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Kawasaki-Like Multisystem Inflammatory Syndrome in Children with SARS-Cov-2 Infection in Republic of Moldova- Case Reports

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Summary- Infection with the new type of coronavirus SARS-CoV-2 is a real challenge for the entire medical and scientific community. It forces the health care institutions to deal with a record number of patients, and often, there are contradictory statements about this virus because of its chameleonic features. As the COVID-19 pandemic continues to expand, several clinical cases with the multisystem inflammatory syndrome in children (MIS-C) similar to the Kawasaki disease have reported in many studies. The exact pathophysiological mechanisms are still unknown, but most children have multiple organ dysfunctions, while respiratory damage is less pronounced than adults. Typical clinical manifestations of MIS-C include fever and impairment to two or more organ systems, with evidence data of inflammation and laboratory or epidemiological evidence of SARS-CoV-2 infection. The present paper describes the clinical manifestations of 5 clinical cases with Kawasaki disease that met the criteria for the MIS-C case definition issued by the WHO.

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Kawasaki-Like Multisystem Inflammatory Syndrome in Children with SARS-Cov-2 Infection in Republic of Moldova– Case Reports

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Summary- Infection with the new type of coronavirus SARS-CoV-2 is a real challenge for the entire medical and scientific community. It forces the health care institutions to deal with a record number of patients, and often, there are contradictory statements about this virus because of its chameleonic features. As the COVID-19 pandemic continues to expand, several clinical cases with the multisystem inflammatory syndrome in children (MIS-C) similar to the Kawasaki disease have reported in many studies. The exact pathophysiological mechanisms are still unknown, but most children have multiple organ dysfunctions, while respiratory damage is less pronounced than adults. Typical clinical manifestations of MIS-C include fever and impairment to two or more organ systems, with evidence data of inflammation and laboratory or epidemiological evidence of SARS-CoV-2 infection. The present paper describes the clinical manifestations of 5 clinical cases with Kawasaki disease that met the criteria for the MIS-C case definition issued by the WHO.

Keywords: kawasaki disease, multisystem inflammatory syndrome, sars-cov-2, child, clinical case.

I. Introduction

Although the first published studies reported a relatively slight benign course of SARS-CoV-2 infection in children, in late April - early May 2020, appears a new presentation of Covid-19 in the pediatric population, as the pediatric multisystemic inflammatory syndrome temporarily associated to the SARS-CoV-2 infection, which has similar characteristics to other pediatric inflammatory conditions such as the Kawasaki disease, staphylococcal and streptococcal toxic shock syndrome, bacterial sepsis, macrophage activation syndrome. It can also debuted with excessively high inflammatory markers and abdominal syndrome, which can mimic appendicitis or typhoid fever [1]. The Kawasaki disease (KD), also called and amucocutaneous lymph node syndrome, is one of the most common acute systemic vasculitides of childhood, involving medium-sized arteries, especially coronary arteries; the clinical picture describes an acute-onset with high fever, generalized polymorphic exanthema, palmoplantar erythema, symmetric nonpurulent conjunctivitis, usually unilateral cervical lymphadenopathy which is lasting approximately 12 days, and mucosal enanthema with red and chapped lips [2].

The etiology, immunology, and pathophysiology of KD are not yet fully understood, although elements of the immune system play an key role [3]. KD, in both its typical and atypical presentations, has been described as being associated with infectious agents such as Streptococcus pyogenes, Staphylococcus aureus, and Yersinia pseudotuberculosisas well as viral infections such as adenoviruses, enteroviruses, Ebstein-Barr virus, and coronaviruses non- SARS-CoV-2 [4,5], and approximately 2% of children may develop macrophage activation syndrome [6].

Scientists have concluded that KD is the leading cause of coronary heart disease in the pediatric population. The most worrying complication of KD is aneurysmal dilation of the coronary arteries, which can be detected by echocardiography starting with the 2nd week of the convalescence stage [2]. Recently, several scientific journals have published a series of KD cases associated with SARS-CoV-2 infection, among the most consistent being those reported in the United Kingdom, Italy, France, the United States, Turkey [7- 12].

