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Case report

Multi-System Inflammatory Syndrome in Children (MIS-C) Reported in COVID-19 Positive 2.5-Year Old Boy

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Abstract

Multi-System Inflammatory Syndrome in Children (MIS-C) has been recently described as a newly emerging serious condition linked to COVID-19.

We, hereby, describe and report the clinico-laboratory characteristics of a 2.5-year-old boy who tested positive for SARS-CoV2 and exhibited an image of MIS-C. We seriously want to spotlight this new entity in Saudi Arabia where the peak of SARS-CoV2 is descending whereas MIS-C case might be increasing. The same scenario had occurred in other countries. We recommend reporting possible cases of MIS-C to our local, state, or territorial health department. We expect increased reporting cases of COVID-19-associated MIS-C in Saudi Arabia and Arabian Gulf region.

Keywords: ***COVID-19, SARS-CoV2, MIS-C, Multi-System Inflammatory Syndrome in Children, Saudi Arabia, Riyadh, Pediatrics***

Introduction

Multi-System Inflammatory Syndrome in Children (MIS-C) has been recently described as a newly emerging serious condition linked to COVID-19. As delineated in the CDC Health Advisory, the case definition for COVID-19 associated MIS-C is: An individual aged <21 years presenting with [1]:

- Fever ≥38.0°C for ≥24 hours,
- Laboratory evidence of inflammation (Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6, elevated neutrophils, reduced lymphocytes and low albumin)
- Evidence of clinically severe illness requiring hospitalization,
- Multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological)
- No alternative plausible diagnoses.
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.

Methods and materials

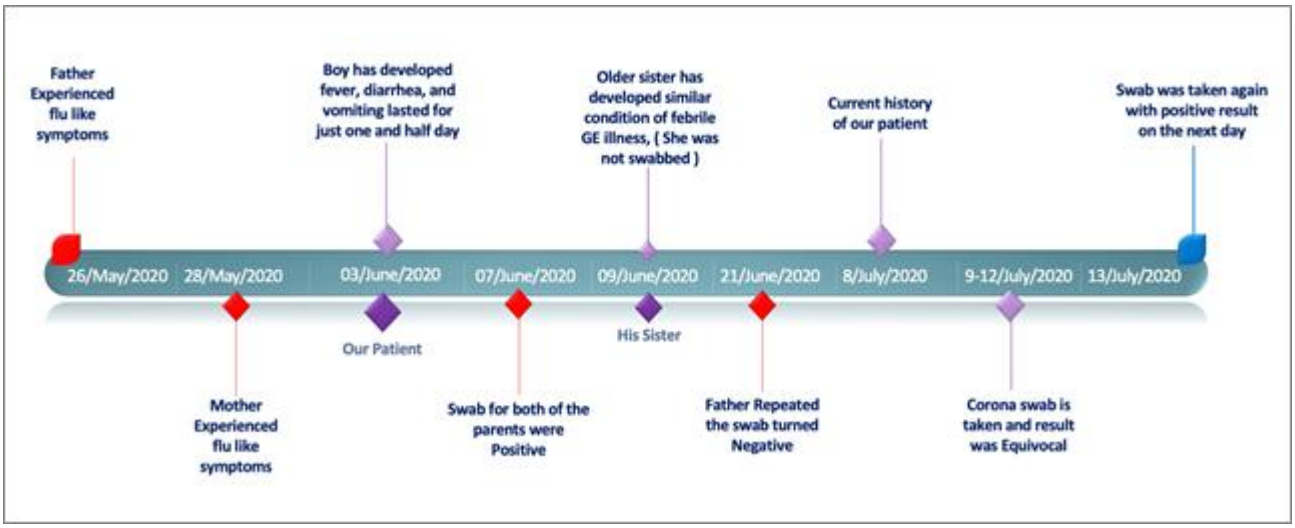
We, hereby, describe and report the clinico-laboratory characteristics of a 2.5-year-old boy who tested positive for SARS-CoV2 and exhibited an image of MIS-C.

Case Report

On July 2020, we admitted a 2.5-year-old Jordanian boy, who is previously healthy, to our pediatric ward. He had presented with a 5-day history of documented-at-home high-grade fever (more than 39) in conjunction with a constellation of clinical symptomatology that appeared 24 hours prior to admission, these were diarrhea, vomiting, decreased oral intake, and non-itching skin rash. It is worth noting that parents of the above-mentioned child, were tested positive for a symptomatic SARS-CoV2 infection one month before the current hospitalization of their son which he had been screened for on the first day of febrile episode, which was done in another hospital, and turned out to be negative in advance of his clinical deterioration.

