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Case Report

Multisystem Inflammatory Syndrome Associated with COVID-19 in Pediatrics: A Case Report in Saudi Arabia

Rola A. Sleiman*, Waleed A. Okash, Abdulaziz S. Alruwaili, Dareen A. Elkhateeb, Ammar Youcef, Reham Harb

Dr. Sulaiman Al-Habib Group, Al-Rayan Hospital, Riyadh, Saudi Arabia

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) affects more adults than children worldwide, and infected children have low mortality rates; however, COVID-19 can be complicated by an inflammatory Kawasaki-like syndrome called multisystem inflammatory syndrome associated with COVID-19 (MIS-C). We report a case of MIS-C from Riyadh, Saudi Arabia, in a 4-year-old Saudi girl who presented with acute febrile gastroenteritis and persistent fever. Her condition improved spontaneously during admission and she did not require pediatric intensive care unit admission.

1. INTRODUCTION

Coronaviruses are a large family of viruses that cause illnesses ranging from the common cold to more severe diseases such as Middle East respiratory syndrome coronavirus and Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV).

Coronavirus Disease 2019 (COVID-19) is a new coronavirus disease caused by SARS-CoV that first appeared in the Chinese city of Wuhan at the end of December 2019. Saudi Arabia counted 255,825 cumulative cases between March 2, 2020 and mid-July 2020 and has reported a COVID-19 mortality rate of 1%.

Multisystem Inflammatory Syndrome in Children (MIS-C) is an inflammatory condition caused by COVID-19 that affects different body organs in children, including the brain, eyes, heart, lungs, kidneys, gastrointestinal organs, and skin. The U.S. Centers for Disease Control (CDC) issued an alert on May 14, 2020 urging pediatricians to consider MIS-C when evaluating pediatric patients with COVID-19. The first MIS-C case was described in April 2020, and no MIS-C cases were diagnosed in Saudi Arabia until the time we wrote this case report.

2. CASE REPORT

A 4-year-old female child was admitted with a 3-day history of mild acute febrile illness and gastrointestinal manifestation in the form of repeated nonbilious or projectile or bloody vomitous. Her condition was associated with periumbilical abdominal pain and watery, nonbloody, nonmucoid diarrhea 3–4 times per day. The child had high levels of inflammatory markers, thrombocytopenia, and neutrophilia.

The family denied any history of contact with individuals with COVID-19. The child had no respiratory symptoms, and her senses of smell and taste were preserved. A physical examination showed a sick girl who was dehydrated and extremely tired but with stable vital signs. Her throat was erythematous with no cervical lymph node enlargement. The abdominal exam findings were normal.

A Complete Blood Count (CBC) examination showed neutrophilia and lymphopenia. The C-reactive protein level was high. Stool virology tests for adenovirus and rotavirus and a stool culture were negative.

She was started on ceftriaxone and intravenous fluid for rehydration. The next day, her condition worsened and her fever spiked and became higher and more frequent. The fever was unresponsive to paracetamol; therefore, ibuprofen every 6–8 h was started with diclofenac suppositories given every 12 h.

On the third day, a macular rash (non-itchy, blanchable on pressure) appeared, mainly on the trunk (Figure 1) and somewhat over the limbs and the face (Figure 2) with bilateral nonpurulent bulbar (limbus-sparing) conjunctivitis.

A urinary workup initially showed proteinuria and hematuria with negative culture results. A repeat CBC showed a decreased platelet count, hypoalbuminemia, high ferritin level, high lactate dehydrogenase level, and high D-dimer level.

*Corresponding author. Email: rolasleimanbarada@gmail.com
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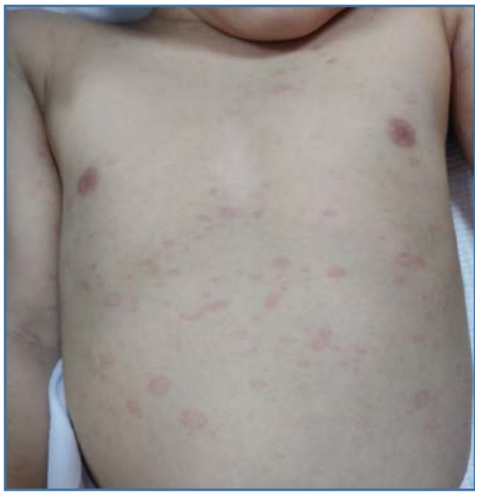

Figure 1 | Macular rash over the trunk.

