Diagnosis and Treatment of West Nile Infections

Sandra Abadie Kemmerly, MD

Section on Infectious Diseases, Ochsner Clinic Foundation, New Orleans, LA

ABSTRACT

West Nile Virus (WNV) should be considered in the differential diagnosis for patients presenting with symptoms of viral meningitis, encephalitis, and flaccid paralysis. The activity for 2003 started with human cases in July and is expected to continue spreading throughout the United States. Only 1 in 150 WNV infections result in severe neurologic illness, which is more common in the elderly population. Testing for the IgM antibody against WNV in both serum and spinal fluid is the diagnostic test of choice. Treatment is generally supportive, and no specific anti-viral agents have been determined in trials to be beneficial. Prevention includes the elimination of mosquito breeding sites and the use of pesticides and insect repellents.

Dr. Kemmerly is a fellow of the infectious Diseases Society of America and Govenor of the Louisiana Chapter of the American College of Physicians.

Prior to 1999, West Nile Virus (WNV) infections were not present in the United States. Over the past 3 years, the infection has spread rapidly throughout the country infecting birds, mosquitoes, humans, and horses. In 2002, the Centers for Disease Control and Prevention (CDC) reported more than 4000 human infections and 284 deaths in the US from 44 states and the District of Columbia. As of July 2003, 34 states had reported cases of avian, animal, or mosquito infections. The first human cases in 2003 were reported in early July (1).

WNV infection should be included in the differential diagnosis of a febrile illness or unexplained meningitis or encephalitis, and a high index of clinical suspicion should be present regarding results of specific laboratory tests. Considering the summertime predilection for this infection and the rapidity with which it has moved across the country, all areas within the continental US, and perhaps Canada and Mexico, should be on alert for WNV-associated illness.

This mosquito-borne virus may cause a wide range of symptoms of varying severity in humans. The incubation period in humans ranges from 3 to 15 days. Most human infections are not clinically apparent. However, symptoms may begin with a mild febrile illness and can include fever, headache, myalgias, lymphadenopathy, and a roseolar or maculopapular rash in 20%-50% of persons infected (2,3). It is estimated that only 1 in 150 individuals infected with WNV develops neurologic involvement (such as meningitis or encephalitis) that may result in death. There are limited data to suggest that immunocompromised patients or those who developed WNV infection following organ transplantation may be at increased risk for severe WNV disease (4).

DIAGNOSTIC STUDIES

Cranial MRI appears to be superior to CT for distinguishing central nervous system inflammation. In the 1999 New York outbreak, none of the 43 CT scans showed evidence of acute disease, whereas 31% of those scanned with MRIs had abnormal findings suggesting inflammation. Spinal fluid analyses in this study showed a normal glucose level and elevated protein level with a lymphocytic pleocytosis (3). Both electromyograms and nerve conduction studies may be useful in patients that exhibit neuromuscular abnormalities.

LABORATORY STUDIES

The most common diagnostic method used is IgM-capture enzyme-linked immunosorbent assay (ELISA). The sensitivity of this test is 95%-100% in both serum and spinal fluid (5). In most cases, the IgM is detectable in the serum and cerebrospinal fluid by onset of disease (communication from CDC). This testing methodology is available through state and local health departments. WNV-specific IgM antibody is not detected until the end of the viremic period, which may approach the fourth day of illness. High IgM WNV antibodies in a person with encephalitis or meningitis likely represent infection; however, the IgM may persist from several months to more than a year. Additionally, an intrathecal IgM specific for WNV strongly suggests central nervous system infection, as humoral IgM antibodies do not cross the blood-brain barrier (2).

There is a close antigenic relationship among the flaviviruses. Recent immunization with yellow fever or Japanese encephalitis vaccines may result in false positive results on IgM antibody testing for WNV. Other infectious agents may also cross-react with WNV testing, including dengue, St. Louis encephalitis, and other arboviruses. However, a four-fold change in neutralizing antibody titer should still be sought to provide a specific diagnosis of WNV infection. CDC-defined IgM and IgG ELISAs that use specified antigens are preferred and are available from many state laboratories (6). Plaque reduction neutralization tests comparing the titers to cross-reacting agents can help determine false-positive IgM antibody capture test results. Both viral culture and polymerase chain reaction (PCR) testing, albeit promising, have been shown to be less sensitive that the ELISA for routine testing (2). In the New York outbreak, among the specimens tested by real-time PCR, 16 of 28 (57%) and 4 of 28 (14%) were positive for WNV genome (3).

Diagnosis can also be made by brain biopsy from surgery or autopsy. The pathological findings in fatalities have shown diffuse inflammation of the brain and spinal cord with small hemorrhages, perivascular cuffing, and extensive neuronal degeneration. These findings result from WNV replication causing injury, cytotoxic response, and inflammation (2).

In a group of patients who died and were autopsied, brain tissue was positive for WNV antigen on immunohistochemical analysis and positive for WNV genome on real-time PCR (3). In the cases in which transmission occurred via an organ transplantation, including the subsequent death of one organ recipient, the brain tissue at autopsy was positive for viral culture, WNV PCR, and immunohistochemical staining (4).

TREATMENT

Treatment for WNV infection is supportive. There is no WNV-specific therapy to reduce the injury or resulting edema. Ribavirin in high doses and interferon-α 2b has demonstrated efficacy against the WNV in vitro; however, there are no clinical trials to support the efficacy of either agent (6,7). There have been no controlled studies of the use of steroids, seizure medications, or osmotic agents in the management of WNV encephalitis (6), and no vaccine is currently available for prevention.

PREVENTION

Clearly prevention is paramount in controlling the spread of this viral infection. Primary prevention in humans includes effective mosquito repellents (those containing DEET), avoiding locations where mosquitoes are biting, and barrier methods such as long sleeve clothing, long pants, and window screens. Additionally, active surveillance of the avian population by health departments and the reduction of mosquitoes through coordinated spraying of pesticides in highly populated mosquito areas are all strategies to help in the control of WNV.

REFERENCES

1. West Nile virus activity -- United States, July3-9, 2003. MMWR Morb Mortal Wkly Rep 2003; 52:646.
2. Marfin AA, Gubler DJ. West Nile encephalitis: An emerging disease in the United States. Clin Infect Dis 2001; 33:1713-1719.
3. Nash D, Mostashari F, Fine A, et al. Outbreak of West Nile virus infection in the New York City area in 1999. N Engl J Med 2001; 344:1807-1814.
4. Iwamoto M, Jernigan DB, Guasch A, et al. Transmission of West Nile virus from an organ donor to four transplant recipients. N Engl J Med 2003; 348:2196-2203.
5. Tardei G, Ruta S, Chitu V, et al. Evaluation of immunoglobulin M (IgM) and IgG enzyme immunoassays in serologic diagnosis of West Nile Virus infection. J Clin Microbiol 2000; 38:2232-2239.
6. Petersen LR, Marfin AA. West Nile virus: a primer for the clinician. Ann Intern Med 2002; 137:173-179.
7. Anderson JF, Rahal JJ. Efficacy of interferon alpha-2b and ribavirin against West Nile virus in vitro [letter]. Emerg Infect Dis 2002; 8:107-108.