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MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN AND ADOLESCENTS IN YAKUTIA

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Generally, COVID-19 is milder in children than in adults. But already in May 2020, information about a multisystem inflammatory disease that affects children and adolescents began to arrive from around the world. The pathogenesis and pathological picture of COVID-19 are characterized by the development of thrombus inflammation, generalized microangiopathy in the form of destructive-proliferative viral vasculitis and coagulopathy with secondary damage to the skin, internal organs, central nervous system, hemophagocytosis. This paper presents the observation of ten patients aged from 6 months to 14 years treated at the Children's Clinical Infectious Diseases Hospital in Yakutsk from September 2020 to March 2021 with a diagnosis of U07.2 - Coronavirus infection caused by COVID- 19, no virus identified, M30.3 Kawasaki-like syndrome. The presence of prolonged fever, damage to two and whiter systems of the body, laboratory markers of inflammation without obvious foci of an acute infectious process was the criteria for making a diagnosis. Also, a prerequisite for establishing a diagnosis was the presence of contact with patients with COVID-19 or antibodies to SARS-CoV-2. There were no patients with complicated cases that required intensive care among the observed patients, but there were severe cardiac lesions in some children. All our patients were of Yakut nationality. In contrast to the available literature data, we did not observe a significant violation of the blood coagulation system; in some patients, thrombocytosis was prominent. We observed a subarachnoid haemorrhage in one patient.

Keywords: multisystem inflammatory syndrome, children, fever.

Introduction. Symptoms of the multisystem inflammatory syndrome (MIS) are similar to those of Kawasaki disease. Kawasaki disease characterized by self-limiting vasculitis. As a rule, the disease affects only children, and a prolonged increase in body temperature is its first sign [1,2]. The new syndrome is called pediatric multisystem inflammatory syndrome or MIS. It is now clear that this condition is a delayed consequence of new coronavirus infection. According to the WHO recommendations, preliminary criteria for recognizing a case of MIS require the presence of at least one of the following two symptoms: rash; hypotension or shock; cardiac arrhythmia; signs of coagulopathy; acute gastrointestinal symptoms; elevated markers of inflammation without obvious microbial causes of inflammation; infection with coronavirus or direct contact with patients with COVID-19 [3]. They indicate that the time interval from contact with a Covid-19 patient can range from 6 to 51 days, and in most cases, children with MIS had antibodies to SARS-Cov-2 [2]. The most frequently affected gastrointestinal tract (92%), cardiovascular (80%) and respiratory system (70%), haematological changes had 76% of patients [1,2]. Also, several authors note a high frequency of MIS cases among the Mongoloid and Afro-Caribbean population, mainly boys who are ill [4]. Intravenous immunoglobulins and systemic corticosteroids are effective treatments [2,4]. The incidence of confirmed SARS-CoV-2 infection in children and adolescents was 322 per 100,000 people in this age group, and MIS-C - 2 per 100,000 people [5]. In 2020, 6098 children were diagnosed with Covid-19 in the Republic of Sakha (Yakutia), 857 of them needed inpatient treatment.

The purpose of this study is an analysis of clinical and laboratory data of multisystem inflammatory syndrome in children, determination of the features of the course of this disease in patients of Yakut nationality.

Research methods and materials. We observed 10 patients with the multisystem inflammatory syndrome. The criteria for establishing the diagnosis were: severe condition, fever for at least 48 hours, damage to 2 or more body systems, laboratory signs of an inflammatory process, signs of a new coronavirus infection (determination of antibodies to SARS-Cov-2 IgG class by enzyme-linked immunosorbent assay, detection of the virus by polymerase chain reaction), contact with patients with Covid-19.

Results and discussion. Between September 17, 2020, to March 19, 2020, we observed 10 patients with multisystem inflammatory syndrome, of which nine were boys and one girl. The ages of the children were very different: 6 months, 1 year, 5 years - 2 children, 6 years old, 7 years old, 8 years old, 10 years old, 13 years old and 14 years old. All patients were of Yakut nationality (Sakha). When analyzing the epidemiological history, the fact that six patients had family contact with patients with Covid-19. The terms of contact were: 14 days (in 2 cases), 1 month (3 cases) and 1.5 months (1 case). The PCR examination took place among contacted persons, results were negative in all cases. It worth noticing that in all cases, the diagnosis of Covid-19 in family members was laboratory confirmed. Three children had clinical signs of ARVI, and two of them also had anosmia, which was short-lived and stopped within 2 weeks. The course of ARVI in everyone on the usual basic therapy had no complications, and recovery came on the 5-7th day. Three patients showed no clinical signs of the disease at the time of contact. One patient, 11 days before this hospitalization, underwent inpatient treatment with a diagnosis of "Coronavirus in-

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fection caused by the COVID-19 virus." Three patients had no history of contact with COVID-19 patients. At the time of admission to the children's infectious diseases hospital, all patients by ELISA determined antibodies to SARS-Cov-2 of the IgG class in titers above 20. It was not possible to isolate the virus genome by PCR in any patient.

Children were admitted to an infectious diseases hospital with referral diagnoses of acute respiratory viral infections in 7 patients and two with a diagnosis of acute respiratory infections. One boy was admitted with a referral diagnosis "Coronavirus infection caused by the COVID-19 virus, no virus identified." He was initially hospitalized in the Central District Hospital with a diagnosis of Kawasaki Syndrome, the examination revealed antibodies to SARS-Cov-2 of the IgG class, and he was transferred to the DIKB in Yakutsk. In all cases, the onset of the disease (multisystem inflammatory syndrome) was acute - with a rise in body temperature from 38.4 ° C to 40.2 ° C, there was hyperemia of the throat, signs of intoxication. Three had a dry cough in two cases, and one child had a wet cough with a discharge of mucopurulent sputum. At the time of hospitalization, three patients had lymphadenitis in varying degrees of severity and with different localization. Seven children had skin rashes of various localization. The diarrheal syndrome was noted in two children. Hospitalization was carried out on the 4th day in four patients, in three on the 2nd day, one patient was admitted to the hospital on the 3rd, 7th and 9th days of illness.

