

# Case report: Pediatric patients with COVID-19 presented as multi-system inflammatory syndrome

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## Case Report

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# Abstract

## Background

COVID-19 in pediatric patients is typically associated with minimal manifestations and is less severe than adult patients. Recently, there are reports of children with COVID 19 and myocardial involvement from Europe and America that first were assumed to be Kawasaki disease or its atypical presentation. However world health organization has set a new designation for this state; “multi-system involvement syndrome” in children with COVID-19; (MIS-C).

## Case presentation:

Here we report two COVID-19 pediatric patients (two girls aged 10 and 13 years old) with MIS-C.

## Conclusion

Presence of Kawasaki like signs in COVID 19 patients should be an alarming point to consider multi-system inflammatory syndrome; a syndrome with extensive organ involvement and yet indistinct exact pathophysiology.

## Background

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) originated in Wuhan in December 2019 and has now spread to affecting about 213 countries around the world. (1, 2)

Children do not appear to account for a large proportion of COVID-19 disease; in some studies it was reported up to 12.3 (3, 4, 5, 6) and they have less severe manifestations than adult (7). The most common symptoms of children with COVID-19 are: fever and cough (8).

Recently, there are reports from Europe and North America that described clusters of children and adolescents requiring admission to intensive care units with a multisystem inflammatory condition similar to Kawasaki disease or toxic shock syndrome. The presentation is generally of acute illness accompanied by a hyper inflammatory syndrome, leading to multiorgan failure and shock. Children with these manifestations have been treated with anti-inflammatory medications, including parenteral immunoglobulin and steroids. (9, 10, 11)

WHO has developed a preliminary case definition and case report form for multisystem inflammatory disorder in children and adolescents. The preliminary case definition reflects the clinical and laboratory features observed in children reported to date, and serves to identify suspected or confirmed cases both for the purpose of providing treatment and for provisional reporting and surveillance. (12)

The syndrome should be considered in children with features of typical or atypical Kawasaki disease or toxic shock syndrome.

Preliminary case definition:

Children and adolescents 0–19 years of age with fever > 3 days

AND two of the following:

- a) Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
- b) Hypotension or shock.
- c) Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
- d) Evidence of coagulopathy (by PT, PTT, and elevated d-Dimers).
- e) Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain).

AND

Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

AND

No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

AND

Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

Herein we describe patients with COVID-19 presenting with multi-system inflammatory syndrome. (12)

## Case Presentation

### Case 1

A 10 years old girl was referred to emergency room with a complaint of fever and lethargy. She had fever, abdominal pain and diarrhea from 6-days 3 days and one day before admission respectively. Physical examination revealed maculopapular rash on trunk, erythema of both hands, strawberry tongue and non-purulent conjunctivitis. Vital signs were: blood pressure (BP):90/40, heart rate: 133/min. , respiratory rate: 32 /min. and temperature: 39 °C.

Laboratory data revealed : WBC:25900 (PMN:95%,Lymphocyte:3/2%) ,CRP:150, D-dimer:7900.

She was transferred to pediatric intensive care unit in Namazi Hospital in Shiraz with the impression of atypical Kawasaki disease. Namazi Academic Hospital is the largest hospital in south of Iran with more than 1000 beds and serves as the main tertiary referral center in south of Iran with an 18 bed general PICU. On arrival her vital signs were :blood pressure(BP):55/30 ,heart rate(HR) :158,respiratory rate(RR) :35 and temperature was 39 Glasgow coma scale (GCS) :7/15 so she was intubated and inotrope started and RT-PCR for COVID-19 with nasopharyngeal swab sent for her with a positive result .(Her initial laboratory data are listed in table1.)

Inotrope, vasopressor was started and titrated to reach to an acceptable mean arterial pressure (65 mmHg) in addition to parenteral hydrocortisone, ascorbic acid and thiamine (HAT protocol) and intravenous globulin (IVIG). Echocardiogram findings was: borderline left ventricle function, dilated inferior vena cava (IVC) (it was done while high dose inotrope was infusing).Fortunately the patient responded to the management bundle and inotrope titrated to discontinuation of all inotrope and her partial oxygen content and saturation became acceptable for extubation. On day 6 she was extubated and tolerated o<sub>2</sub> via non rebreather face mask. (Figure 1 and 2 are her initial chest x ray and chest CT )

## Case 2

A 13 years old girl was referred to ER due to decreased level of consciousness, fever and diarrhea. On arrival vital signs were: BP: 110/65 mmHg , HR: 152/min ,RR:22/min and T:40°C . In physical examination GCS was 13/15 central pulses were weak. Despite dopamine infusion, her condition aggravated and the blood pressure decreased to 90/40 mmHg and GCS decreased to 11, so the patient was intubated and transferred to PICU.

Nasopharyngeal swab was taken and sent for COVID-19 RT-PCR and chest CT scan was done that was in favor of COVID-19 .The elevated CRP, troponin , D-Dimer in addition to mentioned signs, fulfilled the criteria of "multi-system inflammatory syndrome.(the initial laboratory data are listed in Table1 and initial CT scan is in Figure 3. )

Echocardiogram revealed poor left ventricle systolic function and borderline right ventricle systolic function with dilated IVC (it was also done with high dose of inotrope and vasopressor).

