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Two Cases of COVID-19 Related Cardiomyopathy in Pregnancy.

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Condensation: Of seven confirmed COVID-19 infections in pregnant women presenting to a single tertiary care center**,** two (28.6%) developed cardiomyopathy.

Keywords: COVID-19, novel coronavirus, pregnancy, cardiomyopathy

Abstract

In our institution, 2 of the initial 7 (28.6%; 95% CI 8.2%-64.1%) pregnant patients with confirmed COVID-19 severe infection developed cardiac dysfunction with moderately reduced left ventricular ejection fractions (LVEF) of 40%-45% and hypokinesis. Viral myocarditis and cardiomyopathy have been reported in non-pregnant COVID-19 patients. A case series of non-pregnant COVID-19 patients demonstrated that 33% of those in intensive care developed cardiomyopathy. More data are needed to ascertain the incidence of cardiomyopathy from COVID-19 in pregnancy, in all pregnant COVID-19 women, as well as those with severe (e.g. pneumonia) disease. We suggest an echocardiogram in pregnant women with COVID-19 pneumonia, in particular those necessitating oxygen, or critically ill, and we recommend handheld, point-of-care devices where possible to minimize contamination of staff and traditional, large echocardiogram machines.

Introduction

Coronavirus 2019 (COVID-19) is a novel coronavirus, responsible currently for a pandemic. The largest cohort to date of over 44,000 individuals from China with COVID-19 infection demonstrated that 81% had mild symptoms up to mild pneumonia, 14% had severe disease (dyspnea, hypoxia, or greater than 50% lung involvement on imaging), and 5% had critical disease (respiratory failure, shock, or multiorgan system dysfunction) [1]. It must be noted that in the original report, asymptomatic patients were not tested. Of those with severe disease, the case fatality rate was 49%, while the overall case fatality rate was 2.3% [1]. As most health care systems and countries are only testing symptomatic patients, the true prevalence of COVID-19 infection is unknown, as well as its true infection fatality rate; this has been recently estimated at about 0.66% [2]. Viral myocarditis and cardiomyopathy have been reported in non-pregnant COVID-19 patients [3-4]. A case series of non-pregnant COVID-19 patients in Washington State demonstrated that 33% of those in intensive care developed cardiomyopathy [3]. Information on COVID-19 in pregnancy is currently limited [4,5,6]. We are not aware of cardiomyopathy reported in pregnant women with COVID-19 infection. We present 2 of the first 7 pregnant patients with confirmed COVID-19 at a single tertiary care center who presented during March 2020, and developed cardiomyopathy.

Case Series

Case 1:

A 45 year-old African-American gravida 4 para 2 at 39 weeks and 2 days presented with contractions and emesis on 3/25/2020.The patient had a history of 2 full term vaginal deliveries and was a diet-controlled gestational diabetic (GDMA1). Her BMI was 44.6 m^2/kg. Her past medical history was significant just for obesity and advanced maternal age. Her only medication was a daily prenatal vitamin. The patient had no known contact with COVID-19 cases and had not traveled outside of the United States in the past month. She was found to be tachycardic with heart rate in the 120s beats/minute, fetal tachycardia with baseline fetal heart rate (FHR) in the 170s beats/minute, and initial temperature of 99.6° F. She was admitted for intravenous fluid hydration and prolonged monitoring. The patient developed a fever of 100.8° F two hours after admission, and work-up revealed a chest radiograph with pulmonary edema and a ground glass appearance. Six hours after presentation she developed severe range hypertension with blood pressure of 183/114 mmHg, HR in the 130s beats/minute, respiratory rate (RR) of 26/minute, temperature of 100.7° F and an oxygen saturation (SpO2) of 96%. Given the severe range blood pressures, a preeclampsia panel was sent which revealed a proteinuria of 1+, platelets of 274,000 per mcL, an aspartate aminotransferase (AST) of 32 IU/L and alanine aminotransferase (ALT) of 24 IU/L. A working diagnosis of preeclampsia was established, and magnesium sulfate was initiated for seizure prophylaxis. The patient's

