik H. Klontz: A specimen of CSF was sent to a reference laboratory where PCR testing for

Powassan virus was performed. The diagnosis of Powassan virus infection requires a high degree of clinical suspicion because it is rarely, if ever, included on multiplex PCR assays. Unfortunately, there is no single test for Powassan virus infection that is sensitive in all patients; therefore, it is critical to ascertain the timing of infection and the patient's immune status (Fig. 3).[9]

In immunocompetent hosts, the presence of Powassan virus RNA is transient and often undetectable by the time many patients seek care. As with other arboviruses, most diagnoses of Powassan virus infection are made by the detection of virus-specific IgM antibodies, with confirmation obtained by means of plaque-reduction neutralization testing. However, patients with

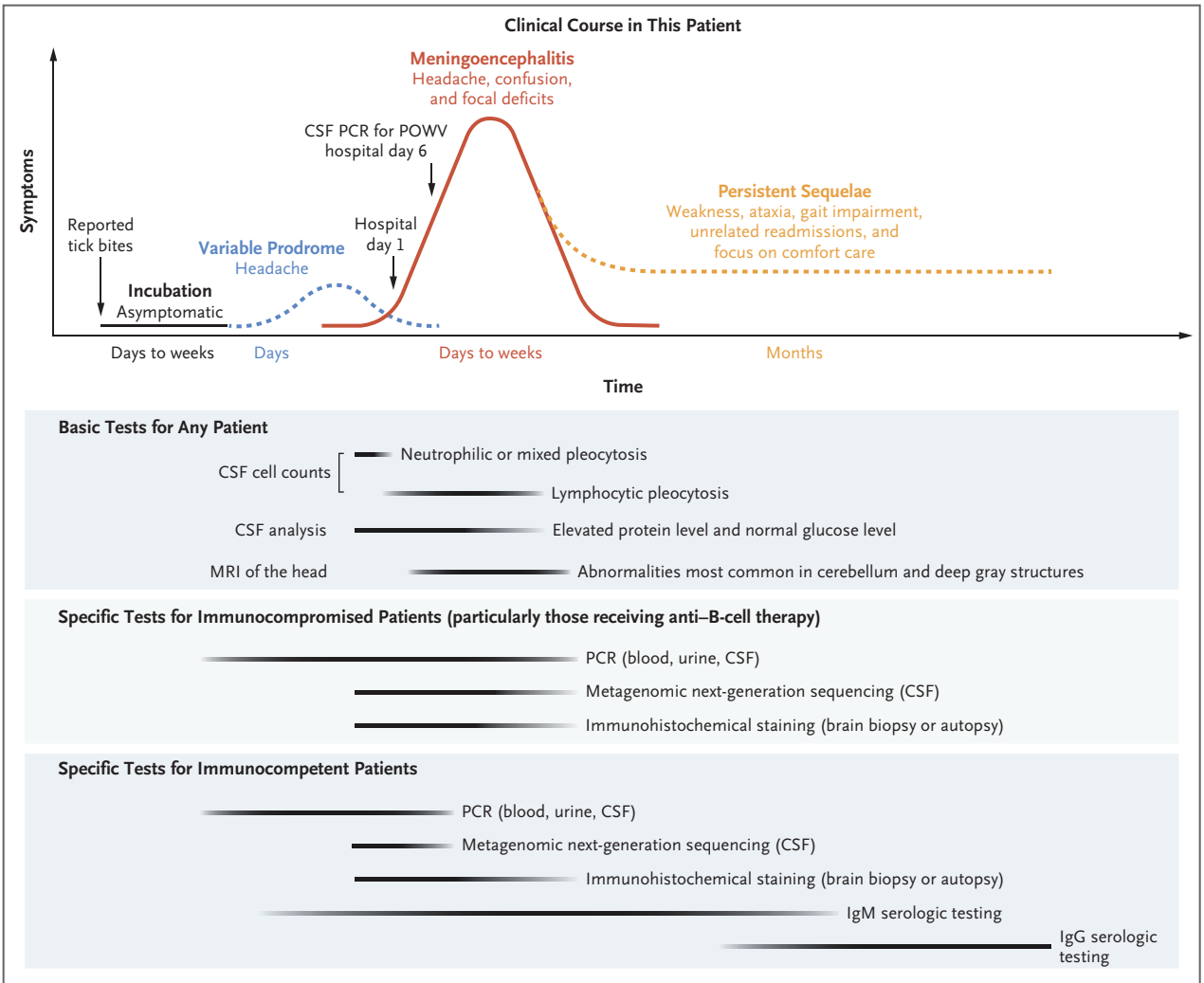

Figure 3. Laboratory Testing Options for Diagnosis of Powassan Virus Infection.

Shown is the timeline of the patient's clinical course and laboratory testing options for Powassan virus infection. Diagnostic testing strategies for Powassan virus should be based on patient-specific risk factors and the estimated time of possible infection. The most sensitive test depends on the timing of infection and the immune status of the patient. In immunocompetent patients, the presence of RNA is transient and may be undetectable by the time patients seek care. In such cases, IgM serologic testing is the most sensitive option in all but the earliest and latest stages of disease. Immunocompromised patients, particularly those receiving anti–B-cell therapy, may never have seroconversion, which makes serologic testing an insensitive testing method for Powassan virus. However, immunocompromised patients often have more severe infections or delayed viral clearance, features that make molecular tests, such as PCR, highly sensitive options. CSF denotes cerebrospinal fluid, PCR polymerase chain reaction, and POWV Powassan virus.