Medical history of the family: Family is composed of the child parents, his older 42-month-old sister, and our patient.

Figure 1: Timeline events for the case.



Date	Event
26/May/2020	Father Experienced flu like symptoms
28/May/2020	Mother Experienced flu like symptoms
03/Jun/2020	Our patient developed fever, diarrhea and vomiting lasted for just one and half day
07/Jun/2020	Swab for both parants were positive and for the patient was Negative
09/Jun/2020	His older sister developed similar condtion of febrile GE illness, However she was not swabbed
21/Jun/2020	Father had repeated swab and that turned Negative
8/July/2020	On Evening, the current history of our patient has started
09-12/July/2020	Corona swab taken and result on 12/July was equivocal
13/July/2020	Swab is taken again with positive result obtained on the next day

Upon presentation, his vital signs were HR: 148 bpm, BP: 95/48, RR: 25, Temperature: 39.2 C, O2sat: 97%. On initial physical examination, he was febrile, ill-looking, and hyper excitable. He has small-sized lymph nodes (less than 1 cm) in the groin, axilla, and neck, injected throat, and maculo-papular rash over his torso, trunk, both buttocks, and less condense in the face, and it spares palms and soles (figures 2, 3, and 4). He has no any other clinical criteria of Kawasaki disease. Rest of his clinical examination revealed non-evident abnormalities.

The initial blood work-up demonstrated Pancytopenia, high inflammatory markers, hyponatremia, hypoalbuminemia, and lymphopenia. LDH, Fibrinogen, Troponin, liver enzymes, PT, and PTT all are normal. (Details and progression of Labs are in Table 1):

Table 1: Result of Blood investigations, details and progression.

Labs / Date	12/7	15/7	17/7	18/7	24/7	Reference Range
WBC	3	7.85	8.01	10.34	6.61	5-15 *1000 10e9/L
ANC	2440	6100	5580	4940	350	1.5-6 *1000 10e9/L
Neutrophils%	81%	78%	69.67%	47.74%	53%	25-60 %
Lymphocytes	279	1150	2002	4427	2411	5-9 *1000 10e9/L
Lymphocytes%	9.25%	14.6%	24.99%	42.82%	36.50%	20-70 %
Hemoglobin	10.2	8.3	8.8	8.2	9.0	11-14 g/L
PLT	55	52	195	293	906	140-450 *1000 10e9/L
Potassium	4.3	3.3	3.8	3.7	4.5	3.4-4.7 mmol/L
Sodium	133	137	136	131	141	136-145 mmol/L
Albumin	34	25	26	24	29	38-54 g/l
D-dimer	3.77	3.95	3.86	5.38	6.01	0 – 0.5 mcg/ml
ESR	60	___	65	91	26	< 11 mm/1Hour
CRP	111.6	158	94.9	64.2	4.1	< 5 mg/L
Procalcitonin	5.33	9.47	45.48	___	0.26	< 0.5 ng/ml

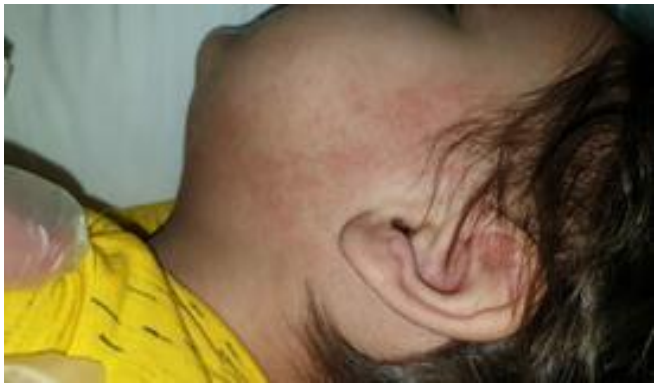
LDH	174	___	___	___	___	120-300 U/L
Ferritin	638.17	587.78	335.9	281.61	143.20	5.3-99.9 ng/mL
Fibrinogen	314	___	226.4	182.8	109	200-400 mg/dl

The fever was unremitted and poorly responds to paracetamol. He was started on maintenance IV fluid, IV ceftriaxone, and regular dose of paracetamol. We have investigated other related possible diagnoses such as EBV (Ebstien-Barr Virus), Adenovirus, Brucellosis, and Enteric fever. Peripheral blood film revealed normal shape of neutrophils and lymphocytes, normocytic normochromic anemia, mild anisocytosis, and Poikilocytosis, and large platelets. Abdominal ultrasound detected mild hepatomegaly liver size 13 cm, edema of gallbladder wall, and mild to moderate ascites.

