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Polymorphism of clinical manifestations, experience of diagnosis and treatment of multisystem inflammatory syndrome associated with COVID-19 in children

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Purpose — to analyze the literature data on possible variants of the course of pediatric multisystem inflammatory syndrome (PIMS-TS) in children; to describe our own experience in the diagnosis and treatment of some cases of PIMS-TS in children of different age groups; to present possible variants of clinical manifestations of the above disease; to draw attention to the need for early diagnosis and team care and treatment of such children.

This novel clinical syndrome later identified as PIMS-TS temporally associated with SARS-CoV-2. In contrast with KD, PIMS-TS appears to occur in children at an older age with a predominance of gastrointestinal symptoms, hemodynamic instability, and myocardial dysfunction. However, the exact pathomechanism remains to be understood. Nevertheless, the post-viral immunological reaction is postulated to be the underlying mechanistic underpinnings.

The paper describes the clinical course of the disease in a 5-year-old boy who complained of abdominal pain and hyperthermia, and the disease was masked by surgical pathology. The phenomena of intoxication syndrome, polyserositis, skin manifestations in the form of a polymorphic rash, hyperemia of the conjunctiva, swelling of the feet and hands increased in dynamics. The course of the disease in a 10-year-old girl who had symptoms of a viral infection is also described. However, upon going to the hospital, both children were diagnosed with a serious condition, they were hospitalized and given appropriate treatment.

Therefore, the multifaceted nature of the PIMS-TS' course underlines the need for early recognition and multispecialty care and management.

The research was carried out in accordance with the principles of the Helsinki Declaration. The informed consent of the patient was obtained for conducting the studies.

No conflict of interests was declared by the authors.

Keywords: PIMS-TS, COVID-19, SARS-CoV-2-19, MIS-C, children.

Поліморфізм клінічних проявів, досвід діагностики та лікування мультисистемного запального синдрому, асоційованого із COVID-19, у дітей

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Мета — проаналізувати літературні дані про можливі варіанти перебігу мультисистемного запального синдрому в дітей; описати власний досвід діагностики і лікування деяких випадків мультисистемного запального синдрому в дітей різних вікових груп; навести можливі варіанти клінічних проявів вищезазначеного захворювання; звернути увагу на необхідність ранньої діагностики та командного догляду і лікування таких дітей.

Відомо, що мультисистемний запальний синдром у дітей має відносно легкий перебіг, на відміну від дорослих. Однак нещодавні дані показали, що в підгрупи дітей розвинулася системна запальна відповідь, яка нагадує атипову/типову хворобу Кавасакі і синдром токсичного шоку. Пізніше цей новий клінічний синдром ідентифікували як педіатричний запальний мультисистемний синдром, тимчасово пов'язаний із SARS-CoV-2. Однак запальний мультисистемний синдром частіше розвивається в дітей старшого віку з переважним ураженням шлунково-кишкового тракту, нестабільністю гемодинаміки та дисфункцією міокарда. Водночас точний патомеханізм поглиблено досліджується. Визначено, що поствірусна імунологічна реакція є основним тригерним фактором розвитку мультисистемного запального синдрому.

Описано клінічний перебіг хвороби у хлопчика віком 5 років, який скаржився на біль у животі та гіпертермію, а захворювання маскувалося під хірургічною патологією. У динаміці наросли явища інтоксикаційного синдрому, полісерозит, шкірні прояви у вигляді поліморфного висипу, гіперемії кон'юктив, набряку стоп і кистей. Також описано перебіг захворювання в дівчинки віком 10 років, яка мала прояви вірусної інфекції. Однак на момент звернення до лікарні в обох дітей встановлено тяжкий стан, їх госпіталізовано та проведено відповідне лікування.

Отже, різнобічний характер перебігу мультисистемного запального синдрому в дітей підкреслює необхідність його ранньої діагностики, багатопрофільної допомоги та найшвидшого лікування.

Дослідження виконано відповідно до принципів Гельсінської декларації. На проведення досліджень отримано інформовану згоду батьків дітей.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: PIMS-TS, COVID-19, SARS-CoV-2-19, MIS-C, діти.