On admission, the condition of all children was assessed as serious. At least two systems were involved in the pathological process.

Fever (febrile or hyperthermic) occurred in all children. The duration of the fever ranged from 5 to 12 days and depended on the duration of hospitalization and the appointment of glucocorticosteroid therapy. One patient had a second wave of fever after two days of normal body temperature.

Damage to the cardiovascular system, to one degree or another, was detected in all patients according to ECG data. One child was diagnosed with myocarditis, two children were diagnosed with coronaritis. In the remaining patients, the instrumental examination was diagnosed with violations of the cardiac conduction system: in three cases - atrioventricular block of 1 degree, in two children - incomplete blockade of the right bundle branch. Three children have diagnosed with grade 2 cardiomegaly.

Lymph node involvement was quite common (in 7 patients). In addition to the submandibular lymph nodes, the axillary, cubital and inguinal lymph nodes were affected. The lymph nodes were dense, not welded to the underlying tissues, painful on palpation ranging from 1 cm to 2.5 cm. Ultrasound of the cervical lymph nodes was performed in one child, due to a sharp pain in the lymph nodes, to exclude an abscess. Also, scleritis and photophobia were noted in 6 patients.

In 4 patients from the first days of illness (2-3 days) maculopapular rashes were noted. The rash had a confluent character, protruded above the level of the skin. In one patient, the rash spread, almost all over the body and bullae with serous contents were noted. In this patient, the rash was practically the only clinical sign. In one patient, the rash was petechial in nature. The duration of the rash ranged from 2 to 6 days and also depended on the timing of the administration of glucocorticosteroids. In one patient, without exanthema syndrome, on the 12th day of illness, peeling was noted on the tips of the fingers. In one child, in the acute period, there was pasty and soreness of the skin of the soles and palms, there was no peeling later. The defeat of the respiratory system was diagnosed in 6 patients. In four cases - acute bronchitis, in two - community-acquired bilateral lower lobe pneumonia, moderate severity. No patient had respiratory failure. The lesion of the gastrointestinal tract was noted in 5 patients and was represented by pain in the abdomen and four patients had loose stools. The duration of the episode of diarrhoea ranged from 4 to 6 days. Thus, the observed patients showed damage from 2 to 4 body systems.

In laboratory research, we revealed significant changes. In the general analysis of blood, all patients showed a neutrophilic shift in the leukocyte formula: stab neutrophils accounted for up to 59%, seminiferous neutrophils up to 79%. Moreover, leukocytosis occurred only in four patients. An increase in ESR to high values was characteristic, and there was a negative trend during the course of the disease. The maximum ESR values were in a six-month-old child who was diagnosed with myocarditis. On the 2nd day of illness, ESR was 57 mm. rt. Art., on the 12th day - 70 mm. rt. Art. Three children had severe thrombocytosis, which also increased over time. One patient had thrombocytopenia (88 × 109).

In a biochemical blood test, the cytolytic syndrome was determined in all patients: an increase in ALAT levels (up to a 7-fold increase) and ASAT (up to a 6-fold increase). It should be noted that in all cases during the therapy there was a rapid normalization of these parameters. Indicators of total bilirubin increased slightly in two children, less than 1.5 times.

All patients had increased CRP indices, and significantly: from 20-fold to 100-fold increase. Against the background of ongoing therapy and clinical improvement, the CRP value reached the norm in only two patients. Also, five patients showed an increase in procalcitonin: two up to 10 ng/ml, two - 2 ng / ml. and 0.8 ng / ml. All children had a significant increase in the level of D-dimer, the maximum value was 2280 ng/ml.

An increase in ceatinine values was noted in 5 patients, in three of them, the norm was slightly exceeded, in two - 2 times higher than the norm. The parameters of creatinine kinase were not changed in any patient. Unfortunately, the level of ferritin was investigated only in four patients, in two cases an increase in this indicator was noted by 1, and 1.9 times.

The study of the blood coagulation system did not reveal significant changes. Two patients had a slightly increased

activated partial thromboplastin time (APTT), and in one patient the level of fibrinogen reached 6.3 g / L. The prothrombin index was not changed in any child. The duration of bleeding in Duka and coagulation according to Sukharev remained normal in all patients.

All patients received pathogenetic therapy: three children - normal human immunoglobulin, six - dexamethasone and prednisolone - two children. Therapy began within 1 to 3 days after hospitalization and, respectively, from 2 to 11 days from the onset of the disease. Against the background of the therapy, all patients showed positive dynamics: the body temperature returned to normal within 2 to 4 days, on average by 2.9 days. Moreover, the duration of the fever before hospitalization ranged from 1 to 11 days. On average, patients were in the infectious diseases hospital for 8.4 days (from 1 to 14 days). Four patients were transferred to the Department of Cardioreheumatology of the Pediatric Center of the National Center of Medicine for further examination and treatment. Six children were discharged home in satisfactory condition under the supervision of an outpatient cardio rheumatologist.

Conclusion. Thus, all observed children had signs of MIS. Despite the incomplete symptom complex, the clinical

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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