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CASUISTIC PAPER

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Diagnostic and therapeutic difficulties of tick-borne encephalitis – a two case reports

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ABSTRACT

Introduction. The paper presents epidemiology, routes of infection, forms of the disease, diagnostic and treatment methods, and prophylaxis of tick-borne encephalitis.

Aim. In this paper, we present two descriptions of the cases of tick-borne encephalitis.

Description of the cases.

Case 1. A 60-year-old man with fever up to 39 degrees for 3 days, multi-site headache and other body aches, as well as an ear-stuck feeling. The day before hospitalization, there was a feeling of numbness on the right side of the face from eye level to the chin and speech distortion.

Case 2. A 60-year-old patient with headaches and an increase in temperature to 39 degrees for 3 days, who, approximately, three weeks earlier was ticked by a tick in the lower parts of the back.

Conclusion. It is also important for doctors to take a broader view and to make society aware of that Lyme disease is not associated only with Lyme disease. Further work is also needed towards effective treatments for Tick-borne encephalitis (TBE).

Keywords. diagnostic, tick borne encephalitis, treatments

Introduction

Tick-borne encephalitis (TBE) is still a significant diagnostic difficulty due to the lack of specific symptoms. Another problem is the lack of effective treatment for the disease. Currently, the only effective method of preventing disease is vaccination. Tick-borne encephalomyelitis also called Central European Encephalitis (CEE), Russian Spring-Summer Encephalitis (RSSE), tick borne encephalitis (TBE) to flavivirus disease (TBEV) from the Flaviviridae family, which belongs to the group of arboviruses.[1] In Europe, two subtypes of this virus are distinguished: eastern, which is transmitted by Ixodes

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persulcatus ticks and causes Russian spring-summer encephalitis, and western (European) that causes Central European encephalitis, transmitted by ticks of the species Ixodes Ricinus.[2,3] It is the latter species of the tick that is most important in Poland in the spread of the TBE virus from an infected animal to a human.[4,5]

