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Research Article

The Study of the Association of Kawasaki Disease and it's Variants in Pediatric COVID-19 Cases

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Abstract

Background: A recent trend in the COVID-19 patients showing post-infectious hyper-inflammatory syndrome like Kawasaki disease (KD) and its variants like atypical KD and KD shock syndrome have been reported all around the United States and Europe especially in the pediatric population.

Methods: In this systematic review, we examined pediatric cases of COVID-19 viral infection progressing to KD and its variants with literature search using PubMed/Medline, Web of Science, SCOPUS and Google Scholar.

Results: We reviewed twenty seven (10 females/13 males/4 unknown sex) cases (mean age, SD; 9.0 ± 3.7) who developed KD and its variants like atypical KD and KD shock syndrome with concurrent COVID-19 infection. Out of 27 patients 7 (25.9%) were SARS-CoV-2 positive on PCR while 20 (74.0%) had positive antibodies. We found 6 (22.2%) cases with atypical KD, 15 (55.5%) cases of KD shock syndrome and 6 (22.2%) with classic KD symptoms. Out of 27 cases, 24 (88.9%) required pediatric intensive care unit (PICU) admission, who responded well with inotropes, steroids and intravenous immunoglobulin treatment leading to recovery. One reported death was due to infarction of right middle and anterior cerebral arteries. Regarding coronary artery dilatations, one case had severe bilateral coronary artery dilatation, one had mild left coronary artery dilatation whereas two cases had right coronary artery dilatation. Three cases (11.1%) required extracorporeal membrane oxygenation (ECMO) for respiratory support.

Conclusion: Pediatricians should have a very high index of suspicion for the development of post-infectious KD and its variants in children affected by COVID-19 which may warrant emergent care in the PICU setting. Although most of the cases described had excellent outcomes, few cases may decompensate rapidly due to hemodynamic instability.

Keywords: *COVID-19; Kawasaki Disease; Kawasaki Shock Syndrome; Atypical Kawasaki Syndrome; Systematic Review*

Introduction

Kawasaki disease (KD) is an acute systemic vasculitis of medium-sized vessels affecting mostly infants and children. It is considered as the most common childhood primary vasculitis. Classic symptoms of KD include fever, symmetric non-purulent conjunctivitis, erythema of skin, palms and soles and mucous membranes and unilateral cervical lymphadenopathy [1]. Nearly 1/3rd of patients are at higher risk of developing complications particularly coronary artery aneurysms [2,3]. COVID-19 viral infection also known as Systemic Acute Respiratory Syndrome Coronavirus type-2 (SARS-CoV-2) was first started in Wuhan, China in December 2019; has shown human to human trans-

mission via contact or droplets with a mean incubation period of 2 - 14 days [4]. Symptoms usually begin with fever, cough, shortness of breath and also associated with runny nose, fatigue, headache, sore throat, nausea, diarrhea and anosmia in some patients. It also includes complications like pneumonia, acute respiratory distress syndrome and other systemic manifestations [5]. In the pediatric population, there have been few case-reports of classic KD, atypical KD or KD shock syndromes with moderate to severe prognosis [6]. There has been surge in the cases of multisystem inflammatory syndrome in children(MIS-C) affected with COVID-19 defined by CDC as inflammation of eyes, heart, lung, kidneys, brain as well symptoms like vomiting, diarrhea and blood shot eye [7]. However, this study primarily focuses on Kawasaki disease and it's variants. The cases with overlapping features of macrophage activation syndrome and KD shock syndrome have been excluded from the study [8].

Aim of the Study

The aim of this paper is to review pediatric cases of KD and its variants following COVID-19 infection and along with associated complications and outcomes.

Methods

A thorough search in PubMed/Medline, Web of Science, SCOPUS and Google Scholar was performed from January 1st, 2020 to June 14th 2020 for case reports and case series. Our search strategy included the key term: COVID-19 combined with KD, atypical KD or KD shock syndrome. All the published case reports written in English were included in the final analysis. Data from the article were curated and summarized in the form of country of origin, age and gender of the patients, their presenting complaint, any coexisting comorbidities, medical interventions during the course of hospitalization and their outcome (Table 1 and 2). Continuous variables were presented as means ± standard deviations and categorical data as absolute values and percentages.

