

Case Report

Coronavirus Disease 2019 (COVID-19)–Related Multisystem Inflammatory Syndrome in a Pregnant Woman

Moti Gulersen, MD, MSc,
Cara Staszewski, MD,
Evelina Grayver, MD,
Hima Tam Tam, MD,
Eric Gottesman, MD,
Donnie Isseroff, MD,
Burton Rochelson, MD,
and Clarissa Bonanno, MD

BACKGROUND: Recent reports have described a rare but severe complication of coronavirus disease 2019 (COVID-19) in nonpregnant adults that is associated with extrapulmonary organ dysfunction and appears to be secondary to a hyperinflammatory state.

CASE: A multiparous woman at 28 weeks of gestation, diagnosed with COVID-19 4 weeks prior, was admitted with chest pain. Evaluation indicated myocarditis and marked elevations of inflammatory markers consistent with multisystem inflammatory syndrome in adults. The patient developed cardiogenic shock and required mechanical ventilation. Treatment with intravenous immunoglobulin and high-dose corticosteroids was associated with a favorable maternal and fetal outcome.

CONCLUSION: Multisystem inflammatory syndrome in adults associated with COVID-19 in pregnancy is a critical illness, presenting several weeks after initial

Teaching Points

1. Multisystem inflammatory syndrome in adults is an atypical presentation of COVID-19 in pregnancy, which may present several weeks after infection.
2. Multisystem inflammatory syndrome in adults in pregnancy is a critical illness that requires multidisciplinary management to optimize maternal and fetal outcomes.
3. As described in nonpregnant patients, intravenous immunoglobulin and high-dose corticosteroids should be considered for treatment of multisystem inflammatory syndrome in adults in pregnancy.

infection. Treatment with intravenous immunoglobulin and corticosteroids was associated with a favorable outcome.

(*Obstet Gynecol* 2020;00:1–5)

DOI: 10.1097/AOG.0000000000004256

Whereas patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection may experience a range of clinical manifestations,¹ severe or critical coronavirus disease 2019 (COVID-19) in pregnant and nonpregnant individuals most commonly affects the lungs.^{2–7} Recent reports describe a rare, but potentially severe, complication of COVID-19 in adults likely caused by a hyperinflammatory state, similar to the multisystem inflammatory syndrome reported in children.^{8–11} Multisystem inflammatory syndrome in adults is defined by extrapulmonary organ dysfunction and absence of respiratory illness.^{8–11} The effect of multisystem inflammatory syndrome in adults in pregnancy is unknown. We report the case of a preterm gravid woman with multisystem inflammatory syndrome in adults, which developed 4 weeks after her COVID-19 diagnosis.

CASE

A 31-year-old woman, gravida 4 para 1112, presented at 28 4/7 weeks of gestation reporting a 1-day history of fever and chest pain. This pregnancy was complicated by diagnosis of COVID-19 with mild symptoms 4 weeks prior, confirmed by qualitative real-time polymerase chain reaction (PCR) testing. The patient was managed with supportive outpatient care, with resolution of initial symptoms (ie, cough, myalgias, and diarrhea) after approximately 1 week. Her medical history was significant for class 1 obesity and childhood asthma.

From the Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, the Department of Cardiology, the Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, and the Department of Anesthesiology, North Shore University Hospital–Zucker School of Medicine at Hofstra/Northwell, Manhasset, New York.

Each author has confirmed compliance with the journal's requirements for authorship.

Corresponding author: Moti Gulersen, MD, MSc, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, North Shore University Hospital, Manhasset, NY; email: mgulersen1@northwell.edu.

Financial Disclosure

The authors did not report any potential conflicts of interest.

