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VIRAL TIC-BASED ENCEPHALITIS IN A PREGNANT WOMAN. CLINICAL CASE.

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Summary

The course of acute infections, preeclampsia with symptoms of damage to the central or peripheral nervous system - require to be alert for infectious diseases. In doubtful cases, it is necessary to conduct a bacteriological, virological, serological study of the biomaterial, if necessary, an analysis of the cerebrospinal fluid. A timely correct clinical diagnosis based on a multidisciplinary approach to patient management has a significant impact on a positive outcome of the disease and perinatal outcome.

The article presents a case of tick-borne encephalitis, polyradiculoneuritis form, acute course. Shown on a specific example, the difficulty of diagnosing this disease.

The information presented in the article is useful for: obstetrician-gynecologists, neonatologists, general practitioners, infectiologists.

Key words: Tick-borne encephalitis, infectious diseases, damage to the central nervous system, pregnant women.

Резюме

ВИРУСНЫЙ КЛЕЩЕВОЙ ЭНЦЕФАЛИТ У БЕРЕМЕННОЙ. КЛИНИЧЕСКИЙ СЛУЧАЙ.

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Течение острых инфекций, преэклампсии с симптомами поражения центральной или периферической нервной системы – требуют быть настороженным в отношении инфекционных заболеваний. В сомнительных случаях необходимо проводить бактериологическое, вирусологическое, серологическое исследование биоматериала, при необходимости анализ спинномозговой жидкости. Своевременно поставленный правильный клинический диагноз, основанный на мультидисциплинарном подходе к тактике ведения пациентки, существенно влияет на положительный исход заболевания и перинатальный исход.

В статье представлен случай клещевого энцефалита у беременной женщины, полирадикулоневритическая форма, острое течение. Показана, на конкретном примере, трудность диагностики данного заболевания.

Информация, представленная в статье полезна для: акушер-гинекологов, неонатологов, врачей общей практики, инфекционистов.

Ключевые слова: Клещевой энцефалит, инфекционные заболевания, поражение центральной нервной системы, беременные.

Түйіндеме

**ЖҮКТІ ӘЙЕЛДЕГІ ВИРУСТЫ КЕНЕ ЭНЦЕФАЛИТІ
КЛИНИКАЛЫҚ ЖАҒДАЙ****Наталья Н. Клебан¹**, <https://orcid.org/0000-0003-1149-343X>**Динара С. Рахметова¹**, <https://orcid.org/0000-0002-9937-7734>**Татьяна Н. Щербина¹**, <https://orcid.org/0000-0003-1315-057X>**Аина Н. Балтабекова¹**, <https://orcid.org/0000-0001-8005-7194>¹ ШЖҚ КМК "Облыстық перинаталдық орталығы",
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Жедел ағымды инфекциялар, орталық немесе перифериялық жүйке жүйесінің зақымдануымен жүретін преэклампсия-жұқпалы аурулардан сақ болуды талап етеді. Күмәнді жағдайларда биоматериалды бактериологиялық, вирусологиялық, серологиялық зерттеу, қажет болған жағдайда ми-жұлын сұйықтығын талдау қажет. Пациентті басқару тактикасына көпсалалы тәсілге негізделген уақтылы дұрыс клиникалық диагноз қойылуы аурудың оң нәтижесіне және перинаталдық нәтижеге айтарлықтай әсер етеді.

Мақалада жедел ағымды кене энцефалиті, полирадикулоневритикалық түрі туралы жағдай келтірілген. Бұл ауруды диагностикалаудың қиындығы нақты мысалда көрсетілген.

Мақалада келтірілген ақпарат пайдалы: акушер-гинекологтарға, неонатологтарға, жалпы тәжірибе дәрігерлерге, инфекционистерге.

Түйінді сөздер: кене энцефалиті, жұқпалы аурулар, орталық жүйке жүйесінің зақымдануы, жүкті әйелдер.

