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A Pregnant Adolescent with COVID-19 and Multisystem Inflammatory Syndrome in Children

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Abstract

Multisystem inflammatory syndrome in children (MIS-C), a new condition related to coronavirus disease 2019 (COVID-19) in the pediatric population, was recognized by physicians in the United Kingdom in April 2020. Given those up to the age of 21 years can be affected, pregnant adolescents and young adults are susceptible. However, there is scant information on how MIS-C may affect pregnancy and whether the presentation differs in the pregnant population. We report a case of a pregnant adolescent with COVID-19 and MIS-C with a favorable outcome. This case highlights the considerations in managing a critically ill pregnant patient with a novel illness and the importance of a multidisciplinary team in coordinating care.

Keywords
- multisystem inflammatory syndrome in children
- COVID-19
- pregnancy
- critical illness

The novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged from Wuhan, China in late 2019 and has spread across the globe. Its associated disease, COVID-19, has affected millions worldwide. Children were thought to be relatively spared compared with adults, with only 1.7% of infections in the United States occurring in persons younger than 18 years.[1] In late April 2020, however, physicians in the United Kingdom described the emergence of a severe inflammatory syndrome in children with recent or current SARS-CoV-2 infection.[2] This disease, now known as multisystem inflammatory syndrome in children (MIS-C), comprises features of Kawasaki disease and toxic shock syndrome. Criteria for diagnosis include age younger than 21 years, fever for more than 24 hours, laboratory evidence of inflammation, dysfunction in more than two organ systems, no plausible alternative diagnosis, and either current or recent SARS-CoV-2 infection or known exposure within 4 weeks prior to symptom onset.[3]

Given that MIS-C can affect adolescents and young adults, a population capable of pregnancy, it follows that some of those with the disease will be pregnant. We present the case of a pregnant adolescent with MIS-C.

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Case Report

The patient is a 16-year-old female, G2P0010, at $24^{6/7}$ weeks' gestation who presented to the emergency department with 1 week of chest pain, dyspnea, subjective fever, and known COVID-19 exposure. Her chest pain worsened when she was supine and improved with leaning forward. She was otherwise healthy with no known medical problems and had an uncomplicated pregnancy to date.

Upon presentation, she was febrile to 40°C, tachycardic up to 146 beats per minute, and hypotensive with blood pressure as low as 78/52 mm Hg. Her oxygen saturation remained more than 97% on room air and she was alert and oriented. Initial workup included chest X-ray which demonstrated cardiomegaly, computed tomography of the chest which was negative for pulmonary embolism but remarkable for ground glass opacities, and echocardiogram showing reduced left ventricular systolic function with ejection fraction 51%. Coronary arteries were normal. Electrocardiogram demonstrated sinus tachycardia with nonspecific ST/T wave changes. Laboratory tests were notable for elevated inflammatory markers including D-dimer 890 ng/mL (normal $<$ 230 ng/mL), C-reactive protein (CRP) 167.3 mg/L (normal 0–5 mg/L), and procalcitonin 0.57 ng/mL (normal $<$ 0.05 ng/mL). Ferritin was initially normal at 130 ng/mL (normal 5–204 ng/mL). Elevation of troponin I to 0.43 ng/mL was also noted (normal $<$ 0.04 ng/mL). White blood cell count was 23.2×10^3 µL (normal $4.2–9.4 \times 10^3$ µL). Nasopharyngeal swab for SARS-CoV-2 was negative, as were blood and urine cultures.

Despite negative nasopharyngeal swab result, the patient was presumed to have COVID-19 given symptoms, laboratory and imaging findings, and known exposure. She remained hypotensive despite fluid boluses and was thus transferred to the intensive care unit for blood pressure support and further management with presumed diagnosis of COVID-19 pericarditis, myocarditis, and pneumonia.

The patient was managed by a multidisciplinary team including critical care, pediatric cardiology, infectious disease, and maternal–fetal medicine. A discussion was held regarding her clinical status, gestational age, and maternal–fetal implications of periviable birth. The fetus had recently demonstrated appropriate estimated fetal weight for gestational age. The patient stated she desired full intervention for maternal or fetal indications and consent for classical cesarean delivery was obtained. It was decided that delivery would be performed for maternal deterioration, to improve resuscitative efforts, or for nonreassuring fetal status. Given her wishes and critical illness, a course of betamethasone was administered. Fetal surveillance was performed with daily nonstress tests, which was noted to be reassuring.

Over the next several days, she became progressively more tachypneic and hypoxic, requiring supplemental oxygen via nasal cannula then high-flow nasal cannula. Two additional nasopharyngeal swabs for SARS-CoV-2 were sent over this time and resulted as negative. She ultimately required intubation on hospital day 3. Nasopharyngeal swab from the tracheal aspirate taken at the time of intubation returned positive for SARS-CoV-2.

The patient was initially treated with azithromycin, hydroxychloroquine, and zinc for COVID-19, as well as ceftriaxone for possible superimposed bacterial pneumonia. Methylprednisolone was given due to hypotension refractory to volume expansion as well as to treat rapidly progressing acute respiratory distress syndrome (ARDS) and cytokine storm. Approval for compassionate use of remdesivir was obtained and administered following intubation. Prone positioning was utilized while the patient remained intubated, with care taken to cushion and support the gravid abdomen. She required blood pressure support with norepinephrine and was started on a heparin drip for elevated D-dimer.

