CLINICAL VIGNETTE

West Nile Virus Encephalitis Disguised as a Cerebrovascular Accident

Luciano Castaneda, MD and Patrick Poquiz, MD

An 80-year-old man presented to the emergency room (ER) for generalized weakness and lightheadedness. His past medical history includes paroxysmal atrial fibrillation (AF) on anti-coagulation, hypertension, hyperlipidemia, ischemic stroke with no residual deficits, and coronary artery disease status-post percutaneous intervention. He had been experiencing symptoms for a few days and reported chills without fever, decreased appetite, and a recent mechanical fall due to weakness without significant injury or head trauma. His prior level of function was described as ambulatory without any need for assistive devices, and he walked 2-3 miles per day, and was independent with all activities of daily living. He denied any palpitations or vertigo. He had recently seen his primary care provider and a head CT angiogram was unremarkable.

Upon arrival at the ER his vital signs included a temperature of 38.2°C, tachycardia of 110 BPM, respiratory rate of 18/min, blood pressure of 134/88, and room air O_2 saturation above 90%. His physical exam was notable for appearing fatigued, having dry mucous membranes, and an irregularly irregular rhythm on cardiac exam. Laboratory results were notable for hyponatremia of 127 mmol/L. An EKG showed AF with RVR with a ventricular rate of 130 BPM. Portable chest x-ray showed no acute pathology. A viral panel for influenza, RSV, and COVID-19 was negative, urinalysis was normal. Blood cultures were drawn under sepsis protocol and he was admitted to telemetry for AF, weakness, and sepsis. Continuous intravenous diltiazem was started and titrated.

The initial days of his hospitalization were tumultuous. He was continuously in and out of rapid ventricular rate (RVR) and Cardiology was consulted. Echocardiogram showed a preserved ejection fraction at 55% with wall movement consistent with AF without any other significant abnormalities. Treatment of his sepsis was complicated by copious IV fluids for his hypotension. This may have been a combined effect from septic as well as cardiac origin. He continued to have waxing and waning mental status and progressive generalized weakness. Infectious diseases and Neurology were consulted. During his periods of lucidity, he exhibited word-finding difficulty and expressed frustration that he was unable to articulate his thoughts. Although he was started on empiric ceftriaxone for treatment of sepsis, there was no clinical improvement, and his initial blood and urine cultures remained negative. The differential diagnosis was broadened to include encephalitis.

He became critically ill with acute respiratory failure, requiring transfer to the ICU. He required non-invasive airway support with BiPAP. Intravenous amiodarone was started for heart rate control. He was started on empiric IV acyclovir for possible herpes encephalitis, and West Nile Virus (WNV) serum antibody was also drawn. With judicious diuresis, his critical state improved and he was weaned to low flow nasal cannula oxygen. He continued to exhibit generalized weakness and word-finding difficulties. After he was stable, an MR of the brain was performed and revealed no acute abnormalities. A lumbar puncture was not performed due to anticoagulation, however his WNV serum IgM and IgG returned positive. After completing seven days of IV acyclovir, this was discontinued once WNV had been confirmed. He was intermittently febrile above 38.0°C for the first week, before defervescence. He received supportive treatment including rehabilitation evaluations from physical, occupational, and speech therapy. They recommended placement in the acute rehabilitation unit (ARU) given his prior level of function, and he was transferred to the ARU after 14 days of hospitalization. He underwent comprehensive rehabilitation for an additional 17 days with significant improvement in his physical debility as well as his speech, communication, and memory recall. Two months after discharge from the ARU he followed up with his primary care provider and notably continued to show improvement.

Discussion

This 80-year-old man initially presented with a concern for sepsis with non-specific fever, malaise, and generalized weakness. His hospitalization was complicated by AF with RVR and exacerbation of acute congestive heart failure secondary to fluid resuscitation for sepsis. Broad spectrum antibiotics were initiated without improvement. He developed acute aphasia and the differential narrowed towards neurologic etiologies, including encephalitis. A cerebrovascular accident remarked on the differential, but his final diagnosis was WNV encephalitis.

WNV was first detected in the United States in New York in 1999 with the first California case reported in July 2003.[1] It has now been seen in every continent with cases usually seen in the early summer and continuing until mid to late autumn. At the time of our patient's presentation, there were 70 prior cases of WNV infection reported in the region. Fifty-seven patients had neuroinvasive disease with 3 deaths.[2]

WNV is an RNA virus in the *Flaviviridae* family that is transmitted to humans via a mosquito bite, more commonly the *Culex* species.[3] Symptoms range from asymptomatic infection, fever with malaise, to encephalitis with severe neuroinvasive disease. The more common presentations include approximately five days fever with a headache for about ten days that may concurrently include fatigue for up to a month.[4] Less than 1% of WNV cases include neuroinvasive disease.[5] Morbidity increases for those over the age of 50 and with medical co-morbidities, such as our patient.

Objective diagnostic findings include serologic testing for IgM antibody in either blood or cerebrospinal fluid. Imaging typically does not show findings. However, patients with neuroinvasive disease can show nonspecific MRI abnormalities several weeks after symptom onset. These include increased signal intensity on FLAIR and T2 imaging involving the meninges, basal ganglia, thalami, caudate nuclei, and/or the brainstem. Other microbes should be kept in the differential including Herpes simplex 1, St Louis encephalitis, Dengue fever and bacterial meningitis, which can present similarly. It is important to keep a broad differential as locally acquired Dengue fever has been reported.[6]

The treatment for WNV is supportive and there are no current treatment guidelines nor any FDA-approved medications. Ongoing research into the potential use of ribavirin, interferon-alpha and IVIG.[6] Case reports describe early use of interferon-alpha having benefit. However, use during outbreaks in Israel and the United States did not show benefit.[6] Similarly, case reports have shown benefit with IVIG, but no clinical trials have been completed.[6] With increasing cases, additional studies should be performed. Improvement in neurologic impairment begins six to eight weeks after onset of the infection and plateaus at twelve weeks. Our patient had significant improvement four weeks after presentation to the ER with continued improvement three months later.

WNV infection presents with a variety of symptoms. Our patient's encephalitis was a severe neuroinvasive manifestation. Neuroinvasive disease occurs in less than 1% of WNV cases and occurs more often in patients over age 50 and with increasing co-morbidities. There is currently no cure for WNV. With increasing numbers of cases in the United Statues, heightened awareness is warranted during the summer to autumn seasons. While more research is needed in finding a cure, early use of IVIG currently shows some benefit in WNV encephalitis.

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