profound immunocompromise, particularly those with a history of B-cell–depleting therapy (such as this patient), are typically not able to mount a detectable serologic response, which limits the sensitivity of IgM testing.[10] At the same time, patients with immunocompromise often have more severe infections with delayed viral clearance, which greatly increases the chances of detecting virus-specific RNA. Therefore, in this patient population, PCR and metagenomic sequencing are excellent tests. When PCR testing is performed, it is important that the laboratory tests for both lineages of Powassan virus (I and II). Powassan virus lineage I is clinically and serologically indistinguishable from lineage II (also known as deer tick virus), but these two viruses are genetically divergent, and both are relevant to human disease.[11] In this patient, PCR testing for Powassan virus was positive for Powassan virus lineage II.

MICROBIOLOGIC DIAGNOSIS

Powassan virus encephalitis.

HOSPITAL COURSE AND FOLLOW-UP

Dr. G. Kyle Harrold: The patient's clinical status worsened during the first 5 days of his hospitalization while awaiting lumbar puncture for CSF analysis, and he was treated with empirical antimicrobial therapy. Intravenous acyclovir therapy was started to treat a possible infection with herpes simplex virus (HSV) or VZV, and it was stopped once PCR testing of the CSF returned a negative result. Treatment with ampicillin was initiated for possible listeria infection, and ceftriaxone and vancomycin were started empirically for bacterial meningitis; however, once there was a lower level of suspicion for this entity, vancomycin was discontinued. Ceftriaxone was continued for possible Lyme disease.

Given the concern about the possibility of CNS recurrence of DLBCL, treatment with intravenous dexamethasone was administered after the first lumbar puncture, followed by treatment with a tapering dose of oral dexamethasone. The patient received dexamethasone treatment after the lumbar puncture was performed so that the results of CSF analysis and flow cytometry for lymphoma would not be affected. In addition, he received intravenous immune globulin for empirical treatment of an autoimmune cause of his symptoms and because it is sometimes used off-label in patients with arboviral encephalitis. However, high-quality data that support the latter indication are lacking.

On the 14th hospital day, PCR testing for Powassan virus returned a positive result, treatment with ampicillin and ceftriaxone was stopped, and the dose of dexamethasone was further reduced. Prophylaxis with oral acyclovir, fluconazole, and trimethoprim–sulfamethoxazole was continued.

