COVID-19 Myocarditis
A Case Report, Overview of Diagnosis and Treatment

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Abstract: Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), emerged in Wuhan, China, and rapidly led to a global pandemic that affected 213 countries, more than 5.8 million cases, and 360,000 deaths worldwide as of May 28, 2020. The United States currently has the highest number of COVID-19 cases in the world and contributes to nearly a third of the global death rate. The prevalence of COVID myocarditis is unclear but generally considered rare, with estimates up to 7% of COVID-related deaths. However, these patients suffered catastrophic worsening disease with respiratory compromise requiring intubation and often death. We report the case of a patient with COVID-19–induced myocarditis who was successfully treated with dexamethasone and review the literature.

Key Words: COVID, SARS, myocarditis

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CLINICAL CASE

A 49-year-old African American man with medical history significant for mild intermittent asthma and obesity (body mass index of 35.93 kg/m^2) presented to an outside hospital with a 1-day history of shortness of breath and chest pain. He reported some general malaise and subjective fevers for 2 days prior to admission and noted increasing dyspnea unrelieved with multiple doses of albuterol. He then developed sudden-onset substernal chest pain associated with diaphoresis lasting 3 minutes and presented to the hospital. He had a family history of undefined cardiac disease in his mother in her 60s and his sister who had a heart attack in her 50s. He was a never-smoker, denied alcohol or drug abuse, and worked as a truck driver.

Upon arrival to the emergency department, an initial electrocardiogram (ECG) demonstrated sinus rhythm with 1- to 2-mm concave ST elevations in I and aVL with slight ST depression in lead III and troponin T of 1.020 ng/mL (Fig. 1). A rapid Cepheid COVID-19 (coronavirus disease 2019) test was also administered that returned positive. He was given aspirin 325 mg, clopidogrel 300 mg, and morphine 4 mg and started on heparin drip with 4000 U bolus and continued at 1000 U/h. Given his chest pain and abnormal ECG, the decision was made to emergently transfer him for evaluation to a percutaneous coronary intervention–capable hospital.

Upon his arrival, examination by cardiology revealed symptoms that were predominantly dyspnea with mild chest pressure. His chest x-ray noted bilateral lower lung hazy opacities concerning for atypical pneumonia or pneumonitis; however, given his COVID diagnosis and decompensated heart failure, lack of fever, and only mildly elevated white blood cell count, fluid was more likely (Fig. 2A). He had a point-of-care cardiac ultrasound performed, which demonstrated biventricular dysfunction with a globally hypokinetic left ventricle and right ventricle. The left ventricular ejection fraction was estimated to be 30% to 40%. Blood pressure was 91/68 mm Hg, pulse 90 beats/min, temperature 98.5°F, respiratory rate 40 breaths/min, and oxygen saturation of 100% on 4-L nasal cannula. He had orthopnea and dyspnea speaking full sentences from decompensated heart failure. His laboratory test results from the outside institution also reflected multiorgan failure with lactate of 4 mmol/L, transaminitis with aspartate transaminase (AST)/alanine transaminase (ALT) of 1023/641 U/L, acute renal failure with a creatinine of 2.1 mg/dL, and a pro–brain natriuretic peptide of 23,909 pg/mL. Laboratory test results were also notable for relative lymphopenia of 11.6% and absolute lymphocyte count of 1.43×10^3 lymphocytes/μL, as is commonly seen with COVID-19 infections, hyponatremia to 129 mmol/L, and anion gap of 20 mmol/L. In-house laboratory test results also showed a troponin I of 8.648 ng/mL and elevated inflammatory markers including ferritin of 19,957.2 ng/mL and C-reactive protein (CRP) of 475 mg/L. The repeat ECG showed persistent patterns as from the outside hospital, but was also felt to be possible early repolarization and not ischemic in nature, especially because there were no overt reciprocal changes in the other leads.

Given his overall clinical picture, inflammatory profile, and tenuous respiratory and renal status, the suspicion was higher for COVID-19 myocarditis with possible end-organ involvement from decompensated heart failure and an underlying acute inflammatory process. Because an acute ischemic event was lower on the differential, cardiac catheterization was felt to be a greater risk than potential benefit at the time, and he was medically managed in the intensive care unit. He received a central line and was started on a dobutamine drip that was titrated to a central venous pressure of less than 12 mm Hg, with close monitoring of his intake and output. His respiratory status improved, and his O_2 supplementation was titrated down to room air. Clinically, his lactate also normalized, and renal function improved slightly to a creatinine of 1.9 mg/dL that evening.

Overnight, troponin I initially stabilized from a peak of 10.748 to 10.671 ng/mL, but then progressed to 18.695 ng/mL in the morning. Using an estimated central venous saturation using the central line, his cardiac index was 2.06 L/min per m^2, and systemic vascular resistance was 1499 dyn/s per cm^{-5}. Given that his respiratory status and renal function had improved, and benefit of cardiac catheterization outweighed risk, decision was then made to rule out acute coronary syndrome with right- and

