West Nile Virus Meningoencephalitis in an Infant With Seizures and Abnormal Neuroimaging

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Received April 14, 2013; accepted July 18, 2013; electronically published October 31, 2013.

In August 2012, a 41-day-old, full-term female presented to Texas Children’s Hospital after a 1-day history of fever, irritability, and a disinterest in breastfeeding. On physical examination, she had a temperature of 100.6°F, a heart rate of 170/minute, and a respiratory rate of 40/minute, with normal pulse oximetry. She weighed 4.7 kg (71 percentile). She was irritable but consolable. Her anterior fontanel was soft and flat. She had no conjunctival injection or discharge, no rhinorrhea, and her oropharynx appeared normal. She had clear breath sounds, and her heart examination was normal except for a rapid rate. She had normal pulses and capillary refill time. Her abdominal and musculoskeletal examinations were normal. She had no lymphadenopathy or rash. She had no evidence of nuchal rigidity and had a normal cry and suck without facial palsy. She had normal tone and moved all extremities equally. Her deep tendon reflexes were equal in all extremities. She had a normal grasp and palmar reflex and a normal Moro reflex. Her peripheral white blood cell count (WBC) was 13 470/mm³ with 13.4% neutrophils and 43.4% lymphocytes; hemoglobin was 11.5 g/dL and platelet count of 381 000/mm³. Her urinalysis was normal. Her cerebral spinal fluid (CSF) had a WBC of 85 cells/mm³ (monocytes [64%], lymphocytes [19%], and neutrophils [14%]), a red blood cell (RBC) count of 6 cells/mm³; protein of 79 mg/dL and glucose of 39 mg/dL. Her CSF gram stain was negative. Blood and CSF were sent for enterovirus polymerase chain reaction (PCR) testing. Ampicillin and cefotaxime were administered.

On her second hospital day, she developed rhythmic right eye deviation and right face twitching for 20 seconds. She had 8 similar episodes, the longest lasted 12 minutes, which spontaneously resolved followed by a postictal period. The pediatric Neurology team recommended starting levetiracetam antiepileptic therapy. Due to concerns for herpes simplex virus (HSV) encephalitis, a lumbar puncture was attempted for HSV PCR testing and was unsuccessful. On day of life 44, the patient’s blood was sent for an HSV PCR and a serum arbovirus panel (which included immunoglobulin [Ig] M and IgG antibody testing for West Nile, Western Equine Encephalitis, Eastern Equine Encephalitis, California Encephalitis Group, and St. Louis Encephalitis). She was started on intravenous acyclovir (20 mg/kg per dose every 8 hours). Magnetic resonance imaging of the brain revealed a hypodense focus in the left thalamus (4 mm in diameter), suggestive of a lacunar infarct and leptomeningeal enhancement at the left posterior cranial vertex, most prominent along the central sulcus (Figure 1).

On her fourth hospital day, the patient had no further seizures and blood and CSF cultures were negative for bacterial growth. Her antibiotic treatment was discontinued. On day of life 47, additional CSF was obtained for HSV PCR testing and was improved with a WBC count of 35 cells/mm³ (lymphocytes [63%], monocytes [36%], neutrophils [1%]), a RBC count of 475 cells/mm³, protein of 74 mg/dL, and glucose of 30 mg/dL. Her mother felt that she was eating and acting better. On further discussions with the patient’s mother she stated that she herself had experienced 3 days of “tiredness,” mild headache, body rash, and nonbloody diarrhea the week before her infant became sick but denied feeling ill or having similar symptoms during her pregnancy. The infant had not been in contact with any additional persons who were ill, had no known mosquito exposure, and had no recent travel outside of their hometown (a suburb of Houston, Texas).

On her day of discharge to home, the patient’s HSV PCR testing in the blood and CSF were both negative and
her acyclovir therapy was stopped. She was discharged to home receiving levetiracetam. The week after her discharge, her serum arbovirus panel returned and was positive for West Nile (IgM 5.38 internal validation [IV], reference range [RR]: 1.11 IV and IgG 0.5 IV, RR: 1.29 IV) and the remainder of her arbovirus diagnostic panel was negative. Our patient’s CSF was not tested for West Nile virus (WNV) IgM, which is a highly sensitive test for West Nile virus neuroinvasive disease (WNND) and would have assisted in confirming her diagnosis. At 6 weeks post-discharge, she had no further seizure activity and her levetiracetam antiepileptic medication was discontinued. At a 6-month follow-up visit, she had a normal neurologic exam and normal development for age, with no additional seizure activity.

