

Kawasaki-Like Disease in Children during COVID-19 Pandemic: Two Case Reports

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Abstract

Background: Kawasaki disease (KD) is an acute vasculitis that affects small and medium-sized arteries. During the coronavirus disease 19 (COVID-19) pandemic, a significant increase in KD symptoms was reported among patients who had taken COVID-19, known as the multisystem inflammatory syndrome in children (MIS-C). We describe 2 cases of KD following the COVID-19.

Case presentation: Two 2.5 and 3.5 year-old boys presented to the Shahid Sadoughi Hospital with weakness, fever, nausea, and vomiting for several days. The other symptoms were maculopapular rash, cracked lips, erythematous palms, conjunctivitis, and lymphadenopathy. Respiratory symptoms were observed in none of them. The course of the disease was moderate to severe in both, and they were treated entirely.

Conclusions: COVID-19 infection in children may be presented without any respiratory symptoms. Thus, Pediatricians should consider these atypical presentations and not restrict COVID-19 tests only for patients with typical presentations in order not to miss such cases and prevent irreversible complications.

Key Words: Coronavirus Infections, Iran, Kawasaki disease, Pediatrics.

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1- INTRODUCTION

Kawasaki disease (KD) is an acute systemic febrile disease leading to vasculitis; and usually occurs in children under five years of age (1, 2). Viral infections, particularly those that involve the respiratory system, can lead to the creation of immune complexes that do not cleave rapidly in a subset of patients, triggering a type III allergic immune response; and can cause KD or KD-like symptoms in some patients (1-3).

The coronavirus disease 19 (COVID-19) has spread throughout the world, since December 2019; and its severity and mortality are mainly associated with age. Cases of COVID-19 are primarily adults, with a small percentage of patients under 18 years of age (4-6).

The symptoms of COVID-19 in children are the same as those in adults, although they are usually milder or even asymptomatic. Among the typical symptoms, gastrointestinal complaints have been described more in pediatric patients (1, 4, and 6). Nevertheless, it can occur in some children beyond respiratory and gastrointestinal disorders such as vasculitis, myocarditis, and cutaneous involvement (7). Currently, the reports of COVID-19 cases accompanied by KD, presented with overlapping features of COVID-19 and KD, are increased in children and adolescents (1, 5, and 8). Here, we describe two cases of KD following the COVID-19 infection who were admitted to the pediatric department of Shahid Sadoughi Hospital, Yazd, Iran, in May and September 2020.

2- CASE PRESENTATION

2-1. Case 1

A 2.5-year-old boy with fever, lethargy, nausea, vomiting, and loss of appetite from five days ago, and the recent onset of generalized maculopapular rash and edema, especially in lower extremities,

was brought to the pediatric emergency department. He exhibited no respiratory symptoms. There was no history of recent sick contact, leaving home, or travel. Overall, he was a healthy, fully vaccinated boy.

His vital signs at the time of referral are listed in **Table 1**. Dry and cracked lips, as well as the erythematous eruption of the palms and soles were presented. No appreciable lymphadenopathy was noted. Also, fine crackles were heard at the base of both lungs.

Laboratory testing was remarkable for leukocytosis, anemia, hypoalbuminemia, and elevated inflammatory parameters (**Table 1**). The patient was tested for COVID-19 and other viral infections. All results were negative. Ultrasound detected mild left-sided pleural effusion and mild pelvic ascites. A Computed Tomography scan of chest showed modest patchy ground-glass opacities in lungs, so the Kaletra and Hydroxychloroquine were prescribed for the patient.

Nevertheless, the patient's fever and rash remained. On day 6th of hospital stay, the echocardiogram demonstrated dilation of the left coronary artery (LCA), mild mitral regurgitation, and normal left ventricular function, suggesting KD. Without delay, Aspirin and intravenous immunoglobulin (IVIG) were administered. About 48 h following the first infusion, fever and rash were suppressed, and oxygen saturation was raised, and he was discharged home on the 9th day of hospitalization in good general condition and remained well without any complications one the later week in a follow-up visit.

Due to solid suspicion, COVID-19-specific antibodies were tested in the follow-up visit, in which a positive IgG was shown.

2-2. Case 2

A 3.5-year-old boy was admitted to the pediatric emergency department with lethargy, fever, and non-pitting edema of extremities. He also had nausea and vomiting from three days ago without any other gastric or respiratory symptoms. The patient's initial vital signs can be seen in **Table 1**. On examination, he had bilateral, nonexudative conjunctivitis and his throat was erythematous without exudates. No sensitive and enlarged cervical lymph nodes were perceived. Reduction of respiratory sounds was observed in lung auscultation. Abdominal examination revealed mild generalized tenderness and hepatosplenomegaly.

Similarly, pleural effusion and hepatosplenomegaly were indicated by ultrasound. Laboratory workup showed leukocytosis, anemia, hypoalbuminemia, hyponatremia, and increased inflammatory markers (**Table 1**). Among other diagnostic tests ordered to find infections, only Reverse Transcription Polymerase Chain Reaction (RT-PCR) COVID-19 was positive. Antiviral therapy was started, but the fever continued. The patient was evaluated by echocardiography, which was normal, but with the possibility of atypical Kawasaki, treatment with Aspirin and IVIG was begun. Fever resolved, the limbs' edema decreased, and white blood cell count fell to normal. Within 24 hours, he found palms and soles scaling. After improvement, he was discharged with Aspirin for six weeks, s. At follow-up, he was entirely well and had no specific findings on examination.