RR increased to the 40s/minute and SpO2 dropped to 80% on oxygen via nasal cannula. After a discussion with maternal-fetal medicine, anesthesia, general obstetrics and gynecology, and cardiology, the decision was made to deliver the fetus to aid maternal resuscitation. The patient underwent a primary cesarean delivery 7.5 hours after presentation on 3/26/2020. On postoperative day (POD) #0 a maternal arterial blood gas (ABG) showed pH of 7.27, pCO2 of 31 mmHg, pO2 of 117 mmHg, HCO3 of 16 mEq/L, and a base excess of -11 mmol/L. A repeat chest radiograph revealed small peripheral bilateral opacities with differential diagnoses including atypical pneumonia, viral pneumonia, and congestive heart failure. Due to suspicion of congestive heart failure, magnesium sulfate was discontinued and furosemide was administered IV. Cardiology was consulted to perform an echocardiogram, which showed a moderately reduced left ventricular ejection fraction (LVEF) of 40% with global hypokinesis, and she was diagnosed with acute heart failure with reduced EF. Given the clinical picture of fever, tachypnea, and the chest radiograph findings amidst the background of a pandemic, a GeneXpert COVID-19 RNA polymerase chain reaction (PCR) test was performed and returned positive. Further laboratory investigation demonstrated a normal troponin of 0.046 ng/mL, a brain natriuretic peptide (BNP) of 114 pg/mL (normal <100 pg/mL), and a procalcitonin of 0.13 ng/mL (normal < 0.10 ng/mL). On POD #4, chest radiograph demonstrated worsening bilateral lung infiltrates, and despite oxygen therapy, the SpO2 could not be maintained above 90%. An electrocardiogram was performed with non-specific T-wave abnormalities otherwise a normal EKG, with a QT/QTc of 354/465 ms (both normal). Serum potassium was 3.7 mEq/L (normal). As the patient failed to improve, she was started on methylprednisolone IV 60mg every 3 hours and

hydroxychloroquine 400mg orally every 12 hours for 24 hours, followed by 400mg orally daily. That evening, after the initial doses were administered, she began desaturating to 86% on 6 liters of nasal cannula. An ABG revealed a pH of 7.07, pCO2 of 75 mmHg, pO2 of 85 mmHg, HCO3 of 21.7 mEq/L, and a BE of -2 mmol/L. She was placed on a non-rebreather at 15 liters, which initially improved the SpO2 to 90% and on POD #4 methylprednisolone 100mg IV daily was started. On POD #5 the patient again desaturated to the low 80's%. As our institutional COVID-19 protocol calls to avoid non-invasive mechanical ventilation which could aerosolize viral particles, the patient was intubated by anesthesia, but without improvement. The heart rate decreased to the 30's and the patient developed pulseless electrical activity (PEA). Cardiopulmonary resuscitation (CPR) was initiated and return of spontaneous circulation (ROSC) was obtained after 5 minutes of CPR. Post arrest her troponin level peaked at 0.930 ng/mL (normal <0.4 ng/mL), with a BNP of 323 pg/mL. After CPR the patient was started on a norepinephrine drip, initially at 8 mcg/minute and was titrated up to a maximum of 20 mcg/min. The patient was administered one dose of Tocilizumab, an interleukin-6 (IL-6) receptor antagonist 800mg IV. As of the writing of this article (4/2/2020), the patient is currently POD #7 and remains intubated and ventilated in the ICU, is arousable and moving all four extremities, with an SpO2 of 96%, continuance of the norepinephrine drip at 20 mcg/min, daily methylprednisolone 100mg IV daily, and hydroxychloroquine 400mg PO daily. Her significant laboratory values are: troponin 0.046 ng/mL and a markedly elevated procalcitonin of 48.21ng/mL.

Case 2:

A 26 year-old Latin American gravida 3 para 1 at 33 weeks and 6 days presented with shortness of breath, dyspnea, and decreased fetal movement on 3/27/2020. The patient has a history of 1 full-term vaginal delivery and the patient's husband was known to be positive with COVID-19 infection. Her BMI was 37 m^2/kg. Her past medical history was significant also for polycystic ovary syndrome, and her only medication was a daily prenatal vitamin. The patient's initial vital signs were HR in the 130s beats/minute, BP of 110s/70s mmHg, RR in the mid-20's/minute, an SpO2 of 95%, and an initial temperature of 99.3° F. The SpO2 improved to 97% on 2L nasal cannula. About 8 hours after presentation, her RR increased to the 40s/minute, with a HR in the 130s/minute, and SpO2 of 95%. An ABG showed a pH of 7.32, pCO2 of 18 mmHg, pO2 of 107 mmHg, HCO3 of 14 mEq/L, and a BE of -14 mmol/L. CXR demonstrated bilateral infiltrates. Work-up for metabolic acidosis with respiratory alkalosis was significant for an anion gap of 19, which when investigated, only demonstrated an elevated beta-hydroxybutyrate of 3.61 mmol/L (normal 0.02 to 0.27 mmol/L). Lactic acid was 0.6 mmol/L (normal 0.4 to 2.0 mmol/L) and the other differential diagnoses for anion gap acidosis were ruled out. As there was suspicion for COVID-19 infection, a general respiratory panel was sent and was negative, C-Reactive Protein (non cardiac) was 7.68 mg/dL (normal <3.0 mg/L), ferritin of 86 ng/mL, BNP of <10 pg/mL, procalcitonin of 0.17 ng/mL, troponin-I of <0.015, AST of 47 IU/L, and an ALT of 52 IU/L. Becton Dickinson COVID-19 testing, which was sent on 3/28/2020, returned positive. The patient was managed with fluid restriction, supplemental oxygen via nasal cannula, ceftriaxone IV and azithromycin IV. Given our contemporary experience with the patient presented in Case #1, out of precaution an echocardiogram was performed that demonstrated a moderately reduced

