Tick-borne Encephalitis (TBE)

Tick-borne encephalitis, or TBE, is a human viral infectious disease involving the central nervous system. TBE is caused by the tick-borne encephalitis virus (TBEV), a member of the family *Flaviviridae*, and was initially isolated in 1937. Three virus sub-types are described: European or Western tick-borne encephalitis virus, Siberian tick-borne encephalitis virus, and Far eastern Tick-borne encephalitis virus (formerly known as Russian Spring Summer encephalitis virus, RSSEV).

The family *Flaviviridae* includes several tick-borne viruses affecting humans. These viruses are closely related to TBEV and Far-eastern TBE, and include Omsk hemorrhagic fever virus in Siberia, Kyasanur Forest disease virus in India and its close relative, Alkhurma virus in Saudi Arabia. Louping ill virus (United Kingdom) is also a member of this family; it causes disease primarily in sheep and has been reported as the cause of a TBE-like illness in laboratory workers and persons with contact to sick sheep (e.g., veterinarians, butchers). In the USA and Russia, another tick-borne flavivirus, Powassan virus, is responsible of encephalitis in human.

Transmission

Ticks, specifically hard ticks of the family *Ixodidae*, act as both the vector and reservoir for TBEV. The main hosts are small rodents, with humans being accidental hosts. Large animals serve as feeding hosts for the ticks, but do not play a role in maintenance of the virus.

The virus can chronically infect ticks and is transmitted both transtadially (from larva to nymph to adult ticks) and transovarially (from adult female tick to eggs). TBE cases occur in humans most frequently in rural areas and during the highest period of tick activity (between April and November). Infection also may follow consumption of raw milk from infected goats, sheep, or cows. Laboratory infections were common before the use of vaccines and availability of biosafety precautions to prevent exposure to infectious aerosols. Person-to-person transmission has not been reported with the exception of vertical transmission, from an infected mother to fetus.

Signs and Symptoms

The incubation period of TBE is usually between 7 and 14 days and is asymptomatic. Shorter incubation times have been reported after milk-borne exposure.

In contrast to Far-eastern TBE, European TBE is more severe in adults than in children where meningitis is more frequently observed.

In approximately two-thirds of patients infected with the European TBE virus, only an early (viremic) phase is experienced; symptoms are nonspecific and may include fever, malaise, anorexia, muscle aches, headache, nausea, and/or vomiting. After about 8 days of remission, a second phase of disease occurs in 20% to 30% of patients. These patients may experience a clinical illness that involves the central nervous system with symptoms of meningitis (e.g., fever, headache, and a stiff neck), encephalitis (e.g., drowsiness, confusion, sensory disturbances, and/or motor abnormalities such as paralysis), or meningoencephalitis.

The convalescent or recovery period can be long and the incidence of sequelae may vary between 30% and 60%, with long-term or even permanent neurologic symptoms. Neuropsychiatric sequelae have been reported in 10-20% of patients.

The range of clinical manifestations can be observed following infection by any of the TBE virus subtypes. Biphasic symptomatology (fever then neurological disorders) is frequent after infection with the European or Western TBE subtype. Infections by the Far-eastern TBE subtype are generally more severe and the case-fatality rate is higher. The Siberian subtype in children could be responsible for chronic encephalitis.

In general, mortality is rare, about 1% to 2%, with deaths occurring 5 to 7 days after the onset of neurologic signs in European TBE. During Far-eastern TBE, signs and symptoms are more severe and mortality is higher (5-20%).

Risk of Exposure

TBE is an important infectious disease in many parts of Europe, the Former Soviet Union, and Asia, corresponding to the distribution of the ixodid tick reservoir. The annual number of cases (incidence) varies from year to year, but several thousand cases are reported annually, despite historical under-reporting of this disease.

In disease endemic areas, people with recreational or occupational exposure to rural or outdoor settings (e.g., hunters, campers, forest workers, farmers) are potentially at risk for infection by contact with the infected ticks. Furthermore, as tourism expands, travel to areas of endemicity broadens the definition of who is at risk for TBE infection.

Diagnosis

During the first phase of the disease, the most common laboratory abnormalities are a low white blood cell count (leukopenia) and a low platelet count (thrombocytopenia). Liver enzymes in the serum may also be mildly elevated. After the onset of neurologic disease during the second phase, an increase in the number of white blood cells in the blood and the cerebrospinal fluid (CSF) is usually found. Virus can be isolated from the blood during the first phase of the disease. Laboratory diagnosis usually depends on detection of specific IgM in either blood or CSF, usually appearing later, during the second phase of the disease.

Treatment

There is no specific drug therapy for TBE. Meningitis, encephalitis, or meningoencephalitis requires hospitalization and supportive care based on syndrome severity. Anti-inflammatory drugs, such as corticosteroids, may be considered under specific circumstances for symptomatic relief. Intubation and ventilator support may be necessary.

Prevention

Like other tick-borne infectious diseases, TBEV infection can be prevented by using insect repellents and protective clothing to prevent tick bites. A vaccine is available in some disease endemic areas (though not currently in the United States).

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