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PEDIATRICS

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DIAGNOSIS AND TREATMENT OF SEPSIS IN AN INFANT WITH CONGENITAL LACTASE INSUFFICIENCY (case report)

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Abstract: The article presents the results of clinical observation of the infant suffering from the sepsis and congenital lactase deficiency. The first symptom of the disease in the first day of life was diarrhea. Lactose insufficiency was diagnosed. Later blood has appeared in the feces. Condition of the child stated to get worse and the child was hospitalized. Condition remained to be grave during 2 weeks, symptoms of intoxication, enlargement of liver were marked, stool was up to 15 – 16 times a day, it contained blood mixed with feces, blood blobs and streaks. Analysis of clinical symptoms and result of laboratory investigations gave motive to diagnose sepsis, congenital lactose insufficiency, anemia, and hypotrophy. The treatment included diet (lactose-free formula), antibiotics, infusion, probiotics, vitamins. Results of investigation normalized. The child was discharged from the hospital in satisfactory condition.

KeyWords: infant, lactose insufficiency, sepsis, therapy

CASE STUDY

A 1.5-months-old Miron K. was admitted to Kharkiv Regional Children Clinical Hospital No.1 (RCCH No.1) with frequent (up to 13-15 times a day) liquid stool with mucus and blood, lethargy, weakness, poor sucking ability, and lack of body weight gain.

According to his medical history he was born from the mother with complicated fourth pregnancy. For three years the woman had been suffering from infertility, then she had three spontaneous abortions. This pregnancy proceeded with gestational toxicosis in the second half of pregnancy, and eclampsia. She gave birth at the term of 37 weeks of gestation by caesarean section due to intrauterine fetal hypoxia.

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The child was born with asphyxia, estimated 3.5 points according to Apgar score. His body weight was 3100 g, height – 50 cm, head circumference – 32 cm, chest circumference – 30 cm. He was breastfed on the second day and was discharged from the hospital on the third day.

On the 5th day of life the child had diarrhea with mucus, stool frequency being up to 15 times a day. The pediatrician referred the child to the City Perinatal Center, where he stayed for 7 days. During that period the child was examined at the specialized Kharkiv Regional Medical Genetic Center where he was diagnosed with primary lactase deficiency. The nutrition was corrected and his diet was changed to lactose-free formula. The child's condition normalized in 8 days and he was discharged home.

On the third day of being at home the child's condition worsened, and stool frequency increased to 15 times a day, the stool contained mucus and blood. The condition was progressively worsening. He was referred to RCCH No.1 by a district doctor. At the Intensive Care Unit of the clinic the child was diagnosed with intestinal bleeding, and he was hospitalized to the Department of Surgery.

At admission the child's condition was severe. The severity of the condition was caused by intoxication, dehydration, neurological disorders. The child was dull and adynamic. His skin was pale, subcutaneous fat got thin, turgor and elasticity of tissues were reduced and neonatal reflexes were weak. He had a reduced muscle tone, puerile breathing in the lungs and respiratory rate of 50 breaths per minute. His heart sounds were muffled, clean, rhythmic; heart beat rate was 152 beats per minute. The abdomen was soft, the liver was palpated 3 cm below the edge of the costal arch and the spleen was 1.5 cm. Stool was liquid, watery and mixed with blood. Urination was normal.

The child was diagnosed with congenital lactase insufficiency, gastroenterocolitis, 1st degree hypotrophy, hypoxic and ischemic lesion of the central nervous system, neurotony depression syndrome and early recovery period. Differential diagnostic included necrotizing enterocolitis of newborns, and surgical pathology, accompanied with intestinal bleeding. The child was transferred to the ward for younger children of RCCH No.1.

Follow-up examination for 15 days showed that his condition remained severe, intoxication symptoms persisted, diarrhea was up to 15-16 times a day and the stool contained blood mixed with feces, as well as blood blobs and streaks.

Laboratory and instrumental findings essential for diagnosis were as follows:

Blood count: (indice fluctuated during the follow-up): Hb – 72 - 102 g/L; erythrocytes– 3.3 – 4.0*1012 /l; Ht – 26 - 28%; platelets– 140-192*109/l; leukocytes– 5.4 – 17.6*109/l; neutrophils – 60 - 82%; stab neutrophils – 1 - 17%.

Urinalysis: microscopy of sediment – 3 and 4 to 57 in sight, leukocytes – 2 - 3 in sight up to ½.

Coprogram: epithelial cells –10-20 in sight, leukocytes – 10-25 in sight, erythrocytes – 50-70 in sight, large amount of iodophilic flora.

The reaction for occult blood was positive.

Bacteriological blood test (twice with an interval of 2 days) revealed Staphylococcus saprophyticus sensitive to Lincomycin, Tetracycline, Vancomycin, Rifampicin, Chloramphenicol.

Bacteriological urine test: Escheriehia coli, Enteroccus faeciane, Klebsiella pneumoniac.

