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MIS-C among return visits for fever in a pediatric emergency department during the COVID-19 pandemic

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1. Case report

Fever is the most common symptom associated with severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) infections in children. Although majority of cases in children have been mild, severe complications such as Multisystem inflammatory syndrome in children (MIS-C) can occur. These children are often critically ill with a mortality rate of 2–4%. Initial symptoms of MIS-C are non-specific and mimic other viral illness making early diagnosis challenging. We report five patients who were evaluated for fever and discharged from our PED and were subsequently diagnosed with MIS-C (n = 3) or Kawasaki Disease (n = 2) during their RV within 7 days. All patients presented with fever during the initial visit and three of the five children had gastrointestinal symptoms. They were all noted have persistent tachycardia during the index visit. Three patients presented in cardiogenic shock and echocardiographic abnormalities were noted in four patients during the RV. Significant interventions were required in majority of these children (PICU admission: 4, inotropes: 3, mechanical ventilation:2). Clinicians need to maintain a high index of suspicion for diagnosis of MIS-C especially in those who present with persistent fever and have abnormal vital signs during the COVID-19 pandemic.

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1. Case report

Fever is the most common symptom associated with severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) infections in children. Although majority of cases in children have been mild, severe complications such as Multisystem inflammatory syndrome in children (MIS-C) have occurred. The return visits (RV) of children who were evaluated for fever and discharged home during the pandemic is unknown. We performed a retrospective chart review of RV of children ≤18 years of age who were evaluated for fever and discharged from our pediatric emergency department (PED) during the first six months (4/1/2020–12/31/2020) of the Corona Virus Disease 2019 (COVID-19) pandemic to identify those children who were diagnosed with Multisystem Inflammatory Syndrome in children (MIS-C) or Kawasaki Disease during the RV. Our PED is an inner city level 1 trauma center attached to a free standing children’s hospital with approximately 85,000 visits/year.

Among the seventy seven children who had a seven day RV after an index visit for fever, five children (5/77; 0.6%) were diagnosed with MIS-C (n = 3) and Kawasaki disease (n = 2). These children ranged in age from 1 to 15 years. Sixty percent were male and African American. Three children had gastrointestinal symptoms and one child had a rash. All children had persistent tachycardia during the index visit. One of these children had a screening evaluation for MIS-C during the index visit which was only abnormal during the RV. The laboratory results are noted in Table 1b. All children had elevated CRP (median: 263; IQR: 279.85) and D-Dimer (median: 2.29; IQR: 17.81). Lymphopenia was noted in three children. Serum troponin was abnormal in four children and...
Table 1a
Description of children with a return visit diagnosis of MIS-C/Kawasaki Disease (KD).

| ID | Age in years | Sex | Past medical history | First visit symptoms | Physical exam-first visit | Physical exam-return visit | Admit to PICU | Treatment | COVID PCR | COVID IgG | Diagnosis | Hospital LOS |
|----|--------------|-----|----------------------|----------------------|--------------------------|---------------------------|----------------|-----------|-----------|-----------|-----------|------------|---------------|
| 1  | 3            | Female | None                | Fever (2 days)        | Fever Tachycardia        | Ill-appearing              | Yes           | IVIG Inotropic support (epinephrine-1 day) | Negative | Not performed | MIS-C     | 4 days       |
| 2  | 15           | Male  | Asthma, Obesity     | Fever (2 days)        | Fever Tachycardia Pharyngeal erythema | Shock with severely depressed myocardial function | Yes           | IVIG Infliximab Inotropic support (epinephrine -4 days), Mechanical ventilation - 4 days | Negative | Not performed | MIS-C     | 8 days       |
| 3  | 11           | Male  | Asthma, Eczema      | Fever (2 days)        | Fever Tachycardia Pharyngeal erythema | Ill-appearing Tachycardia Tachypnea Rash Shock | Yes           | IVIG Infliximab Inotropic support (dopamine and epinephrine -4 days) Mechanical ventilation – 6 days | Negative | Not performed | MIS-C     | 9 days       |
| 4  | 1            | Male  | None                | Fever (2 days)        | Fever Tachycardia         | Ill-appearing Tachycardia  | No            | IVIG Aspirin | Negative | Negative | Kawasaki Disease | 6 days      |
| 5  | 5            | Female | None                | Fever (3 days)        | Fever Tachycardia Cervical lymphadenitis | Ill-appearing, Tachycardia Red eyes Dry cracked lips Rash Cervical lymphadenitis | Yes           | IVIG (twice) Infliximab Aspirin | Negative | Negative | Kawasaki Disease | 6 days      |

Table 1b
Laboratory, electrocardiogram, and echocardiogram findings on initial and return visits of patients ultimately diagnosed with MIS-C or Kawasaki.