3- DISCUSSION

Although the leading cause of KD is still unknown, since its incidence increases significantly during certain seasons, infectious agents seem to be one of the leading causes. On the other hand, the higher incidence in Eastern population indicates genetic factors (9-11).

There is some evidence that shows a 30-fold increase in KD during COVID-19 pandemic compared to the same time in the past five years (10, 11). What's more, it occurs several weeks later because of post-infectious hyperinflammatory response; so that it is said that there is an association between the COVID-19 and KD development. The Centers for Disease Control and Prevention of the United States have named it multisystem inflammatory syndrome in children (MIS-C) (1, 11-13).

The prevalence of COVID-19 among children is much lower, milder, and less lethal than among adults (3, 14). According to the prior studies, children with COVID-19 mainly have not shown pulmonary involvement at first, and only 4.4% of them may experience a severe course of the disease (5, 9). Nevertheless, it can increase the risk of MIS-C and subsequently increase the duration, deterioration, and complications of KD (4, 5, 14). Although MIS-C Clinical features show many similarities with KD, it has some characteristics that distinguish it from KD, which are explained as follows: In around 80% of MIS-C patients presented with gastrointestinal symptoms (versus one in three patients in KD), cardiac disorders occur more common and more severe. (4, 14) Furthermore, it affects older children (1, 5, 9). In a cohort study, a positive IgG in all MIS-C patients who mimicked KD symptoms demonstrated a previous infection in the last two weeks or more (1). Due to the low viral load in the pediatric nasopharynx, COVID-19 RT-PCR was mainly negative in them; whereas, high loads of virus have been observed in nasopharyngeal secretion in adults with severe COVID-19 infection (1, 9). Hence, pediatricians should first request a COVID-19 RT-PCR test and then its serological test to prevent false-negative results. (1).

Table-1: Clinical and laboratory features of the patients at the time of admission and discharge

Gender Age, year	Case 1		Case 2	
	Male 2.5		Male 3.5	
Condition	Admission	After treatment	Admission	After treatment
Vital signs				
Pulse rate	186	105	138	85
Respiratory rate	46	25	54	20
Temperature, °C	38.5	36.7	38.1	36.3
O2 Saturation, %	95	98	95	99
Blood pressure, mmHg	90/60	100/60	90/50	100/50
Hematology				
Hemoglobin, g/dl	9.2	-	9.4	-
White blood cell, ×10 ⁹ /L	16	13.2	18.8	10.1
Platelet, mg/dl	104	394	83	255
Inflammatory markers				
ESR, mm/h	40	21	90	40
CRP	3+	+	2+	+
Ferritin, g/l	200	-	320	-
Biochemistry				
Albumin, g/dl	3	-	2.6	-
Na, mmol/L	136	135	125	133
Triglyceride	241	-	200	-
LDH, U/L	663	-	526	-
CPK	41	-	43	-
Virology				
COVID-19 PCR	Negative		Positive	
COVID-19 IgG	Positive		-	
CMV IgG/IgM Ab	Negative		Negative	
HIVAb	Negative		Negative	
ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; LDH: Lactate Dehydrogenase; CPK: Creatine phosphokinase; COVID-19: Coronavirus disease 2019; RT-PCR: Reverse Transcription Polymerase Chain Reaction; CMV IgG/IgM Ab: Cytomegalovirus Immunoglobulin G/M Antibody; HIV Ab: The human immunodeficiency virus antibodies				

IVIg is the cornerstone of treatment coupled with high dose Aspirin to avoid thrombosis (1, 9). Likewise, both of our cases were treated by receiving IVIg as well. Immunosuppressants should be prescribed as a subsequent treatment in patients with severe MIS-C courses who

do not respond to IVIg (1, 9, and 11). Its administration may also be beneficial for reducing inflammatory cytokine storm and development of vasculitis (1, 11).

4- CONCLUSION

COVID-19 infection in children may involve other organ systems beyond respiratory system. Thus, many cases are easily missed if the diagnostic tests are limited to patients with typical clinical features of COVID-19. Early diagnosis and proper treatment can significantly prevent the progression of MIS-C to cardiac dysfunction. Pediatricians should consider such atypical presentations to reduce invasive diagnostic evaluations, costs, and particularly, irreversible complications.

5- ABBREVIATIONS

KD, Kawasaki Disease; COVID-19, Coronavirus disease 2019; CDC, Disease Control and Prevention of the United States; MIS-C, Multisystem Inflammatory Syndrome in Children; IVIG, Intravenous Immune Globulin; CMV IgG/IgM Ab, Cytomegalovirus Immunoglobulin G/M Antibody; ESR, Erythrocyte Sedimentation Rate; CRP, C-Reactive Protein; RT-PCR, Reverse Transcription Polymerase Chain Reaction; LDH, Lactate Dehydrogenase

6- ACKNOWLEDGMENT

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7- CONFLICT OF INTEREST

None

8- REFERENCES

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