West Nile Neurologic Disease Gaining Ground

In some states, the incidence of WNV encephalitis is at least 25-fold greater than herpes encephalitis.

BY BRUCE JANCIN

VAIL, COLO. — West Nile virus has very quickly become the most important cause of arbovirus encephalitis in the United States.

West Nile virus (WNV) first appeared in the Western Hemisphere in New York City in 1999. Yet today the overall frequency of West Nile encephalitis in the United States approaches that of herpes simplex encephalitis, Dr. Kenneth L. Tyler observed at a conference on pediatric infectious diseases sponsored by the Children's Hospital, Denver.

"If you account for the fact that most West Nile cases are concentrated in the summer months and in certain geographic areas, whereas herpes of course is year-round and not with any geographic predilection, in some of those areas the relative incidence of West Nile encephalitis over herpes simplex encephalitis is actually quite large," said Dr. Tyler, professor of neurology, medicine, and microbiology at the University of Colorado, Denver.

The often-cited figure for the U.S. incidence of herpes simplex encephalitis is four cases per 1 million population per year. That means in the central states, where WNV is concentrated, the incidence of WNV encephalitis is actually at least 25-fold greater than herpes encephalitis, he added.

Neurologic disease caused by WNV takes three forms: encephalitis, accounting for 55%-60% of cases; meningitis, accounting for 25%-40%; and the often-devastating acute flaccid paralysis, comprising 5%-10%.

Patients with meningitis or encephalitis typically develop fever, headache, nausea and vomiting, and myalgia. Rash, diarrhea, and arthralgia are also common.

Hallmarks of encephalitis, in which the infection involves brain tissue, are a change in mental status and a variety of movement disorders, including postural or kinetic tremor and parkinsonism. Weakness is often impressive. Ataxia and myoclonus are common. Seizures are not.

The cranial nerves most often involved are the second, manifested in blurring and other visual changes, and the seventh, with a uni- or bilateral facial paralysis in a Bell's palsy–like pattern, the neurologist continued.

Unlike in herpes simplex encephalitis, where well over 90% of biopsy-proven affected patients display intracranial neuroimaging abnormalities, that's true for only about half of patients with WNV encephalitis, and even then special MRI techniques such as flare or fast-spin often are required.

The cerebrospinal fluid (CSF) can provide a clue to the diagnosis of WNV meningitis and encephalitis. Unlike in the classic picture of CNS viral infections, where the CSF shows lymphocytic pleocytosis, Dr. Tyler demonstrated in a study of 250 patients with WNV meningitis or encephalitis that 37% of encephalitis patients and 45% of meningitis patients had polymorphonuclear leukocytes as the predominant cell type in their CSF, a pattern that often persisted for a week or more (Neurology 2006;66:361-5). The CSF contained normal glucose levels, elevated protein, and a mean of about 226 cells/mm^3.

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DR. TYLER

Another diagnostic clue is that the CSF of a patient with WNV CNS disease often appears highly reactive, "almost like a cancer," according to Dr. Tyler.

Studies within the last year indicate the recovery phase following symptomatic WNV infection may be more prolonged than originally thought, even in patients with West Nile fever rather than neurologic disease. In a not-yet-published 108-patient Texas study, 60% of patients reported persistent symptoms of weakness, fatigue, memory deficits, personality change, new-onset depression, or walking difficulties after 1 year; 42% had continued complaints after 5 years.

However, in a more rigorous longitudinal study using validated test instruments, Dr. Mark Loeb of McMaster University, Hamilton, Ont., and his coinvestigators found that recovery from the physical, mental, mood, and fatigue symptoms of WNV took about 1 year on average, with patients having neuroinvasive disease taking slightly longer than those with West Nile fever (Ann. Intern. Med. 2008;149:232-41).

Acute flaccid paralysis is a poliomyelitislike disorder that is marked by the acute onset of rapidly progressive asymmetric flaccid weakness. Nearly 90% of affected patients reach their maximum degree of involvement in less than 24 hours.

"I've seen patients who were fine in the morning and quadriplegic in the evening. That's how rapidly it can progress," Dr. Tyler said.