© 2020 by the American College of Obstetricians and Gynecologists. Published by Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0029-7844/20



On presentation, the patient reported severe left-sided chest pain, worse with inspiration, and shortness of breath. She had no obstetric symptoms. Physical examination revealed a normotensive, ill-appearing woman with fever (temperature 100.8°F), tachycardia (heart rate 122 beats per minute), and oxygen saturation of 100% on room air. She had no abdominal or uterine tenderness on palpation. Initial laboratory studies were significant for leukocytosis (white blood cell count of 16,450 mm³ with 84% neutrophils) and an elevated C-reactive protein (13.06 mg/dL). Serum coagulation studies, a complete metabolic panel, cardiac enzymes, lactate, ferritin, and procalcitonin were within normal limits. The results of routine respiratory viral testing using PCR on nasopharyngeal swab specimen were negative. The patient's SARS-CoV-2 PCR test result was positive, and her SARS-CoV-2 immunoglobulin G index was positive at 6.89 arbitrary units/mL (1.40 arbitrary units/mL or greater). An electrocardiogram revealed sinus tachycardia, computed tomography angiography of the chest was negative for pulmonary embolism and other lung pathology, and the results of a lower extremity Doppler ultrasound scan were normal. A transthoracic echocardiogram revealed a hyperdynamic left ventricle (ejection fraction of 65–70%), normal right ventricular function, and a trace pericardial effusion. A fetal nonstress test was reactive. Owing to concern for sepsis and the low likelihood of recurrent COVID-19 infection,¹² ceftriaxone was initiated. The cardiology team suspected a diagnosis of pericarditis, and the patient was treated with pain medication and dexamethasone (intravenous 6 mg daily).

On hospital day 4, her clinical condition deteriorated and she was transferred to the medical intensive care unit, where she remained febrile with worsening tachycardia as well as new-onset hypotension (blood pressure 83/41 mm Hg) and tachypnea (respiratory rate 55 breaths/minute). Repeat laboratory evaluation was notable for marked elevations in several serum markers: C-reactive protein 31.46 mg/dL (from 13), D-dimer 1,225 ng/mL (from 577), troponin T 146 ng/L (from undetectable), creatinine kinase-MB 4 ng/mL (from undetectable), serum pro-brain natriuretic peptide 1,668 pg/mL (from 549), leukocytosis 18,630 mm³ (from 11,920), fibrinogen 1,225 ng/dL, and SARS-CoV-2 immunoglobulin G 59.60 arbitrary units/mL (from 6.89). An electrocardiogram showed sinus tachycardia without ischemic changes, and transthoracic echocardiogram revealed severe global biventricular dysfunction with a trace pericardial effusion. Oxygen saturation remained at 100% on room air.

A multidisciplinary team including members from maternal-fetal medicine, cardiology, critical care, anesthesiology, infectious disease, neonatology, and nursing discussed the patient's critical status and plan of care. Cardiogenic shock secondary to myocarditis in the setting of multisystem inflammatory syndrome in adults was suspected. The patient expressed clearly that she wished for all possible interventions to prioritize her health and that she wanted to avoid any intervention that would increase her

personal risk, even if that decision would increase the risk for the fetus. Because delivery in her immediate condition could be life-threatening, delivery for fetal indication was not being considered and fetal monitoring was deferred.

The decision was made to intubate the patient and assess invasive cardiac hemodynamics with a Swan Ganz catheter to provide more detailed information regarding her care. Mechanical circulatory support options, including intraaortic balloon pump (Impella) or extracorporeal membrane oxygenation, were available if needed. After intubation and placement of the Swan Ganz catheter, as well as initiation of dobutamine and vasopressor support, cardiac function stabilized.

Intravenous immunoglobulin and high-dose dexamethasone (intravenous 10 mg every 6 hours) therapy were initiated. The patient's serum inflammatory markers remained elevated, including interleukin-6 (8.3 pg/mL). Therapeutic anticoagulation with intravenous unfractionated heparin to maintain a partial thromboplastin time of 60–80 seconds was initiated given her multiple risk factors for venous thromboembolism. After 4 days of immunoglobulin and corticosteroid therapy, the patient's cardiac function improved, at which time she required only low-dose dobutamine, and she was extubated on hospital day 8.