S. No	Author	Age/Sex	Country	COVID-19 testing method	Presenting symptoms
1	Blondiaux., *et al*. [9]	6/	France	SARS-CoV IgG test positive	Fever for 7 days, abdominal pain, vomiting, diarrhea
2	Blondiaux., *et al*. [9]	8/	France	SARS-CoV IgG test positive	Fever for 4 days, abdominal pain
3	Blondiaux., *et al*. [9]	12/	France	SARS-CoV IgG test positive	Fever for 5 days, abdominal pain, vomiting and diarrhea
4	Blondiaux., *et al*. [9]	11/	France	SARS-CoV IgG test positive	Fever since 2 days, vomiting, abdominal pain and fatigue
5	Chiu., *et al*. [12]	10/M	USA	SARS-CoV PCR nasopharyngeal swab positive	Fever for 7 days, fatigue, diarrhea, cough, rash, and conjunctivitis
6	Chiotos., *et al*. [10]	5/F	USA	SARS-CoV PCR test positive	Fever for 4 days, mucosal changes, conjunctivitis, swollen hands, nuchal rigidity
7	Chiotos., *et al*. [10]	5/F	USA	SARS-CoV IgG test positive, SARS-CoV nasopharyngeal swab negative	Fever for 5 days, bilateral conjunctivitis, irritability, lethargy, nuchal rigidity
8	Chiotos., *et al*. [10]	9/F	USA	SARS-CoV PCR test positive	Fever, diarrhea, intermittent periumbilical pain
9	Chiotos., *et al*. [10]	12/M	USA	SARS-CoV RT-PCR nasopharyngeal swab Negative, SARS-CoV PCR test positive	Fever for 6 days, abdominal pain, diarrhea, mucus membrane changes, fissured lips
10	Chiotos., *et al*. [10]	14/F	USA	SARS-CoV RT-PCR nasopharyngeal swab Negative, COVID 19 antibody titer positive	Fever for 5 days, diarrhea, rash, headache
11	Greene., *et al*. [13]	11/F	USA	SARS-CoV PCR nasopharyngeal swab positive	Sore throat for 4 days, malaise, poor appetite, generalized rash on hands

12	Jones., *et al*. [14]	0.5/F -Term infant	USA	RT-PCR nasopharyngeal swab positive	Fever, fussiness and refusal to eat
13	Leon., *et al*. [11]	6/F	USA	RT-PCR nasopharyngeal swab positive	Fever for 6 days, rash, reduced oral intake, hypotension
14	Licciardi., *et al*. [15]	12/M	Italy	RT-PCR nasopharyngeal swab negative, COVID-19 antibody titer positive	Fever for 2 days and abdominal pain
15	Licciardi., *et al*. [15]	7/M	Italy	RT-PCR nasopharyngeal swab negative, COVID-19 antibody titer positive	Fever for 5 days, nausea, vomiting, diarrhea and abdominal pain, tachycardia, hypotension
16	Riphagen., *et al*. [16]	4/M	UK	SARS-CoV nasopharyngeal swab negative, SARS-CoV IgG test positive	Fever of >39°C for 4 days, diarrhea and vomiting, abdominal pain, rash, conjunctivitis
17	Riphagen., *et al*. [16]	6/M	UK	SARS-CoV nasopharyngeal swab negative, SARS-CoV IgG test positive	Fever of >39°C for 4 days, odynophagia, rash, conjunctivitis
18	Riphagen., *et al*. [16]	6/F	UK	SARS-CoV nasopharyngeal swab negative, SARS-CoV IgG test positive	Fever of >39°C for 5 days, myalgia, diarrhea and vomiting for 3 days, conjunctivitis
19	Riphagen., *et al*. [16]	8/F	UK	SARS-CoV nasopharyngeal swab negative, SARS-CoV IgG test positive	Fever of >39°C for 4 days, odynophagia, diarrhea for 2 days, vomiting, abdominal pain
20	Riphagen., *et al*. [16]	8/M	UK	SARS-CoV nasopharyngeal swab negative, SARS-CoV IgG test positive	Fever of >39°C for 5 days, non-bloody diarrhea, abdominal pain, conjunctivitis, rash
21	Riphagen., *et al*. [16]	12/M	UK	SARS-CoV nasopharyngeal swab negative, SARS-CoV IgG test positive	Fever of >39°C for 4 days, diarrhea and vomiting for 2 days, abdominal pain, rash, odynophagia, headache
22	Riphagen., *et al*. [16]	13/F	UK	SARS-CoV nasopharyngeal swab negative, SARS-CoV IgG test positive	Fever of >39°C for 5 days; non-bloody diarrhea, abdominal pain, conjunctivitis
23	Riphagen., *et al*. [16]	14/M	UK	SARS-CoV nasopharyngeal swab negative post-mortem	Fever of >40°C for 4 days, 3 days non-bloody diarrhea, abdominal pain, headache
24	Rivera-Figueroa17	5/M	USA	SARS-CoV PCR nasopharyngeal swab positive	Fever for 8 days, rash, extremity edema, conjunctivitis, diarrhea, dysuria
25	Waltuch., *et al*. [18]	5/M	USA	RT-PCR nasopharyngeal swab negative, COVID-19 antibody titer positive	Fever for 5 days and abdominal pain for one day
26	Waltuch., *et al*. [18]	10/M	USA	COVID-19 antibody titer positive 17 days ago	Known case of asthma presented with fever, rash, fatigue, cough and poor oral intake
27	Waltuch., *et al*. [18]	16/M	USA	RT-PCR nasopharyngeal swab negative, COVID-19 antibody titer positive	Known case of hypothyroidism presented with fever for 6 days, rash for one day, cough, myalgia and fatigue