II. Aim

The present article aims to highlight an overview of the main features of MIS-C temporarily associated with SARS-CoV-2 infection similar to the Kawasaki disease.

III. Materials and Methods

This is a single-center prospective observational study. This case series report describes five pediatric patients with MIS-C, admitted between April 22 and October 9, 2020, in a tertiary Pediatric Health Care Institution named Institute of Mother and Child from Chisinau. The analyzed variables included anamnestic data, demographic information, general clinical manifestations, epidemiological data certifying exposure to SARS-CoV-2 infection, the laboratory results and imaging investigations, and the evolution of the disease by the implemented therapeutic tactics.

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The MIS-C patients included in the study met the recently revised WHO definition - Children and adolescents aged 0 to 19 years with fever ≥ 3 days, plus 2 of the following: a) Rash or bilateral non-purulent conjunctivitis or signs of mucocutaneous inflammation (oral, hands, feet); b) Hypotension or shock; c) Characteristics of myocardial dysfunction, pericarditis, valvulitis or coronary artery abnormalities, including imaging evidence (echocardiography) and laboratory tests (increased troponin levels and / or NT-proBNP); d Evidence of coagulopathy (eg, increased prothrombin time / INR, time of partially activated thromboplastin, level of D-dimers); e) Acute gastrointestinal symptoms (vomiting, diarrhea) or abdominal pain; and Increased inflammatory markers, such as ESR, PCR, or procalcitonin, and No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndrome, and Proof of COVID-19 (RT-PCR, positive serological tests), or possible contact with patients tested positive for COVID-19.

The Kawasaki disease was defined conforming to the criteria of the American Society of Cardiology, including both classic types (fever≥ five days plus four or more of the following clinical criteria: non-exudative bulbar conjunctivitis, changes in the lips or oral mucosa, non-suppurative later cervical lymphadenopathy, erythematous polymorphous skinrash, erythema of the palms or soles, firm induration of the hands or feet, or both - for the complete type of disease, and fever ≥ five days plus 2 or 3 mentioned clinical criteria - for the incomplete type).

IV. Results

The age of the five patients diagnosed with MIS-C similar to the Kawasaki disease was between 8 months and ten years. When looking at gender distribution, a female prevalence (80%) to males (20%) was noted. Table 1 shows the characteristics of patients admitted for Kawasaki-like multisystem inflammatory syndrome in children. All patients included in the study had at least one evidence of SARS-CoV-2 infection, 2 (40%) of whom were tested positive by RT-PCR in the nasopharyngeal swab. In contrast, the other 3 (60%) showed positive serological evidence data of anti-SARS-CoV-2 IgG and IgM. Patients 3 and 5, concomitant with serological evidence of SARS-CoV-2 infection, also presented serological evidence of latent Ebstein Barr virus (EBV) infection. Clinical manifestations present at time of the admission to hospital included persistent drug-resistant fever, polymorphic skin rush without blisters or crusts and non-pruritic, signs of peripheral skin inflammation expressed by palmar or plantar erythema, and abdominal pain in 100% of cases. Four (80%) of the five patients showed non-exudative bulbar conjunctivitis and signs of damage to the oral mucosa manifested by red and cracked lips, raspberry tongue with hypertrophied papillae and diffuse oropharyngeal erythema. Unilateral cervical lymphadenitis was present in patients 1, 2, and 3 (60%); in patient 4 bilateral cervical lymphadenitis was found, while in patient five, it was not detected. Patients 2 and 5, at the beginning of the disease, also presented clinical manifestations from the digestive system expressed by diarrhea and single vomiting.