Bacteriological feces test: Staphylococcus saprophyticus sensitive to Rifampicin, Chloramphenicol, Klebsicella, Sensitive to Rifampicin, Tetracycline.

Feces test for dysbacteriosis: Lactobacilli were not found. Conditionally pathogenic enterobacteria – Klebsiella 108 (N – 104).

Ultrasound examination of the brain and internal organs revealed hypoplasia of the thymus, other organs were without abnormalities.

Immune status was checked twice but no pathology was revealed.

Endoscopic examination of the esophagus, stomach, duodenum, sigmoid colon, and rectum revealed no pathology.

Test of calprotectin revealed no pathology.

Findings of investigations performed at Kharkiv Regional Medical Genetic Center:

Biochemical blood test: total cholesterol – 2,52 mmol/l (normal – 2.95 - 5.25 mmol/l), uric acid – 3.06 U/l (normal – 1,37 - 2.98 U/l), calcium – 2.13, ALT, phosphorus, creatinine, creatininase, lactate dehydrogenase, total bilirubin, gammaglutamyl/transferase – within normal range.

Investigation of lactose activity: the patient was found to have lactose activity insufficiency: polymorphism of lactose 13910 C/T gene (LCT) – polymorphism of C/C in homozygous state.

The diagnosis of lactose insuficiency was confirmed by the symptoms, history data, laboratory and instrumental findings. The use of lactose-free formula was recommended. Supplementations containing lactose enzyme (Mamalak, Koliprev, Lactazar) were recommended before taking infant formula according to age.

Due to certain difficulties in the treatment of the patient, poor efficiency of the administered therapy was discussed at the consultation with the specialists – geneticists, pediatricians, surgeons, gastroenterologist, and immunologist.

Findings of the multidisciplinary case management

team: considering the history, presentation, laboratory and instrumental findings which include a diagnosed congenital abnormality – congenital lactase insufficiency, a progressive increase in the severity of the child's condition due to accompanying inflammatory process – hemorrhagic colitis; pyelonephritis, anemia and hypotrophy; bacteremia (presence of Staphylococcus saprophyticus in the blood, Staphylococcus saprophyticus and Klebsiella in the feces, Escheriehia coli, Enteroccus faeciane, Klebsiella pneumoniac in the urine) identified in laboratory investigations; erythrocytes in coprogram, signs of inflammation in the blood test- leukocytosis, neutrophilia; primary lactose deficiency confirmed by the second investigation carried out at the RMGC, the diagnosis should be specified as follows:

Primary diagnosis – congenital lactose insufficiency accompanied by sepsis of septicopyemic type, enterocolitis, pyelonephritis.

Concomitant diagnosis – hypoxic- ischemic encephalopathy, depression syndrome, tonicity disorders, early recovery period.

Complications – 1st degree deficiency anemia, 1st degree hypotrophy.

Laboratory and instrumental findings allowed to exclude immunological failure, and surgical pathology.

The child received the following treatment: nutritional care (a formula of Nutrilon malabsorption, later lactose-free formula (Nestle), infusion therapy – 5% glucose, 0.9% sodium chloride), antimicrobial therapy in accordance with the sensitivity of detected flora, Kreon, Biogaia, Smecta, vitamins B1 and B6.

The child's condition improved: dysfunction of the intestine subsided, stool characteristics returned to normal, laboratory data (blood, urine, feces, bacteriological investigation) normalized. The child's weight started to increase. The child was discharged from the hospital on the 28th day in satisfactory condition. Follow-up examination of the district pediatrician, gastroenterologist, geneticists was advised.

Clinical findings showed a severe course of a combination of lactose insufficiency and infectious process accompanied by the development of hypotrophy and deficiency anemia.

Lactase insufficiency.

Breast milk sugar – lactose is one of the most important components of breast milk. This sugar is found in nature only in the milk of mammals, and its highest concentration is in women's milk. Fetal lactase activity is observed from 10-12 weeks of gestation; it begins to increase from 24 weeks and reaches its maximum to 38-40 weeks, persisting for the first year of a child's life. The disease is triggered by mutation of the structural gene LCT (beta glycosidase complex of lactase- phlorizin hydrolase) of the small intestine, which leads to insufficiency of the enzyme. The gene is mapped on the short arm of the 21st chromosome 2q21 [1].

Lactose provides about 40% of the energy required by the child and is necessary for the brain development. In the small intestine a larger molecule of lactose is broken by lactase into two smaller molecules – glucose and galactose. Glucose is an important source of energy whereas galactose becomes a part of galactolipids necessary for the development of the central nervous system.

Lactose which is not broken down in the small intestine (for example, due to deficiency of lactase) moves further and stimulates the formation of intestinal bacterial colonies of Lactobacillus bifidus. These fermenting bacteria provide the acid medium in the gastrointestinal tract, inhibit pathogenic bacteria, fungi and parasites.