Introduction

The 2019 coronavirus disease pandemic (COVID-19), which was reported as severe infection of the acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2), has spread rapidly around the world. Data from the World Health Organization (WHO) as of early February 2021 showed that COVID-19 affected more than a hundred million people and caused two million deaths [17,30].

It is reported that SARS-CoV-2 infection symptoms in children's group is mild compared to adults [17,26]. However, recent data have shown that groups of children may develop a significant complications as systemic inflammatory reaction,

which resembles atypical / typical Kawasaki disease (KD) and toxic shock syndrome [28]. This new clinical syndrome was later recognized as pediatric inflammatory multisystem syndrome, which is associated with SARS-CoV-2 (PIMS-TS). Following the advent of PIMS-TS, the WHO, the American Centers for Disease Control and Prevention (CDC) and the European Center for Disease Prevention and Control (ECDPC) have defined this syndrome [6,17,29,23]. Since the release of various identified cases from these organizations, a number of scientific publications from different regions of the world have been published, studying the mechanisms of their development, reporting on clinical cases and treatment outcomes using PIMS-TS.

Epidemiology

In April 2020, the UK National Health Service raised the alarm for children with major hypersensitivity syndrome, some of whom had laboratory-confirmed COVID-19. Since then, other countries have begun to report the same clinical syndrome (France, USA, Italy, Spain and India) [3,15,17,22,24,27]. It was noted that compared to Kawasaki disease (KD), there are consistent epidemiological characteristics of PIMS-TS (MIS-C). Multisystem inflammatory syndrome is reported to occur in children of all racial and ethnic groups, unlike KD, which mainly affects the East Asian group of children. Based on the age group, MIS-C mainly affects children of older age groups in comparison with the typical KD (average age group is about 9–15 years versus 2–5 years, respectively) [9,17,28].

Following guidance from the NHS England and the British Society for Pediatric Intensive Care on unexplained cases of multisystem inflammatory syndrome in the UK, on 1 May 2020 the Royal College of Pediatrics and Child Health (RCPCH) published guidelines and definitions for this syndrome and independence from SARS-CoV-2 [17,23]. Since then, the WHO and the CDC have also developed a definition of this relatively new disease. Diagnostic criteria for this syndrome are presented in table.

Presumptuous PIMS-TS mechanism. Although PIMS-TS may indeed be associated with SARS-CoV-2 infection, the pathophysiology of PIMS-TS remains unclear. However, some evidence and reports suggest several mechanisms of this new clinical nosology. The first possible hypothesis is that PIMS-TS is an immunologically mediated or post-infectious process caused by non-neutralizing IgG antibodies due to enhanced antibody synthesis (antibody-dependent enhancement — ADE) [5,17, 25,27].

Cases of PIMS-TS have been reported since the peak of SARS-CoV-2 infection in some countries. It was found that most patients were more likely to test positive for SARS-CoV-2 antibodies than for nasopharyngeal PRL, which increases the likelihood of engaging acquired immunity in the development of this syndrome [17,25,28]. This evidence is confirmed by the conclusion of a multicenter study among 78 children who had signs of PIMS-TS, with which sick children were admitted to the Pediatric Intensive Care Unit (PICU) in the UK [9,17]. This study showed that 96% of patients had antibodies to SARS-CoV-2, but negative for PCR. This result confirms the evidence that PIMS-TS may not be an acute COVID-19 infection, but most likely a post-immunological reaction [9,17]. However, according to a number of authors, this theory of ADE is still unclear, as there was no information on the deterioration of patients' condition with COVID-19 who received convalescent plasma [17,25].

The second proposed PIMS-TS hypothesis is a cytokine storm, which is caused by the ability of the coronavirus to block responses to type I and III interferon in patients with a previously high viral load or in patients who failed to replicate the virus, leading to excessive cytokine activation [17,25].