When analyzing the results of laboratory investigations, the increase of acute phase reactants of inflammation was detected in 100% of cases, varying for each case. Thereby, the erythrocyte sedimentation rate and hyperfibrinogenemia were recorded in 60% of cases (patients 1, 2 and, 4), while there was an increase in the C-reactive protein in 100% of cases, its values varying between 12 and 96 mg / L. In the early stages of the disease, leukocytosis was present in 80% of patients (except patient 4), neutrophilia in 60% of cases (patients 2,3 and 5), lymphopenia (except patient 1), and anemia (patients 1,2, 4, 5) in 80% of cases, which on the background of treatment returned to reference values. In patients 3 and 5 (40%) changes in platelet count showed thrombocytopenia, and patients 1, 3, and 4 (60%)had thrombocytosis. Patient 3 initially presented with thrombocytopenia and later developed thrombocytosis. Other changes found in the analysis of biological blood samples were syndrome of nitrogen retention manifested by elevated serum creatinine and urea levels in patients 2 and 5 (40%), increase of the liver transaminases in patient 3 (20%),and elevation of the MB fraction of creatinekinase in 80% of cases (except for 1). Patients 2 and 5, along with the syndrome of nitrogen retention, also presented insignificant proteinuria, which on the background of the corticosteroid therapy was negative. Echocardiographic examinations performed during hospitalization showed no signs of impaired myocardial contractility, pericardial suffusion, or aneurysmal dilatation of the coronary arteries in any of the five patients, while on examination by electrocardiogram prolonged QT interval in patient 5 was detected. 80% of patients hadtypical imaging signs for uni- or bilateral pneumonia, detected via chest radiographs, even though they presented poor respiratory symptoms.

All 5 cases required at least 24 hours of monitoring in the intensive care unit; patient two also needed oxygen support. The treatment included corticosteroids, antibiotics, antiaggregant drugs, and symptomatic therapy depending on the situation. The therapeutic response was positive in 100% of cases. Patients were discharged with recommendations to return later for a check on the long-term course of the disease and early identification of possible complications specific to the Kawasaki disease that may occur remotely. To date, none of the patients included in the study have developed any complications.

Table N.1: Characteristics of patients admitted for Kawasaki-like multisystem inflammatory syndrome

