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## Multisystem Inflammatory Syndrome Associated with COVID-19. Own Experience

**Conflict of interest:** nothing to declare.

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### Abstract

**Introduction.** In the context of a pandemic, cases of multisystem inflammatory syndrome (MIS-C) are increasingly being reported. Complication is insidious by a variety of manifestations and high efficiency of multiple organ disorders.

**Purpose.** To demonstrate a clinical case of a syndrome associated with SARS-CoV-2 MIS-C complicated by shock, pleural and pericardial effusion in order to increase the vigilance of doctors of various profiles in relation to this condition.

**Materials and methods.** A clinical case of SARS-CoV-2-associated multisystem inflammatory syndrome in an 11-year-old child, which began with abdominal manifestations that mimicked an acute abdomen, followed by the development of shock, pericardial and pleural effusion, and cardiac dysfunction, is presented.

**Results.** This case clearly demonstrates the variety of clinical manifestations of MIS-C in children. The condition requires a team approach by specialists of different profiles for the timely detection and prevention of possible complications.

**Keywords:** COVID-19, multisystem inflammatory syndrome, shock, pleural effusion, pericardial effusion

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## Мультисистемный воспалительный синдром, ассоциированный с COVID-19. Собственный опыт

**Конфликт интересов:** не заявлен.

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### Резюме

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**Введение.** В условиях пандемии все чаще регистрируются случаи мультисистемного воспалительного синдрома (MIS-C). Осложнение коварно разнообразием проявлений и высокой частотой полиорганных нарушений.

**Цель.** Демонстрация клинического случая ассоциированного с SARS-CoV-2 MIS-C-синдрома, осложненного шоком, плевральным и перикардальным выпотом, с целью повышения бдительности врачей различного профиля по отношению к данному состоянию.

**Материалы и методы.** Представлен клинический случай ассоциированного с SARS-CoV-2 мультисистемного воспалительного синдрома у ребенка 11 лет, который начинался с абдоминальных проявлений, имитировавших «острый живот» с последующим развитием шока, перикардального и плеврального выпота и кардиальной дисфункции.

**Результаты.** Данный случай наглядно демонстрирует разнообразие клинических проявлений MIS-C у детей. Состояние требует командного подхода специалистов разного профиля для своевременного выявления и предотвращения возможных осложнений.

**Ключевые слова:** COVID-19, мультисистемный воспалительный синдром, шок, плевральный выпот, перикардальный выпот

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### ■ INTRODUCTION

Since March 2020, a pandemic has been recorded worldwide due to the spread of SARS-CoV-2. An important aspect of the childhood pandemic is the development of the so-called multisystem inflammatory syndrome (MIS-C). This complication of COVID-19 reflects polymorphic symptoms and can lead to severe multiorgan reports. According to the survey (Panigrahy Neha et al. 2020), 91.8% of visitors with MIS-C have fever, disorders of the gastrointestinal tract, which include abdominal pain (52.8%), pasting (44.8%), diarrhea (39.5%), conjunctivitis (44.0%), rash (38.2%), respiratory distress (20.9%) and neurological lesions (17.5%). Cardiovascular symptoms include ventricular dysfunction (39.3%), tachycardia (18.4%), coronary artery dilatation (13.4%), cardiogenic shock (7.1%), chest pain (2.6%), and ventricular arrhythmia (0.3%) [1]. Clinically, the syndrome

is very similar to Kawasaki disease, but against a reduction in the incidence of coronary artery aneurysms in people with MIS-C relative to the bottom, and at the same time when the accession of general heart function is recorded, showing myocardium and/or pericarditis [2]. In addition, Kawasaki disease is more common in children under 5 years of age, while MIS-C occurs in older children [3].

Both diseases are associated with a significant storm of cytokines, which leads to systemic inflammation and myocardial dysfunction [4, 5]. Also, elevated ferritin levels in these patients are a marker of macrophage activation syndrome (MAS) [6]. It was noted that high levels of ferritin are associated with severe disease in MIS-C associated with SARS-CoV-2 [7].