In endemic areas of Europe, the percentage of infected ticks varies between 0.5-5%. Incidence occurs seasonally, in spring and summer, when tick feeding is intensified.[4] Currently in Poland, the number of cases of full-blown TBE over the past 10 years is estimated at 150 to over 250 cases per year. In 2014, 195 cases were recorded, and in 2015, 150 cases of TBE Epidemiological studies show that these are underestimated data.[5] The highest risk of illness is observed in northern, northeastern and eastern Poland. Exposure to tick sting is particularly beneficial for some professions. This risk group includes forest workers, farmers (especially those who have farms located in close proximity to forests), people dealing in collecting undergrowth, but also border guards patrolling border areas.[6] It is worth emphasizing that people professionally involved in working in the forest can be naturally immunized as a result of numerous tick bites and the introduction of minimal, subliminal doses of TBE virus that do not cause disease symptoms, but induce the production of specific antibodies.[7] Human infection most often occurs as a result of pricking by an infected tick (the virus is transmitted along with its saliva during blood suction). In addition, infection can occur through the digestive tract by consuming raw, unpasteurized milk and milk products (yogurt, cheese, butter) from infected animals, i.e. cows, sheep, goats.[8,9] The existence of this route of infection is due to the fact that the virus can penetrate from the blood into the mammary glands of infected animals, and also remains active in an environment at pH 2.75-11.55 for about 24 hours, and therefore is not inactivated in the stomach. According to studies, TBEV retains the ability to virulence in the milk of infected animals for up to 8 days.[9,10] In milk, butter or cheese, the virus can survive for many months. Pasteurisation of dairy products provides full protection against infection, because TBEV is sensitive to temperature changes.[11,12] As a result of transmission of the virus through the digestive tract, a characteristic form of the disease may develop, i.e. biphasic milk fever. This type of infection accounts for around 10-20% of all TBEV cases in Europe.[9] Occasionally, infection can also occur through the inhalation route through the olfactory epithelium when inhaling the suspension of viral particles, since it has been proven that the virus remains infectious in air for up to 6 hours at room temperature.[12] In addition, cases of infections due to cuts during laboratory work and transfusional infections have been described.[13,14] The virus is not transmitted from person to person. The incubation period of the KZM virus is from 7 to 14 days after a tick bite, and from 3 to 4 days in the case of gastrointestinal infection.[14-17] Sensitivity to infection is common, but the disease is usually asymptomatic.[4] Central European tick-borne encephalitis has a two-phase course.[4] The first phase of the disease lasts on average 4 days (1-8) and is characterized by a sudden onset. It is associated with the virus getting into the blood after being pricked by an infected tick. Wiremia is accompanied by an increase in body temperature not exceeding usually 38°C, less often reaching 40°C with non-specific flu-like symptoms, i.e. malaise, increased psychophysical fatigue, increased sweating, headache, nausea and vomiting, muscle and joint pain, photophobia, catarrhal upper respiratory tract, conjunctivitis. Some patients may have a maculopapular rash mainly on the torso. During this period, leukopenia and thrombocytopenia, as well as an increase in CSB albumin can be observed in laboratory tests.[8] In about 13 -26% of infected, the disease ends with the first phase, followed by recovery and in the remaining patients (about 74-87%), usually after an average of 8 days (1-33) of well-being, the second phase of so-called neurological.[18] 23-50% of patients only have symptoms of the second phase of the disease without first phase symptoms.[11,19] The neurological phase is associated with the entry of the virus into the central nervous system. Again, body temperature rises 39-40°C. There are severe headaches, nausea, vomiting, meningeal symptoms and muscle and joint pain.[8] Depending on the location of the inflammatory process in the central nervous system (CNS) and the clinical picture of the disease, the following forms of KZM can be distinguished: meningitis, encephalomyelitis (encephalomeningitis), meningitis, encephalitis and spinal cord (meningoencephalomyelitis), meningitis, encephalomyelitis (meningoencephaloradiculitis).[8] The meningeal form is the most common, occurs in about 49% of patients, has the mildest course. Symptoms are typical for lymphocytic meningitis. A more severe course is characterized by meningitis. In its course may occur: ataxia, disturbances of consciousness up to and including coma, sometimes cranial nerve palsy. About 10% of patients suffer from the most severe meningitis. It leads to anterior horns of the spinal cord and flaccid limb paralysis. Positive meningeal symptoms, symptoms of focal CNS, nerve roots and peripheral nerves are found.[8] Prognosis worsens the involvement of the medulla and brainstem. KZM mortality is up to 5% .[8] Most patients recover fully. In some cases, there is a prolongation of the disease process and its transition into a chronic form with periods of disease progression and its stabilization.[20-22] A lighter course is usually more common in children and adolescents than in adults. In people over 60 years of age, the course of KZM is usually more severe and sometimes leads to permanent neurological or psychological consequences. The frequency of neurological complications is estimated at 20-50%.[8] The most common among them are: paralysis or paresis of

cranial nerves, multi-nerve damage with paralysis of various muscle groups - most often the shoulder belt with muscle atrophy, mainly deltoid muscle, flaccid paralysis of the limbs, damage to the cerebellum (gait and speech disorders, nystagmus, intentional tremor), sensory disorders, neuralgia, focal or generalized epileptic seizures, intellectual disorders: concentration disorders, attention, persistent and fresh memory, perception (hallucinations), thinking (delusions), mood and emotions (depression, mania, anxiety) or personality and behavioral disorders and insomnia.[8,22-25]

The basis for diagnosis is the detection of specific antibodies in the IgM and/or IgG class in blood serum and pmr by ELISA.[8] IgM antibodies are detected in the serum of patients with TBE after about 7-10 days from the time of infection and they persist for an average of 40 days, and IgG antibodies appear later, about 14 days after the infection, but they can be detected in serum up to several dozen years after infection. It should be noted that usually in routine diagnostics of TBE with developed TBEV-induced neuroinfection both of the abovementioned classes of antibodies are detected simultaneously. In the cerebrospinal fluid, however, in patients with active TBE, specific IgM and IgG immunoglobulins appear later than in the blood and are detected for a shorter time than when they are present in the serum.[7] It is also possible to demonstrate the genome of the TBE virus by RT-PCR (reverse-transcriptase polymerase chain reaction) in serum and CSF in the acute phase of the disease. This is of little importance in routine diagnostics, because in the neurological phase, which usually occurs during the hospitalization period, the virus is already absent in serum and in CSF.[8] The CSF general examination is important in the diagnosis of TBE Inflammatory changes in PMR usually persist for 4 to 6 weeks, less often for several months in the form of increased protein and cytosis.[26-28] It should be noted that the lack of characteristic epidemiological data in the patient's history (tick bite, seasonality) does not allow the exclusion of any tick-borne disease.[4] When TBE is found, only symptomatic treatment is used. It involves the administration of antipyretic, analgesic, anti-inflammatory, anti-edema drugs, and in severe cases also glucocorticosteroids.[29] The most effective form of prevention is vaccination.