	Case 1	Case 2	Case 3	Case 4	Case 5
Age, years	8 months	7	10	1.5	7
Sex	Female	Female	Female	Male	Female
Date of admission	May 22, 2020	June 10, 2020	July 10	August 28, 2020	October 9,2020
Clinical features	Fever, conjunctivitis, unilateral cervical lymphadenopathy, maculo-papular rush, cough, abdominal pain, hepato- and splenomegaly (+2,5-3,0 cm), tachycardia.	Fever, conjunctivitis, unilateral cervical lymphadenopathy, maculo-papular rush, diffuse erythema of the oral mucosa, intensely red and cracked lips, signs of peripheral skin inflammation (palms and soles),myalgias, arthralgias,headache, abdominal pain, vomiting and diarrhea, lethargy, tachycardia, hypotension, hepatomegaly (+2,5 cm); Down syndrome.	Fever, conjunctivitis, unilateral cervical lymphadenopathy, maculo-papular rush, diffuse erythema of the oral mucosa, intensely red and cracked lips, signs of peripheral skin inflammation (palms and soles), myalgias, arthralgias, lethargy, headache, abdominal pain, tachycardia.	Fever, conjunctivitis, bilateral cervical lymphadenopathy, maculo-papular rush, diffuse erythema of the oral mucosa, intensely red and cracked lips, signs of peripheral skin inflammation (palms and soles), abdominal pain, general malaise, he refuses to drink and eat, tachycardia, hepatomegaly (+1,5 cm).	Fever, abdominal pain, maculo-papular rush, diffuse erythema of the oral mucosa, signs of peripheral skin inflammation (palms and soles), lethargy, tachycardia, abdominal pain, headache and diarrhea.
Duration of fever, days	16	8	5	9	6
Laboratory results: Inflamatory markers	CRP – 24 mg/L; ESR – 52 mm/h; fibrinogen – 6,6 g/L	CRP – 96 mg/L; ESR – 40 mm/h; fibrinogen – 4,34 g/L.	CRP – 12mg/L; ESR – 8 mm/h; fibrinogen – 3,77 g/L	CRP – 24mg/L; ESR – 33 mm/h; fibrinogen – 4,88 g/L	CRP – 96mg/L; ESR – 10 mm/h; fibrinogen – 2,2 g/L; ferritin – 388ng/mL.
Laboratory results: General blood test	WBC - 16,3; neutrophil – 21,0; lymphocyte -68%; platelet – 449; Hb-94g/L	WBC - 11,8; neutrophil – 83,0; lymphocyte -12%; platelet – 201; Hb-90g/L	WBC - 20,7; neutrophil – 87,0; lymphocyte -11%; platelet – initially 77, later547; Hb- 156 g/L.	WBC - 5,8; neutrophil – 64,0; lymphocyte -34%; platelet – 1047; Hb-102 g/L	WBC - 17,4; neutrophil – 89,0; lymphocyte -6%; platelet – 71; Hb-99 g/L.
Laboratory results: Renal fuction& serum electrolytes	Creatinine – 38 μmol/L; urea – 0,6 mmol/L; Na – 129 mmol/L; K-4,10 mmol/L ; protein in the urine-negative	Creatinine – 65 μmol/L; urea – 16,3 mmol/L; Na –143 mmol/L; K- 3,91 mmol/L; Ca – 2,07 mmol/L; protein in the urine- 0,08 g/L.	Creatinine – 67 μmol/L; urea – 5,77 mmol/L; Na – 147 mmol/L; K- 3,71 mmol/L; protein in the urine- negative	Creatinine – 47 μmol/L; urea – 2,82 mmol/L; Na –139 mmol/L; K- 5,39 mmol/L; protein in the urine- negative	Creatinine – 107 μmol/L; urea – 11,83 mmol/L; Na –146 mmol/L; K-4,30 mmol/L; protein in the urine – 0,04g/L
Laboratory results: Liver function & other biochemistry	ALT – 30,6 iu/L; AST – 13,8 iu/l; LDH – 244 iu/L; CK – 46 iu/L.	ALT – 26,5 iu/L; AST – 25,4 iu/l; LDH – 317 iu/L; CK – 51 iu/L; total protein – 53,1 g/L; triglycerides – 3,10 mmol/L.	ALT – 99,0 iu/L; AST – 48,0 iu/l; LDH – 249 iu/L; CK – 46 iu/L; total protein – 55,0 g/L; triglycerides – 2,20 mmol/L.	ALT – 15,6 iu/L; AST – 22,5 iu/l; LDH – 276 iu/L; CK – 26 iu/L; ; total protein – 61 g/L; triglycerides – 1,65 mmol/L; pH – 7,44, HCO3- 16,9; BE – 7,3 mmol/L; lactate – 2,55 mmol/L.	ALT – 22,8 iu/L; AST – 27,4 iu/l; LDH – 230 iu/L; CK – 47 iu/L; total protein – 43,3 g/L;
Laboratory results: Cardiac markers	CK MB – 57,7 iu/L.	CK MB – 23,7 iu/L.	CK MB – 29,1 iu/L.	CK MB – 36,0 iu/L.	CK MB – 38,6 iu/L.
Imaging	CXR:Signs of bronchitis.	CXR: Signs of	CXR: Signs of	CXR: Signs of	CXR: Signs of

