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LISTERIOSIS. CONGENITAL NEONATAL SEPSIS. CLINICAL CASE

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Abstract. Neonatal listeriosis, related to intraurine infection, has a high mortality rate, this is due to the morphology and physiology of the pathogen, the rate of infection and the organs that are affected. This article discusses the main characteristics of the microorganism and the clinical case of the course of this disease.

Key worlds: *neonatal listeriosis; congenital neonatal sepsis; antibacterial therapy; ittraurine infections; hydrocephalus syndrome.*

ЛИСТЕРИОЗ. ВРОЖДЕННЫЙ НЕОНАТАЛЬНЫЙ СЕПСИС. КЛИНИЧЕСКИЙ СЛУЧАЙ

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Резюме. Неонатальный листериоз, относящийся к внутриутробным инфекциям, имеет высокий процент летальности, связано это с морфологией и физиологией патогена, характером течения инфекции и органами, которые поражаются. В данной статье рассмотрены основные характеристики микроорганизма и клинический случай течения данного заболевания.

Ключевые слова: *неонатальный листериоз; врожденный неонатальный сепсис; антибактериальная терапия; внутриутробные инфекции; гидроцефальный синдром.*

Listeriosis is an infectious disease of bacterial etiology. The causative agent is *Lysteria monocytogenes*, a gram-positive facultative intracellular bacillus, stable in the environment and temperatures down to –1.5 °C. Outside the cell they are capable of "tumbling" motility; when moving inside the cell, the actin rockets mechanism is activated. It is a catalase-positive microorganism.

The disease is transmitted nutritionally (by eating unpasteurized milk, raw cheeses, meat, fish), the bacterium is able to pass through the intestinal barrier; invasion occurs due to the interaction

of internalin A (InlA) and E-cadherin (hEcad) with the participation of the phosphoinositide-3-kinase (PI3-K), which subsequently leads to secondary hematogenous dissemination [1, 2].

In addition to the nutritional route of transmission, a transplacental route is possible. When working with experimental models, it was proven that transplacental transmission occurs due to the interaction of the proteins internalin A (InlA) and B (InlB) on the bacterial cell surface in complex with c-Met and E-cadherin (hEcad), which being a transmembrane protein, is located on the apical and basement membranes of syncytiotrophoblasts (SYN) [3], and the interaction of InlB with c-Met is critical for the activation of PI3-K in SYN and is required for InlA-mediated entry of *L. monocytogenes* across the placental barrier [4]. The possibility of its participation in this type of distribution of internalin P (InlP) is also currently being studied [14].

The toxin synthesized by bacteria, listeriolysin O (LLO), which is necessary for the exit of the bacterial cell from the host cell vacuole, has an active influence on the infection process; its ability to modulate signaling pathways is also considered in modern studies [5]. Phosphatidylinositol-specific lipase C (PICA) and lecithinase are also required for phagosome exit, and metalloproteinase carries out post-translational modification of lecithinase.

The ActA protein regulates actin polymerization, mediating bacterial movement and invasion [7].

Risk factors are pregnancy, immunodeficiency, and old age. The incubation period ranges from 3 to 70 days, with an average of 21 days [8, 9].

The most common form of listeriosis is neurolisteriosis in pregnant women, which is extremely rare. In newborns, two forms of listeriosis are distinguished: with early onset with the manifestation of infection on the 1st–2nd day after birth, the mortality rate can reach 50%; late-onset listeriosis develops after 10–12 days and is associated with nosocomial infection [15, 16].

Infection in the first half of pregnancy is accompanied by chorioamnionitis, flu-like symptoms, with fever observed in 85% of cases, spontaneous abortions, and the formation of fetal malformations [10, 11].

Infection in the second half of pregnancy leads to premature labor, stillbirth, meningitis, sepsis, neonatal pneumonia, and damage to the nervous system [12, 13].

Infection as a result of aspiration of amniotic fluid intrapartum is also possible. Such infection is characterized by a later development of symptoms, usually in the form of meningitis. With such an infection, transient colonization is possible, which will not lead to the development of the disease.