Table 1: *Clinical and demographics, comorbidities and presentation profile of Kawasaki disease associated with COVID-19 infection.*

Abbreviations: M: Male; F: Female; SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus; COVID-19: Coronavirus Disease-2019; RT-PCR: Reverse Transcriptase Polymerase Chain Reaction; IgG: Immunoglobulin-G.

	Author	Age(Yr)/ Sex	Kawasaki symptoms	Lab findings	Chest imaging	ECHO	Complications	Treatment	Outcome
1	Blondi-aux., *et al*. [9]	6/-	cheilitis, cervical ad-enopathy, trunk and palm rash	Elevated BNP, troponin, CRP	_	Transient systolic dysfunction	_	IVIG, inotro-pes	Recovered
2	Blondi-aux., *et al*. [9]	8/-	Kawa-saki disease shock syn-drome with myocardi-tis, cheilitis, conjunctivi-tis, rash	Elevated BNP, troponin, CRP	Normal	Transient systolic dys-function	_	IVIG, inotro-pes	Recovered
3	Blondi-aux., *et al*. [9]	11/-	Kawa-saki disease shock syn-drome with myocardi-tis, palmar rash	Elevated BNP, troponin, CRP	Bilateral opacities	Transient systolic dys-function	_	IVIG, inotro-pes	Recovered
4	Blondi-aux., *et al*. [9]	12/-	Kawa-saki disease shock syndrome with myo-carditis, conjunctivi-tis, rash on trunks	Elevated BNP, troponin, CRP	Normal	Transient systolic dys-function	Myocarditis	IVIG, aspirin	Recovered
5	Chiu., *et al*. [12]	10/M	dry cough, diarrhea, conjunctivi-tis and rash	Elevated pro-BNP, d-dimers, ferritin, LDH, fibrinogen, INR	_	Severely diminished LV sys-tolic function with trace pericardial effusion	Myocarditis	Dopamine	Critical
6	Chiotos., *et al*. [10]	5/F	KD shock syndrome, hypoten-sion	Elevated Pro-BNP, troponin and inflamma-tory markers. Hypoalbu-minemia and thrombocyto-penia	Mild infil-trates	Mild dilata-tion of LV, mildly di-minished LV function	_	IVIG, steroids, dopamine, epinephrine	Recovered