Aim

In this paper, we present two descriptions of the cases of tick-borne encephalitis.

Description of the cases

Case 1.

A 60-year-old man was admitted to the Department of Neurology with the following symptoms: fever up to 39 degrees for 3 days, multi-site headache and other body aches, as well as an ear-stuck feeling. The day before hospitalization, there was a feeling of numbness on the right side of the face from eye level to the chin and speech distortion. About 5 days before hospitalization, the patient ended 10-day antibiotic therapy due to upper respiratory tract infection. In addition, about 3 weeks earlier he was ticked by a tick around the lower parts of the back without extensive erythema. Upon admission to the Department by neurological examination for deviations from the normal state, it was found: somewhat dysartic speech, distortion of the sensation from the height of the eye socket down on the right side of the face, smoothing of the right nasolabial fold, weaker tooth grinding on the right, the patient was not upright. Computed tomography of the head performed in the urgent mode, transthoracic echocardiography of the heart and laboratory tests did not reveal any significant deviations from the norm. Pre-diagnosed neuroinfections. Lumbar puncture was performed, cerebrospinal fluid was taken for general examination and Borrelia burdorferii antibodies in the IgM and IgG class (negative results were obtained in the following days of hospitalization). The pmr study found: a slightly increased protein level of 55.7 mg / dl, pleocytosis of 37 cells /mcl, percentage of cells with a monoplane nucleus 41%, multiplane 59%. Due to the features of V and VII neuropathy of the cranial nerve, diagnostics was expanded to include magnetic resonance imaging of the head with contrast. The study describes on average numerous (about 20) hyperintensive foci in the T2 and Flair sequences, invisible in the T1 and DWI sequences, not enhancing the signal after the contrast agent - most likely foci of deep white matter ischemia for differentiation with demyelinating lesions in both frontal and parietal lobes. In addition, old painting pits in the left parietal lobe, amygdala and bridge were described. On the basis of the overall clinical picture, acute meningitis and encephalitis were diagnosed, most likely of viral etiology. Antiviral and anti-inflammatory treatment was implemented - acyclovir and dexamethasone Otolaryngological consultation was performed due to the patient's feeling of tapping in the ears and the features of damage to the right nerve of the VIIth patient. The study did not find an ear-like aetiology of the aforementioned ailments, further treatment in the Department of Neurology was recommended. On the first day of hospitalization, the patient continued to fever to approximately 39.2 degrees. There was a sharp deterioration in the general and neurological condition. The patient reported shortness of breath, feeling cold, and general weakness. Swallowing difficulties arose as a result of which the patient choked. Chest x-ray (x-ray of the klp) was taken - no pathology. The patient was moved to the intensive neurological supervision room and monitoring of vital functions began. In the neurological examination, the previously described deviations involuntarily joined face movements mainly around the mouth, grunting, nystagmus when looking to

