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Tricky Presentation of Multisystem Inflammatory Syndrome in Children (MIS-C) with in Pediatric

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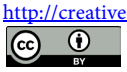

Abstract

Introduction: In emergence a COVID patient with multisystem inflammatory syndrome in children (MIS-C), associated with SARS-CoV-2, has shown increasing number among pediatric. Even the same presentation of Kawasaki disease we have to keep in mind MIS-C, in order to reach a consensus on this new disease in the future. Three variations of the disease patterns were reported: a group of children with increase in inflammatory activity and persistent fever, without criteria for Kawasaki disease, a second group with Kawasaki disease criteria, and a third group with shock, coronary aneurysms, severe cardiac dysfunction, and gastrointestinal symptoms. Classic Kawasaki disease is self-limited vasculitis which affects medium-sized vessels, almost occurred in children under five years old. Here, we bring a Saudi case, present to emergency department in Prince Sultan Military Medical City. **Case report:** 10 years old female, medically free, presented with abdominal pain, fever and skin rashes. Patient had history of COVID-19 infection 1 month before presentation. Initial investigations showed acute kidney injury with elevated inflammatory markers. **Conclusion:** Further evidence of the increase in the incidence of pediatric MIS-C, temporarily is associated with SARS-CoV-2. Physician should give more attentions to this new diagnosis with more fatal outcomes than Kawasaki cases.

Keywords

Kawasaki or Kawasaki-Like Syndrome, Vasculitis, Multi Organ Failure, Myocarditis, Fever, Abdominal Pain, Skin Rash, Intravenous Immunoglobulin, Acute Kidney Injury and Raised Inflammatory Markers

1. Introduction

China, on December 19th, 2020, reported first case of (SARS-CoV-2) COVID-19. In addition to the involvement of the respiratory system it shows a more benign evolution [1] [2] [3] [4] [5]. However, there are reports of frequent gastrointestinal involvement [6] and, among other symptoms, an incidence increase of Kawasaki or Kawasaki-like syndrome, when associated with SARS-CoV-2 [7] [8].

On April 7, 2020, the first case report of Kawasaki like disease (KD) and COVID-19 a six-month-old child with was published in the US. Cases occurred shortly after exposure to COVID-19 suggesting a possible temporal correlation with SARS-CoV-2 infection, as some patients had positive polymerase chain reaction (PCR) or serology. This syndrome was called the "multisystem inflammatory syndrome in children (MIS-C)" [9] [10] [11].

2. Case Illustration

2.1. History

A 10 year old girl not known to have any medical illness came to emergency with a history of fever for the last five days and lower abdominal pain. The patient seek medical advice in a private hospital where she was diagnosed as having a urinary tract infection for which she received IV ceftriaxone injection for three days after which she developed generalized skin rash. As a result her parent stopped the medication and brought her to our emergency. In addition to the above patient had vomiting, diarrhea, decreased activity and poor oral intake. There is past history of Covid-19 infection 1 month ago. Patient is developmentally normal and fully vaccinated with average school performance.

2.2. Examination

Unwell looking female patient presented with fever, diffuse abdominal pain without tenderness, generalized body ache and widespread macular rashes all over the body. She was vitally stable and other systemic examination was unremarkable.

2.3. Diagnosis Work Up and Therapeutic Interventional

Normal Saline bolus given and blood investigations were extracted which showed (**Table 1** below) abnormally elevated inflammatory markers and renal function tests. Imaging also requested to rule out any abdominal emergencies. No signs of Intestinal Obstruction were seen in abdominal x ray and abdominal ultrasound showed mild hepatomegaly with free fluid collection in the pelvis otherwise unremarkable findings, while Chest x ray showed bilateral infiltrates with no ARDS picture.

When all items put together including history, clinical presentation, investigations, the patient met the CDC criteria of Multi system inflammatory syndrome of COVID in children (MIS-c).

Two hours later, the patient misbehaved and showed hypotension, tachycardia

Table 1. Initial laboratories result.

Item	*Result*	*Reference range*
RBCS	4.74	4.00 - 5.20
Platelet count	78,000	150,000 - 450,000
HB	96	115.0 - 155.0 gr/L
D-dimer	10,774	0 - 500 ng/L
LDH	365	120 - 300 unit/L
Creatinine	134	29 - 56 mcmol/L
Urea	12.7	2.8 - 8.1 mmol/L
Procalcitonin	14.20	Less than 2 mcg/L
CRP	133.91	0 - 6 mg/L
Ferritin	1637	7 - 140 micg/L

and signs of respiratory distress, for that she received additional 2 boluses of Normal Saline (20 ml/kg) and PICU was called for respiratory support and further management.

Choosing antibiotics was tricky as patient had query history of ceftriaxone hypersensitivity (skin rashes) with acute kidney injury.On the other hand, we needed good coverage of antibiotics with minimal side effects, so decision made to start Linezolid and Meropenem intravenously as empirical antibiotics. Respiratory distress was observed on the second day of admission, in the form of increasing oxygen requirement, so the patient was hooked to high flow nasal cannula then she was attached to BIPAP.