7	Chiotos., *et al*. [10]	5/F	KD shock syndrome, hypotension	Elevated Pro-BNP, troponin and Inflammatory markers. Lumbar puncture showed aseptic meningitis	Right peribronchial thickening with patchy infiltrates	Moderately diminished LV systolic function	_	Steroids, epinephrine	Recovered
8	Chiotos., *et al*. [10]	9/F	conjunctivitis, edema of extremities, fissured and strawberry tongue	Elevated Pro-BNP, troponin and inflammatory markers	Pulmonary edema	Normal	_	_	Recovered
9	Chiotos., *et al*. [10]	12/M	KD shock syndrome	Elevated Pro-BNP, troponin, inflammatory markers	Diffuse bilateral infiltrates	Diminished RV systolic function	_	IVIG, ECMO, steroids, inotropes	Recovered
10	Chiotos., *et al*. [10]	14/F	Incomplete KD	Elevated ESR, CRP, ferritin. Thrombocytopenia, hyponatremia	Bilateral pulmonary- infiltrates	Right coronary artery dilatation	+	IVIG, inotropes, antibiotics	Recovered
11	Greene., *et al*. [13]	11y/F	4 days of sore throat, malaise, poor attitude, generalized rash on hands	Elevated pro-BNP, troponin, WBC. Lymphopenia	Normal	LV systolic function mildly decreased	_	IVIG, norepinephrine, milrinone, antibiotics	Recovered
12	Jones., *et al*. [14]	0.5/F	Fever, Erythematous non pruritic rash, Extremity edema, Limbic sparing conjunctivitis, prominent tongue	Left shift in WBC, normocytic anemia, elected ESR and CRP, hyponatremia	Faint opacity in the left midlung zone	Normal	_	IVIG, Aspirin, Tocilizumab	Recovered
13	Leon., *et al*. [11]	6/F	conjunctivitis, rash, extremity edema	Elevated WBC, ESR, CRP and LDH	Patchy pulmonary-opacities	Reduced systolic function	Myocarditis	IVIG, antibiotics, dopamine	Recovered

14	Licciardi., *et al*. [15]	12/M	Classic KD, conjunctivitis, erythema, cracked lips, rash, extremity edema	Elevated ESR, CRP, Lymphocytopenia	Normal	Pericardial effusion	_	Steroids	Recovered
15	Licciardi., *et al*. [15]	7/M	bilateral conjunctivitis, rash on palms and soles, scrotal erythema	Elevated ESR, CRP. Lymphocytopenia	Normal	Reduced Systolic function	_	IVIG, steroids, antibiotics	Recovered
16	Riphagen., *et al*. [16]	4/M	Kawasaki disease shock syndrome, unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral edema, and generalized extremity pain with significant gastrointestinal symptoms	Elevated troponin, mechanical ventilation required	Pleural effusions	Not done	Mechanical ventilation required	IVIG, Noradrenaline, Adrenaline, antibiotics	Recovered
17	Riphagen., *et al*. [16][1]	6/M	KD shock syndrome, unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral edema, and generalized extremity pain with significant gastrointestinal symptoms	Elevated CRP, troponin, pro-BNP	_	Dilated LV, pericoronary hyperechogenicity	Non-invasive ventilation required	IVIG, steroids, tocilizumab, milrinone, antibiotics	Recovered

18	Riphagen., *et al*. [16]	6/F	KD shock syndrome, unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral edema, and generalized extremity pain with significant gastrointestinal symptoms	Elevated CRP, troponin, pro-BNP	_	Mild LV systolic impairment	Non-invasive ventilation required	IVIG, steroids, dopamine, noradrenaline, milrinone	Recovered
19	Riphagen., *et al*. [16]	8/M	KD shock syndrome, unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral edema, and generalized extremity pain with significant gastrointestinal symptoms	Elevated troponin, mechanical ventilation required	Pleural effusions	Mild biventricular dysfunction, severely dilated coronaries	Severely dilated coronary arteries, mechanical ventilation required	IVIG, steroids, infliximab, noradrenaline, adrenaline, antibiotics	Recovered
20	Riphagen., *et al*. [16]	8/F	KD shock syndrome, unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral edema, and generalized extremity pain with significant gastrointestinal symptoms	_	_	Moderate LV dysfunction	Mechanical ventilation required	IVIG, steroids, Tocilizumab, noradrenaline, adrenaline, milrinone, antibiotics	Recovered