During the next 48 h he began deteriorating with worsening respiratory condition, acral coldness, delayed capillary refill and tachycardia, tachypnoea and relatively low blood pressure. His repeated chest X-ray revealed worse infiltrations (figure 5), and Echocardiogram showed signs of mild carditis with mild pericardial effusion, mild mitral and tricuspid regurgitation, and prominent coronary arteries without ectasia or aneurysm. He required to be transferred to PICU, where we commenced him on anti-inflammatory management of 2 doses IVIG 2 gram/kg of each, high doses of Aspirin, and methylprednisolone pulse therapy. CRP, Ferritin were both trended down. But Pro-calcitonin has increased to 43 that indicated extending antibiotic coverage on which had reduced to 11. He was connected to low flow nasal cannula of oxygen. No mechanical ventilation or other invasive procedures have been required.

Patient improved and discharged home on tapering oral steroid therapy, low-dose Aspirin, and regular follow up in the general and cardiac clinics.

Figure 2, 3 and 4: Depicted below are the child's pictures.



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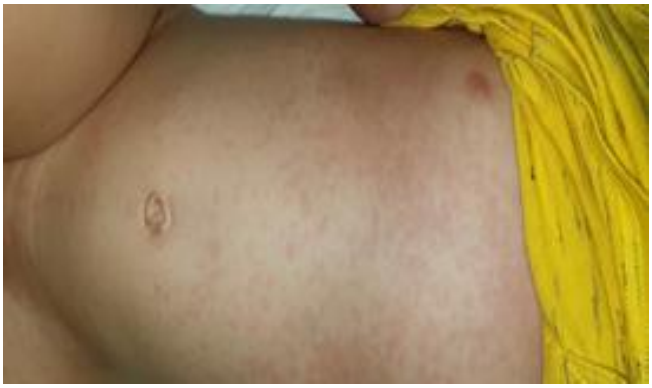

(3)

(4)

''Upon Admission''

''Before shifting him to PICU''

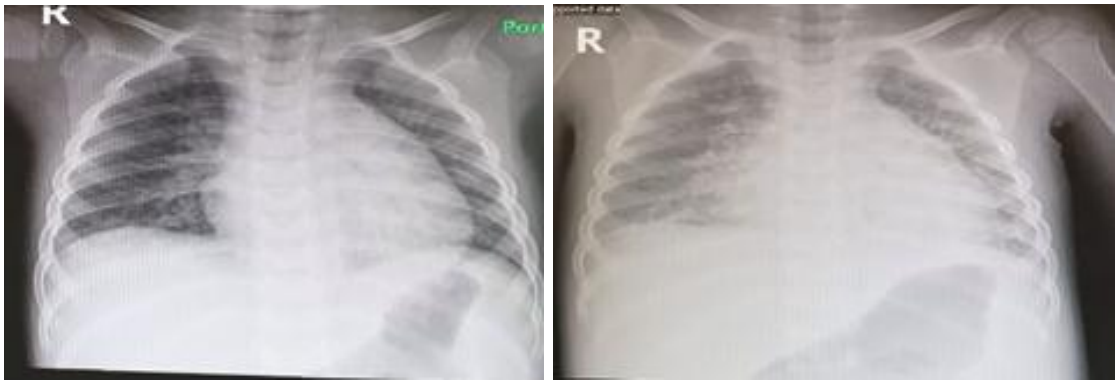

Figure 5. Chest X-Ray of our patient.

Discussion

Emerging reports from Europe and the United States have suggested that COVID-19 may be associated with MIS-C (also referred to as pediatric multisystem inflammatory syndrome–temporally associated with SARS-CoV-2 [PMIS-TS]). The syndrome was first described in the United Kingdom, were previously healthy children with severe inflammation and Kawasaki disease-like features were identified to have current or recent infection with SARS-CoV-2 [2]. Additional cases of MIS-C have been reported in other European countries, including Italy and France [3,4]. Emerging data suggest that MIS-C may be associated with pediatric patients who are slightly older than children typically seen with Kawasaki disease, and some cases of MIS-C in young adults have been reported [5].