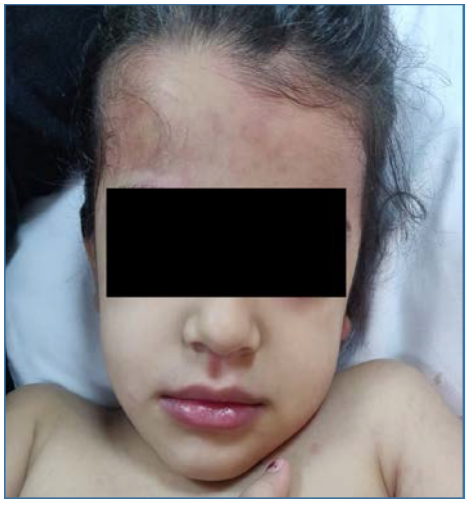

Figure 2 | Kawasaki-like syndrome showing erythema and red lips.

The child's condition continued to worsen throughout the third day, she looked very sick, and she had a persistent fever and tachycardia. Her oxygen saturation was 100% on room air, and her blood pressure was stable. Electrocardiography (ECG) showed abnormal nonspecific changes in the ST-segment and T-wave, whereas echocardiography findings were unremarkable. Abdominal ultrasonography performed owing to the persistent severe crampy pain revealed mesenteric lymphadenitis. Chest radiography showed a right-sided infiltrate.

At that point, the need for Intravenous Immunoglobulin (IVIG) and referral to the pediatric intensive care unit was discussed with the parents because of the possibility of incomplete Kawasaki or multisystem inflammatory syndrome associated with COVID-19. The father admitted that he had tested positive for COVID-19 4 weeks prior to her admission. The child had been swabbed at that time, but the result was negative.

Upon learning this information, we immediately took a COVID-19 swab and tested her immunoglobulin G level; both came back positive. Fortunately, the child started to improve, the fever became less frequent, the rash faded, and she started to eat without abdominal pain. The platelet count increased on the fifth day after admission. She was discharged home on no medication with good clinical follow-up on the seventh day after discharge. All viral workups including serology for Epstein–Barr virus, cytomegalovirus, and parvovirus were negative.

Informed consent was obtained from the girl's parents for publication of her details and these figures.

2.1. Laboratory Values

Results of her laboratory tests are shown in Tables 1–3.

3. DISCUSSION

Since the start of the COVID-19 pandemic, children have been less commonly affected than adults. With the percentage of positive pediatric cases varying from 1% to 5% [1], Saudi Arabia shows a similar incidence [2]. Children rarely develop respiratory distress syndrome. Unfortunately, since March 2020, a new complication has appeared in pediatric patients related to an inflammatory response to COVID-19 that mimics the mysterious Kawasaki disease. The number of patients with Kawasaki disease suddenly increased, and all tested positive for COVID-19. An Italian study reported a 30-fold increase in Kawasaki disease during the COVID-19 outbreak [3].

After the CDC advisory about MIS-C was delivered in mid-April [4], many cases were reported worldwide, with more than 1000 cases at the time we wrote this article. By definition, MIS-C involves the association between COVID and an inflammatory syndrome marked by signs of Kawasaki disease such as a rash and red eyes with a persistent fever and gastrointestinal manifestations with increased inflammatory markers that can occur 2–4 weeks after COVID-19 exposure.

The relationship between coronaviruses and Kawasaki disease is not new. In 2005, a group from the United States reported a higher prevalence of human coronavirus in respiratory swabs of children with Kawasaki disease compared with a control group. They raised suspicions about the role of the coronavirus family in the pathogenesis of Kawasaki disease [5].

This case is one of a few MIS-C and COVID-19 cases diagnosed in one of Saudi Arabia's private tertiary hospitals and is the second published case report. The first case was of a child with glucose-6-phosphate dehydrogenase deficiency who died after COVID-19 exposure but was not diagnosed with MIS-C [6].

Upon comparing MIS-C to Kawasaki disease, we found that they share several clinical manifestations such as fever, skin rash, and conjunctivitis. However, gastrointestinal manifestations in the form of severe abdominal pain seem more frequent with MIS-C with a prevalence of up to 81% [7], similar to our patient. The main finding of abdominal ultrasound is mesenteric adenitis. The typical thrombocytosis of Kawasaki disease is absent in MIS-C; however, thrombocytopenia is a characteristic laboratory finding.

Our patient had tachycardia with ECG changes, but the echocardiography findings were normal. We were worried about myocarditis or pericarditis, which have been described in many series, but fortunately neither affected our patient [8].