Fever. Persistent fever is one of the criteria for determining the case of PIMS-TS. The duration of fever for PIMS-TS is more than 24 hours [6,17] or 3 days [17,29], in contrast to KD, which is ⩾5 days [10,17]. Fever is one of the clinical signs of inflammation along with other inflammatory signs such as rash or conjunctivitis. Almost all patients with PIMS-TS had a history of fever that occurred 4–8 days before treatment [9,13,15,17,19,20,27,28]. Temperatures ranging from 38 to 40°C and torpid to antipyretics, in seven children with PIMS-TS reported by M. Pouletty et al., the temperature reached over 40°C [17,20,26,]. However, it is difficult to distinguish between PIMS-TS and KD solely on the basis of fever characteristics, as both have the same clinical features. The onset of fever is extremely important because it helps to identify

Table

Identification of cases of pediatric inflammatory multisystem syndrome from the Royal College of Pediatrics and Child Health, WHO and Centers for Disease Control and Prevention

Royal College of Pediatrics and Child Health (UK) [6]	World Health Organization [4]	Centers for Disease Control and Prevention (USA) [5]
• A child with persistent fever, inflammation (neutrophilia, increased CRP, and lymphopenia) and evidence of single or multiple organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal, or neurological pathology) with additional symptoms. This may include children who meet the full or partial criteria for KD*	• Children and adolescents 0–19 years old with fever >3 days and two of the following: a) Rash or bilateral purulent conjunctivitis or signs of mucocutaneous inflammation (hands or feet, mouth cavity). b) Hypotension or shock. c) Features of myocardial dysfunction, development of pericarditis, valvulitis or coronary abnormalities (including ECHO data or elevated troponin / NT-proBNP). d) Evidence of coagulopathy (using PT, PTT, increasing the level of D-dimer). e) Acute gastrointestinal problems (diarrhea, vomiting or abdominal pain)	• A person under the age of 21 years old with fever**, laboratory data of inflammation*** and clinically severe diseases requiring hospitalization, with multisystem (>2) lesions of organs, heart, kidneys, respiratory system, gastrointestinal tract, dermatological, hematological and neurological disorders)
• Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, myocarditis-related infections such as enterovirus (waiting for the results of these studies should not delay with a specialist)	• increased markers of inflammation, such as ESR, C-reactive protein or procalcitonin	• lack of alternative plausible diagnoses
• PCR testing for SARS-CoV-2 can be positive or negative	• no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndrome	• positive for current or recent SARS-CoV-2 infection by RT-PCR, serological or antigenic test; or exposure to COVID-19 for 4 weeks before symptoms appear
	• evidence of COVID-19 (RT-PCR, antigen test or positive serological evaluation), or probable contact with patients with COVID-19	
Additional comments: Some individuals may meet the full or partial criteria for KD, but this should be considered if they meet the definition criteria for MIS-C. Consider MIS-C in any infant death with evidence of SARS-CoV-2 infection		

Notes: * — Criteria for KD include persistent fever and 4 of the 5 main clinical signs: erythema and cracked lips, strawberry tongue and / or erythema of the oral and pharyngeal mucosa; bilateral bulbar injection of the conjunctiva without exudate; rash (maculopapular, diffuse erythroderma); erythema and swelling of the wrists and feet and / or periungual desquamation; lymphadenopathy; ** — Fever >38.0°C for >24 hours or report of fever lasting >24 hours; *** — Laboratory data, including but not limited to: elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase or interleukin-6 (IL-6); elevated levels of neutrophils; lymphocytopenia; and low albumin levels.

the course of the disease and follow-up after treatment.

In KD, intravenous immunoglobulin (IVIG) administration within 10 days of fever effectively reduces the risk of coronary artery aneurysm [10,17]. Most often, fever in PIMS-TS decreased after the onset of IVIG (at a dose of 2 g/kg) [8,17,20]. However, patients with IVIG-resistant fever, defined as a duration of fever of at least 36 hours but less than 7 days, should be given a second infusion of immunoglobulin [17,20,26].

Moreover, unexplained fever, signs of inflammation, and laboratory findings in children with a personal or family history of COVID-19, especially in an area with a high incidence of SARS-CoV-2, should be considered as suspected PIMS-TS. If laboratory tests (general blood test and biochemical parameters of blood, CRP, ferritin, albumin) showed the presence of hyperinflammation, additional tests should be ordered to detect myocarditis (troponin, procalcitonin and ECHO-cardiography) or cytokine storm syndrome (lactasate dehydrogen, PTT, INR) [4,17].

Hemodynamic instability. Most children had a shock syndrome that did not respond to volumetric resuscitation, which ultimately required the support of vasopressors. A study of a number of cases in the UK by S. Riphagen et al. found that for 10 days in April 2020, eight children who were previously in satisfactory condition and tested negative for SARS-CoV-2 had hyperinflammatory syndrome with multiorgan damage, similar to Kawasaki disease shock syndrome (KDSS), which eventually evolved into vasoplegic shock [17,24].