21	Riphagen., *et al*. [16]	12/M	KD shock syndrome, unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral edema, and generalized extremity pain with significant gastrointestinal symptoms	Elevated CRP, troponin, pro-BNP	_	Severe biventricular impairment	Mechanical ventilation required	IVIG, steroids, heparin, noradrenaline, adrenaline, milrinone	Recovered
22	Riphagen., *et al*. [16]	13/F	KD shock syndrome, unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral edema, and generalized extremity pain with significant gastrointestinal symptoms	Elevated CRP, troponin, pro-BNP	Not done	Moderate to severe LV dysfunction	_	IVIG, noradrenaline, milrinone, antibiotics	Recovered
23	Riphagen., *et al*. [16]	14/M	KD shock syndrome	Elevated Troponin, pro-BNP, CRP, procalcitonin	Bilateral basal lung consolidations and diffuse nodules	RV dysfunction/ elevated RVSP;	Ileitis, generalized gall bladder edema and dilated biliary tree	IVIG, Dopamine, noradrenaline, Argipressin, Adrenaline, milrinone, hydrocortisone, antibiotics	Right MCA and ACA Ischaemic Infarction, demise
24	Rivera-Figueroa., *et al*. [17]	5/M	Cracked erythematous lips, non-exudative conjunctivitis, bilateral cervical lymphadenopathy	Elevated ESR, CRP. Leukocytosis, thrombocytopenia, hyponatremia	Prominent cardiac silhouette	Small Pericardial effusion	_	IVIG, steroids	Recovered

25	Waltuch., *et al*. [18]	5/M	bilateral conjunctivitis, cervical lymphadenopathy, Classical KD, possible TSS	Elevated ESR and CRP	Normal	Mildly dilated proximal LAD	_	IVIG, Toclizimab, Inotropes, antibiotics	Recovered
26	Waltuch., *et al*. [18]	10y/M	Generalized maculopapular rash, bilateral conjunctivitis, atypical KD/TSS	Elevated WBC, CRP, LDH, ESR	Peribronchial thickening with ill-defined opacities in the Rt.mid-lower lung	Mild MR and TR	_	IVIG, Toclizimab, Inotropes, antibiotics	Recovered
27	Waltuch., *et al*. [18]	16/M	Cheilitis, stomatitis, bilateral conjunctivitis, maculopapular rash, desquamation, cervical lymphadenopathy, atypical KD and an element of TSS	Elevated WBC, ESR, CRP, LDH, Troponin, BNP	New hazy opacities in lower lung lobes suggestive of viral pneumonia	Moderately depressed systolic LVEF	Coronary artery dilatation	Tocilizumab, Anakinra Inotropes, Antibiotics	Recovered

Table 2: *Diagnostic symptoms, laboratory investigations and outcomes of Kawasaki syndrome with COVID-19 infection. Abbreviations: WBC: White Blood Cell Count; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; LDH: Lactate Dehydrogenase; BNP: B-Type Natriuretic Peptide; KD: Kawasaki-Disease; IVIG: Intravenous Immunoglobulin; LV: Left Ventricle; LVEF: Left Ventricular Ejection Fraction; RV: Right Ventricle; MR: Mitral Regurgitation; TR: Tricuspid Regurgitation; TSS: Toxic Shock Syndrome.*

Results

Our search identified 92 articles; out of which 42 were excluded due to duplication and 40 were excluded as they lacked individual patient-level data. Finally, 10 articles describing 27 patients (mean age, SD = 9.0 ± 3.7) for the analysis were included [9-18]. A total of 13 (48.1%) cases were from the United States of America (USA), 8 (29.6%) were from the United Kingdom (UK), 4 (14.8%) were from France whereas 2 (7.4%) were from Italy. (Table 1). Of 27 cases, 13 (48.16%) were males, 10 (37.03%) were females and 4 cases (14.81%) with unknown sex. Among the cases we reviewed, we found 6 (22.2%) had atypical KD, 15 (55.5%) had KD shock syndrome and 6 (22.2%) had

classic KD symptoms. All of the cases were tested for COVID-19 infection by either RT-PCR of the nasopharyngeal swab or by measurement of COVID-19 antibody titers. Seven (25.92%) of them were found to be positive by PCR and 20 (74.07%) had positive antibody titers.