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Introduction

Cases of tick-borne encephalitis often have atypical symptoms and are difficult to diagnose. Misdiagnosis in pregnant women can have fatal consequences for the mother and fetus. At the same time, conventional laboratory and instrumental research methods and high-tech neuroimaging methods may be ineffective in diagnosing the disease [4].

Tick-borne encephalitis (TBE) is an acute infectious disease of viral etiology, with transmissible transmission, occurring in various clinical forms, with a predominant lesion of the central and peripheral nervous system. The causative agent is an arbovirus of the Flaviviridae family [3].

TBE in Kazakhstan is characterized by sporadism and a pronounced seasonality associated with the dynamics of tick activity. The peak of activity is observed in May-July, it can last until October. You can become infected with TBE not only by a tick bite, but also by drinking raw goat (cow, sheep) milk. Natural foci belong to the mountain forest belt of the Tien-Shan, Dzungarian and Zailiysky Alatau, Tarbagatai, the valleys of the Aksu, Tentek, Irtysh, Ulba and Bukhtarma rivers, which are distinguished by lush vegetation. Ticks *Ixodes persulcatus*, *D. pictus*, *D. marginatus*. Infection of ticks in natural foci is 0.5-10%. Once infected, the tick retains the virus forever, passing it on to offspring [1].

Of the total number of patients with TBE, up to 70% of patients are residents of rural areas, but more and more often, tick attacks occur in the city. So, for example, at the peak of the epidemiological season (April-May-June) in 2021 in 5 regions - Akmola, Almaty, East Kazakhstan, North Kazakhstan and Almaty - 6,947 people applied for tick bites. In the North Kazakhstan region, more than 30 residents were affected. Among all the victims, 9 cases of infection with tick-borne encephalitis and one case of tick-borne borreliosis were registered. For the same period in 2020, there were 14 cases of TBE [1].

An acute onset of the disease is characteristic: a sudden rise in body temperature to 38-39 °C, after a prodromal period of 1-2 days: weakness, malaise, weakness, myalgia, headache. Fever (viremia) in TBE has a two-wave character: short-term primary viremia, and then repeated, coinciding in time with the reproduction of the virus in the internal organs and its appearance in the central nervous system [2].

The following forms of the disease are distinguished: asymptomatic, general infectious, meningeal, meningoencephalitic, meningoencephalopolyomyelitis, polyradiculoneuritis. The ratio of clinical and asymptomatic forms ranges from 1:300 - 1:1000.

- The general infectious form is characterized by a favorable course with a quick recovery. The duration of the

fever is 3-5 days. The main manifestations are toxic-infectious: headache, weakness, nausea with mild neurological symptoms. CSF parameters without deviation from the norm.

- Meningeal form. The cephalgic syndrome dominates. Characterized by vestibular and dyspeptic (nausea, single or repeated vomiting) disorders, pain when moving the eyes, photophobia, stunning. Rigidity of the neck muscles, symptoms of Kernig and Brudzinsky are determined. Meningeal symptoms persist throughout the febrile period. In the cerebrospinal fluid, a moderate increase in the content of lymphocytes, an increase in protein concentration is determined. Increased intracranial pressure. The duration of the fever is 7-14 days. The outcome is favorable.

- The meningoencephalitic form is severe. The clinical picture is dominated by impaired consciousness, cephalgic and meningeal syndromes. Rigidity of the occipital muscles, symptoms of Kernig and Brudzinsky are expressed. Often there are delusions, hallucinations, psychomotor agitation with loss of orientation in place and time, epileptiform seizures. Characterized by the appearance of hemiparesis, subcortical hyperkinesia, stem disorders, as well as focal lesions of the cranial nerves: III, IV, V, VI, VII, IX, X, XI and XII pairs. In the study of cerebrospinal fluid in the acute period, lymphocytosis and an increased protein content are noted. CNS lesions are detected against the background of cerebral and toxic-infectious manifestations. The recovery period lasts up to 2 years. The frolicking atrophic paralysis of the muscles is partially restored.