Hemodynamic instability has previously been reported in adults with SARS-CoV-2 sepsis. All of them met the clinical criteria for shock and were positive for PCR from SARS-CoV-2 nasal smear and with predominant lung, kidney, liver and

heart damage, as well as coagulation disorders. Meanwhile, children with PIMS-TS had no noticeable pulmonary or renal symptoms, and none of the laboratory markers were elevated except for D-dimer levels. Thus, according to the authors, there is a significant differentiation between adults with viral sepsis and children with PIMS-TS [9,17].

Mucosal skin manifestations. Both PIMS-TS and KD have similarities in mucocutaneous inflammation [17,23,27]. Maculopapular rash, conjunctivitis, and cheilitis are the most common clinical mucosal skin symptoms found in children with PIMS-TS. However, there were no further detailed descriptions of mucosal and skin lesions, including the appearance or predisposition to localization of the rash in PIMS-TS compared with KD. It should be noted that the presence of skin lesions and other symptoms, including abdominal pain, increases the likelihood of PIMS-TS [3,16,17].

Gastrointestinal symptoms. Patients with PIMS-TS often have gastrointestinal symptoms, unlike KD. More than 50% of patients with PIMS-TS, in addition to fever, experienced abdominal pain, nausea, vomiting or diarrhea. A detailed description of abdominal pain has not yet been described, although the degree of pain is probably severe. Message from J. Toubiana et al. [26] shows that 21 patients with multisystem inflammatory syndrome similar to Kawasaki had gastrointestinal symptoms that arose at the beginning of the disease from acute abdominal pain, and 95% had vomiting and diarrhea. In addition, four patients showed effusion in the peritoneum, two of them underwent surgery for acute abdomen. Moreover, among patients who had diarrhea, it was not bloody [17,26].

M. Cabrero–Hernández et al. (2020) in one Spanish hospital described five children who went to the emergency department (ED) with complaints of abdominal pain and vomiting for 2–5 days. Three of them localized pain in the right iliac region. They later developed hemodynamic instability and were transferred to intensive care unit (ICU) on suspicion of abdominal sepsis. All patients underwent ultrasound / computed tomography (CT) and inflammation of the intestine without any disease requiring surgical treatment. Microbiological confirmation of bacterial infection from the collected cultures was not obtained. On admission, PCR testing for SARS-CoV-2 by nasal swab was negative in 4 of 5 patients. Meanwhile, despite the negative PCR results, all patients were treated empirically as SARS-CoV-2 and discharged 2–13 days after hospitalization. Prior to discharge, patients tested positive for IgG SARS-CoV-2 and PCR SARS-CoV-2 [3,17]. Thus, these findings prove the postimmune response as a trigger for hyperinflammatory syndrome with gastrointestinal symptoms as one of the most common major complaints [2,3,5,13, 15,17,18,20,21,24,26,28].

Cardiac damage in COVID-19 and PIMS-TS can be explained by genetic predisposition, myocardial damage caused by a cytokine storm, and direct viral invasion of SARS-CoV-2 into cardiac myocytes [15,17,18]. It is believed that the post-viral immunological reaction is also the cause of myocardial dysfunction. Apparently, after the introduction of IVIG there is a significant restoration of myocardial function and a decrease in inflammatory biomarkers.

A number of critically ill children with PIMS-TS were diagnosed with acute myocarditis in medical institutions in Paris (France), which was less severe than normal myocarditis. They also had intense systemic inflammation, in contrast to acute myocarditis due to KDSS, manifested by elevated platelet and neutrophil counts and CRP levels. However, the main mechanism remains unclear, as none of them underwent a biopsy [13,17]. Elevated levels of troponin and sodium B-type uretic peptide are common in patients with heart disease, and most have elevated levels of C-reactive protein, ferritin, lactate dehydrogenase, and D-dimer. Patients with PIMS-TS tend to be older, with more significant inflammation and myocardial damage than patients with KD.