A study conducted by British scientists (Shema Hameed et al. 2020) in 51% of 35 cases of children with MIS-C revealed cardiac dysfunction, manifested by myocardial dysfunction, myocarditis, pancarditis, pericardial effusion and coronary artery aneurysms [8].

In addition, there are data on the occurrence of vasculitis of small and medium-sized vessels, similar to those observed in patients with Kawasaki disease [9].

Detection of autoantibodies in patients with MIS-C has also been reported. Studies show that target antigens for autoantibodies are expressed in mucosal and cardiac tissues, endothelial cells, and cytokine molecules [10, 11]. These autoantigens are also reported in patients with Kawasaki disease [12]. Neutrophils and monocytes expressing Fcγ receptors are responsible for the pathogenesis of the disease, probably by interacting with autoantibodies and leading to the formation of immune complexes [10].

A recently published cohort study (Jackeline J Rodriguez-Smith, et al. 2021) of inflammatory biomarkers in COVID-19-associated MIS-C in children, Kawasaki disease, and macrophage activation syndrome found similar concentrations of S100 protein and interleukin-18 in diseases Kawasaki and MIS-C, but significantly different ligand frequencies of 9-induced IFN $\gamma$  chemokine (CXCL9). The authors suggest that CXCL9 may be a useful biomarker for distinguishing MIS-C from Kawasaki disease, and may also be used to diagnose the severity of MIS-C with high sensitivity and specificity [13].

At present, the pathophysiological mechanisms of this syndrome remain completely unknown and the study of this syndrome and its impact on the cardiovascular system continues.

It is also extremely important to introduce specific clinical biomarkers to distinguish between hyperinflammatory diseases and to determine the clinical severity of MIS-C. Such biomarkers will be essential as the COVID-19 pandemic continues and seroconversion is likely to increase. In addition, research results indicate that biomarkers can be used for clinical monitoring of MIS-C and thus improve diagnostic and treatment algorithms.

## ■ PURPOSE OF THE WORK

To demonstrate diagnostically complicated clinical case of SARS-CoV-2-associated multisystem inflammatory syndrome complicated by shock and pericardial effusion in an 11-year-old patient to increase the vigilance of physicians of various profiles regarding postcovid MIS-C.

## ■ DESCRIPTION OF THE CLINICAL CASE

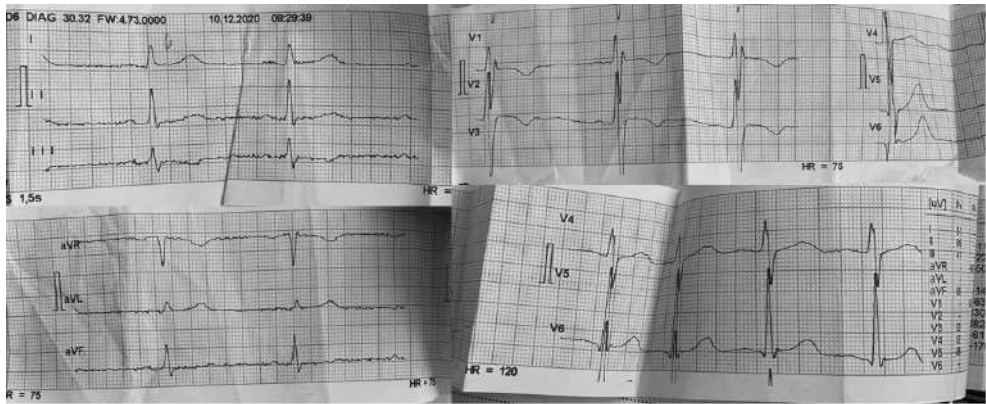
An 11-year-old child went to the doctor with complaints of fever, abdominal pain and skin rash within one day. The family doctor regarded the disease as scarlet fever and

