Pearls & Oy-ster: Bilateral thalamic involvement in West Nile virus encephalitis

PEARLS

- Bilateral thalamic inflammation in the presence of a clinical picture suggestive of viral encephalitis should raise concern for West Nile virus infection.
- Other members of the Japanese encephalitis serocomplex, particularly Japanese encephalitis, may give a similar radiologic appearance.
- Other causes of bilateral thalamic injury include influenza A and ischemic infarction involving the artery of Percheron.

OY-STER

- Initial serology for West Nile infection frequently returns false-negative results, particularly in patients who are immunosuppressed.

PATIENT 1 A 46-year-old man with a history of pancreas and kidney transplants presented after 3 weeks of progressive abdominal pain, emesis, fever, and diffuse weakness. He was receiving mycophenolate mofetil and tacrolimus for immunosuppression related to organ transplant. He developed worsening weakness and altered mental status, eventually becoming comatose. CSF collected 3 days after admission showed 69 nucleated cells (85% lymphocytes, 2% neutrophils, 13% monocytes), 7 red blood cells, a glucose concentration of 53 mg/dL (appropriate for serum glucose concentration), and a protein level of 100 mg/dL, consistent with viral encephalitis. Initial ELISA was negative for West Nile virus (WNV) immunoglobulin G (IgG) and immunoglobulin M (IgM). Brain MRI showed signal hyperintensity in bilateral thalamic nuclei on fluid-attenuated inversion recovery (FLAIR), extending to the lower cervical spinal cord (figure, A). Foci of restricted diffusion were seen in bilateral thalamic nuclei, the medulla, and the tegmentum (figure, B). CSF collected 11 days after admission subsequently returned positive for WNV infection on ELISA IgM, microsphere immunofluorescence assay IgM (MIA), and real-time qualitative PCR.

PATIENT 2 A 23-year-old woman with a history of cardiac and renal transplants presented with several days of progressive abdominal pain, emesis, and diarrhea. She was receiving mycophenolate mofetil and tacrolimus for immunosuppression related to organ transplant. She gradually became comatose and developed status epilepticus. CSF collected on admission showed 160 nucleated cells (90% lymphocytes, 6% neutrophils, 4% monocytes), 2,350 erythrocytes, a glucose concentration of 76 mg/dL (appropriate for serum glucose concentration), and a protein level of 153 mg/dL, consistent with viral encephalitis. WNV ELISA returned positive at one laboratory for IgG and IgM and negative at a second. MIA was positive for IgM on initial CSF, and repeat CSF collected 14 days after admission was positive for IgG and IgM. Brain MRI also showed signal hyperintensity in bilateral thalamic nuclei on FLAIR imaging extending to the brainstem (figure, C).

DISCUSSION WNV encephalitis (WNVE) outbreaks are increasingly common in the United States. According to the Centers for Disease Control and Prevention, in 2012, 2,873 cases of neuroinvasive WNV were reported in the United States, with over 5,600 total infections and 243 reported deaths. This incidence is dramatically increased from 2011, when 486 cases of neuroinvasive WNV were reported. The signs and symptoms of WNVE are generally nonspecific and can make diagnosis challenging. The most common symptoms found are fever, diffuse weakness, fatigue, headache, and confusion. When found, acute flaccid paralysis due to myelitis, cranial neuropathies, myoclonus, and meningitis may aid in diagnosis. Radiologic findings can also be important in the diagnosis of WNVE because initial serology is often falsely negative. False-negative results may be particularly common when patients are immunosuppressed.

WNV may preferentially affect the thalamic nuclei. This finding is similar to other members of the Japanese encephalitis serocomplex, which includes Japanese encephalitis, Murray Valley

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encephalitis, Kunjin encephalitis, and St. Louis encephalitis.7–9 However, this finding is not always present.2,6 Neuroimaging is frequently normal, with normal MRI findings in up to 30% of cases. Hyperintensity seen on T2 and FLAIR imaging with normal intensity on T1 is typical of WNVE, and diffusion restriction can be seen in up to 50% of cases. A predilection for the thalami, basal ganglia, brainstem, and cerebellum has been reported.2 While bilateral thalamic inflammation occurs in other diseases, identification of this radiologic pattern should raise suspicion for WNVE.10 Repeat CSF testing may be indicated when initial serology is negative.

AUTHOR CONTRIBUTIONS
Dr. Guth: drafting/revising the manuscript for content, study concept, analysis of data. Dr. Futterer: drafting/revising the manuscript for content. Dr. Hijaz: drafting/revising the manuscript for content. Dr. Liotta: drafting/revising the manuscript for content. Dr. Rosenberg: drafting/revising the manuscript for content. Dr. Naidech: drafting/revising the manuscript for content. Dr. Maas: drafting/revising the manuscript for content.

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REFERENCES
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