In PICU her blood pressure was 72/30 mmHg and HR was 158 mm/Hg, so central venous catheter was inserted and epinephrine was added. Vasopressin was added an hour later to attain the acceptable mean arterial pressure (MAP of 65 mmHg). Inotropes were tapered over the next four days but due to severe hypoxemia (Pao<sub>2</sub>/Fio<sub>2</sub>:65) she needed mechanical ventilation till the 10<sup>th</sup> day of admission .Then she was extubated and tolerated oxygen via mask but on the 14<sup>th</sup> day presented with ventricular fibrillation(VF)and asystole and unfortunately didn't responded to cardiopulmonary resuscitation and expired.

## Discussion And Conclusion

Fifty years ago Tomisaku Kawasaki reported cases that were later entitled Kawasaki disease (13) with unknown cause. There have been several hypothesis for the disease but the most accepted one is “an aberrant response of the immune system to one or more unidentified pathogens in genetically predisposed patients” (14). It has been supposed that viruses of coronavirus family could be the triggering pathogens in Kawasaki disease. Nowadays, again in the Era of COVID-19, there are reports of Kawasaki like illness in pediatrics that is known as “Multisystem Inflammatory Syndrome in Children”(MIS-C) associated with COVID-19 (15).

Since the beginning of COVID-19 pandemic, cardiac involvement had been described in adult patients with COVID-19 (16) but myocardial involvement in pediatric population is reported in the setting of this syndrome.

In a cohort from Imperial College of London, with a similar case definition patients developed shock, diarrhea ,gastrointestinal manifestation, myocardial involvement and oxygen requirement in 75%, 59.5%, 57%, 51% and 51% of cases respectively.

In the New York cohort, 97% of patients had gastrointestinal involvement, 76% developed shock, 70% had acute kidney injury, 58% showed neurocognitive involvement, 58% developed myocardial involvement and 52% required supplemental oxygen .Comparing to patients affected with Kawasaki disease, the above mentioned patients were older and had higher inflammatory markers, as well as higher rates of shock, coronary abnormalities and abdominal problems.

Regarding the management, 100% of the UK cases received fluid resuscitation. 62% of them received intravenous immunoglobulin, and 51% received corticosteroids. In the New York patients, all received intravenous immunoglobulin and 30% received a second dose.

About 88% received aspirin, 70% received methylprednisolone and 42% received enoxaparin.

Both of our two patients fulfilled the newly defined syndrome with a highly elevated troponin level that reflects a severe myocardial injury both received IVIG and HAT protocol in addition to broad spectrum antibiotics.

In the beginning of COVID-19 pandemic, there was less concept about the degree of organ involvement and severity in pediatric patients which it was maybe due to lower reports of severe cases but now with the new reports, maybe it's the time for those who involve in the care of pediatric patients to be aware of new manifestations related to COVID-19 in patients who present with fever such as multi-system inflammatory syndrome; a syndrome with extensive organ involvement that can be fatal with yet indistinct exact pathophysiology.

## Abbreviations

BP: blood pressure; COVID-19: Coronavirus disease; HR: heart rate; GCS: Glasgow coma scale; MIS-C: multi-system involvement syndrome; RR: respiratory rate; VF: ventricular fibrillation

## Declarations

### **Ethics approval and consent to participate:**

This study was approved by the ethics committee of Shiraz University of Medical science (IR.SUMS.REC.1399.336). Written informed consent was obtained the parents guardians and sent to the ethics committee.

### **Consent for publication:**

Obtained

### **Availability of date and material:**

Data and material is ready for any purpose.

### **Competing interests:**

The authors declare that they have no competing interest.

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### **Authors' contributions:**

A.S. planned the study and wrote the manuscript. E.S. gathered patients' data and submitted the manuscript. A.S.D. data interpretation .A.S.D. and S.H.G edited the manuscript and were scientific consultant .All authors discussed the results and contributed to the final manuscript.

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## Table

**TABLE 1:** Initial laboratory data

	Case 1	Case 2
Ferritin (ng/ml) M: 22.81-275 F: 4.63-204	>2000	539
COVID Realtime PCR	Positive	Negative
Typical Chest CT finding	Patchy infiltration	Bilateral patchy ground glass
White blood cells(count/ml)	25900	3300
Lymphocyte	950	260
Procalcitonin ≤ 0.3	14.2	89.9
C- reactive protein <6 (mg/L)	150	105
Creatine phosphokinase (U/L) M: < 171 F:< 145	322	2470
Lactate dehydrogenase (U/L) < 480	664	1240
Troponin (ng/ml) < 19	62.5	1163
D-Dimer (ng/ml) < 500	5193	2754
Total bilirubin 0.1-1.2	0.9	0.6
Direct bilirubin < 0.3	0.5	0.2
Aspartate transaminase (U/L) M: < 37 F: < 31	55	114
Alanine aminotransferase (U/L) M: < 41 F: < 31	37	42
Albumin	2.8	2.9
Blood urea nitrogen (mg/dl) 8 - 20	24	30
Creatinine M: 0.8 - 1.3 F: 0.6 - 1.2	0.8	1
Pt /INR	17.1/1.27	24.1/1.79
Ptt	32	31.9
Blood culture	Negative	Negative
ESR	78	54
Fibrinogen (200-400)	426	411
Platelets	113000	102000
Sodium	140	132

# Figures



**Figure 1**

initial chest x ray



**Figure 2**

chest CT



**Figure 3**

initial CT scan