- The meningoencephalomyelitic form is characterized by the early development of flaccid symmetrical paresis of the muscles of the neck, trunk, and upper limbs on the 3-4th day of the disease against the background of general toxic and meningeal phenomena. Less commonly, the intercostal muscles, muscles of the diaphragm and lower extremities are involved in the process. The patient is not able to keep his head in a vertical position, there are no movements in his hands. In the future, a pronounced atrophy of individual muscle groups of the shoulder girdle, chest, and limbs develops [7].

In Kazakhstan, febrile (40.3%) and meningeal (37.8%) forms are predominantly recorded. Other forms are less common: meningoencephalitic (18.5%), meningoencephalopolyomyelitis (0.8%) and mixed (2.5%) forms [1].

List of main diagnostic measures: general blood test, general urine test, acid-base state, blood electrolytes, examination of cerebrospinal fluid (for meningeal and meningoencephalitic forms), ELISA: determination of antibodies of the IgM, IgG class to the tick-borne encephalitis virus, PCR RNA TBEV (blood and cerebrospinal fluid), ECG, R-graphy thorax, MRT of the brain [5].

Special temporary inpatient treatment is the most effective and helps to avoid conflicts. The main thing in the treatment is etiotropic therapy with specific human immunoglobulin against tick-borne encephalitis (at the rate of 0.1 ml / kg of body weight). Preventive vaccination of the population in endemic regions is required [8].

It is necessary to strictly adhere to the algorithm for tick bites in regions endemic for tick-borne encephalitis:

immediately contacting the victim to the emergency room, examining the tick for infection with TBE in the parasitological laboratory of sanitary and epidemiological examination, seroprophylaxis with immunoglobulin against TBE of the victim (including pregnant women from the 2nd trimester), if the tick is contagious or the study was not conducted [6].

Description of the clinical case

The authors of the article share with colleagues the experience of treating a pregnant woman with a diagnosis of Tick-borne encephalitis, polyradiculoneuritis form, acute course (Ig M against TBE were detected). The presented clinical cases of tick-borne encephalitis proceeded under the guise of gestational pyelonephritis, intrahepatic cholestasis and severe preeclampsia.

Pregnant N., 33 years old, was delivered to the Petropavlovsk RC from a multidisciplinary regional hospital on May 16, 2021 at 18:15 with complaints of an increase in body temperature to 38.2 0C, severe weakness, drowsiness during the day, insomnia at night, poor appetite, dry mouth.

Anamnesis of the disease: from 05.12.21, the pregnant woman developed weakness, malaise, chills, dry mouth, an increase in body temperature to 38.0 C. She took tab. paracetamol 0.5 g 2 times a day with a short effect. Hyperthermia persisted at the previous figures, weakness and drowsiness increased. In connection with the deterioration of health called the ambulance team. Hospitalized in the department of pathology of pregnancy MRD with a preliminary diagnosis: 2-Pregnancy 37 weeks. ARI. Gestational pyelonephritis. Rhesus negative blood factor. Antibacterial cefazolin 1.0 *3 r IV, antiviral therapy Nomides 75 mg* 2 r, paracetamol 0.5 g* 3 r, infusion therapy 800 ml IV per day. During treatment, hyperthermia persisted up to 38 0C with heavy sweat and chills, weakness, lethargy, sleep disturbance increased, and a decrease in the amount of urine excreted was noted. According to laboratory data: decrease in Hb to mild anemia Hb-98g / l, thrombocytopenia up to 150 * 109, proteinuria from 0.1 to 5 g / l, leukocyturia, urobilin, bilirubin, ketone bodies +++ in urine, hypoproteinemia up to 54 g/l, elevated transaminases ALT-330U/L, AST-184U/L, Coombs test positive (+++). Exhibited clinical diagnosis: 2-Pregnancy 37 weeks 3 days. Severe preeclampsia. SARS moderate. Intrahepatic cholestasis of pregnancy. Anemia is moderate. Moderate thrombocytopenia. Rhesus negative blood factor. Angiopathy of the retina OU. Moderate low water. Taking into account severe preeclampsia, the pregnant woman was transferred to the Regional Perinatal Center of Pavlodar for delivery.