While intubated, an erythematous rash was noted on her palms that then desquamated. She also developed diarrhea. Testing for *Clostridium difficile* was performed and returned negative. Repeat echocardiogram demonstrated stable but reduced ejection fraction at 50 to 55% as well as dilation of the left ventricle. Her troponin normalized. The peak values of her inflammatory makers were D-dimer 1,003 ng/mL, CRP 249 mg/L, ferritin 670 ng/mL, and procalcitonin 0.57 ng/mL. All eventually downtrended throughout her course. In addition, she developed a significant anemia with hemoglobin nadir of 6.6 g/dL for which she received a total of three units packed red blood cells. The anemia was attributed to her illness as there was no evidence of active bleeding and she was not anemic prior to presentation.

She was extubated on hospital day 7, weaned off supplemental oxygen, and transitioned to room air. Fetal nonstress tests were appropriate for gestational age throughout her admission. The patient was discharged on hospital day 12 with scheduled follow-up with pediatric cardiology and maternal–fetal medicine. She remains stable and undelivered at the time of this writing.

Discussion

To our knowledge, this is the first case of a pregnant adolescent with MIS-C. She meets criteria based on her age, fever, cardiac, respiratory, gastrointestinal, and dermatologic organ system involvement, multiple elevated inflammatory markers, and positive SARS-CoV-2 tracheal aspirate. The patient presented prior to the first description of MIS-C and therefore this diagnosis was recognized retrospectively.

The first report of MIS-C includes eight children who presented with features similar to Kawasaki disease and toxic shock syndrome.[2] The children had fever, rash, conjunctivitis, edema, and gastrointestinal symptoms. They progressed to shock and there was one death. A 30-fold increase in Kawasaki-like disease was then reported in the Bergamo province of Italy.[4] Some though not all of the affected children in both studies tested positive for SARS-CoV-2 or had known COVID-19 exposure. Similar cases were reported in the United States, prompting the Centers for Disease Control and Prevention to issue a health advisory to further draw attention to this emerging entity.[3]

Current evidence suggests MIS-C is due to an immune-mediated response to the virus rather than direct infection. MIS-C lagged behind the peak of reported infections by

approximately one month. In addition, some children who tested negative for SARS-CoV-2 via nasopharyngeal swab were found to have positive immunoglobulin G antibodies, suggesting past but not current infection.[5]

Proposed therapies include those typically given for Kawasaki disease such as intravenous immunoglobulin and aspirin as well as methylprednisolone, antibiotics, and anticoagulation.[2,4,6] Immunomodulating agents such as interleukin-6, interleukin-1, and tumor necrosis α inhibitors have also been proposed as treatment given the presence of markedly elevated cytokines and immune-mediated basis of the disease.[5] Since MIS-C had not been fully characterized at the time of our patient's presentation, she was not offered some of these therapies and instead was treated with recommended medications for COVID-19 in adults at that time including hydroxychloroquine and remdesivir. Importantly, she did receive a course of high-dose methylprednisolone. Though it was started for refractory hypotension, severe ARDS and cytokine activation as measured by elevated inflammatory markers, it may have helped treat her MIS-C as well. She also received antibiotics and anticoagulation. With both COVID-19 and MIS-C, the benefits of many therapies are uncertain, and more evidence is needed.

MIS-C, like other critical illness, has the potential for maternal deterioration and the risks and benefits of delivery at the patient's particular gestational age should be discussed. It is unclear how delivery may affect the clinical course of MIS-C especially when considering fluid shifts in the setting of compromised cardiac function. Fortunately, this patient did not have signs of fetal compromise during her hospitalization and delivery was not necessary. Obstetric care and the decision to deliver should be individualized and when possible, the patient should be involved in discussions about the risks and benefits of medical interventions and fetal surveillance. Management of critically ill pregnant women often requires a multidisciplinary team approach including maternal–fetal medicine specialists along with experts in medicine and various subspecialties as appropriate.

It is unknown if MIS-C has any effects on ongoing pregnancy or increases risk for preterm delivery. Our patient's cardiac function remains a concern, especially as she enters the third trimester when cardiac demand is at its greatest. However, one series found that cardiac dysfunction resolved in 71% of cases.[6] She will be followed with serial echo assessments to evaluate if she is adequately adapting to the increased cardiovascular demands of pregnancy. It is also uncertain if MIS-C or SARS-CoV-2 infection affects the placenta or developing fetus. However, early reports suggest the virus may be cultured from the placenta[7] and placentas of women with SARS-CoV-2 show increased prevalence of arteriopathy and malperfusion.[8] More data are needed and will be obtained as the pandemic continues and women who experienced SARS-CoV-2 infections remote from delivery progress through their pregnancies.

Obstetricians should be aware of MIS-C as the affected population can overlap with the pregnant population. Multidisciplinary care and a team-based approach should be undertaken to optimize maternal and fetal outcomes.

Conflict of Interest
None declared.

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