Acute flaccid paralysis is predominantly a lower motor neuron phenomenon. The paralyzed limbs typically have decreased or absent reflexes but preserved sensation. Cranial nerve involvement is a feature in 70% of cases.

Among the more common manifestations are dysphagia, extraocular eye movements, facial paralysis, and vocal cord paralysis. Respiratory failure occurs in 40% of cases. The mortality in patients with respiratory impairment is 50%, Dr. Tyler said.

Survivors of acute flaccid paralysis show variable improvement, coming mostly in the first 4 months. Persistent weakness is common among survivors who have respiratory involvement. ■

Japanese Encephalitis Vaccination Urged for Travel to Asia

BY MIRIAM E. TUCKER

ATLANTA — Japanese encephalitis was identified in four U.S. travelers who returned from Asia during 2003-2008.

The four are the only known cases of Japanese encephalitis among U.S. residents to have occurred since the licensure of a vaccine against the mosquito-borne infection in 1992.

All were civilian travelers or Asian expatriates, the Centers for Disease Control and Prevention reported (MMWR 2009;58:737-40).

Japanese encephalitis should be suspected in a patient with evidence of a neuroinvasive viral infection such as encephalitis, aseptic meningitis, or acute flaccid paralysis, who recently returned from a Japanese encephalitis-endemic country in Asia or the western Pacific.

The virus circulates in parts of China, India, Japan, and Southeast Asia, and all travelers to endemic countries should be advised of the risks of Japanese encephalitis disease.

Health care providers should contact their state or local health department or the CDC's Division of Vector-Borne Infectious Diseases at 970-221-6400 for assistance with diagnostic testing, the CDC said.

In June, the CDC's Advisory Committee on Immunization Practices recommended Japanese encephalitis vaccination for travelers who plan to spend a month or longer in endemic areas during transmission season.

The committee also advised that vaccination be considered for short-term (less than 1 month) travelers to endemic areas during transmission season if they will both travel outside of urban areas and engage in activities that increase the risk of exposure to mosquito bites.

The virus circulates in parts of China, India, Japan, and Southeast Asia, and all travelers to endemic countries should be advised of the risks of Japanese encephalitis disease and the importance of measures to reduce mosquito bites.

However, vaccination is not recommended for short-term travelers whose visit will be restricted to urban areas or whose visit will occur outside of a well-defined Japanese encephalitis virus transmission season, which varies by region, according to the ACIP. The CDC usually follows the recommendations of the committee.

Japanese encephalitis is the leading cause of encephalitis in Asia, with 35,000-50,000 cases annually, a case-fatality rate of 20%-30%, and a 30%-50% risk for significant sequelae among survivors.

There is no antiviral therapy, Dr. Marc Fischer, of the CDC's Arboviral Diseases Branch, said at the ACIP meeting.

One of the four Japanese encephalitis cases, a previously healthy unvaccinated 22-year-old student returning from a study-abroad program in Thailand, was initially reported in 2004. She recovered without apparent sequelae (MMWR 2005;54:123-5).

The other three cases had not been reported until now. All three patients were Asian immigrants or family members who traveled to Asia to visit friends or relatives and had not been vaccinated against Japanese encephalitis.

All recovered, but two had residual neurologic deficits, the CDC said.

In March 2009, the Food and Drug Administration licensed a new Japanese encephalitis vaccine, Intercell's Ixiaro (distributed by Novartis), for use in adults aged 17 years and older.

The only other Japanese encephalitis vaccine available in the United States, JE-Vax (Biken/Sanofi Pasteur), was associated with hypersensitivity reactions (20-600 cases per 100,000 vaccine recipients) as well as rare neurologic events (0.1-2 cases per 100,000 recipients).

JE-Vax is licensed for children and adults aged 1 year and older, but is no longer being produced. Sanofi Pasteur maintains a stockpile for children 1-16 years of age who meet the travel criteria, Dr. Fischer noted at the ACIP meeting. ■

More information about Japanese encephalitis (including seasonality) is available at the CDC Web site at www.cdc.gov/ncidod/dvbid/jencephalitis.