That same day, new-onset mild-range hypertension (blood pressure 140–156/90–99 mm Hg) and acutely rising aspartate aminotransferase (828 units/L), alanine aminotransferase (630 units/L), lactate dehydrogenase (757 units/L), and proteinuria (4+ protein on urinalysis) levels were noted. In the absence of multisystem inflammatory syndrome in adults or other pathology to explain these new findings, the diagnosis of preeclampsia with severe features was suspected, and delivery was indicated for maternal benefit. Intravenous magnesium was initiated for seizure prophylaxis and fetal neurologic benefit. Ultrasound scan confirmed a fetal heart rate of 144 beats per minute before delivery. An uncomplicated repeat cesarean birth was performed under general anesthesia, resulting in delivery of a 1,290-g male newborn with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. Transesophageal echocardiography to evaluate cardiac function was used throughout the cesarean birth, and mechanical support options were available if needed.

The patient's postoperative course showed continued improvement in cardiac function, with treatment of hypertension with hydralazine for afterload reduction, as well as downtrending liver enzymes. She was extubated 1 day postpartum and advanced on all postoperative milestones by postoperative day 2. She received intravenous immunoglobulin and high-dose corticosteroids for a total of 5 and 10 days, respectively, and was discharged home on postoperative day 7. Normal cardiac function was visualized on echocardiogram and magnetic resonance imaging before discharge. Newborn SARS-CoV-2 PCR test results using nasopharyngeal swab specimen were negative, and he remains in the neonatal intensive care unit with complications related to prematurity.



DISCUSSION

Multisystem inflammatory syndrome and its association with COVID-19 was first reported as a life-threatening illness in previously healthy children and adolescents.^{13–15} Clinical characteristics include fever, abdominal pain, cardiovascular shock, and hyperinflammation, as well as mucocutaneous manifestations similar to those of Kawasaki disease.^{13–15} The emergence of this syndrome appeared in patients with negative SARS-CoV-2 PCR test results and after several countries had reported a downtrend in infection rates, suggesting a delayed onset of this critical illness after infection.⁸ Recently, several reports have described a similar multisystem inflammation syndrome in adults, which differed from severe or critical COVID-19 based on the presence of minimal respiratory symptoms, hypoxemia, or the common radiographic abnormalities such as bilateral opacities or consolidation.^{8–11}

The Centers for Disease Control and Prevention outlined the clinical course of 27 patients with multisystem inflammatory syndrome in adults from the United States and the United Kingdom, in which cardiac dysfunction was seen in almost all patients.⁸ Our patient met all five criteria for diagnosis (Table 1). The majority of patients with multisystem inflammatory syndrome in adults survived (24/27, 89%), and they were most commonly treated with intravenous immunoglobulin and corticosteroids; use of inotropes and vasopressor support was also common.⁸

Given the associated risks of venous thromboembolism, seven patients included in the Centers for

Disease Control and Prevention analysis were treated with therapeutic anticoagulation.⁹ Six patients (6/27, 22%) required mechanical ventilation, and the three patients who died had comorbid conditions such as obesity, hypertension and diabetes, a previous respiratory illness, and significant radiographic lung disease on presentation.⁸ Survivors were discharged home 5–25 days after hospitalization.⁸

The time interval between SARS-CoV-2 infection and development of multisystem inflammatory syndrome in adults varies and has reportedly been between 2 and 5 weeks, whereas median onset of critical COVID-19–associated respiratory illness is 10–12 days after symptom onset, emphasizing the distinct distribution of the two clinical courses in nonpregnant patients.^{1,2,8} Moreover, treatment regimens may be different—patients with severe or critical COVID-19 may benefit from antiviral therapy with remdesivir in addition to corticosteroids,^{1,16,17} whereas patients with multisystem inflammatory syndrome in adults improve with immunoglobulin therapy and corticosteroids.⁸