prescribed appropriate treatment: amoxicillin and antipyretics. The child's condition did not improve for three days. On the third day of the disease, due to the lack of positive dynamics, the child was hospitalized in the infectious department of the children's hospital. At the initial examination: the child is in conscious, focused, body temperature 37.6 °C, the skin on the torso and extremities is covered with a polymorphic rash in the form of pink-red spots and irregularly shaped papules. The phenomena of catarrhal conjunctivitis, papillary "raspberry" tongue, enlarged submandibular lymph nodes, hyperemia of the oropharyngeal mucosa, edema of the palms and soles are noted. Free breathing, respiratory rate 22 / min, heart rate 98 / min, regular rhythm, auscultatory picture of the lungs and heart without significant features. Blood pressure on the brachial artery 106/64 mm Hg, SpO2 96%, capillary filling time 2 sec. Abdomen moderately swollen, sensitive along the intestine, mainly in the right iliac region. The size of the liver and spleen is not increased on palpation. There was no medical history of possible contact with infectious patients, including patients with COVID-19. By this time the child was healthy. Kawasaki-like syndrome was suspected. Screening tests showed slight leukocytosis with neutrophil shift (neutrophils 80%), ESR acceleration to 30 mm/h, elevated CRP to 78 ng/ml, decreased platelet count to 87 /  $\mu$ l, rapid COVID-19-negative test. Due to the increase in abdominal pain, the child was consulted by a pediatric surgeon and a decision was made on urgent surgical treatment. During the operation, the appendix did not look unchanged, the audit of the abdominal cavity did not reveal inflammatory processes. Immediately after surgery, the child's condition suddenly deteriorates due to hemodynamic disorders. At physical inspection pallor of skin is observed, time of capillary filling of 5 sec., BP decreased to 83/46 mm Hg. The child was urgently transferred to the intensive care unit. Septic shock was suspected and treatment was started according to the protocol of this syndrome. Infusion of isotonic NaCl solution in a volume of 20 ml/kg for 20 minutes was not effective. Blood pressure after bolus injection of fluid 78/45 mmHg. Repeated bolus administration of isotonic saline was combined with noradrenaline at a dosage of 0.05  $\mu$ g / kg / min. After the second bolus infusion, hemodynamic parameters improved: BP 92/60 mm Hg, Ps 118 / min. Infusion therapy is continued in a maintenance mode, oxygen therapy through a mask.

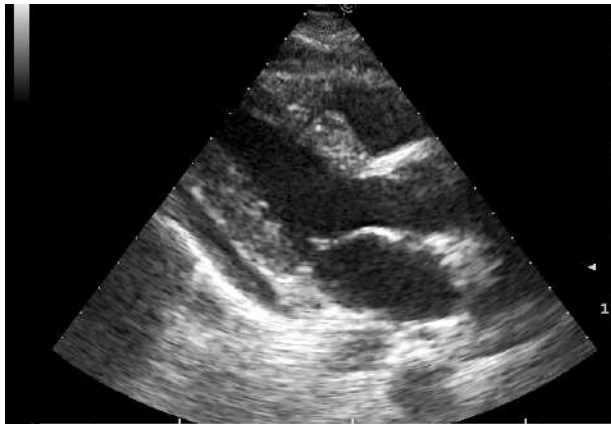
On the fifth day of the disease, laboratory tests were performed in the intensive care unit to verify the diagnosis of Kawasaki-like syndrome. Serum ELISA for the presence of IgG-positive. The level of leukocytes – 14.9 G / l, platelets 85 /  $\mu$ l, neutrophils – 97%, ESR-40 mm/h, D-dimer – 4246.79 ng/ml, ALT – 68 U/l, AST – 45 U/l, bilirubin 36.4  $\mu$ mol/l (direct 28.1  $\mu$ mol/l), creatinine – 55  $\mu$ mol/l, lactate – 2.4 mmol/l, CRP – 98 mg/l, ferritin – 849 ng/ml, procalcitonin – 4.0 ng/ml, APTT – 46 sec, fibrinogen – 3.6  $\mu$ mol/l, IL-6 – 17.2 ng/ml.