Echocardiographic analysis was done to rule out any cardiac anomalies along with coronary artery dilation or aneurysm. Eighteen (66.6%) of the cases were reported to have mild systolic dysfunction and required inotropic support (Table 2). One patient (3.70%) developed right coronary artery dilation, another one (3.70%) had mild left coronary artery dilation, whereas one patient had severely dilated both coronary arteries. Three of the cases (11.1%) required ECMO for respiratory support. All the patients in the case review series had an excellent outcome after treatment with intravenous immunoglobulin (IVIG) and intravenous methylprednisolone along with broad spectrum antibiotics. However, one death (3.70%) was noted with infarction of right middle and anterior cerebral arteries. Five of the cases (18.5%) had confirmed COVID-19 infection in the family, while 2 (7.4%) cases had a history of anosmia without positive COVID-19 results in the family.

Discussion

Recent emergence of the COVID-19 virus has caused a pandemic with variegated presentations affecting various age groups. COVID-19 cases are also noted in the pediatric age group, but with less severe presentation compared to the adult counterparts [5]. However, the recent outbreak of COVID-19 has also led to the development of KD and its other variants in children [8]. There have been various studies conducted which show associations between various infectious etiologies such as adenovirus, enterovirus, human rhinovirus and coronavirus with the development of KD. In this case review series, we studied the pattern of development of KD and its variants like atypical KD and KD Shock Syndrome.

It is hypothesized that the COVID-19 infection causes cytokine storm (IL-6) which can increase vascular permeability, hyperinflammatory response and multi-organ failure requiring PICU admission [19]. One of the reasons through which hyperinflammatory response is seen by cytokines could be attributed to antigen-antibody complex leading to various vasculitis-like presentations causing KD [19,20]. In this case review series, we studied a total of 27 pediatric cases with confirmed COVID-19 infection. The mean age group was found to be 7.7 with male preponderance.

The classic clinical presentation of KD (fever, bilateral conjunctivitis, erythema and swelling of hands and palms) were not noted frequently in the patients with concurrent COVID-19 infection [2,3]. The other two variants that were commonly seen were atypical KD (fever more than 5 days without all the symptoms of classic KD) and KD shock syndrome which included shock features with fever along with echocardiographic abnormalities (mitral or tricuspid regurgitation) leading to multiorgan failure [4]. Macrophage activation syndrome characterized by worsening thrombocytopenia with hepatosplenomegaly along with hemodynamically unstable was recognized in one of the cases [10].

Out of 27 cases, 24 (88.8%) required PICU admission because of shock. A total of 18 (66.6%) of them were kept on inotropes for profound hemodynamic instability. On initial evaluation chest X-ray was done which demonstrated either pulmonary edema or patchy pulmonary infiltrates consistent with viral pneumonia. The common laboratory findings noted were leukocytosis, elevated CRP and ESR levels with increased Pro-BNP and troponin levels [21]. The elevated troponin levels would also be indicative of myocardial injury pointing towards the diagnosis of KD or its variants [10].

Echocardiography was significant for systolic dysfunction in patients with atypical KD and KD shock syndrome in 15 (68.1%) cases out of 22 for whom echocardiography was performed. Consequently, coronary artery involvement was noted in 3 (11.5%) cases [21].

The treatments were the same for most of the cases with broad spectrum antibiotics like cefepime and clindamycin to cover common infections with IVIG and intravenous methylprednisolone to dampen the immune response. Monoclonal antibodies like Tocilizumab were

used to counter the inflammatory effects of interleukin-6 to suppress the immune response. Most of the patients required PICU admission requiring inotropic support for hemodynamic instability. Treatment outcomes were excellent for all of them except for one case, who unfortunately died due to infarction of the right middle and anterior cerebral artery. The mean length of stay for PICU was 5 - 6 days.

Emergency physicians and Pediatricians should keep a high index of suspicion for post infectious cytokine-release storms in COVID-19 infection. The patients with suspected hyperinflammatory response should be kept in PICU for continuous monitoring along with further laboratory investigations inclusive of various inflammatory markers along with Pro-BNP and troponin levels. Rapid worsening can also be seen in these cases, thus in-hospital care team should be prepared for rapid deployment of resuscitative measures along with potential ECMO.