Often, patients with Powassan virus encephalitis have additional acute complications. Some patients, for example, may become encephalopathic to a degree that mechanical ventilation is indicated. Powassan virus infection is known to cause cerebellitis that may lead to occlusion of the fourth ventricle and acute obstructive hydrocephalus, a neurosurgical emergency requiring consideration of an external ventricular drain and suboccipital craniectomy. Patients may also have seizures for which they receive treatment with antiseizure medications. This patient did not have any of these acute complications.

There are no specific treatments for Powassan virus infection; treatment is supportive, and ongoing physical therapy, occupational therapy, and speech and language therapy are considered to be essential to maximize recovery. This patient continued to receive supportive care with physical therapy, occupational therapy, and speech and language therapy, which together resulted in modest improvement. He was discharged to a short-term rehabilitation hospital to continue his recovery.

At a follow-up visit 1 month after discharge, the patient and his wife reported a slow but continued improvement with ongoing rehabilitation therapies. They felt he was close to his baseline cognitive level, but a neurologic examination showed that he still had diplopia on rightward gaze, direction-changing nystagmus, weakness in the right arm and leg, severe ataxia, and inability to walk. Continued rehabilitation therapy was recommended. Five months after hospital discharge, the patient's wife reported that the patient had had multiple intercurrent illnesses unrelated to Powassan virus infection, with stepwise functional decline. The goals of care were transitioned to focus on comfort

measures, and he died 6 months after the current presentation.

FINAL DIAGNOSIS

Powassan virus encephalitis.

This case was presented at Neurology Grand Rounds.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Dr. Shibani S. Mukerji for review of the case history.

AUTHOR INFORMATION

[1]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore; [2]Department of Radiology, Massachusetts General Hospital, Boston; [3]Department of Radiology, Harvard Medical School, Boston; [4]Department of Neurology, Massachusetts General Hospital, Boston; [5]Department of Neurology, Harvard Medical School, Boston; [6]Department of Pathology, Massachusetts General Hospital, Boston; [7]Department of Pathology, Harvard Medical School, Boston.

REFERENCES

1. Balint B. Autoimmune movement disorders. Continuum (Minneap Minn) 2024;30:1088-109.
2. Rosenfeld MR, Dalmau J. Paraneoplastic neurologic syndromes. Neurol Clin 2018;36:675-85.
3. Hermann P, Appleby B, Brandel J-P, et al. Biomarkers and diagnostic guidelines for sporadic Creutzfeldt-Jakob disease. Lancet Neurol 2021;20:235-46.
4. Graciaa DS, Cope JR, Roberts VA, et al. Outbreaks associated with untreated recreational water — United States, 2000–2014. MMWR Morb Mortal Wkly Rep 2018;67:701-6.
5. Charlier C, Poirée S, Delavaud C, et al. Imaging of human neurolisteriosis: a prospective study of 71 cases. Clin Infect Dis 2018;67:1419-26.
6. Adra N, Goodheart AE, Rapalino O, et al. MRI shrimp sign in cerebellar progressive multifocal leukoencephalopathy: description and validation of a novel observation. AJNR Am J Neuroradiol 2021;42:1073-9.
7. Tan CS, Koralnik IJ. Progressive multifocal leukoencephalopathy and other disorders caused by JC virus: clinical features and pathogenesis. Lancet Neurol 2010;9:425-37.
8. Mendoza MA, Hass RM, Vaillant J, et al. Powassan virus encephalitis: a tertiary center experience. Clin Infect Dis 2024;78:80-9.
9. Klontz EH, Chowdhury N, Branda JA. Laboratory testing for Powassan virus: past, present, and future. J Infect Dis 2024;230:Suppl 1:S70-S75.
10. Kapadia RK, Staples JE, Gill CM, et al. Severe arboviral neuroinvasive disease in patients on rituximab therapy: a review. Clin Infect Dis 2023;76:1142-8.
11. Klontz EH, Chowdhury N, Holbrook N, et al. Analysis of powassan virus genome sequences from human cases reveals substantial genetic diversity with implications for molecular assay development. Viruses 2024;16:1653.