According to the results of the ECG (fig. 1) – sinus rhythm, correct, the tendency to tachycardia. Horizontal electrical axis of the heart. Metabolic disorders in the myocardium.

Echocardiography (fig. 2) revealed a decrease in contractile function of the left ventricle (ejection fraction 54%), final diastolic volume – 114 ml, left atrium 28 mm, aortic valve tricuspid, aortic valve size 17/23 mm. Arc left, in the aorta pressure 6 mm Hg Pulsating blood flow in the abdominal aorta, no data on aortic coarctation. Coronary vessels without features. tricuspid valve – speed 0.6, a small return flow through the tricuspid valve (+). Systolic pressure in the right ventricle 35 mm Hg mitral valve V 0.9, a small backflow through the mitral valve. In the right pleural cavity, the accumulation of free fluid up to 2 cm, in the left pleural cavity –2.5 cm (fig. 3).



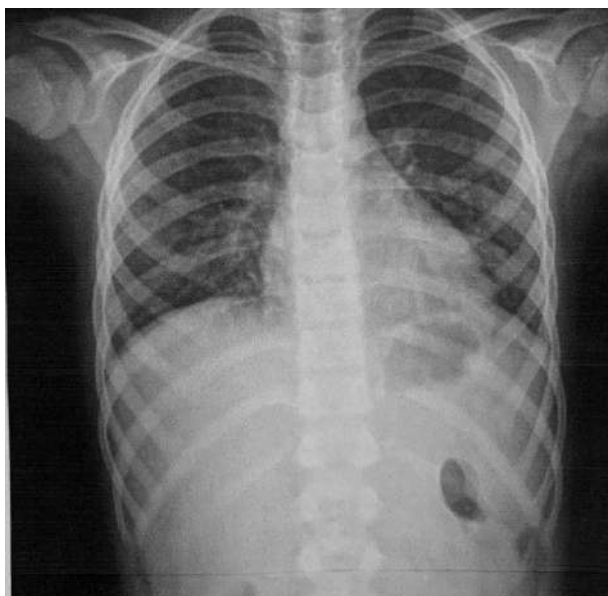
**Fig. 1. Electrocardiography data of a patient with Kawasaki-like syndrome**



**Fig. 2. Echocardiography. Visualization of pericardial effusion in the pleural cavity**



**Fig. 3. Pleural effusion**



**Fig. 4. Chest radiography**

According to the results of X-ray examination (fig. 4) pulmonary fields without pathological shadows, the pulmonary pattern is enhanced by peribronchial infiltration. The roots are unstructured, heavy.

According to the clinical picture and examination results, the child met the criteria of the Ministry of Health of Ukraine for multisystem inflammatory syndrome associated with COVID-19 [14]. According to the accepted recommendations, human immunoglobulin was prescribed for intravenous administration in a dosage of 2 g/kg. Prior to the exclusion of bacterial etiology, he received antibacterial therapy (imepenem/cilastatin and vancomycin) and anti-inflammatory therapy (dexamethasone). Against the background of immunoglobulin receiving, a significant reduction in the cutaneous manifestations of the syndrome (rash) and conjunctivitis was visually observed. Decreased levels of hepatic aminotransferases and bilirubin were observed in the laboratory. In total, the patient spent 11 days in the intensive care unit. Against the background of positive clinical and laboratory dynamics (decrease in the level of leukocytes from the peak  $41.8 \cdot 10^9$  to  $9.6 \cdot 10^9$ , decrease in the level of D-dimer, decrease in ESR, normalization of APTT, decrease in visual manifestations – rash and conjunctivitis) pediatric department. He was discharged for outpatient observation after 25 days of inpatient treatment in a satisfactory condition.

## ■ CONCLUSIONS

Manifestations of MIS-C in children are diverse and require a team approach by specialists of different profiles (supervision of surgeons, infectious disease specialists, cardiologists). Diagnosis of MIS-C is complicated by the lack of pathognomonic clinical picture and specific diagnostic methods.

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