While patient was in PICU, serology for Covid-19 tested positive and an ECHO showed dilated left ventricle with moderate mitral regurgitation and depressed ejection fraction to 35% with no pulmonary embolism and normal coronary arteries, therefore IV Lasix started (1 mg/kg/day). Additionally the patient was on continuous infusion of Inotrope (Dopamine 10 mic/kg/min& epinephrine dose 0.05 mic/kg/min which shifted to Milronine 0.3 mic /kg/min). In addition to that an Intravenous Immunoglobulin (IVIG) (1 gram/Kg/dose) was given for 2 doses with pulse doses of methylprednisolone IV (30 mg/kg/dose) for 5 days. The Infectious Disease team recommended to continue Linezolid and Meropenem IV as started in ER and to add oral Favipiravir. Hematology point of view was to start enoxaparin subcutaneously once daily.Five days later, pulse methylprednisolone and furosemide were shifted to oral form with addition of oral Captopril.

Cardiac and respiratory functions improved by clinical and imaging basis, so respiratory support weaned gradually to room air after 5 days of admission.

Blood and urine culture showed no growth after 5 days and ECHO repeated and showed improvement of cardiac functions. Oral intake was allowed gradually and was tolerated.

3. Discussion

Currently, there are two criteria to diagnose MIS-C, CDC and WHO criteria. Our patient met almost all the items of CDC criteria in the form of age < 21 years, clinical presentations which included fever > 38 C, high inflammatory markers (elevated CRP, Fibrinogen, D-dimer, ferritin, LDH, procalcitonin), multi-system involvement (respiratory, renal, cardiac, gastrointestinal, hematological and dermatological) in addition to severe illness requiring hospitalization with positive serology of COVID-19.

Three variations of the disease patterns were reported: a group of children with increase in inflammatory activity and persistent fever, without criteria for Kawasaki disease, a second group with Kawasaki disease criteria, and a third group with shock, coronary aneurysms, severe cardiac dysfunction, and gastrointestinal symptoms [12].

Classic Kawasaki disease is self-limited vasculitis which affects medium-sized vessels, almost occurred in children under five years old [13] [14].

The American Heart Association (AHA) definition of Kawasaki's definition, persistent fever for a period of five days or more, plus four out of five mucocutaneous criteria are required (last updated in 2017), Despite an undefined etiology, there is suggestive evidence that an infectious agent triggers an inflammatory cascade that leads to Kawasaki disease [15] [16]. Gastrointestinal symptoms, such as nausea, diarrhea, lack of appetite and abdominal pain were much more frequent in MIS-C than in Kawasaki disease, showing in 100% of cases in the French study [8] [9] [10] [11].

Untreated children, 20% develop coronary aneurysm with a significant increase in the risk of infarction and thrombosis in adulthood. More severe cases can occur with Kawasaki shock syndrome, and rarely with macrophage activation syndrome [7].

Mild cases of MIS-C could be treated as classic Kawasaki, with immunoglobulin infusion (IVIG) 2 g/kg; biological agents such as anti-interleukin 1, and corticosteroids.

In more severe cases of MIS-C, in addition to IVIG and aspirin, the use of methylprednisolone in the form of pulse therapy is recommended—at a dose of 30 mg/kg/day, for three days, for severe cases, and in moderate cases, 10 - 20 mg/kg/day for one to three days, followed by a maintenance dose. Mild-to-moderate cases of MIS-C can be managed with a prophylactic dose of enoxaparin and severe cases with a therapeutic dose [17] [18] [19].

Our patient classified as severe form of MIS-C. When current guidelines were applied to our patient, the patient dramatically improved clinically and laboratory.

The total length of stay was 14 days, 10 days in PICU and 4 days in pediatric ward.

Patient discharged in good healthy condition with the following home medications in the form of tapering dose of oral prednisolone, aspirin 81 mg/day, oral

Captopril 12, 5 mg and oral Lasix. Follow up with cardiology and rheumatology was planned after 2 weeks of hospital discharge.

4. Conclusion

Further evidence of the increase in the incidence of pediatric MIS-C, temporarily is associated with SARS-CoV-2. Physician should give more attentions to this new diagnosis with more fatal outcomes than Kawasaki cases. The diagnosis is challenging due to the variety of clinical and laboratory manifestations, with either positive or negative COVID-19 results, but that should not delay therapy as soon as the diagnostic suspicion is generated. Follow-up is important, as these complications may appear later. We await further studies, given the novelty of the disease to improve the diagnosis and care of the pediatric population.

Ethics approval

Signed informed consent for participation and republication of medical details was obtained from the parent of this child. The confidentiality of the patient data was secured all the time.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviation

MIS-C: Multisystem Inflammatory Syndrome in Children;
SARS-CoV-2: Sever Acute Respiratory Syndrome-Corona Virus 2;
ARDS: Acute Respiratory Distress Syndrome;
CDC: Centers for Disease Control and Prevention;
PICU: Paediatric Intensive Care Unit;
BIPAP: Bilevel Positive Airway Pressure;
WHO: World Health Organization.