and laboratory picture made it possible to establish this diagnosis of "Multi-inflammatory syndrome". Some peculiarities were revealed in patients in the Republic of Sakha (Yakutia). All patients were representatives of the Mongoloid race, the majority were boys. The most frequently affected cardiovascular and respiratory systems. The blood coagulation system was not significantly impaired, while half of the patients had significant thrombocytosis. Also, a dynamic increase in changes in some laboratory parameters was revealed, even against the background of stabilization of the general condition of the patients. This raises the question of the need to study the follow-up of patients with MIS.

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A CLININCAL CASE OF LOUIS-BAR SYNDROME EARLY ONSET IN A CHILD

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Abstract: The article represents a clinical case of Louis-Bar syndrome. The pediatricians should be alert to genetic disorders when revealing signs of immunodeficiency. Immunoassay examination is of extreme importance in early diagnosis of primary immunodeficiency.

Keywords: immunodeficiency, immunoglobulins, cerebellar ataxia, telangiectasia, replacement therapy

Introduction. Louis-Bar syndrome (OMIM#208900) is an autosomal recessive disorder which is characterized by ataxia, oculocutaneous teleangioctasis, immunodeficiency, predisposition to oncological disorders, infertility and premature aging. Louis-Bar syndrome refers to syndromes characterized by chromosomal instability, which occurs in balanced chromosomal rearrangement within the immune system cells. The characteristic feature of the syndrome is in cerebral neurodegeneration resulting in early fatality [1,4]. Recent investigations revealed that aneuploidy for chromosome is increased from 3 to 5 times in cerebral cells of the patients, thus, up to 30-50% of cerebral cells turn to be aneuploid [4].

Progressing cerebral ataxia with early onset is a principal clinical manifestation, epileptic attacks are not rare. Teleangioctasia of the conjunctiva, auricles and cheeks appear at the age of 3-6 years. 80% of cases are predisposed to infections due to immunodeficiency [2,3,5].

Immune abnormality is resulted from selective IgA deficiency. It is characterized by the signs of the damaged cell immunity leading to circulating T-lymphocytes reduction [3,5].

Clinical features of Louis-Bar syndrome. The authors represent a clinical feature of Louis-Bar syndrome in a 6-year old girl. A girl is of Russian ethnicity, born from the 6th pregnancy and 3rd labor. Pregnancy was characterized by gestational toxicosis and gestosis. The delivery was on the 40th week. The birth weight was 3800g, height was 50 cm. The child was lactated till the 6th month. Psychomotor development: she could raise her head since 2 month, roll over since 5 months, she walks since 1 year and 4 months and talks from 1 year and 2 months.

Family history is not complicated. The parents refuse chronic disorders.

At the age of 6 months the general condition was assessed as satisfactory. No signs of abnormalities were revealed. The skin was clean and pale. No fever revealed. The pharynx was with no signs of abnormality. Peripheral lymphatic nodes were impalpable. Nasal breathing was free without discharge. Respiration was puerile, weak in the lower lobes of the lungs, without rales. Respiratory rate was up to 35 per minute. Heart rate was 120 per minute. The abdomen was soft and painless. The liver and the spleen were not enlarged. Stool and diuresis were not disturbed. The complete blood count showed: hemoglobin (HGB) – 120 g/dL (Reference range (RR): 120-160 g/dL); erythrocytes (RBC) – 4.4x10^{12}/L (RR: 4.1-5.2x10^{12}/L); platelets (PLT) - 250 10^{9}/L (RR: 150 – 450x10^{9}/L); leukocytes (WBC) -2.2x10^{9}/L (RR: 5.5 – 12.5x10^{9}/L); lymphocytes (LYMF) – 55% (RR: 50-65%); monocytes – 3% (RR: 4-10%);

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stab neutrophils - 5% (RR: 1-5%); segmented neutrophils - 35% (RR: 20-35%); eosinophils - 2% (RR: 0-5%); erythrocytes sedimentation rate (ESR) by Panchenkov's micromethod -10 mm/hour (RR: 1-15 mm/hour). Complete blood count revealed leukopenia.

The child suffered of acute viral respiratory infections 6 times during his first year of life, had 3 cases of tonsillitis thus confirming clinical signs of immunodeficiency.

The patient was referred to the specialized hematological department at the age of 1 year. There he was examined. The complete blood count showed: hemoglobin (HGB) - 122 g/dL; erythrocytes (RBC) – $4.35x10^{12}$/L; platelets (PLT) – $200x10^{9}$/L; leukocytes (WBC) – $3.5x10^{9}$/L (RR: 4.5 – $13x10^{9}$/L); lymphocytes (LYMF) - 65% (RR: 45-65%); monocytes –10% (RR:4-10%); stab neutrophils - 5% (RR: 1-5%); segmented neutrophils - 15% (RR: 20-35%); eosinophils – 5.0% (RR: 1-4%); erythrocytes sedimentation rate (ESR) by Panchenkov's micromethod – 6.0 mm/hour. Complete blood count revealed leukopenia and neutropenia. Biochemical analysis of blood was within the norm.