In the United States, from April 16 through May 4, 2020, the New York City Department of Health and Mental Hygiene received reports of 15 hospitalized children with clinical presentation consistent with MIS-C. Subsequently, the New York State Department of Health has been investigating several hundred cases and a few deaths in children with similar presentations, many of whom tested positive for SARS-CoV-2 infection by reverse transcriptase polymerase chain reaction (PCR) or serology [6]. Several other states are now reporting cases consistent with MIS-C.

On May 15 the CDC issued a Health Advisory to define MIS-C and to warning physicians and health care providers for this new entity.

The last update data about Epidemiology of MIS-C on July 2020 in United State disclosed that the incidence of Multisystem Inflammatory Syndrome in Children (MIS-C) was 2 per 100,000 in the time period from March 1 through May 10, 20. The number of cases may have been underestimated due to mild MIS-C cases that did not involve hospitalization, lack of recognition of an emerging syndrome, and absence of a full panel of inflammatory markers [7].

MIS-C may be a post-infectious inflammatory response rather than a direct viral process [8], which is supported by the clinical and laboratory features of hyperinflammation [9],[7], the timing of onset in relation to SARS-CoV-2 infection [9],[7],[10] and similarities with disease pattern in adults [9]. The role of asymptomatic infection and timing between SARS-CoV-2 infection and MIS-C are unknown, and a causal relationship has not been established [8].

MIS-C management decisions should involve a multidisciplinary team of pediatric specialists in intensive care, infectious diseases, cardiology, hematology, and rheumatology. Clinical course and treatment are not well defined. Management is mainly supportive. There are insufficient data to recommend for or against any therapeutic strategy for management of MIS-C, and the role of COVID-19 therapies is not clear. Antiplatelet and anticoagulant therapy, along with IV immune globulin, corticosteroids, and other immunomodulators are considered at many centers [11, 12].

Locally in Saudi Arabia, a published case of Saudi G6PD deficient girl died with Pediatric Multisystem Inflammatory Syndrome-COVID-19 as described by authors. She was, by far, the only reported MIS-C case at the national level due to scant data on this regard [13]. However, as per our local conducting research in other facilities in Riyadh, and other provinces, where several similar cases are reported.

Our case has met all CDC definition criteria of COVID19-associated MIS-C with positive results for both SARS-CoV2 PCR and IgG serum antibodies. The positive High IgG serology might suggest a possible subsequent post-infectious process mechanism. However, this is not simply to ascertain the mechanism of COVID19-associated MIS-C.

The negative result of SARS-CoV2 PCR from the first nasopharyngeal swab taken within the first 24h of our patient's illness can be explained by a false negativity. The antibiotics covering our patient was guided by clinical and laboratory references. We upgraded this coverage from ceftriaxone and azithromycin to meropenem and teicoplanin. However, blood and urine cultures had no growth.

Conclusion

We seriously want to spotlight this new entity in Saudi Arabia where the peak of SARS-CoV2 is descending whereas MIS-C case might be increasing. The same scenario had occurred in other countries. We recommend reporting possible cases of MIS-C to our local, state, or territorial health department. We expect increased reporting cases of COVID19-associated MIS-C in Saudi Arabia and Arabian Gulf region.

Author Contribution

MAA; Co-author, Planning the case report conception and design, reviewing relevant literature, the final writing
ASA; Co-author, reviewing the case report scenario
ADA; Co-author, reviewing Labs
WAO; Co-author, Discussion

List of Abbreviations

Abbreviation		Full Form
COVID-19	:	CoronaVirus Disease 2019
SARS CoV2	:	Sever Acute Respiratory Syndrome CoronaVirus 2
MIS-C	:	Multi-System Inflammatory Syndrome in Children
SA	:	Saudi Arabia
CDC		Center for Disease and Control
PICU	:	Pediatric Intensive Care Untie
RT-PCR	:	Reverse Transcriptase Polymerase Chain Reaction
WBC	:	White Blood Cell
ANC		Absolute Neutrophils Count
BUN	:	Blood Urea Nitrogen
ALT	:	Alanine AminoTransferase
AST		Aspartate Transminase
PLT	:	Platelet
HR	:	Heart Rate
BP	:	Blood Pressure
RR	:	Respiratory Rate

Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethical Approval

This article does not contain any studies with human participant or animals performed by any of the authors.

Informed Consent

Informed consent was obtained from the legal guardian of the child included in the study.

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