A damage to the fetus is associated both directly with an infection and decrease in the number or disturbances in the functioning of T-regulatory cells (Treg), which consists in a decrease in their regulatory ability, which leads to immune-mediated fetal death [17].The stimulation of immune system cells by cytokines produced by T-lymphocytes leads to the formation of granulomas — listeriomas, which are systemic in nature and are considered as granulomatous sepsis.

CLINICAL CASE

G.K. was born prematurely at 25 6/7 weeks, as a result of the second pregnancy, the first was in 2019, term labor. The course of pregnancy was unremarkable; according to ultrasound at the 25th week, polyhydramnios, grade III hemodynamic disturbances, and chronic placental insufficiency were revealed. The birth weight was 940 g (1 centile corridor), the body length was 30 cm (1 centile corridor), the head circumference was 25 cm (1 centile corridor), the chest circumference was 23 cm (1 centile corridor). Apgar score was 2/3 points.

The condition at birth is regarded as extremely severe due to respiratory failure, prematurity, morphofunctional immaturity, and severe intrapartum asphyxia. Resuscitation measures were carried out and she was connected to an artificial lung ventilation device (ALV). She responded to the examination with increased motor activity, muscle tone and reflexes of the newborns were reduced. Respiration was weakened, crepitus was heard, saturation decreased to 70%, weakened breathing on the right — right-sided hydrothorax, according to ultrasound of the pleural cavities on both sides, traces of effusion were determined, the lungs showed signs of interstitial inflammation. A pleural puncture and drainage were performed.

A clinical blood test revealed thrombocytopenia and anemia. Acid-base state (ABS) — mixed acidosis, lactic acidosis. EchoCG — tricuspid regurgitation of the 1st degree. Neurosonography (NSG) — increased periventricular echo density in the frontal-parietal-occipital regions. Full-blooded

choroid plexuses, intraventricular hemorrhages of degree II on the left, degree I on the right, expansion of the occipital horns.

According to ultrasound of the abdominal organs and kidneys, a diffuse change in the renal parenchyma was observed with depletion of blood flow in the periphery, a moderate amount of free fluid in all parts of the abdominal cavity of an anechoic nature.

Examination by an ophthalmologist — the retina is in the stage of vascularization (zone II).

According to the results of histology of the placenta, the following were identified: acute focal chorioamnionitis, choriodeciduitis, acute subchorionitis, productive placentitis, chronic subcompensated placental insufficiency, acute placental insufficiency.

Based on the totality of clinical and laboratory data, a diagnosis of "early neonatal sepsis" was made.

According to blood and sputum cultures and from the ear fold, there was growth of bacteria of the genus *Lysteria*, as a result of which the child was diagnosed with neonatal listeriosis. An antibacterial therapy was prescribed with ciprofloxacin, amikacin and meropenem.

In the first two weeks, the condition was interpreted as extremely severe, a negative intracranial clinical picture was observed with an increase in intracranial hemorrhages, central hemodynamic parameters were unstable, inotropic and vasopressor therapy was carried out. Due to insufficient diuresis, edema syndrome developed to anasarca; a laparocentesis was performed due to ascites. In the second week, the drainage in the abdominal cavity began to drain intestinal contents; during the operation, it was discovered that the wall of the ileum in the distal section for 15 cm was flabby, with multiple perforations, and therefore a section of the small intestine was resected ileocecal angle, a double enterocolostomy was performed, by the end of the second week the child's condition worsened due to the cessation of the stoma and a change in the infection status with an increase in leukocytosis. A lumbar puncture was performed due to hydrocephalic syndrome.

According to neurosonography, a picture of slow negative dynamics of increase in ventriculomegaly was observed against the background of persistent increased periventricular echo density in the frontal-parietal-occipital regions, full-blooded choroid plexuses, intraventricular hemorrhages of the second degree on the left, second degree on the right, and a pronounced expansion of the occipital horns. The hydrocephalic syndrome did not progress after lumbar puncture. According to the results of a repeat study, two days later there was a stabilization of ventriculomegaly.

During the third and fourth weeks, the child's condition was extremely severe with positive dynamics, the course of the disease was wavy, the exit of the eventrated strand of the omentum between the sutures at the diverting stoma was noted, surgical intervention was performed, in addition, due to anemia and hypocoagulation, a transfusion of erythrocyte suspension and fresh frozen plasma was carried out. The dynamics showed stabilization of the condition; due to the possibility of spontaneous breathing, the child was extubated, but respiratory support through nasal cannulas was maintained.