Cardiomyopathy and myocardial injury associated with COVID-19 in pregnancy have been reported.^{18,19} However, each patient with cardiac disease simultaneously presented with severe or critical COVID-19 respiratory illness or hypoxemic respiratory failure, and cardiac disease was present relatively early in the disease course compared with the findings described in nonpregnant patients with multisystem inflammatory syndrome in adults and our patient.^{8,18,19}

Table 1. Diagnostic Criteria of Multisystem Inflammatory Syndrome in Association With Our Patient's Presentation

CDC Diagnostic Criteria for Multisystem Inflammatory Syndrome in Adults	Case Patient Presentation
Severe illness requiring hospitalization in a person aged 21 y or older	31 y old
Positive test result for current or previous SARS-CoV-2 infection (nucleic acid, antigen, or antibody) during admission or in the previous 12 wk	Positive SARS-CoV-2 PCR test result from nasopharyngeal swab specimen on admission and 4 wk prior, positive SARS-CoV-2 IgG antibody on admission
Severe dysfunction of 1 or more extrapulmonary organ systems (eg, hypotension or shock, cardiac dysfunction, arterial or venous thrombosis or thromboembolism, or acute liver injury)	Myocarditis, shock
Laboratory evidence of severe inflammation (eg, elevated CRP, ferritin, D-dimer, or interleukin-6)	Elevated CRP, ferritin, D-dimer, and interleukin-6
Absence of severe respiratory illness (to exclude patients in which inflammation and organ dysfunction might be attributable simply to tissue hypoxia)	No respiratory symptoms, maintained oxygen saturation at normal levels on room air, no lung pathology on imaging

CDC, Centers for Disease Control and Prevention; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; PCR, polymerase chain reaction; IgG, immunoglobulin G; CRP, C-reactive protein.



Of note, our patient developed new-onset hypertension, proteinuria, and an acute rise in liver enzymes 5 days after initiating intravenous immunoglobulin and high-dose corticosteroid therapy. At that time the patient was otherwise clinically improving, suggesting her inflammatory syndrome responded appropriately to therapy. Although the diagnosis of preeclampsia was suspected and has been associated with COVID-19,²⁰ it is a clinical diagnosis that requires the absence of any underlying pathology that may explain such findings. This was unclear in our patient, because her transaminitis may have reflected another extrapulmonary organ dysfunction characterized by multisystem inflammatory syndrome in adults. However, the patient's downtrending liver enzymes soon after delivery supports the diagnosis of preeclampsia. Our patient highlights the need for maintaining a broad differential diagnosis when considering clinical conditions associated with COVID-19 in pregnancy.

In conclusion, clinical features in our patient included persistent fevers, shock, cardiac dysfunction, and elevated serum inflammatory markers, which developed weeks after initial infection. A multidisciplinary team approach and treatment with intravenous immunoglobulin and high-dose corticosteroids were associated with a favorable outcome for the mother and her newborn. Although our patient required delivery for a subsequent pregnancy-related complication, the rapid improvement in her clinical status after treatment suggests that prolonging pregnancy may be considered a reasonable option in other antepartum patients with multisystem inflammatory syndrome in adults, depending on the clinical scenario and gestational age at presentation. A better understanding of this rare complication of COVID-19 in pregnancy is urgently needed to optimize care for this challenging illness.