To date, there is only one study that reports MRI results in patients with PIMS-TS. The result showed diffuse myocardial edema, without signs of fibrosis or focal necrosis [2,17]. This finding also confirmed the hypothesis of a postviral immune response as a potential mechanism of KD-like development of PIMS-TS due to the presence of macrophages and neutrophil infiltration in the myocardial interstitium, in contrast to myocardial cell degeneration in viral myocarditis [2,14,17].

In addition to myocardial dysfunction, children with PIMS-TS are also at risk for developing coronary artery aneurysms [1,2,13,17,20,21,27,28]. However, the study by Whittaker et al. (2020) showed that among 58 children with PIMS-TS in the UK, no association was found between levels of markers of inflammation and the development of coronary artery aneurysms. This finding suggests that the severity of inflammation does

not always cause changes in the coronary artery. Moreover, it emphasizes the importance of routine ECHO-cardiographic tests to detect any coronary aneurysm in the entire spectrum of PIMS-TS [17,28]. Among children with coronary artery pathology without objective dilation, «ECHO-bright» imaging on ECHO-cardiography was observed, which can be explained by the presence of inflammation of the endothelium of the coronary arteries [17,21,24,26]. Therefore, close monitoring of these parameters is required in patients with PIMS-TS.

Another single-center study by T. Ramcharan et al. (2020) among 15 children with PIMS-TS in the main pediatric hospital in the UK found 13 patients (87%) who had arrhythmiometric regurgitation of the valve (10 patients with mitral regurgitation) during hospitalization, with improvement after 1–2 days, indicating presence of transient valvulitis [17,21].

For the age group, patients with PIMS-TS, in general, are older than patients with KD — from 8 to 15 years; whereas KD affects infants or children under 5 years of age. Inflammation data and PIMS-TS symptoms in most cases match KD symptoms. However, gastrointestinal manifestations such as abdominal pain, nausea, vomiting, and diarrhea are more common in PIMS-TS. Myocardial dysfunction and shock occur more often in PIMS-TS compared with classic KD. Both have almost the same laboratory findings deviations; the levels of D-dimer protein and ferritin in PIMS-TS are generally higher than in KD [17,21].

Taking to consideration the abundance of asymptomatic cases of SARS-CoV-2 during this pandemic, clinicists encountering patients who have any symptoms similar to KD, especially those with a predominance of gastrointestinal symptoms, should consider MIS-C as one of the differential diagnoses options [17].

The SARS-CoV-2 pandemic did not bypass Ukraine either. At the peak of the increase in morbidity, in October-December 2020, the Khmelnytsky pediatrician began to detect cases of the disease in children with symptoms similar to KD with prevalence of intestinal symptoms, and who had contact with patients with COVID-19 or positive IgG on SARS-CoV-2. These were children aged 5 to 15 years. They were diagnosed with multisystem inflammatory syndrome (MIS-C) associated with SARS-CoV-2. 10 children aged 5–15 were successfully treated at the Khmelnytsky City Children's Hospital. We would like to present two cases.

The purpose of the study — to conduct an analysis of literature data on possible variants of the course of multisystem inflammatory syndrome in children; to share your own experience of diagnosis and treatment of some cases of multisystem papular syndrome in children of different age groups; to familiarize with the possible variants of clinical manifestations of this disease and pay attention to the need for early diagnosis and team care and treatment of such children.

The research was carried out in accordance with the principles of the Helsinki Declaration. The informed consent of the patient was obtained for conducting the studies.

Clinical case 1

A boy, 5 years old, Khmelnytsky, was admitted to the hospital in KP «Khmelnytsky City Children's Hospital» on October 18, 2020, with complaints of fever up to 38–39°C, pain in the lower abdomen and around navel, nausea, bloating. From the anamnesis it is known that the boy was ill during the last three days when the above-mentioned complaints arose. Two days before hospitalization, the child was examined by a surgeon in the emergency department. Acute surgical pathology was ruled out, antispasmodics, antipyretics were prescribed. However, gradually the pain intensified, the temperature rose to 39°C, and dyspeptic symptoms persisted. They turned to the surgeon again. Hospitalized on suspicion of appendicitis. On the same day he underwent surgery and was diagnosed with acute gangrenous appendicitis. The first days after the operation the boy felt well. The condition worsened on the third day after surgery with the appearance of systemic edema syndrome with a predominant localization in the area of the feet and hands. The next day there was a polymorphic rash (on the palms, upper extremities, neck and back), enlarged cervical lymph nodes, conjunctival hyperemia. Heart tones are muffled, tachycardia, systolic murmur at the apex. The liver and spleen enlarged. Ultrasound of the heart revealed signs of dilatation of the left ventricle and atrium, fluid in the pericardium along the left ventricle (2–3 mm). On both sides in a pleural sinus the liquid of 5–8 ml (anechogenic), signs of marginal atelectasis is visualized. Ultrasound of the abdominal cavity revealed signs of hepatosplenomegaly, reactive changes in the liver, abdominal lymphadenopathy, polyserositis (ascites, hydropericardium, pleurisy).