| Type                  | Patient 1 Initial | Patient 1 Return | Patient 2 Initial | Patient 2 Return | Patient 3 Initial | Patient 3 Return | Patient 4 Initial | Patient 4 Return | Patient 5 Initial | Patient 5 Return |
|-----------------------|-------------------|------------------|-------------------|------------------|-------------------|------------------|-------------------|-------------------|-------------------|-------------------|
| CRP mg/L              | 39.3              | 263              | 322               | 16.2             | 20                | 297              |
| Sodium mMol/L         | 136               | 126              | 137               | 135              | 14                | 124              |
| ALT Units/L           | 20                | 35               | 77                | 14               | 225               |
| Albumin gm/dl         | 3.5               | 3.3              | 4                 | 4.7              | 3.5               |
| Ferritin ng/mL        | 101.5             | 860              | 615               | 37.4             | 390               |
| Troponin ng/L         | 22                | 119              | 1797              | 5                | 10                |
| BNP pg/ml             | 858               | n/a              | 1090              | n/a              | 21                |
| ALC Units/L           | 1.6               | 1.1              | 0.6               | 2                | 0.9               |
| D Dimer mg/L          | 2.29              | 2.95             | 1.68              | 0.46             | 3.5               |
| Electrocardiogram     | Sinus             | ST-T wave changes | Junctional rhythm or ventricular rhythm | NA               | Normal            |
| Echocardiogram        | Normal            | Mild left ventricular dysfunction and mitral regurgitation | Severe left ventricular dysfunction | NA               | Normal            |
|                       |                   |                   |                   |                   |                   |

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brain natriuretic peptide was abnormal in three children. EKG abnormalities were noted in two children with MIS-C and included junctional rhythm in one and ST-T wave changes in another. Echocardiogram was abnormal in one patient and included mitral regurgitation in three patients, mild left ventricular dysfunction in two patients, severe left ventricular dysfunction in one patient and pulmonary regurgitation in one patient. Four children required admission to the intensive care unit, three required inotropic support and two required mechanical ventilation (table 1a). There were no deaths in our cohort.

2. Discussion

The World Health Organization (WHO) declared COVID-19 caused by SARS-CoV-2 as a pandemic on March 11, 2020. As of early December 2021, 7 million children have tested positive for COVID-19 [1]. MIS-C is a rare complication of children with COVID-19 with a reported incidence of 2 per 100,000 [2]. It is associated with a mortality of 2–4% [3] and with cardiogenic shock and coronary artery aneurysms in 20% of patients [4,5]. The Center for Disease Control (CDC) and WHO have published guidelines for diagnosis and work up of children with suspected MIS-C [6,7]. Early recognition and timely management is critical for favorable outcomes in children with MIS-C.

Presenting symptoms of MIS-C include fever, gastrointestinal symptoms such as abdominal pain vomiting and diarrhea, rash and conjunctival injection. Since these symptoms often mimic other common viral illness clinical distinction is often difficult. However, children diagnosed with MIS-C in our case series demonstrated persistent tachycardia and nearly two thirds of them presented in cardiogenic shock. Thus, it is critical for clinicians to be vigilant of abnormal vital signs and maintain a high index of suspicion for diagnosis of MIS-C especially in those who present with persistent fever and elevated inflammatory markers. Common laboratory findings noted in children with MIS-C include elevated inflammatory markers such as C reactive protein, ferritin, and lactate dehydrogenase as well as hyponatremia, acute kidney injury and elevated D-dimers. Since MIS-C often develops a few weeks after SARS-CoV-2 infection or exposure, serology testing is often recommended in addition to RT-PCR testing. Though children with MIS-C often have elevated inflammatory markers, it is important to note that the screening evaluation for MIS-C can be misleadingly normal if the children have been symptomatic only for a short duration (≤ 24 h). Hence, it is critical to arrange for a timely follow up as well repeat the screening labs for MIS-C for the subset of children who continue to be symptomatic.

The major morbidity noted in children with MIS-C results from cardiac abnormalities which include ventricular dysfunction, coronary artery dilation and aneurysms, arrhythmia, and conduction abnormalities [8]. Patients with severe illness often present in cardiogenic shock requiring inotropic support, mechanical ventilation and extracorporeal membrane oxygenation. Given the frequent association with cardiac abnormalities, all patients with suspected MIS-C should undergo evaluation with an electrocardiogram, echocardiogram as well serial monitoring of troponin and BNP. Prompt recognition and admission to a pediatric intensive care unit of children with cardiac involvement at risk for hemodynamic compromise is essential to improve mortality and morbidity.

Funding and disclosures

None.

Declaration of Competing Interest

None.

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