Despite WNV being the most common neuroinvasive arboviral disease in the United States, our patient’s clinical presentation with WNV meningoencephalitis as a manifestation of WNND was unique given her age at the time of her presentation, her associated seizure activity, and her abnormal brain imaging [1]. This case is the only known infant case of WNND with documented abnormal neuroimaging with subsequent normal development at 6 months of age.

Our case’s presentation with WNND in August 2012 occurred during a seasonal epidemic of WNV disease in the state of Texas, which accounted for 32% of all WNV cases nationwide in 2012. Forty-five percent of Texas’ cases were reported in the northeast corner of the state: Dallas (371 cases), Tarrant (242 cases), and Denton (177 cases) counties. Our case was from the southeast area of the state in Waller County, which reported this single case and is located adjacent to Harris County, which reported 60 cases in 2012 [2].

Due to the epidemic of WNV in Texas at the time her presentation, we suspected that our patient acquired her disease via a mosquito vector, which is the most common mode of transmission of WNV. An in utero transmission from her mother seemed less likely given her age at the time of her presentation, and her positive IgM serologies seemed suggestive of an acute rather than convalescent infection [3]. Given her mother’s symptoms 1 week before the infant’s illness, another consideration included transmission via breast milk, although this mode of transmission is rare [4]. Further testing of her mother (serum and breast milk for WNV antibody levels) could have assisted in determining our patient’s mode of viral acquisition.

The most interesting clinical dilemma raised in the management of this case was the likelihood of HSV meningoencephalitis as the cause of her illness. Given her age and rapid clinical improvement, HSV meningoencephalitis was thought to be less likely the cause of her illness, but it could not be excluded without further diagnostic studies for HSV [5].

HSV meningoencephalitis is more common than WNND in infants. Most congenitally or perinatally acquired cases of HSV meningoencephalitis occur in neonates less than 28 days of age (usually 11–17 days), and “late cases” at 4–6 weeks occur but are uncommon [5]. Only 28 pediatric WNV cases less than 12 months of age have been reported in the United States since 2002; 17 of whom had a diagnosis of WNND, and only 5 of the WNND cases were less than 8 weeks of age. Of those less than 8 weeks of age, none were definitively confirmed as congenitally acquired [1].

Over 50% of infants with central nervous system (CNS) HSV and 22% of infants with disseminated HSV disease present with seizures, compared with the less than 1% of pediatric WNND cases. Sixty-five percent of neonates with CNS HSV have abnormal brain imaging with either

Figure 1. Magnetic resonance imaging of brain with and without contrast, isotropic diffusion-weighted sequence, revealing a hypodense focus in the left thalamus (4 mm in diameter) and leptomeningeal enhancement at the left posterior cranial vertex, along the central sulcus (11 mm in diameter).
multifocal disease or abnormalities in the frontotemporal regions [5]. Many patients with HSV meningoencephalitis have persistent neurologic abnormalities, 66%–69% of whom have abnormal neurodevelopmental outcomes at 12 months of age [5]. Although severe neurological disease from WNND can occur in children, few have neurologic sequelae, and younger age is protective of recovery [6]. There is a paucity of published case reports of neuroimaging findings in children or adults with WNND, and most cases have normal imaging or subtle neuroimaging abnormalities. However, severely ill patients often have lesions involving the deep gray matter, the medulla, and brainstem from vascular injury secondary to inflammation [7]. In addition, in those with a diagnosis of WNV-associated acute flaccid paralysis syndrome, areas in inflammation can be found in the anterior horn cells of the spinal cord [8]. Our patient’s multifocal inflammation was similar to published case studies (most often involving adult patients) with the lesions primarily in the lacunar deep, gray matter of the brain.

This 5-week-old case of WNND presenting as meningoencephalitis is one of few reported pediatric cases of WNND in this age group and the only known case with documented abnormal neuroimaging with subsequent normal development at 6 months of age. As more cases of WNND in children are described, selected clinical features may be shown to help distinguish this condition from other causes of viral meningoencephalitis.

Acknowledgments

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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