REFERENCES

- Centers for Disease Control and Prevention. Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19). Accessed October 19, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>
- National Institutes of Health. Clinical presentation of people with SARS-CoV-2 infection. Accessed October 19, 2020. <https://www.covid19treatmentguidelines.nih.gov/overview/clinical-presentation>
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020;323:1061–9. doi: 10.1001/jama.2020.1585
- Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. Coronavirus disease 2019 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. *Am J Obstet Gynecol MFM* 2020;2:100118. doi: 10.1016/j.ajogmf.2020.100118
- Lokken EM, Walker CL, Delaney S, Kachikis A, Kretzer NM, Erickson A, et al. Clinical characteristics of 46 pregnant women with a severe acute respiratory syndrome 2 infection in Washington state. *Am J Obstet Gynecol* 2020;19:S0002–9378(20)3055–8. doi: 10.1016/j.ajog.2020.05.031
- Pierce-Williams RAM, Burd J, Felder L, Khoury R, Bernstein PS, Avila K, et al. Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a US cohort study. *Am J Obstet Gynecol MFM* 2020;2:100134. doi: 10.1016/j.ajogmf.2020.100134
- Blitz MJ, Rochelson B, Minkoff H, Meirowitz N, Prasanna L, London V, et al. Maternal mortality among women with coronavirus disease 2019 admitted to the intensive care unit. *Am J Obstet Gynecol* 2020;223:595–9.e5. doi: 10.1016/j.ajog.2020.06.020
- Morris SB, Schwartz NG, Patel P, Abbo L, Beauchamps L, Balan S, et al. Case series of multisystem inflammatory syndrome in adults associated with SARS-CoV-2 infection—United Kingdom and United States, March–August 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1450–6. doi: 10.15585/mmwr.mm6940e1
- Chau VQ, Giustino G, Mahmood K, Oliveros E, Neibart E, Oloomi M, et al. Cardiogenic shock and hyperinflammatory syndrome in young males with COVID-19. *Circ Heart Fail* 2020;13:e007485. doi: 10.1161/CIRCHEARTFAILURE.120.007485
- Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP, et al. Large-vessel stroke as a presenting feature of COVID-19 in the Young. *N Engl J Med* 2020;382:e60. doi: 10.1056/NEJMc2009787
- Magro C, Mulvey JJ, Berlin D, Nuovo G, Salvatore S, Harp J, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. *Transl Res* 2020;220:1–13. doi: 10.1016/j.trsl.2020.04.007
- Centers for Disease Control and Prevention. Duration of isolation and precautions for adults with COVID-19. Accessed October 19, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html>
- Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. *N Engl J Med* 2020;383:334–46. doi: 10.1056/NEJMoa2021680
- Whittaker E, Bamford A, Kenny J, Kafouru M, Jones CE, Shah P, et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. *JAMA* 2020;324:259–69. doi: 10.1001/jama.2020.10369
- Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J, et al. COVID-19-associated multisystem inflammatory syndrome in children—United States, March–July 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1074–80. doi: 10.15585/mmwr.mm6932e2
- Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the treatment of COVID-19—final report. *N Engl J Med* 2020;2007764. doi: 10.1056/NEJMoa2007764



17. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL. Dexamethasone in hospitalized patients with COVID-19—preliminary report. *N Engl J Med* 2020:2021436. doi: 10.1056/NEJMoa2021436
18. Juusela A, Nazir M, Gimovsky M. Two cases of coronavirus 2019-related cardiomyopathy in pregnancy. *Am J Obstet Gynecol MFM* 2020;2:100113. doi: 10.1016/j.ajogmf.2020.100113
19. Pachtman Shetty SL, Meirowitz N, Blitz MJ, Gadowski T, Weinberg CR. Myocardial injury associated with coronavirus disease 2019 in pregnancy. *Am J Obstet Gynecol* 2020 [Epub ahead of print]. doi: 10.1016/j.ajog.2020.10.014
20. Brandt JS, Hill J, Reddy A, Schuster M, Patrick HS, Rosen T, et al. Epidemiology of coronavirus disease 2019 in pregnancy: risk factors and associations with adverse maternal and neonatal outcomes. *Am J Obstet Gynecol* 2020:S0002-9378(20)31134-0. doi: 10.1016/j.ajog.2020.09.043

PEER REVIEW HISTORY

Received October 26, 2020. Received in revised form November 12, 2020. Accepted November 19, 2020. Peer reviews and author correspondence are available at <http://links.lww.com/AOG/C151>.