Epidemiological history: According to the pregnant woman, on April 2, 21 (40 days before seeking help), she found a live tick on her body. In the right armpit, a patch of reddening of the skin was noted for several days. I removed the tick myself. She did not seek medical help. The tick was submitted by relatives to the sanitary and epidemiological examination laboratory for research and a conclusion was obtained that the tick is not contagious. About a week later, for several days, I was bothered by sweating and itching at night. Then the condition returned to normal and until 12.05.21, the state of health did not suffer. On 12.05.21, the above complaints appeared. After hospitalization in the PC, when clarifying the facts of the anamnesis, it was found that

the tick was found not on 02.04.21 but on 24.04.21 (18 days before treatment), the tick was not examined.

Objectively

General condition is severe due to intoxication, neurological symptoms. Body temperature - 36.4 gr. Neurological status: Consciousness - GCS 14-15 points. Oriented in space and time. Reluctant to make contact. Depletes quickly. Pupils S=D. There is no nystagmus. The face is symmetrical. Tongue in the midline. The speech is clear. Swallowing is not disturbed. Tendon reflexes S=D, live. Muscle strength in the limbs 4-5 points. Muscle tone is preserved. Sensitivity saved. There are no meningeal or pathological signs. CP is doing it right. Symptoms of tension (symptom of Lasegue on 2 sides). Normosthenic physique, moderate nutrition. The skin is pink, of normal humidity, at the sites of intravenous injection of hematoma. The mucous membrane on the lips is dry with cracks. Scleras are light. There are no peripheral edemas. Tongue coated with past plaque, dry. There are no catarrhal phenomena from the nose and oral cavity.

On the part of the organs of the chest, abdominal cavity deviations from the norm were not revealed. RR - 24 in 1 min. Heart rate - 98-110 rpm 1 min. BP - 120/80 mm Hg. Diuresis is reduced. Obstetric status corresponds to a gestational age of 37 weeks. The condition of the fetus is satisfactory.

According to the laboratory data of the GBT: anemia, moderate Hb-89g / l, moderate thrombocytopenia - platelets - 152 * 109. GUT: proteinuria 1 g/l, leukocyturia up to 16 p/c. HD: hypoproteinemia - 42.7 g/l, increased transaminases ALT-200 U/L, AST-152 U/L, increased alkaline phosphatase - 225 U/L, increased lactate dehydrogenase -557U/L, increased CRP-90 mg/l, ferritin-184 ng/ml, Coombs test positive (+++). Procalcitonin is normal. According to acid-base balance: mixed alkalosis, hypokalemia.

Instrumental examination:

- ECG 05.17.2021: sinus tachycardia 102.
- X-ray of the chest 17.05.2021: Signs of chronic bronchitis.
- Ultrasound of the hepatobiliopancreatic region on 17.05.2021: Hepatomegaly, diffuse structural changes in the liver parenchyma, congestion of the contents of the gallbladder.
- Ultrasound of the kidneys on 17.05.2021 signs: hydronephrosis on the left, hydronephrosis on the right, nephromegaly on both sides, diffuse structural changes in the renal sinus, kidney parenchyma.
- MRI of the brain with contrast on 21.05.21: macrostructural changes in the brain and areas of pathological deposition of paramagnetic in the substance and membranes of the brain were not detected.

Exposed preliminary diagnosis: Pregnancy 37 weeks 3 days. Fever of unknown origin. Intoxication Syndrome. Encephalopathy. Gestational pyelonephritis. Hepatitis? Intrahepatic cholestasis of pregnancy? Anemia is moderate. Moderate thrombocytopenia. Angiopathy of the retina OU. Rhesus negative blood factor without antibody titer. Moderate low water.