the right, paresis of the right side of the face, facial muscles, paresis of the palate, throat and tongue, paresis of the middle right upper limb, weakness of hand grip after right. Urgent head magnetic resonance imaging was ordered, excluding fresh ischemia. The image showed no significant differences compared to the previous study. In the following hours the patient's general condition continued to deteriorate rapidly. Due to acute respiratory failure, the patient was intubated and transferred to the Anaesthesiology and Intensive Care Unit (ICU). After admission to the above-mentioned ward, the patient's condition remained severe. The fever was up to 38.2 degrees. The patient was connected to a respirator. He required analgosedation, dopamine infusion for hypotension and stimulation of furosemide diuresis. Bilateral inflammatory changes of the lungs, probably after aspiration, have been reported in the x-ray of the klp. Antiviral treatment was maintained. Antibiotic therapies were used with good effect (in the X-ray of the chest, the complete regression of the inflammatory changes previously described was seen). In the following days the patient's neurological condition continued to deteriorate. During the entire hospitalization at the ICU, the patient was consulted neurologically several times. The next neurological examination revealed: medium-wide pupils, poorly responsive to light, trace corneal and ciliary reflexes, no ocular-head reflex. Periodic involuntary serial movements of the supraorbital region, lips and tongue, flaccid paralysis with extremely weak deep reflexes and lack of plantar reflexes. In control computed tomography of the head, fresh pathologies within the brain were excluded. The patient was consulted by a doctor of Infectious Diseases, diagnostic recommendations were implemented. In the differential diagnosis of symptoms presented by the patient, Guillain-Barry syndrome (Miller-Fischer variant), autoimmune encephalitis, subacute sclerosing encephalitis (SSPE), neuroborreliosis, tuberculosis of the nervous system, tick-borne encephalitis (KZM) were taken into account. Therefore, CSF was again collected for general examination, virological and anti-neuronal antibodies. Anti-neuronal antibodies and antibodies against GM1 and GQ1b gangliosides were determined in the blood. Re-examination of the cerebrospinal fluid showed slightly increased pleocytosis (8 cells/mcl) and high protein levels (313.4 mg/dl) - features of protein-cell cleavage. In this situation, taking into account the clinical picture together with the results of the CSF, suspected acute inflammatory polyradiculoneuropathy - Guillain-Barre syndrome with a possible Miller-Fischer variant. High doses of intravenous glucocorticosteroids were used followed by intravenous infusion of immunoglobulins without the expected clinical effect. In connection with the above, 5 plasmapheresis procedures were performed. Despite the treatment, the patient was still in a severe general condition. In a non-contact neurological examination, eyes opened spontaneously, four-limb limp paresis. On the 16th day of hospitalization, the ENG examination was performed, which did not show the characteristics of acute inflammatory radiculoneuropathy. The study found features of a significant degree of nerve damage at the trunk level in the area of sensory and motor fibers, which gave a picture of sensorimotor polyneuropathy mainly of an axonal nature with a demyelination component. In the performed electroencephalographic examination, an abnormal, encephalopathic record was found. On the 23rd day of hospitalization, results of tests for KZM were obtained - anti-TBEV antibodies: positive in the IgM class 4.27 and border IgG 1.02 (descriptive norm: <0.8 negative, 0.8-1.1 border > 1,1-positive). Based on the results of laboratory tests, presented by the patient's symptoms and medical history, tick-borne meningitis, encephalomyelitis was diagnosed. Due to the lack of effective causal treatment, supportive treatment was carried out. In the next days of hospitalization the patient's condition remained very severe. On the 36th day of hospitalization, the patient experienced tremors of facial mimics. Neurologically consulted. The study found: residual elements of consciousness, lying patient, the only motor activities are partial opening of the eyelids, periodic facial grimaces, periodic symmetrical series of myoclonic seizures of both cheeks and upper lips, scanty movements of tongue tightening, periodic floating eye movements to the sides, knobs eyes set straight ahead, in a slight divergent strabismus, medium wide pupils, symmetrically correctly responsive to light, corneal and ciliary reflexes preserved, symmetrical, ocular-head reflex absent, assisted breathing, tracheostomy, unable to swallow and effective expectoration of upper respiratory tract secretion , nourished by PEG, suctioned, flaccid four-limb paralysis with no deep and plantar reflexes - areflexia, Babinski's symptom and foot-shake bilaterally absent. Symptomatic epilepsy was diagnosed in the form of myoclonic seizures on both sides of the face, most likely a consequence of KZM. Sodium valproate with valproic acid was successfully added to anti-epileptic treatment. Attempts to disconnect the patient from the ventilator have been unsuccessful. After gaining relative circulatory and respiratory stability of the patient in a vegetative state, he was transferred to the Care and Treatment Institution.

Case 2.

A 60-year-old patient who, approximately 5 days before hospitalization, ended ten-day antibiotic therapy due to upper respiratory tract infection. In addition, about three weeks earlier he was ticked by a tick in the lower parts of the back. He did not observe the presence of typical erythema. At the time of admission to the Department of Neurology, he gave a number of non-specific symptoms, including headaches and an increase in temperature to 39 degrees for 3 days. To confirm the initial diagnosis of