LVEF of 40-45% with global hypokinesis. Her SpO2 was 96% on room air. Despite her reduced EF, cardiology did not feel she was clinically in acute heart failure; metoprolol 12.5mg twice a day was initiated and the patient was placed on a telemetry monitoring. Her HR was in the100s, BP of 110s/70s, RR of 20s, with ABG showing a pH of 7.42, pCO2 of 28.7 mmHg, pO2 of 101 mmHg, HCO3 of 18.8 mEq/L, and a BE of -6 mmol/L. Given the unknown course of COVID-19 in pregnancy, as a precaution, and in an effort to deliver the patient before becoming critically ill, the patient underwent a primary cesarean delivery on 4/1/2020 and was recovered with continuous telemetry monitoring. As of the writing of this article (4/2/2020) the patient is currently stable on day #7 of hospital admission and POD #1 from cesarean delivery. She is meeting her POD #1 surgical goals, with an improved respiratory status and SpO2 of 96% on room air. However, overnight the patient developed supraventricular tachycardia (SVT), therefore, cardiology increased her metoprolol from 12.5mg PO q12 to 25mg PO q12. Of note, during her entire hospitalization, the patient never developed a fever >100.4° F. As per Center for Disease Control, both the mother and neonate are being isolated from the general postpartum population in negative pressure rooms with droplet isolation.

Discussion:

A review of the literature demonstrates that cardiomyopathy is a frequent finding in up to 33% of critically ill, non-pregnant COVID-19 patients [3,4]. It is unknown if the rate of developing COVID-19 cardiomyopathy is exacerbated in the pregnant population or

similar to the rate in the non-pregnant patient. Additionally, it is unclear whether the high rate of cardiomyopathy reported in the case series of non-pregnant patients is secondary to multisystem organ dysfunction or a direct complication of COVID-19. It must be highlighted that our cohort of COVID-19 positive pregnant women is currently limited, and that we are only testing symptomatic pregnant patients; the association between cardiomyopathy and COVID-19 infection in pregnancy is possibly less strong than what we found. Our two patients had some risk factors for cardiac disease, including race/ethnic group, obesity, and in one case advanced maternal age.

Pregnancy is an immunocompromised state in which the cardiovascular demands are increased. It is a state of compensated respiratory alkalosis with metabolic acidosis that is vulnerable to respiratory pathogens such as COVID-19. Of the respiratory parameters, respiratory rate remains unchanged in healthy pregnancy, and the finding of tachypnea is a significant finding and should prompt practitioners to further evaluate the patient. While tachypnea and shortness of breath are not unique findings to COVID-19 infection or cardiomyopathy, in the critically ill COVID-19 pregnant woman, or even in the pregnant woman with COVID-19 pneumonia necessitating oxygen, given also the evidence from the non-pregnant literature, performing an echocardiogram should be considered to evaluate for cardiomyopathy. Furthermore, to minimize exposure to echocardiographer technologists and to avoid contamination of the traditional echocardiogram machines that could serve as a fomite and infect the next patient, a policy whereby board certified echocardiography cardiologists perform the study with, for example, a point-of-care handheld General Electric Vscan echocardiography device is

suggested. This small device is easy to decontaminate, is of good technical quality and images are stored, downloaded into the patient's electronic medical record and interpreted into a formal report. The management, evaluation, and ability to anticipate complications in pregnant patients are critical in this COVID-19 pandemic; more experience is needed.

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References:

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA.* Published online February 24, 2020. doi:10.1001/jama.2020.2648
2. Verity R, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet Infect Dis 2020, in press. Published Online March 30, 2020, https://doi.org/10.1016/S1473-3099(20)30243-7.
3. Guo T, Fan Y, Chen M, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol.* Published online March 27, 2020. doi:10.1001/jamacardio.2020.1017
4. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *JAMA.* Published online March 19, 2020. doi:10.1001/jama.2020.4326
5. Di Mascio et al. Outcome of Coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. AJOG MFM 2020; in press. Available at: https://www.sciencedirect.com/science/article/pii/S2589933320300379

6. Breslin N, et al. COVID-19 in pregnancy: early lessons. AJOG MGM 2020, in press. Available at: https://www.sciencedirect.com/science/article/pii/S2589933320300410
7. Dashraath P, et al. Coronavirus Disease 2019 (COVID-1 19) Pandemic and Pregnancy. AJOG 2020, in press. Available at: https://www.ajog.org/coronavirus_guidance.