Bone marrow sample revealed 1% of stromal cells (RR: 0-2%). The number of blasts was 1% (RR: 0-2%). Index of neutrophil maturation was 0.7 (RR: 0.6-0.8). Index of erythroblast maturation – 0.8 (RR: 0.8-0.9). The correlation of white and red blood cells lines 3:1 (RR: 3-4:1). Diagnostic decision: According to the obtained results no pathology was revealed.

After the medical examination the patient was clinically diagnosed with neutropenia of unknown genesis. A regular pediatric check-up was recommended.

Weakness, fatigue, and waddling were revealed at the age of 1.5 years. The general condition was assessed as poor. The child was of correct habitus with malnutrition. The layer of subcutaneous fat was low. The skin was pale. The conjuctiva of the both eyes showed signs of teleangiectasia. The skin surface of the face and auricles were pigmented with freckles, the skin was dry. The visible mucous membranes were pale. The lymphatic nodes of the neck and sublingual part are not matted together and painless. The pulse was 95-100 per minute. Respiratory rate was 30 per minute. Clear pulmonary sound was percussed above the lungs, respiration was vesicular. Heart sounds were muffled, rhythmic. The abdomen was soft and painless to palpation. The liver and the spleen were not enlarged. Stool and diuresis were not disturbed. The neurological status revealed clinical signs of central nervous system damage. The child was slow to contact. Consciousness was clear. The cognitive functions were impaired with unstable attention and poor mimics. The face was symmetrical, the movement of the eyeballs was full. Mild signs of cerebral ataxia were noticed: walked on his own but waddling and feeting his legs apart. Babinski syndrome was absent for the both sides. The mascular tonus was decreased. Tendon reflexes of the arms and the legs were decreased.

The suggested diagnosis: neutropenia of unknown genesis. Cerebral ataxia. Hypotrophy of the 2nd degree. Perinatal encephalopathy. Cerebral atrophy. Readiness for convulsions.

The child was referred to the Russian children's clinical hospital (Moscow) for the further examination. The child was examined by the allergologist-immunologist, who paid attention to the signs of leukopenia, neutropenia and frequent cases of respiratory infections in the child's case history.

The results of ummunogram showed: Ig A - 0 g/L (RR: 0.21-2.82g/dL); Ig M – 0.38 mg/mL (RR: 0.47-2.40 mg/mL); Ig G – 23.7 mg/ммL (RR: 4.83-12.26 mg/mL); Ig E - 1 IU/mL (RR: 0-60Un/mL); CD3+ - 55.00% (RR: 62.0-69.0 %); CD4+ - 35.00% (RR: 28.1-65.0%); CD8+ - 25.00% (RR: 26.0-68.0%). Diagnostic decision: immunoglobulin A absence, sharp decrease of immunoglobulin M, CD3+ subpopulation. The obtained results confirm primary immunodeficiency.

Alpha-fetoprotein test showed 90 IU/mL (RR: 0-58IU/mL). Diagnostic decision: test results reveal an increased level of alpha-fetaprotein.

MRI of the brain revealed signs of the cerebral atrophy, enlargement of IV ventricle.

The electroencephalography (EEG) revealed pulse sharpening between the ranges θ and δ and epileptic spike-and-wave complexes, spikes; hypsarrhythmia.

The geneticist examined the child and described the phenotype as dysplastic with stooping back. Hypersalivation. The palpation of the backbone was painless. The backbone line was not curved. The length of the lower limbs D=S. The movement of the joints was full and painless. Waddling. The skin was pale with coffee-like spots. The abdomen was soft and palpable. The spleen and the liver were within the norm. External genitals were of female type. Stool and diuresis were not disturbed.

The genetic data are: ATM (c.5932G>T, c.450453delTTCT, c.15641565delGA, c.5170G>T (p.Glu1724Ter) + c.748C>T (p.Arg250Ter), g.108115650G>A (p.Trp266*), p.Ala1945_Phe1952delV, p.Glu376fs, p.Ile2629fs/.

The clinical diagnosis is primary immunodeficiency. Louis-Bar syndrome (confirmed by molecular genetic analysis).

The patient is recommended to follow regular check-ups at the local pediatrician and the allergologist-immunologist. Immunogram control. Human immunoglobulin (gabroglobin, Gamunex-C, Ig VENA) is administered as a lifelong therapy.

The patient is regularly examined at the Pediatric center of the Republican hospital #1, National medical center, for the last 4 years. The patient receives replacement therapy of immunoglobulin (Ig VENA) and is examined twice a year. The patient's state is considered as stable at the moment. There is still cerebral ataxia, she suffers from respiratory infections 4-5 times a year. The patient is considered as disabled and she is on home education.