By the end of the fourth week, the condition worsened against the background of progression of the neurological clinical picture with manifestations in the form of apnea.

Subsequently, the condition stabilized, positive dynamics were observed during the treatment, there were no signs of increasing respiratory failure, the patient needed respiratory support through nasal cannulas. Central hemodynamic parameters were compensated.

According to echocardiography, left ventricular hypertrophy was observed, minimal without dynamic obstruction of the left ventricular outflow tract (LVOT). A tricuspid regurgitation of the I degree was noted.

The child was transferred to the neonatal pathology department, where he remained until the operation to close the enterocolostomy; four days later, a repeat operation was performed due to anastomotic failure; relaparatomy, resection of the anastomotic area, and enterocolostomy were performed. Taking into account the data of cultures of the contents of the abdominal cavity with seeding of *K. pneumonia* and *S. maltophilia*, as well as the failure of the anastomosis, which could be caused by the course of the infectious process, a change in antibacterial therapy was carried out according to sensitivity, ciprofloxacin was prescribed, and amikacin, meropenem were canceled.

Two weeks after the operation, the condition worsened: pronounced retraction of the upper aperture of the chest and intercostal spaces during inspiration, pronounced stridor, an attempt

was made to relieve swelling of the larynx and upper respiratory tract by inhalation with adrenaline and dexazone. Intubation was performed due to persistent decompensated respiratory acidosis according to ABS data and severe disturbances in respiratory mechanics such as inspiratory dyspnea. A moderate amount of white sputum was sanitized from the tracheobronchial tree; according to its culture, a fungal infection was detected, and therapy with amphotericin B was started. After stabilization of the condition, a T-shaped ileocoloanastomosis was performed.

The repeated neurosonography was without changes, dynamic ultrasonographic (US) monitoring revealed an increase in the dorsal horns and the cisterna magna, a retrocerebellar cyst/ cerebellar hypoplasia was suspecte. An magnetic resonance imaging of the brain was performed there were signs of cortical-subcortical subatrophy of the cerebral hemispheres and cerebellum, normotonic occlusion at the level of the midbrain aqueduct, triventricular hydrocephalus due to subarachnoid hemorrhage and bilateral intraventricular hemorrhage due to prematurity.

According to US monitoring, the hydrocephalic syndrome did not progress. The Observation was continued by a neurologist together with surgeons due to the need for surgery to close the colostomy. According to US monitoring, it was established that the hydrocephalic syndrome does not progress, there is a developmental delay, and torticollis.

In the postoperative period, the condition was assessed as severe; subsegmental atelectasis was detected in the right lung, for which X-ray control was carried out. Considering the positive X-ray picture and the absence of respiratory failure, no further therapy was needed. A Dynamic observation by an ophthalmologist for retinopathy of prematurity was continued, stabilization was noted.

At the moment, the child's condition has been stabilized due to previous treatment; the girl is under constant observation by pediatricians, neurologists and ophthalmologists.

There is a severe delay in psychomotor development, organic damage to the central nervous system (CNS) as a consequence of hemorrhage in the germinal matrix of both hemispheres of the cerebrum, the vermis and the right hemisphere of the cerebellum, in the lateral and fourth ventricles, the pontocerebellar cistern, right-sided chronic subdural hematoma, stenosis of the aqueduct, expansion of the lateral and third ventricle of the brain, atrophy of the corpus callosum, decrease in the volume of white matter of the brain, atrophy of the vermis, cerebellar hemispheres, pons, medulla oblongata. The Hydrocephalic syndrome is compensated. A Movement disorders syndrome, pyramidal insufficiency, and muscular dystonia syndrome are noted.

CONCLUSION

The described clinical case demonstrates the severity of congenital listeriosis, with the neurological clinical picture manifested by multiple brain injuries. In addition to the central nervous system, other organs and systems are also negatively affected. Stabilization of the condition was achieved through antibacterial, vasopressor and symptomatic therapy, as well as through timely surgical treatment of manifestations of sepsis.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that there have no competing interests.

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Consent for publication. Written consent was obtained from the representative patients for publication of relevant medical information within the manuscript.

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Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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