

# Multisystem Inflammatory Syndrome in Children (MIS-C) associated with Kawasaki Disease in a three-year-old girl with SARS-CoV-2 infection

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## Abstract

Kawasaki Disease (KD) is an acute and restrictive vasculitis. Studies have noted a viral association with the occurrence of this syndrome. This article reports a child with several severe inflammatory syndrome symptoms associated with COVID-19 and KD. The patient, a three-year-old Iranian Kurdish girl without a history of internal diseases and with no history of drug and food allergies, was referred to Imam Hasan hospital three days after diarrhea, nausea, and pain in the inner part of the left thigh. Scattered rashes around the face, neck, and arms during fever were significant. Reverse transcription polymerase chain reaction (RT-PCR) was positive for COVID-19, but the lung high-resolution computed tomography (HRCT) did not show involvement, so the diagnosis of KD associated with viral infection was suggested. In further studies, Wright and 2ME tests, Widal, and purified protein derivative (PPD) tests were declared negative. After intravenous immunoglobulin (IVIG), the patient's fever continued, but other symptoms improved.

Since COVID-19 is a new disease and our understanding of its numerous symptoms is evolving, we recommend physicians to be vigilant about secondary inflammatory syndromes that induce KD; rapid treatment with IVIG and steroids may improve patients' conditions.

## Keywords

Kawasaki Disease, COVID-19, Coronavirus, vasculitis.

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## Introduction

Kawasaki Disease (KD) is an acute and restrictive vasculitis that may be found in children of any age and sometimes difficult to diagnose for the physician [1]. Studies have noted a viral association with the occurrence of this syndrome [2]. If left untreated, there is a 25% chance of serious cardiovascular damage [1, 3]. Coronaviruses are a large family of viruses capable of causing mild pathologies, such as colds, and more severe diseases, such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). SARS-CoV-2 is known as a novel Coronavirus (nCoV), causing COVID-2019. COVID-19 is a viral disease unknown to humans until December 2019 [4]. The virus is very similar to the ones causing MERS and SARS and can cause viral pneumonia with different severities. Initial reports of patients with the virus showed that up to 50% of people with chronic diseases are at risk of death [5-7]. Many children with COVID-19 are asymptomatic or exhibit only moderate symptoms regardless of the prevalence of the COVID-19 pandemic. In the last two months, though, first in Europe and most recently in the United States, a few children have encountered a more serious COVID-19-related inflammatory syndrome, which sometimes leads to hospitalization and needs intensive care [8]. We report the diagnostic and treatment steps of a three-year-old girl with the Multisystem Inflammatory Syndrome in Children (MIS-C) associated with KD and with SARS-CoV-2 infection.

## Patient's medical reports

The patient, a three-year-old Iranian Kurdish girl with a height of 80 cm and a weight of 15 kg with no

history of internal diseases or surgeries or medical and food allergies, referred to the hospital three days after diarrhea, nausea, and pain in the inner part of the left thigh. In the initial examination, vital signs were recorded as fever of 39 degrees, heart rate of 140, respiratory rate of 26, and blood pressure of 90/50. The patient was immediately admitted and monitored under the care of a pediatrician. In laboratory investigation, white blood cells (WBC): 9,200 with neutrophils 81%, lymphocytes 15%, platelets 270,000 and erythrocyte sedimentation rate (ESR): 90 mm/h were evident. The patient's creatine phosphokinase (CPK) and liver tests were normal. Urine and blood cultures were negative for bacteria, and patient fecal cultures were negative for *Shigella spp.* and *Salmonella spp.* In urine dipstick analysis, sugar was observed as two plus.