This clinical case reconfirms that the pediatricians should be alert to genetic disorders when revealing signs of immunodeficiency. Early immunoassay examination of the child is of extreme importance in early diagnosis of the primary immunodeficiency. Replacement therapy may balance development of long-lasting subacute and chronic infectious disorders [5].

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Menkes disease. A clinical case report of a rare disorder of copper metabolism caused by a mutation in the *ATP7A* gene

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The article presents the features of diagnostics and dynamic monitoring of a patient with Menkes disease, a rare disorder of copper metabolism caused by a mutation in the *ATP7A* gene. The data of scientific literature on the epidemiology, etiology, pathogenesis of this disease are analyzed, and the basic principles of therapy and the outcomes of the disease are considered. The described patient was admitted for treatment with a diagnosis of consequences of severe perinatal lesions of the central nervous system with a typical clinical picture for this group of diseases: spastic tetrapresis, pseudobulbar syndrome, structural focal epilepsy. However, during the follow-up process, uncharacteristic symptoms were noted: short blonde coarse hair, bladder diverticulosis and progressive atrophy of the cerebral cortex in dynamics according to MRI. During the diagnostic search, tests for copper concentration and serum ceruloplasmin levels were performed twice, indicating Menkes disease, and complete exome sequencing was performed, which confirmed the presence of a point mutation in the *ATP7A* gene.

Keywords: Copper, ceruloplasmin, hypsarrhythmia, Menkes disease.

Introduction: Most hereditary metabolic disorders are extremely rare, but together they represent a fairly common group of diseases. As a rule, they are incurable and often lead to early disability and death, however, for many hereditary diseases, pathogenic therapy has been developed and with timely diagnosis and early start of treatment therapy, it is possible to achieve a favorable prognosis for life. One of these is hereditary disorders of copper metabolism.

The most famous neurodegenerative disease associated with impaired copper metabolism is Wilson-Konovalov disease, caused by a mutation in the ATP7B gene, which is responsible for the synthesis of copper-transporting ATPase and is characterized by the accumulation of copper in various organs and tissues, with predominant damage to the liver and central nervous system [2. 5, 13]. However, in addition to Wilson-Konovalov disease, there is a much less well-known hereditary disorder of copper metabolism, in which there is an uneven copper deficiency in various organs. This disease is called Menkes disease or curly hair disease and is an X-linked recessive neurodegenerative disease caused by mutations in the ATP7A gene located on chromosome Xq21.1 [1, 13]. Being an X-linked disease, clinical manifestations are possible only in males, in women who are carriers of ATP7A mutations, with the exception of rare cases associated with sex chromosome aneuploidy or X-autosome translocations, the disease is asymptomatic. However, some carriers of the mutant gene have minor hair and skin abnormalities [6, 8, 14].

The ATP7A gene is responsible for the synthesis of the transport protein of the same name, the function of which is to transport copper across cell membranes; this protein is expressed in all organs except the liver. In the small intestine, the ATP7A protein is necessary for the absorption of copper from food by active transport; in the cells of other organs, it acts as a carrier of copper from the cell membrane to the Golgi apparatus, where the synthesis of proteins and enzymes takes place, for the functioning of which copper [5] is required. One of these enzymes is lysyl oxidase, which binds tropocolagen into strong fibrils of mature collagen. When the mechanism of lysol oxidase synthesis is disturbed, defective collagen is formed, the properties of which determine many of the symptoms of Menkes disease. Normally, when there is an excess of copper inside the cell, the same ATP7A protein transports it to the cell membrane and removes the excess from the cell. Mutations in the ATP7A gene lead to the synthesis of a defective protein that is incapable of normal functioning. As a result, the absorption of copper from food in the intestine is sharply reduced, the synthesis of enzymes in the Golgi apparatus is disrupted, and the transport of excess copper from cells is blocked. Ultimately, copper accumulates in the small intestine and kidneys, and in the brain and other tissues, its content becomes catastrophically low, which together contributes to the formation of a kind of clinical picture of the disease [3, 4].

Menkes disease occurs in 1: 250,000-1: 350,000 newborn boys. Manifests, as a rule, in the neonatal period. Early symptoms include hypothermia, hyperbilirubinemia, growth retardation, and multiple stigmas of dysembryogenesis. Hair in the neonatal period, as a rule, looks normal [3, 11, 13].

Upon completion of the first 2-3 months of relatively normal development, a regression of previously acquired skills occurs, followed by a gross delay in psychomotor development. These children are characterized by the appearance of various types of epileptic seizures (focal, generalized, myoclonic) [11], general weakness with further formation of spastic tetraparesis [8]. Over time, a striking distinctive feature of these children becomes obvious - trichoplidystrophy, their hair becomes matted, coarse, gray or ivory [12]. A characteristic feature of the course of the disease is multiple diverticula of the urinary tract, often leading to rupture and secondary infection. Among other signs, it is important to note gen-

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