Laboratory parameters: blood tests showed anemia (100 g/l), leukocytosis (21.5–16.0×10^9), hypochromia thrombocytosis (837×10^9), neutrophilia, lymphocytopenia, elevated ESR (33 mm/h), low total protein (33 g/l), high CRP (24 mg/l), moderately elevated procalcitonin levels (0.62 ng/ml). Coagulogram, ferritin, troponin and D-dimer — within the reference values.

From the anamnesis: the child did not have frequent episodes of respiratory infection and any chronic pathology, allergy history is not present. The child's parents had COVID-19, recovered two weeks before the onset of symptoms of the disease in the child. The child has positive IgG antibodies to COVID-19.

Given the signs of polyserositis (ascites, hydropericardium, hydrothorax), myocardial dysfunction, dry skin and mucous membranes, the presence of spotted erythematous skin rash with characteristic localization on the palms and soles, edema of the hands and feet, bilateral non-purulent conjuctivitus, signs of inflamation in the blood sample, the presence of IgG antibodies to COVID-19, the child was diagnosed with complete MIS-C (multisystem inflammatory syndrome), induced by COVID-19.

Due to the severity of the condition, the child was placed in ICU for about a week.

Treatment: intravenous immunoglobulin (IVING) (2 g/kg), by continuous infusion for 24 hours, antibacterial therapy, infusion therapy, hormone therapy, anti-inflammatory therapy, symptomatic and supportive therapy.

After 20 days of treatment, the boy was discharged home in satisfactory condition under the supervision of primary care physicians with recommendations to continue anti-inflammatory and hormone therapy according to the protocol.

Clinical case 2

A girl, 10 years old, Khmelnytsky, was admitted to the hospital in KP «Khmelnytsky City Children's Hospital» on October 24, 20, with complaints of fever up to 39.5°C, dry cough, lethargy, headache during the last 6 days. She was treated on an outpatient basis, took antibiotics, Nonsteroidal Anti-inflammatory Drugs (NSAIDs), and symptomatic therapy. Despite the therapy, febrile fever and catarrhal symptoms persisted and even worsened. Upon the father's application to the emergency department, the child was hospitalized in serious condition. On admission: body temperature 37.4°C, pain throughout the body (according to the girl), in particular, intense abdominal pain and headache. The skin is pale, dry, polymorphic rash on the neck, face and anterior abdominal wall, edema and redness around the eyes and in the palms and soles, severe hyperesthesia. Heart sounds are muffled, rhythmic, tachycardia (125 beats/min). Breathing 30/min. In the lungs, hard breathing, weakened in the lower parts, isolated wet rales and crepitation in the lower parts on the right. The abdomen is somewhat tense, bloated, peristalsis is preserved. Liver +2 cm, spleen is not palpable. There were no stools at the time of the examination (the previous two days ago, several episodes of loose stools). Urination is independent, diuresis is sufficient. From the next day in the hospital, the patient's condition progressively deteriorated due to increased symptoms of intoxication, hemodynamic disorders, polyserositis, edema, diffuse skin rash, severe hyperesthesia, abdominal syndrome, bilateral non-purulent conjunctivitis. On the 2nd day she was transferred to ICU, where she was treated for 5 days.