Abdominal and pelvic ultrasounds were performed to examine the child's digestive system. No abnormalities were reported, except for a few lymph nodes in the mesentery with a 7 mm diameter reactive view. Hip radiography was performed due to pain in the left thigh and pelvis's median area, and resulted normal. One day after treatment initiation, nausea was controlled, but fever continued. Scattered rashes around the face, neck, and arms during fever were significant (**Fig. 1** and **Fig. 2**). Due to hyperpyrexia, the patient was transferred to a pediatric infectious disease specialist service. The patient underwent a reverse transcription poly-



**Figure 1.** Scattered rashes around the arms.



**Figure 2.** Scattered rashes around the face and the neck.

merase chain reaction (RT-PCR) test in terms of the existence of COVID-19, which was declared positive, but in lung high-resolution computed tomography (HRCT) there was no evidence of pulmonary involvement. Therefore, she was diagnosed with KD associated with a viral infection. During the hospitalization she was under the care of a pediatric infectious disease specialist. Then cardiac echo was performed, and the results were declared normal. An intravenous immunoglobulin (IVIG) dose of 2 g/kg began for the patient and, in further examinations, Wright and 2ME, Widal, and purified protein derivative (PPD) test were negative. After IVIG, the patient's fever continued, then she was transferred to the pediatric hospital five days after treatment. During hospitalization, the child's fever was not controlled despite receiving another IVIG and corticosteroid therapy. The patient was finally discharged after 25 days of hospitalization and was recommended to take dexamethasone at home. Finally, after 35 days of monitorization under an infectious disease specialist, she recovered.

## Discussion

KD and MIS-C have several common symptoms such as skin rashes, lymphadenopathy, strawberry tongue, and increased inflammatory biomarkers. However, MIS-C in COVID-19 has been associated with unique features such as starting at older ages (cases of children in adolescents), the prevalence of abdominal symptoms, and left ventricular systemic failure [9-11]. Previous studies have linked other types of Coronaviruses to KD. In **Tab. 1**, the demographic characteristics of these patients are shown [12, 13].

Loomba et al. have concluded that there may be a link between COVID-19 and KD [2]. Many viruses can cause KD, so there is no doubt about the possible connection [14]. In several studies, the association of viral agents in KD incidence was determined using cytoplasmic RNA extraction [2, 15]. Viruses associated with KD include influenza, enterovirus, adenovirus, parvovirus, reovirus, respiratory syncytial virus, varicella, Epstein-Barr, and

**Table 1.** Demographic characteristics of patients with Kawasaki Disease (KD) associated with Coronavirus.

Number of patients	Age	Symptoms	Countries
15	2-15	Typical symptoms of KD, KDSS, and atypical KD	America
20	2-15	Hyperinflammatory shock similar to that of KD (six times the expected annual result)	Italy
-	2-15	Hyperinflammatory shock	Spain and Portugal

KD: Kawasaki Disease; KDSS: Kawasaki Disease Shock Syndrome.

measles. There were no reports of KD in patients with COVID-19 in the first stage of the Coronavirus pandemic in East Asia and Southeast Asia. This issue was considered after the arrival of the disease to the West. Underlying genetic factor may be a factor that causes the prevalence of KD in the non-Asian population. Cases non-responding to IVIG have been reported in non-Asian patients with KD, with differences between different ethnic groups [14]. At this time, allergic and immunodeficient children and adolescents require proper treatment. Treatment should not be suspended, and telemedicine should be added [16].

## Conclusion

Since COVID-19 is a new disease and our understanding of its numerous symptoms is evolving, we recommend physicians to be vigilant about secondary inflammatory syndromes that induce KD or Kawasaki disease shock syndrome (KDSS), as rapid treatment with IVIG and steroids may improve patients' conditions.

## Abbreviations

COVID-19: Coronavirus Disease 2019

CPK: creatine phosphokinase

ESR: erythrocyte sedimentation rate

HRCT: high-resolution computed tomography

IVIG: intravenous immunoglobulin

KD: Kawasaki Disease

KDSS: Kawasaki Disease Shock Syndrome

MERS: Middle East Respiratory Syndrome

MIS-C: Multisystem Inflammatory Syndrome in Children

nCoV: novel Coronavirus

PPD: purified protein derivative

RNA: ribonucleic acid

RT-PCR: reverse transcription polymerase chain reaction

SARS: Severe Acute Respiratory Syndrome

WBC: white blood cells

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## Informed consent

Informed consent was obtained from all individual participants included in the study.

## Declaration of interest

The Authors declare that they have no conflict of interest. There is no funding source.

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