Tick-Borne Encephalitis Among U.S. Travelers to Europe and Asia --- 2000--2009

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Tick-borne encephalitis virus (TBEV) is the most common arbovirus transmitted by ticks in Europe. Approximately 10,000 cases of tick-borne encephalitis (TBE) are reported annually in Europe and Russia (1). Although TBE is endemic in parts of China, information regarding its incidence is limited (1,2). TBEV is closely related to Powassan virus (POWV), another tick-borne flavivirus that is a rare cause of encephalitis in North America and Russia; TBEV and POWV can cross-react in serologic tests (3,4). Before 2000, two cases of TBE in North American travelers to Europe were reported (5,6). State health officials or clinicians send specimens from patients with unexplained encephalitis to CDC as part of routine surveillance and diagnostic testing. CDC recently reviewed all 2000--2009 laboratory records to identify cases of TBE among U.S. travelers; the five cases identified are summarized in this report. All five cases had TBEV or POWV immunoglobulin M (IgM) antibodies in serum and were confirmed as acute TBE cases by plaque-reduction neutralization tests against both viruses. All four patients who had traveled to Europe or Russia had biphasic illnesses (a common feature of TBE) and made nearly complete recoveries. The fifth patient, the first reported case of TBE in a U.S. traveler to China, had a monophasic illness with severe encephalitis and neurologic sequelae. Health-care providers should be aware of TBE, should counsel travelers about measures to reduce exposure to tick bites, and should consider the diagnosis of TBE in travelers returning from TBE-endemic countries with meningitis or encephalitis.

Case Reports

Case 1. On July 11, 2001, a previously healthy man aged 57 years was admitted to a Utah hospital with fever of 102.7°F (39.3°C), tachycardia, mental status changes, right arm tremors, and right-sided rigidity (Table 1). In June, he had traveled to eastern Russia where he noted having multiple tick bites. On June 26, 15 days before admission, he developed fever, myalgias, and cough, which improved with empiric antibiotics. Ten days before admission, the symptoms recurred and he was treated with intramuscular penicillin. Four days before admission, he developed headache, neck stiffness, and confusion, which progressed over the next few days. On admission to the hospital, the patient was disoriented and stuporous. Cerebrospinal fluid (CSF) showed lymphocytic pleocytosis and elevated protein; bacterial cultures, herpes simplex virus (HSV), and enterovirus polymerase chain reaction (PCR) were negative. Brain magnetic resonance imaging (MRI) revealed left-sided cerebral edema with ischemic changes of the thalamus and striatum. The patient was diagnosed with encephalitis of unknown etiology and treated empirically with antibiotics and corticosteroids, with resolution of fever and recovery of normal mental status the next day. He returned home after 14 days with residual right-sided weakness.
and rigidity and impaired cognition. His motor symptoms resolved during the next 6 months; however, he continued to experience mild cognitive impairment. Serum collected on admission tested positive for TBEV IgM and TBEV-specific neutralizing antibodies (Table 2). Serologic tests for other arboviruses and pathogens* were negative.

**Case 2.** On August 27, 2004, a previously healthy man aged 20 years was admitted to a Wyoming hospital with fever of 104.0°F (40.0°C), conjunctival injection, photophobia, and altered mental status (Table 1). During June--August, he had traveled in Siberia, Russia, and noted having multiple tick bites. On August 3, approximately 3 weeks before admission, he experienced fatigue, nausea, vomiting, and myalgias, which subsequently resolved. However, 8 days before admission, he developed fever and headache, which worsened until the day of admission. A CSF specimen collected on admission to the hospital showed pleocytosis and elevated protein; bacterial cultures and HSV and enterovirus PCR were negative. Brain MRI was normal. The patient was diagnosed with encephalitis of unknown etiology and treated empirically with antibiotics. He was hospitalized for 4 days and recovered fully. Serum collected on admission tested negative for TBEV IgM but positive for POWV IgM and TBEV-specific neutralizing antibodies (Table 2). Serologic tests for other arboviruses† and *Borrelia burgdorferi* were negative.

**Case 3.** On August 19, 2006, a previously healthy man aged 46 years was admitted to a hospital in Connecticut with fever of 102.9°F (39.4°C) and headache (Table 1). During July--August, he had traveled in Sweden and noted having numerous tick bites. On July 25, approximately three and a half weeks before admission, he developed fever and diarrhea requiring a brief hospitalization. His symptoms resolved, but 2 weeks before admission, after returning to the United States, he developed headaches and fever, which subsequently worsened. On admission to the Connecticut hospital, his physical examination was remarkable for diminished deep tendon reflexes bilaterally in the lower extremities. A CSF specimen showed mild pleocytosis and elevated protein. Brain MRI was normal. He was diagnosed with meningitis of unknown etiology, was hospitalized for 3 days, and recovered fully. Serum collected on admission tested positive for POWV IgM, TBEV IgM, and TBEV-specific neutralizing antibodies (Table 2).