At the beginning of hospitalization (25–27.10.2020) in the general analysis of girl's blood: insignificant anemia (102–110 g/l), leukocytosis (45,9–76,3×10^9/l), shift of a leukocyte formula to the left (band neutrophils — 22–25%, Segmented neutrophils — 63–82%, Lymphocytes — 3–8%), ESR — 46 mm/h, platelets were within the reference values (110–128×10^9/l). Blood biochemistry: low total protein (41 g/l); urea, creatinine, bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), electrolytes and sugar — within the reference values; high CRP (24–48 mg/l). Coagulogram: fibrinogen — 4.4 g/l, prothrombin time (PT) — 13.4 s, International normalized ratio (INR) — 1.03; Prothrombin index (PI) — 93.1%. Procalcitonin — 7.65 ng/ml (reference values <0.5 ng/ml). Ferritin — 715 ng/ml (reference values 7–140 ng/ml), CRP — 269.7 ng/ml (reference values <10 ng/ml), D-dimer — 3967 ngFEO/ml (reference values <500 ngFEO/ml), troponin — 356.61 pg/ml (reference values <36.99 pg/ml). General analysis of urine — no deviation.

ECG (25.10.2020): Sinus rhythm. electrical axis of the heart — vertical. Repolarization processes are reduced and changed. Ultrasound of the abdominal cavity (25.10.2020): signs of splenomegaly, mild hepatomegaly, ascites, omentitis, abdominal lymphadenopathy, mesadenitis, intestinal hyperpneumatosis, signs

of toxic nephropathy (changes in the kidneys edematous).

Chest radiography (26.10.2020): vascular-interstitial pattern is moderately enhanced on both sides. On the right in the 1st segment is a zone of reduced pneumatization, the root is expanded. The sinuses are not obstructed. Heart normal according to the age range. *Conclusion:* Right lower lobe pneumonia. Ultrasound of the lungs (26.10.2020): fluid in the pleural sinuses up to 25 mm high.

Echo-KG (26.10.20220): fluid in the pericardium up to 4 mm. Left coronary artery — 2.4 mm, right 2.4–2.8 mm, Coronary wall 2.7 mm. Signs of impaired systolic function of the left ventricle. The walls of the left ventricle are changed (possibly due to edema).

Cytotest COVID-19 (25.10.2020): IgM — negative, IgG — positive.

IFA SARS CoV-2 (27.10.2020): IgM — negative, IgG — positive.

Given the signs of polyserositis (ascites, hydropericardium, hydrothorax), myocardial dysfunction, the presence of skin rash (spot-erythematous), peripheral edema (palms and soles), bilateral non-purulent conjunctivitis, abdominal syndrome, skin and salivary; Acute inflammatory changes in the hemogram, as well as the presence of IgG SARS Cov-2, were diagnosed with complete MIS-C (multisystem inflammatory syndrome) associated with COVID-19.

Therapy: IVIG (2 g/kg), by continuous infusion for 24 hours, antibiotic therapy, infusion support, antithrombotic therapy (under the control of D-dimer), anti-inflammatory therapy, hormone therapy, maintenance therapy.

The dynamic progress was positive. The condition has significantly improved. Laboratory and instrumental parameters gradually normalized. On the 17th day in satisfactory condition discharged home under the supervision of primary care physicians with recommendations: to continue anti-inflammatory and hormone therapy according to the protocol, to repeat in 6 weeks general and biochemical analysis of blood, echocardiography and ultrasound of the kidneys. Supervision by a cardiorheumatologist.

Despite the mildly symptomatic onset of the disease in both clinical cases there was a polymorphism of clinical manifestations with the development of fever, mucosal skin manifestations, gastrointestinal symptoms, cardiac damage, and hemodynamic instability. Patients needed additional extended diagnostics and specific treatment.

Conclusions

PIMS-TS is an important clinical syndrome that resembles atypical / typical KD and has a wide clinical range, including cardiac complications. In contrast to KD, PIMS-TS is found in older children, with a predominance of gastrointestinal symptoms, hemodynamic instability, and myocardial dysfunction. However, the exact pathomechanism still needs to be understood. Detection and diagnosis of PIMS-TS is quite difficult due to the wide range of patients and insufficient study of this problem. The protocol for the treatment of multisystem inflammatory syndrome in children has not yet been approved.

Polymorphism of clinical manifestations of PIMS-TS emphasizes the need for early diagnosis and team care and treatment of children with this syndrome. However, further studies are needed to reflect the long-term prognosis, especially for coronary artery aneurysm in PIMS-TS.

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