If the activity of lactase (the enzyme that breaks down lactose) is reduced or absent (the condition is called lactase deficiency), lactose becomes the food for bacteria in the small intestine and enters the large intestine in significant quantities. There lactose creates a nutrient medium for reproduction of many microorganisms, resulting in liquefaction of the stool and flatulence, as well as intestinal pain. The extremely acidic stool in its turn can cause further damage of the intestinal walls.

Insufficient activity of lactase may lead to the reduction of extra weight, because, firstly, it cannot break down milk sugar, which is an important source of energy, and, secondly, the damage to the intestine leads to the deterio-

ration of absorption and digestion of the other nutrients of breast milk.

There are two types of lactase deficiency – primary and secondary. It is possible to specify another type of lactase deficiency, in which, due to the individual characteristics of lactation and mother's organization of breast feeding, a child having the enzyme in sufficient quantity, however, experiences the similar symptoms.

Primary lactase insufficiency occurs in case the surface cells of the small intestine (enterocytes) are not damaged, but the activity of lactase is decreased (partial lactase insufficiency, hypolactasia) or absent (complete lactase insufficiency, alactasia).

Secondary lactase deficiency occurs when lactase production is reduced due to the damage of the cells that produce it.

Primary lactase insufficiency can be:

1. congenital – due to genetic disease (it is quite rare)

2. transient – in premature babies and those who are immature by the time of birth

3. of adult type

Secondary lactase insufficiency occurs much more often. Usually, it is caused by any acute or chronic disease, such as intestinal infection, allergic reaction to cow's milk protein, inflammatory processes in the intestine, atrophic changes.

The symptoms of lactase deficiency include liquid (often frothy, with a sour smell) stool, which can be both frequent (more than 8-10 times a day) and rare or absent without stimulation (it is typical for babies having artificial feeding with lactase insufficiency); child anxiety during or after feeding, profuse vomiting; bloating; no weight gain or weight loss.

There are several tests allowing in one way or another confirm lactase deficiency – lactose curve, hydrogen test, stool tests for carbohydrates, analysis of coprogram, but the most reliable way to confirm lactase insufficiency – biopsy of the small intestine [2].

Lactase enzyme is usually used to treat lactase deficiency. The enzyme is given in courses. At the age of 3-4 months, when lactase becomes mature, the treatment is often cancelled. It is also important to choose the right dose. If the dose is too small, the symptoms of lactase insufficiency can still persist, if the dose is too high, the stool can become excessively thick, similar to clay, resulting in constipation. The enzyme is usually given before feeding, dissolved in some breast milk. Usually the doctor recommends to give lactase every 3-4 hours, thus, if necessary, the baby can be fed in the intervals.

The intestinal flora and lining should be restored. In treatment of primary LD the basic treatment is accompanied by correction of intestinal dysbiosis.

In secondary lactase insufficiency (the most common condition) the main attention should be given to treatment of the underlying disease that caused the damage of the walls of the bowel (e.g. gastroenteritis), but reducing the amount of lactose in the diet or lactase fermentation should be considered as a temporary measure, necessary before the recovery of the lining of the intestine. In mild cases, it may be necessary to give lactase for some time, so the bowel will recover without any additional treatment [3-5].

Bacteremia and sepsis.

Bacteremia is a disorder of hematopoietic system caused by bacteria. Sepsis (septicemia) is bacteremia, complicated by clinical manifestations of systemic infection. Sometimes the term "septic syndrome" is used with regard to severe systemic infection in which infectious agents or their toxic products are allegedly circulating in the blood.

Both temporary and permanent bacteremia can lead to metastatic infection. Bacteremia often occurs secondary to other diseases or malnutrition; it is, as a rule, intermittent in nature and associated with opportunistic infection. The primary source of infection is usually located in the genitourinary system, gastrointestinal tract, lungs or on the skin.

Transient bacteremia with a small amount of bacteria in blood is often asymptomatic. Persistent bacteremia with a large amount of bacteria in the blood usually gives the clinical picture of systemic infection, including fever, as well as gastrointestinal symptoms (nausea, vomiting, diar-

rhea). In some cases, the first manifestation of the disease is a septic shock with such characteristic signs as alteration of consciousness, hypotension, disorders of breathing.

The diagnosis is confirmed by rapid progressive severity of the condition. There are complications that can be caused by aerobic bacteria apart from gram-negative microorganisms.

According to some authors, at present, microbial associations with more pronounced pathogenic properties than monoculture play the leading role in the etiology of infectious complications. This is because the virulence of microorganisms may increase in associations of several types in the presence of synergistic action. Asporogenous anaerobic bacteria in association with aerobic species can cause development of more severe forms of a disease. An important role in the interpretation of the results of bacteriological studies is played by the degree of patient's colonization by microorganisms, i.e. it is important not only qualitative but quantitative evaluation of the test results.

The factors contributing to the activation of microflora and subsequent development of infection are reduction of general and local immunity, and use of antibiotics disturbing the natural interaction of microorganisms [6].

Conflict of interests

There is no conflict of interests.

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