Conclusion

Patients with concurrent COVID–19 can have post-infectious cytokine release syndrome consistent with the development of KD and its variants. Thus, emergency physicians and pediatricians should have a high index of suspicion for it, as they can decompensate rapidly requiring resuscitation and/or PICU admission. With the prompt diagnosis and treatment, further complications of the KD can be curtailed.

Bibliography

1. Burns JC., *et al.* "Clinical and epidemiologic characteristics of patients referred for evaluation of possible Kawasaki disease". *The Journal of Pediatrics* 118.5 (1991): 680-686.

2. Hsieh YC., *et al.* "Clinical features of atypical Kawasaki disease". *Journal of Microbiology, Immunology and Infection* 35.1 (2002): 57-60.

3. Witt MT., *et al.* "Kawasaki disease: more patients are being diagnosed who do not meet American Heart Association criteria". *Pediatrics* 104.1 (1999): e10.

4. Lu H., *et al.* "Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle". *Journal of Medical Virology* 92.4 (2020): 401-402.

5. Yagnik PJ., *et al.* "Pediatric Characteristics of 2019 Novel Coronavirus: Review of Available Published Literature". *Clinical Pediatrics* (2019).

6. Ronconi G., *et al.* "SARS-CoV-2, which induces COVID-19, causes Kawasaki-like disease in children: role of pro-inflammatory and anti-inflammatory cytokines". *Journal of Biological Regulators and Homeostatic Agents* 34.3 (2020): 767-773.

7. Ebina-Shibuya R., *et al.* "Multisystem Inflammatory Syndrome in Children (MIS-C) with COVID-19: Insights from simultaneous familial Kawasaki Disease cases". *International Journal of Infectious Diseases* 97 (2020): 371-373.

8. Verdoni L., *et al.* "An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study". *Lancet* 395.10239 (2020): 1771-1778.

9. Blondiaux E., *et al.* "Cardiac MRI of Children with Multisystem Inflammatory Syndrome (MIS-C) Associated with COVID-19: Case Series". *Radiology* (2020): 202288.

10. Chiotos K., *et al.* "Multisystem Inflammatory Syndrome in Children During the Coronavirus 2019 Pandemic: A Case Series". *Journal of the Pediatric Infectious Diseases Society* (2020).

11. Deza Leon MP., *et al.* "COVID-19-Associated Pediatric Multisystem Inflammatory Syndrome". *Journal of the Pediatric Infectious Diseases Society* (2020).

12. Chiu JS., *et al.* "Kawasaki Disease Features and Myocarditis in a Patient with COVID-19". *Pediatric Cardiology* (2020).

13. Greene AG., *et al.* "Toxic shock-like syndrome and COVID-19: A case report of multisystem inflammatory syndrome in children (MIS-C)". *American Journal of Emergency Medicine* (2020).

14. Jones VG., *et al.* "COVID-19 and Kawasaki Disease: Novel Virus and Novel Case". *Hospital Pediatrics* 10.6 (2020): 537-540.

15. Licciardi F., *et al.* "SARS-CoV-2-Induced Kawasaki-Like Hyperinflammatory Syndrome: A Novel COVID Phenotype in Children". *Pediatrics* (2020): e20201711.

16. Riphagen S., *et al.* "Hyperinflammatory shock in children during COVID-19 pandemic". *Lancet* 395.10237 (2020): 1607-1608.

17. Rivera-Figueroa EI., *et al.* "Incomplete Kawasaki Disease in a Child with Covid-19". *Indian Pediatrics* 57.7 (2020): 680-681.

18. Waltuch T., *et al.* "Features of COVID-19 post-infectious cytokine release syndrome in children presenting to the emergency department". *American Journal of Emergency Medicine* (2020).

19. Sultan S and Sultan M. "COVID-19 cytokine storm and novel truth". *Medical Hypotheses* 144 (2020): 109875.

20. Rowley AH. "Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children". *Nature Reviews Immunology* (2020): 453-454.

21. Ramcharan T., *et al.* "Paediatric Inflammatory Multisystem Syndrome: Temporally Associated with SARS-CoV-2 (PIMS-TS): Cardiac Features, Management and Short-Term Outcomes at a UK Tertiary Paediatric Hospital". *Pediatric Cardiology* (2020): 1-11.

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