findings and functional examinations	Pulmonary CT: Normal; Echocardiography: Normal function. No pericardial effusion, no coronary arteries dilatation (LCA – 1,9 mm, RCA – 2,3 mm). ECG - Irregular sinus rhythm. Partial block through the right branch of the His beam	unilateral pneumonia on the left. In S3, S10 on the left - small discoidal atelectasis, in S10 on the left - fibroatelectasis. Pulmonary CT:fibro-atelectatic areas in S3, S6, S10 on the left and in S5 on the right. Multiple bilateral basal pleuropulmonary adhesions. Echocardiography: Normal function. No pericardial effusion, no coronary arteries dilatation (LCA – 2,0 mm, RCA – 2,0 mm). ECG - Regular sinus rhythm. The electrical potential of the LV increased.	bilateral pneumonia. Pulmonary CT:pleuropulmonary adhesions associated with moderate left basal pleural thickening in S10 on the left Echocardiography: Normal function. No pericardial effusion, no coronary arteries dilatation (LCA – 3,0 mm, RCA – 2,0 mm). ECG - Sinus rhythm. Bradycardia.	bilateral pneumonia. Pulmonary CT: Normal. Echocardiography: Normal function. No pericardial effusion, no coronary arteries dilatation (LCA – 3,0 mm, RCA – 2,0 mm); ECG - Irregular sinus rhythm. Tachycardia.	unilateral bronchopneumonia on the left. Pulmonary CT: minimal bilateral inflammatory changes in incomplete resorbtion. Solitary micronode in S5 on the left. Echocardiography: Normal function. No pericardial effusion, no coronary arteries dilatation (LCA – Not visible, RCA – 2,0 mm). ECG - Sinus rhythm, tachycardia, pronounced disorders of repolarization processes, prolonged QT syndrome (515 ms)
Microbiological results (bacterial)	Blood culture no growth; No pyuria; Throat swab – no growth	Blood culture no growth; No pyuria; ASOT – >400 iu/mL; Throat swab – Streptococcus viridans 10^5.	Blood culture no growth; No pyuria; ASOT – negative Throat swab – Streptococcus viridans 10^5.	Blood culture no growth; No pyuria; Throat swab – Corinebacterium spp. 10^4.	Blood culture no growth; No pyuria; ASOT – negative Throat swab – Staphylococcus aureus10^3.
Microbiological results (virology)	Nasopharyngeal swab SARS-CoV-2 RT-PCR – positive; SARS-CoV-2 IgG – positive; SARS-CoV-2 IgM - positive;	Nasopharyngeal swab SARS-CoV-2 RT-PCR – negative; SARS-CoV-2 IgG – positive; SARS-CoV-2 IgM - positive;	Nasopharyngeal swab SARS-CoV-2 RT-PCR – negative; SARS-CoV-2 IgG – positive; SARS-CoV-2 IgM - positive;	Nasopharyngeal swab SARS-CoV-2 RT-PCR – positive; SARS-CoV-2 IgG – positive; SARS-CoV-2 IgM - positive;	Nasopharyngeal swab SARS-CoV-2 RT-PCR – negative; SARS-CoV-2 IgG – positive; SARS-CoV-2 IgM - positive;
Treatment	Dexamethasone, Amoxicillin, cefuroxime, Ibuprofen, fluconazole	Prednisolone, Imipenem, Amikacin, Aspirin; Mask oxygen therapy -1day. Fluid bolus 20 ml/kg.	Prednisolone, Aspirin; Ceftazidime	Prednisolone, Ceftriaxone, Azithromycin, Dipyridamole; Fluid bolus 25 ml/kg.	Prednisolone, Amikacin, Ceftriaxone, Dipyridamole. Fluid bolus 30 ml/kg.
Length of PICU Length of hospital stay	1 day 13 days	5 days 14 days	3 days 10 days	2 days 13 days	6 days 13 days

Abbreviations: ALT, alanine transaminase; ASOT, antistreptolysin O titer; AST, aspartate transaminase; CK, creatine kinase; CK MB, creatine kinase MB; CRP, C-reactive protein; CT, computed tomography; CXR, chest X-ray; ECG, Electrocardiography;Hb, hemoglobin; IgG, immunoglobulin G; IgM, Immunoglobulin M; LCA, left coronary artery; LDH, lactate dehydrogenase; LV, left ventricle; PCR, polymerase chain reaction; PICU, pediatric intensive care unit; RCA, right coronary artery; WBC, white blood cell.

V. Discussions

Initially, it was reported that SARS-CoV-2 infection in children had mild clinical manifestations, with few hospitalizations in intensive care units and very few deaths reported. Children infected with SARS-CoV-2 may have asymptomatic evolution or may have a fever, respiratory and gastrointestinal symptoms [13]. As of April 2020, in the United Kingdom, the scientists identified that children with persistent fever, increased acute phase reactants (neutrophilia, increased PCR and lymphopenia), single or multi-organ dysfunction as MIS-C relative to SARS-CoV-2. The phenotypes in this category are typical or atypical KD, KD shock syndrome, toxic shock syndrome, and macrophage activation syndrome (MAS) [14]. In this study, we analyzed only the group of patients who met the criteria for typical or atypical KD, associated with COVID-19. The temporary association between the clinical and paraclinical manifestations of MIS-C and the presence of laboratory evidence of SARS-CoV-2 infection in the five children included in our small cohortsupports the etiopathogenic

hypothesis that this syndrome is the result of a post-infectious immune response. According to recent reports, pediatric multsystemic inflammatory syndrome often begins 1-6 weeks after the SARS CoV-2 infection and may overlap with an acute respiratory presentation of COVID-19 [14].

