Tick-borne encephalitis viruses

Ixodes ricinus

Tick-borne encephalitis virus belongs to the genus Flavivirus and the family Flaviviridae. Flaviviruses are spherical enveloped viruses with a diameter of 40-60 nm that contain +ssRNA of approximately 11 kb in length. A cap (important for mRNA stability) is found at the 5´ end, but the polyA 3´ end is missing. The RNA encodes 7 non-structural proteins and 3 structural proteins - capsid protein C, membrane protein M and glycoprotein E. The 3´ and 5´ ends of the genome are non-coding. Glycoprotein E is inserted into the membrane, which also contains protein M (7kDa). The latter is produced by cleavage of prM (26kDa) by furin and is found only in mature virions. The virus is thermolabile, gradually losing all activity within 10-30 minutes at 50-60 °C, but is more thermostable in milk. The optimum pH for viral activity is around 8.5, but the virus is not inactivated by the low pH of gastric juice, so infection can occur via the alimentary route. The virus can also be inactivated, for example by UV radiation. The virus enters the cell by receptor-mediated endocytosis. Genomic RNA is translated in the cytoplasm of the infected cell and the resulting viral polyprotein is cleaved into individual proteins. RNA polymerase generates -ssRNA complementary to the viral +ssRNA, which becomes the template for the new viral RNA. The next steps of replication take place in the endoplasmic reticulum. Non-infectious immature virions are produced, which are transported through the secretory pathway of the host cell and mature in acidic vesicles after PrM cleavage.

Tick-borne encephalitis virus complex

In addition to the main subtypes of tick-borne encephalitis virus - Western type and Eastern type (from which some authors also distinguish the Siberian type), the tick-borne encephalitis virus complex also includes the Omsk hemorrhagic fever virus, the kyasanur forest disease virus, the Malaysian Langat virus, the Canadian Powassan virus and the Louping ill virus. All viruses belong to the so-called Arboviruses (arthropod-borne virus), i.e. viruses transmitted by arthropods.

Western type - Central European tick-borne encephalitis virus

As the name suggests, natural outbreaks of the virus occur in areas west of the Urals to eastern France. Infections are seasonal with a peak from April to October, but due to climate change, there is an increase in infections as the period of ideal conditions for the ticks that are the vector of the virus (in this case mainly ticks of the genus Ixodes ricinus) is prolonged. The reservoir in nature is small rodents. The virus multiplies in the tick's salivary glands and, when an infected tick attaches itself to humans or other mammals, including domestic animals (goats, cows, sheep, etc.), the infection is transmitted. Human infection can also occur through alimentary routes, e.g. after ingestion of unpasteurised milk from an infected animal. Therefore, people working with these animals or living on the farm were often infected.

The disease has a typical two-stage character. After 1-2 weeks, primary viremia occurs when the virus multiplies in the subcutaneous tissue and regional nodules. It spreads through the blood and lymph to other lymphoid tissues and the disease manifests itself in a similar way to influenza - increased temperature, fatigue, headache and muscle aches. After a few days, the condition improves and recovery may occur. If this does not happen, the second stage, secondary viremia, comes and the condition worsens. The virus enters the cerebrospinal fluid and meninges via the plexus choroideus and multiplies. All cell types can be affected. Both white and grey matter (grey more), the medulla oblongata, cerebellum, anterior horns of the spinal cord are affected. Meningitis, meningoencephalitis or encephalomyelitis may develop. Manifestations include high fever, headache, vomiting, sleep disturbances, tremors, cranial nerve disorders, flaccid paresis of the limbs, and others. There may be minor hemorrhages in the CNS, necrosis and degenerative changes of ganglion cells. Rarely, cerebral edema occurs. The course is milder in children and adolescents. Strong immunity remains after the disease. Studies have shown that the virus is stable under natural conditions and does not undergo significant antigenic changes. However, it is known that both genotype and phenotypic characteristics can change. In addition, the phenotypic expression also changes during transmission from mammal to tick.

Eastern type - Russian spring-summer encephalitis virus

Russian spring-summer encephalitis is similar to the Western type, but has a more severe course and poorer prognosis. Permanent sequelae are more common, with death occurring in up to 30% of cases. Mice, red mink, wood mice and other small rodents are reservoirs of the virus. The vectors are ticks of the genus Ixodes persulcatus. The incubation period is 10-14 days, after which the infected person has high fevers. This is followed by headaches, dizziness and vomiting. A few days after fever, neurological symptoms including convulsions, alteration of consciousness, hyperkinesis, paralysis and spinal cord involvement appear. After several months or years, exacerbation can occur, which can cause epilepsy, psychosis, and spinal and cortical involvement.

Omsk hemorrhagic fever virus

The virus is predominantly in W Siberia. The reservoir is voles and other rodents, the vectors are ticks *Dermacentor pictus*, *Dermacentor marginatus* and *Ixodes persulcatus*. Muskrats are also hosts, infecting water and creatures living in it with their urine, so the infection can also reach humans through this route. Hunters can also become infected in autumn by contact with the blood of an infected animal. The virus multiplies in the endothelial cells of blood vessels and causes bleeding problems. The incubation period is 2-4 days. Manifestations include high fever, headache, decreased leukocyte count. Treatment is usually without consequences.

Kyasanur Forest Disease virus

The virus has been found off the coast of India in humans and monkeys. The source is rats, bats and small mammals, the vector is the *Haemaphysalis spinigera* tick. The incubation period is 2-7 days, and for the next 12 days the infected person suffers constant fever, head and body aches, as well as severe muscle pain, vomiting and diarrhoea. Bleeding occurs in the lumen of the stomach, intestines and lungs. The lethality is 10%, with sufferers dying mainly from pulmonary oedema.

Malaysian Langat virus

The virus was first isolated in Malaysia and Thailand. The virus is similar to Omaha haemorrhagic fever virus, Kiasanurian forest disease virus, Louping ill virus and tick-borne encephalitis virus, but there are no known diseases associated with Langat virus. Antibodies have been found in the serum of infected people, resulting in an attempt to develop a vaccine against tick-borne encephalitis. Although several vaccines were tested at this time and a vaccine based on the Langat virus had the lowest number of infections, it could not be put into practice. The main reasons were twofold - it did not provide complete protection against the disease and it often (1:10,000) caused encephalitis.

Canadian Powassan virus

The virus is found predominantly in Canada and the USA. The vector is the Ixodes cookei tick, which is a parasite of foxes, raccoons, weasels and marmots. Manifestations of the disease include fever and encephalitis. Antibodies against the virus have been found in squirrels.

Louping ill

The virus has been found in the UK mainly in sheep, but also in other domestic animals, birds and humans. The vector is the tick Ixodes ricinus. In the endemic area, about 0.1-0.4% of ticks are infected. In sheep, the incubation period is 6-18 days, followed by 5 days of fever, inappetence and then neurological disturbances. It often ends in death. In humans, the disease has a milder course, manifested by fever and encephalitis. Human infections are rare, but mostly occur in people working with animals. There is a vaccine against Louping ill, but the lack of vaccines and the higher number of ticks increases the likelihood of infection.

Sources

Related articles

- Encephalitis
- Tick-borne encephalitis
- Neuroinfection

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