Received treatment: Antibacterial therapy was adjusted, taking into account the deterioration due to increasing intoxication - meropenem 1 g IV every 8 hours, antipyretics,

hepatoprotective therapy - Heptral 100 mg per day IV, ursodeoxycholic acid 1 caps 3 r, nephroprotectors, antianemic therapy Cosmofer 2.0 IV, infusion therapy, correction of water and electrolyte disorders with sterofundin 1000 ml per day, magnesium therapy, albumin transfusion 20% - 100 ml, B vitamins 4 ml IV, ascorbic acid 1000 mg.

On the background of treatment, the condition of the pregnant woman remained severe with deterioration due to neurological symptoms, intoxication with fibrillary fever, despite the absence of respiratory tract infection and minimal symptoms of gestational pyelonephritis (Nechiporenko analysis, leukocytes 6500, negative urine culture) disproportionate to the severity of intoxication. Episodes of limb tremors, visual hallucinations, sensations of "difficulty swallowing", and choking were added. Throughout the course of the disease, blood pressure was within the normal range.

The following diseases are included in the differential series according to the leading cause of intoxication and damage to the nervous system: tick-borne encephalitis, borreliosis, severe preeclampsia, dysmetabolic encephalopathy against the background of intoxication caused by urinary tract infection and liver damage, cerebrovascular accidents and focal CNS damage.

17.05.21 the results of a specific examination for tick-borne encephalitis immunoglobulins were received: ELISA for tick-borne encephalitis from 17.05.21: Ig M- detected, Ig G - detected. PCR for tick-borne encephalitis - not detected. ELISA for borreliosis-negative.

17.05.21 specific therapy was started: Human immunoglobulin against tick-borne encephalitis (at the rate of 0.1 ml/kg of body weight) at a dosage of 8 ml * 2 times a day IM for 5 days.

17.05.21 according to fetal CTG monitoring, a threatened state of the fetus was recorded. 17.05.21 at 16:30 a pregnant woman was delivered on an emergency basis by a caesarean section in the lower uterine segment. Anesthesia - total intravenous with mechanical ventilation. The total blood loss was 700 ml. A live full-term boy was born with a body weight of 3244 g, a height of -52 cm, with an Apgar score of 7-9 points. The state of the newborn of moderate severity due to neurological symptoms.

From the 2nd day from the start of specific therapy, an improvement in the condition of the puerperal was noted - a persistent regression of all symptoms of the disease began - intoxication, MODS, normalization of all laboratory parameters began, restoration of the vital functions of the puerperal. On the 3rd day, the body temperature returned to normal. On the 5th day, normalization of the neuropsychic status without residual changes. The postoperative postpartum period proceeded against the background of subinvolution of the uterus. Treatment continued: antibiotic therapy up to 10 days, uterotonics, symptomatic therapy. Dynamic observation of a neuropathologist and an infectious disease specialist. Breastfeeding of the newborn was not carried out, given the risks of infection of the newborn. The newborn and mother were discharged from the hospital on the 21st day of illness.

Results

The presented case is exclusive in the practice of PCMOS. The following points complicated the timely

diagnosis and choice of rational tactics of pregnancy management:

- Low incidence of the disease in the region. Lack of accumulated experience in relation to sick pregnant women
- Inaccurate facts of the anamnesis provided to the pregnant woman during the initial visit (the date of detection of the tick outside the incubation period was not correctly named), which made it possible to exclude TBE.
- Lack of alertness for infectious diseases and delayed examination by an infectious disease specialist.
- Incorrect interpretation of the symptoms of a severe form of TE, as the phenomena of intoxication for acute respiratory viral infections and acute pyelonephritis, and the phenomena of multiple organ failure in the form of damage to the kidneys, liver, encephalopathy - due to complications of pregnancy (severe preeclampsia, intrahepatic cholestasis of pregnant women).
- Untimely diagnosis and late appointment of specific therapy, on the 5th day from the onset of symptoms, led to the development of a severe form of the disease with symptoms of multiple organ failure, deterioration of the pregnant woman, threatened fetal condition and emergency operative delivery.
- After verification of the diagnosis, adequate therapy led to a complete recovery.

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