In our cohort, the most common clinical manifestations were drug-resistant prolonged febrile syndrome and skin syndrome. Fatigue, myalgia, arthralgia, headache, frequently described in adults, were less expressed by children, which could be explained by their inability or difficulty to report them (60% of patients included in our study were less than five years old or had difficulty expressing language). Although our patients showed signs and symptoms characteristic of the Kawasaki disease, such as fever, rash, changes in the oral mucosa, conjunctivitis, cervical lymphadenopathy, thrombocytosis (in later stages of the disease), there were some differences from the classic KD, such as affecting older children, affecting the respiratory system (documented by means of imaging methods), gastrointestinal disorders, lymphopenia and thrombocytopenia, which in some cases has progressed to thrombocytosis. The Kawasaki disease is a clinical diagnosis, and there is currently no specific diagnostic test. It may present itself atypically as a KD shock syndrome and rarely as a macrophage activation syndrome. McCrindle BW et al. believe that KD may be a manifest a genetic predisposition to an abnormal immune response to some specific infectious agents [15].

Renal impairment expressed by the syndrome of nitrogen retention and insignificant proteinuria registered at patients 2 and 5 may be explained by the presence of SARS-CoV-2 receptors type ACE 2 in the kidneys. Simultaneously, these two patients also presented clinical manifestations of digestive disorders expressed by diarrhea and vomiting in patient 2, thus suggesting prerenal involvement. The proposed specific mechanisms for COVID-19 secondary renal damage are associated with ACE 2 receptors (angiotensin-converting enzyme 2), recognized as receptors for SARS-CoV-2 and are located on the surface of epithelial cells in the lungs, heart, kidneys, gastrointestinal system, testicles, basal epidermal cells, and hair follicles, as well as central nervous system cells. Thus, the S1 subunit of the viral protein S binds to the ACE-2 receptor, activating angiotensin II. The transmembrane protease serine 2 (TMPRSS2) cleaves and primes the S protein, facilitating the release of viral fusion peptides, thus achieving membrane fusion. In their article„ Multiorgan and renal tropism of SARS-CoV-2„ published online on May, 13th, Puelles VG et al. state that co-expression of ACE-2 and TMPRSS2 plays arelevant role in easing the genome penetration [16]. Through viral invasion, SARS-CoV-2 could have a direct cytopathic effect on renal cells [16]. One of the first studies that aimed to highlight the kidney damage associated to SARS-CoV-2 infection is the one conducted by Stewart DJ et al. in Great Britain. According to this study, about half of the 52 children hospitalized with COVID-19 had evidence of renal dysfunction, and about a quarter of them met the criteria for acute kidney injury [17].

Four of the five children included in the study showed signs of myocardial inflammation expressed by elevated MB creatine phosphokinase, and patient five also had documented driving disorders on the electrocardiography by prolonging the QT interval, which disappeared at the next hospitalization. The pathogenesis of COVID-19-related myocardial injury in children is unknown. A recent Chinese study suggests that SARS CoV-2is much less common in children, because of the lower ACE2 than in adults [18]. Cui et al. reports information on acute myocarditis associated with SARS-CoV-2 infection in a 55-day-old infant who had elevated cardiac troponin levels at admission [19]. Another study that describes heart failure in MIS-C is conducted in the Bronx, NY, by Einat B. and al. on a group of 19 children, where 1 of the three patients with evidence of heart damage developed ectatic dilation of the coronary artery [20]. The pediatric patients mentioned in that study will require dynamic monitoring, taking into account the risk of cardiac damage in later stages of KD and the unpredictable evolution of MIS-C.

VI. Conclusions

The multisystemic inflammatory syndrome in children similar to the Kawasaki disease is an emerging condition; at the same time, knowledge about pathogenetic mechanisms, risk factors, and long-term implications are limited and often contradictory. A multidisciplinary approach is indispensable for the early identification of this nosology and the initiation of correct treatment to prevent long-term complications. It is meaningful to ascertain if MIS-C in children is a new entity or SARS-CoV-2 act like a new trigger for the Kawasaki disease. This specification will avoid delaying prompt and targeted treatment.