meningitis of cerebrospinal fluid, cerebrospinal fluid in which pleocytosis was found - 37 cells/mcl, including the percentage of cells with a monoplane nucleus 41%, multiplane 59%. Acyclovir antiviral treatment was introduced. Due to the rapid progression of neurological symptoms and the increase of respiratory failure, the patient was intubated and transferred to the Anaesthesiology and Intensive Care Unit (ICU). During hospitalization at the ICU, the patient was in a very severe general condition, unaware, with a limb four-limb paresis. In the differential diagnosis of his symptoms, Guillain-Barry syndrome (Miller-Fischer variant), autoimmune encephalitis, subacute sclerosing encephalitis (SSPE), neuroborreliosis, tuberculosis of the nervous system, tick-borne encephalitis (TBE) were taken into account. On the 10th day of hospitalization, in the re-examination of the cerebrospinal fluid, features of protein-cell cleavage (pleocytosis 8 cells/mcl, protein 313.4 mg/dl) were found. Intravenous glucocorticosteroids were included in the treatment followed by intravenous infusion immunoglobulins. In the absence of a therapeutic effect, it was decided to terminate the administration of immunoglobulins and 5 plasmapheresis treatments performed - without a therapeutic effect. On the 16th day of hospitalization, an electroneurographic examination (ENG) was performed, which did not show the characteristics of acute inflammatory radiculoneuropathy. In the following days, the patient required tracheostomy and percutaneous endoscopic gastrostomy (PEG). On day 23 of hospitalization, a positive test for IgM and IgG against TBE virus was obtained. Based on the overall clinical picture and history, severe postinflammatory encephalopathy was diagnosed as a consequence of tick-borne encephalitis. On the 36th day of hospitalization, the patient felt shaky facial mimics. Symptomatic epilepsy was diagnosed in the form of myoclonic seizures on both sides of the face - a possible complication of TBE.

The reason for conducting extensive differential diagnosis in the described patient before proper diagnosis of tick-borne encephalitis is the fact that this disease can cause a number of non-characteristic symptoms, especially at the initial stage. An additional difficulty is the fact that patients often do not notice tick ticks because tick saliva has anesthetic properties.[19,23] Both patients and doctors first consider the possibility of Lyme disease as the most common and most common tick-borne disease. The presented patient should be suspected that the first phase of the disease occurred before hospitalization and was in the form of upper respiratory tract infection. The reason for reporting and admission to the Department of Neurology were mainly severe headaches, high temperature and features of V and VII cranial nerve neuropathy, which were the expression of the beginning neurological phase of KZM. Unfortunately, the patient developed the most severe form of the disease, namely meninges and spinal cord involvement with cranial nerves and the medulla oblongata. Undoubtedly, the patient's advanced age affected such an abrupt and severe course of the disease. Due to the lack of effective treatment, only symptomatic treatment is possible, and the prognosis for further survival is uncertain due to the occurrence of numerous complications: respiratory failure, swallowing disorders, flaccid paralysis, consciousness disorders and symptomatic epilepsy. Due to the great diagnostic difficulties of KZM and the complicated and not always effective methods of treating this disease, it is always worth considering the use of prevention. Its most effective form is the use of passive or active immunization. Two inactivated vaccines with similar composition are available in Poland. They can be used even in states of impaired immunity. The full vaccination course includes three basic doses (second dose after 3 months and another 9 to 12 months after the first) and one booster dose every 3-5 years.[30] Inoculation in winter or early spring provides protection from the beginning of tick activity (from April to October). The vaccine is safe, according to the literature, undesirable vaccination symptoms are very rare and disappear on their own. This vaccination is particularly recommended in specific professional groups and for people staying in endemic areas. Vaccines against tick-borne encephalitis are highly effective - for every 100 people vaccinated over 95, they produce specific protective antibodies that protect against complications. Passive immunization, on the other hand, consists in administering immunoglobulin against the KZM virus up to 96 hours after tick insertion, which aims to obtain immediate immunization of seronegative persons.[5,30-32]

Conclusion

The described cases show how important it is to spread the principles of prevention and the need for preventive vaccinations, especially among people from endemic areas and professions from high risk groups. The basic way to prevent getting TBE is to avoid situations where you may be exposed to a tick by a tick (primarily wearing clothing that protects against getting ticks on your skin). Clothes can be sprayed with permethrin. On exposed parts of the skin outside the face, you can apply so-called repellents (e.g. DEET-N, N-diethyl-meta-toluamide). After staying in tick feeding places, you should carefully examine the skin and to be sure, wash the whole body in the shower with a soft brush. The ticks that are stuck in the skin are removed immediately after being noticed, preferably with tweezers, and the place after the injection should be decontaminated. Pharmacological prevention of the disease is also important.

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