**Case 4.** On July 18, 2007, a previously healthy girl aged 15 years with acute encephalitis of unknown etiology was airlifted from a hospital in Beijing, China, and admitted to a hospital in New York City (Table 1). During June and July, she had traveled with classmates in Tianjin Province, China. She had no known tick bites. On July 4, she developed fever and diarrhea and was admitted to a local hospital. She was transferred to the Beijing hospital on July 9 for persistent fever and confusion. HSV PCR on CSF and tests for Japanese encephalitis virus antibodies in serum were negative. During the next week in the Beijing hospital, despite empiric treatment with antibiotics and acyclovir, her mental status worsened, and she experienced two seizures and developed Bell’s palsy. On admission to the New York City hospital, her physical examination showed aphasia, hemiplegia, and hyperreflexia. A specimen of CSF showed pleocytosis, and MRI revealed bilateral thalamic and basal ganglia lesions. After a prolonged hospitalization, she was transferred to a rehabilitation facility. She fully recovered cognitive function, but had residual severe
dysarthria and mild bradykinesia in the limbs, which improved with dopamine-agonist medications. Serum collected on July 20 tested negative for TBEV IgM but positive for POWV IgM and TBEV-specific neutralizing antibodies (Table 2). Serologic tests for other arboviruses§ were negative.

Case 5. On September 2, 2008, a previously healthy boy aged 14 years was admitted to a hospital in the District of Columbia with fever, headache, and vomiting. During June--August, he had traveled in the Czech Republic and Siberia, Russia, and noted having multiple tick bites. Eleven days before admission, he developed fever and sore throat, which resolved with oral penicillin. Three days before admission, he developed fever and headache, prompting his return home. During the first 3 days of hospitalization, his fever and headache persisted and he developed neck stiffness and abdominal pain. A specimen of CSF showed pleocytosis and elevated protein; bacterial cultures and HSV and enterovirus PCR were negative. Brain MRI was normal. He was diagnosed with meningitis of unknown etiology; treatment included empiric antibiotics and acyclovir. He fully recovered after an 8-day hospitalization. After consultation with CDC, a convalescent serum sample was collected on September 30, and tested positive for POWV IgM, TBEV IgM, and TBEV neutralizing antibodies (Table 2). Serologic tests for other arboviruses and pathogens¶ were negative.

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Editorial Note

TBE is not a nationally notifiable disease in the United States. However, CDC assists state health departments and clinicians with the diagnosis of possible arboviral diseases, including TBE. Although testing for TBEV is available in certain specialized laboratories outside CDC, these five cases are the only TBE cases known to have been diagnosed in the United States during 2000--2009.

Of the four U.S. patients who had traveled to Europe or Russia, all noted having tick bites and had biphasic illnesses. Two had encephalitis and two had meningitis; none had neurologic sequelae. The fifth patient, who traveled to China, had a monophasic illness with severe encephalitis and neurologic sequelae and no history of tick bite. Despite the variable and cross-reactive
TBEV and POWV IgM antibody findings, the virus-specific neutralizing antibody results support the diagnosis of TBE for all five cases.

TBEV includes three subtypes: European, Siberian, and Far Eastern. During the past decade, both the apparent geographic distribution and reported incidence of TBE have increased (1,7,8). TBEV is known to be endemic from western Europe through Siberia and parts of Asia including certain areas in China (1,2). However, no cases have been reported previously from Tianjin Province, China, and this is the first reported case of TBE in a U.S. traveler returning from China. Approximately one third of persons infected with TBEV develop clinical symptoms and about two thirds of patients recall having a tick bite (9). Typically, patients infected with the European subtype have a biphasic illness. The first (viremic) phase consists of a nonspecific febrile illness, often followed by a remission of symptoms (7). Approximately one third of these patients then develop the second, more severe (neuroinvasive) phase of illness, resulting in meningitis (approximately 50%), encephalitis (approximately 40%), or myelitis (approximately 10%) (7,9). The case-fatality ratio for the European and Siberian subtypes is approximately 1%--3%. The Far Eastern TBEV subtype typically causes a more severe monophasic illness with a case-fatality ratio of approximately 20% and neurologic sequelae in up to 80% of survivors (7).

For unvaccinated travelers to areas in which TBE is endemic, the estimated risk for TBE during TBEV-transmission season is approximately one case per 10,000 person-months (10). This estimate of risk varies according to the degree of unprotected outdoor exposure in forested areas. Cases generally occur during March and November (10). No specific antiviral treatment for TBE exists (8). The main preventive measure is avoiding tick bites** by applying insect repellents to clothing and exposed skin; wearing long-sleeved shirts, long pants, socks, and boots; and tucking pant cuffs into socks. †† No TBE vaccines are licensed or available in the United States, but two inactivated TBEV vaccines are licensed and available in Europe and Canada (7).

TBE should be suspected in a patient with evidence of meningitis or encephalitis who recently returned from a TBE-endemic country. Encephalitis or meningitis caused by TBE and other viruses cannot reliably be distinguished clinically. Health-care providers should contact their state or local health department for diagnostic assistance. TBEV testing can be performed at CDC's Special Pathogens Branch (telephone: 404-639-1115), and TBEV and other arboviral disease testing can be performed at CDC's Arboviral Diseases Branch (telephone: 970-221-6400).

References

10. Rendi-Wagner P. Risk and prevention