Table 1 | Laboratory findings in a case of MIS-C in Saudi Arabia

Laboratory test	Reference values	Result on July 7, 2020	Result on July 9, 2020	Result on July 10, 2020
White blood cell count, $\times 10^9$ cells/L	5–15	5.52	5.12	6.16
Neutrophil count	1.5–6	3.86	3.75	3.78
Lymphocyte count	5–9	0.67	0.76	1.51
Hemoglobin	11–14	10.9	9.9	10.0
Hematocrit	33–42	32.8	29.4	31.2
Mean corpuscular volume	73–87	80.4	80.8	80.9
Mean corpuscular hemoglobin	26–32	26.8	27.1	26.0
Platelet count	150–400	124	105	187
C-reactive protein	<5	102.6		118.9
Albumin	38–54			27
Alanine transaminase	<55		17	14
Aspartate transaminase	5–34		27	32
Lactate dehydrogenase				426
Erythrocyte sedimentation rate	<11			51
Ferritin	5.3–99.9			572.25
Potassium	3.5–5.1			4.8
Sodium	136–145			142
Urea	2.78–8.07			4
Creatinine	28–52			31
Carbon dioxide	18			
Prothrombin time				11.2
Partial thromboplastin time	27–35			22.8
International normalized ratio				1.0
D-dimer	0–0.5			3.1

MIS-C, multisystem inflammatory syndrome associated with coronavirus disease 2019 (COVID-19).

Table 2 | Laboratory findings in a case of MIS-C in Saudi Arabia

Blood C/S	No bacterial growth	July 7, 2020
Stool analysis	No ova or parasites	July 8, 2020
Urine C/S	No bacterial growth	July 8, 2020
Stool C/S	No *Salmonella* or *Shigella*	July 8, 2020
Stool rotavirus	Negative	July 8, 2020
Stool adenovirus	Negative	July 8, 2020
C Strep A	Negative	July 8, 2020
COV-IgG	Positive (6.89; ref. <1.4)	July 11, 2020
Urine C/S	No bacterial growth	July 11, 2020
Cytomegalovirus IgG	Negative	July 10, 2020
Cytomegalovirus IgM	Negative	July 10, 2020
Epstein–Barr virus VCA	Nonreactive	July 10, 2020
Epstein–Barr virus EBNA	Nonreactive	July 10, 2020
Parvo B19	Negative	July 10, 2020
Salmonella typhi	Negative	July 10, 2020
Salmonella paratyphi	Negative	July 10, 2020
COV-PCR	COVID-19 RRL-positive	July 12, 2020

COV, coronavirus; C/S, culture and sensitivity; EBNA, Epstein–Barr nuclear antigen; IgG, immunoglobulin G; IgM, immunoglobulin M; MIS-C, multisystem inflammatory syndrome associated with COVID-19; PCR, polymerase chain reaction; RRL, rapid response laboratory; VCA, viral capsid antigen.

Table 3 | Urinalysis findings in a case of MIS-C in Saudi Arabia

Test	July 8, 2020	July 9, 2020	July 11, 2020
Urine specific gravity	1.025	1.030	1.010
Urine protein	++	+	Non
Urine ketones	+++	Non	+
Urine blood	++	++	Trace
Urine nitrite	Non	Non	Non
Urine bilirubin	Non	Non	Non
Urine urobilinogen	Normal	Normal	Normal
Urine leukocytes	Non	Non	Non
Urine red blood cells	5–10	2–5	0–2
Urine white blood cells	0–2	0–2	2–5

MIS-C, multisystem inflammatory syndrome associated with COVID-19.

Our patient experienced spontaneous remission; she was clinically very sick, but her condition improved dramatically on the fifth day after treatment. This is the most common outcome, but death has been reported [8].

A possible explanation for this evolution is that the patient's condition was not severe from the start and she had no bad prognostic criteria mentioned in some cohort studies [8] such as age older than 5 years, ferritin level >1400, no respiratory distress, or obesity. The other possibility is that her condition improved dramatically because of the early use of Nonsteroidal Anti-inflammatory Drugs (NSAIDs). Despite the precaution of using such drugs in confirmed COVID-19 cases, our patient was given generous doses of ibuprofen and diclofenac to control the fever. As she was treated as having gastroenteritis only, those drugs could play a role in the inflammatory process.

We could not identify a clear role of the NSAIDs in the treatment of this case of MIS-C, which is usually treated mainly with IVIG and steroids. Further studies are necessary to confirm such observations.

4. CONCLUSION

Multisystem inflammatory syndrome in children is a new complication of COVID-19. Pediatricians must be aware of the diagnostic criteria established by the U.S. CDC to ensure its early detection. Nonetheless, the treatment and prognosis of affected children require further research. Reporting such cases and sharing clinical experiences will improve our understanding of this mysterious disease.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

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ABBREVIATIONS

CBC, complete blood count; CDC, Centers for Disease Control; COVID-19, coronavirus disease; ECG, electrocardiography; IVIG, intravenous immunoglobulin; MIS-C, multisystem inflammatory syndrome associated with COVID-19; NSAIDs, non-steroidal anti-inflammatory drugs.

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