References Références Referencias

1. Götzinger, FlorianPfefferle, Jasmin et al. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study; The Lancet Child & Adolescent Health, Volume 4, Issue 9, 653 – 661.
2. Younger DS. Epidemiology of the Vasculitides. Neurol Clin 2019; 37:201;
3. A Franco, R Touma, Y Song, C Shimizu, AH Tremoulet, JT Kanegaye, et al. Specificity of regulatory T cells that modulate vascular

inflammation Autoimmunity, 47 (2) (Mar 2014), pp. 95-104;
4. Kikuta H, Sakiyama Y, Matsumoto S et al (1993) Detection of Epstein-Barr virus DNA in cardiac and aortic tissues from chronic, active Epstein-Barr virus infection associated with Kawasaki disease-like coronary artery aneurysms. J Pediatr 123(1):90–92;
5. Komatsu H, Fujisawa T (2008) Kawasaki disease and infection. Nihon Rinsho 66(2):278–282;
6. Viral infections associated with Kawasaki disease. Chang LY, Lu CY, Shao PL, et al. J Formos Med Assoc. 2014;113:148–154;
7. Akca, U.K., Kesici, S., Ozsurekci, Y. et al. Kawasaki-like disease in children with COVID-19. Rheumatol Int 40, 2105–2115 (2020). https://doi.org/10.1007/s00296-020-04701-6;
8. Toubiana J, Poirault C, Corsia A, et al. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. 2020. https://doi.org/10.1136/bmj.m2094.
9. Verdoni L, Mazza A, Gervasoni A et al (2020) An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet 395:1771–1778.
10. Feldstein LR, Rose EB, Horwitz SM et al (2020) Multisystem inflammatory syndrome in US children and adolescents. N Eng J Med 383(4):334–346. https://doi.org/10.1056/NEJMoa2021680.
11. Davies P, Evans C, Kanthimathinathan HK et al (2020) Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK: a multicentre observational study. Lancet Child Adolesc Health 4(9):669–677. https://doi.org/10.1016/S2352-4642(20)30215-7;
12. Riphagen S, Gomez X, Gonzalez-Martinez C et al (2020) Hyperinflammatory shock in children during COVID-19 pandemic. Lancet 395(10237):1607–1608. https://doi.org/10.1016/S0140-6736(20)31103-X;
13. Castagnoli R, Votto M, Licari A, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review [published online ahead of print April 22, 2020]. JAMA Pediatr. 2020. https://doi.org/10.1001/jamapediatrics. 2020;
14. WHO. Multisystem inflammatory syndrome in children and adolescents with COVID-19. https://www.who.int/publications/i/item/multisystem-inflammatory-syndrome-in-children-andadolescents-with-covid-19;
15. McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. Circulation. 2017;135(17): e927-e999.
16. Puelles VG, Lütgehetmann M, Lindenmeyer MT. Multiorgan and renal tropism of SARS-CoV-2. N Eng J Med. 2020 doi: 10.1056/NEJMc2011400. Publishedonline May 13.
17. Stewart DJ, Hartley JC, Johnson M, Marks SD, du Pré P, Stojanovic J. Renal dysfunction in hospitalised children with COVID-19. Lancet Child Adolesc Health. 2020; 4(8): e28-e29. doi: 10.1016/S2352-4642(20)30178-4;
18. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. Pediatrics. 2020; 145: e20200702. doi: 10.1542/peds.2020-0702.
19. Cui Y, Tian M, Huang D, et al. A 55-day-old female infant infected with 2019 novel coronavirus disease: presenting with pneumonia, liver injury, and heart damage. J Infect Dis. 2020; 221:1775–1781. doi: 10.1093/infdis/jiaa113;
20. Einat Blumfield and Terry L. Levin. COVID-19 in pediatric patients: a case series from the Bronx, NY; Pediatr Radiol. 2020 Jul 29: 1–6. doi: 10.1007/s00247-020-04782-2.