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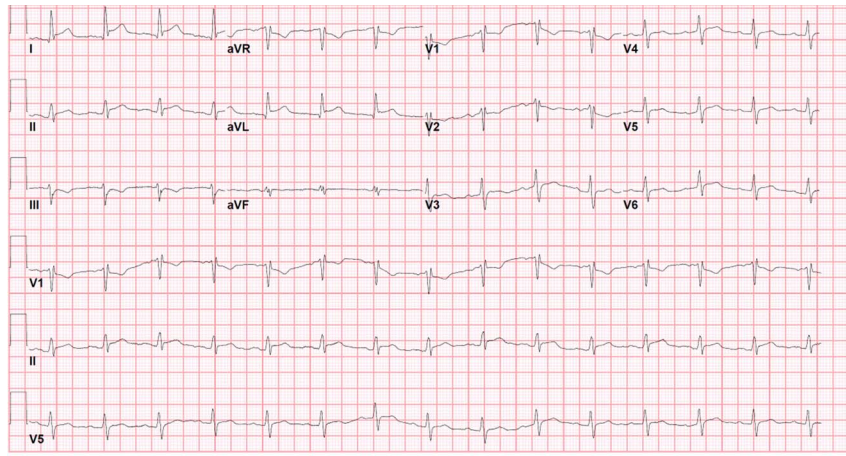


FIGURE 1. Electrocardiogram on presentation to the outside hospital: PR 184 ms, QRS 110 ms, QTc 438 ms. Notable minimal 2-mm ST elevations in lead I and aVL and ST depressions in lead III.

left-sided heart catheterization (Figs. 3A–C). He was determined to have minimal coronary artery disease and clinically diagnosed with COVID-19 myocarditis. A Swan-Ganz catheter was also placed during the procedure to allow for more accurate central venous saturation. During the right-sided heart catheterization, hemodynamics measured are displayed in Figure 3D. Cardiac magnetic resonance imaging and biopsy were not done at the time because it would not affect management, but considered as potential procedures if he continued to worsen and if needed to identify other causes of myocarditis. HIV, antinuclear antibodies, amyloid, viral titers, and Epstein-Barr virus tests were also performed in the meantime, and these were negative.

Given his elevated inflammatory markers and end-organ disease, he was started on dexamethasone 20 mg intravenous daily and considered for tocilizumab if there was no improvement. He was started on intravenous azithromycin 500 mg for potentially augmented pulmonary anti-inflammatory effects. Furosemide drip was started to continue diuresis and titrated to maintain a central venous pressure of less than 10 mm Hg and was discontinued the following day because he was dosed with intravenous pushes as needed.

The patient continued to clinically improve, with no supplemental oxygen or vasopressor requirements the following day. This tracked with his CRP, lactate dehydrogenase, and ferritin levels, which continued to downtrend. Azithromycin was discontinued after 3 doses because of improved chest x-ray findings, strengthening the argument for fluid overload as opposed to developing pneumonia (Fig. 2B).

Interestingly, his D-dimer continued to rise to a peak of 8035 ng/mL on hospital day 3 without any signs or symptoms of venous thromboembolism, and transaminases continued to rise possibly as a result of liver shock or COVID-19–related inflammation to a peak of AST/ALT of 2099/3341 U/L. Based on medical team experience with hypercoagulability in COVID-19 patients, he was continued on therapeutic anticoagulation for the duration of his hospitalization. He was transferred to a telemetry floor on hospital day 4 and medically optimized for his heart failure with losartan, metoprolol, aspirin 81 mg, and steroid taper after 5 days of dexamethasone. He was discharged on hospital day 10, having completed the steroid taper, and was continued on low-dose aspirin, angiotensin-receptor blocker, β-blocker, and a direct oral anticoagulant for 30 days and to be reassessed on outpatient follow-up. Participant provided written informed consent, and the study was approved by the institutional review board of New York University (i20-00473).

DISCUSSION

Cardiac complications of COVID-19 are relatively rare in the infectious spectrum.[1–6] Myocarditis has been identified in case reports of heterogeneous presentation, with severity ranging from

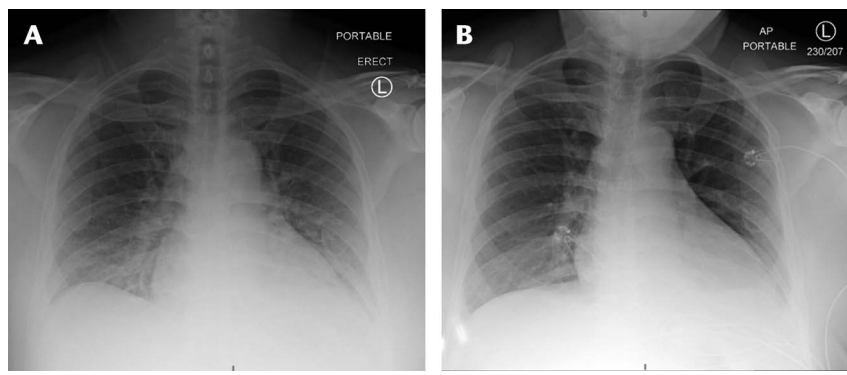
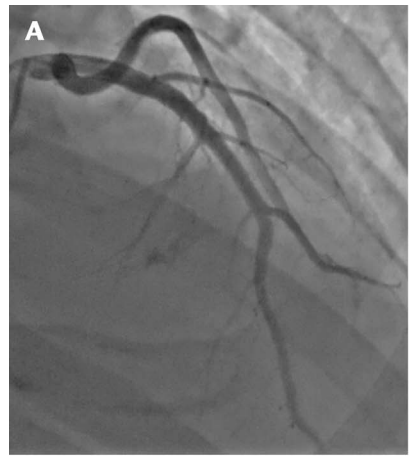
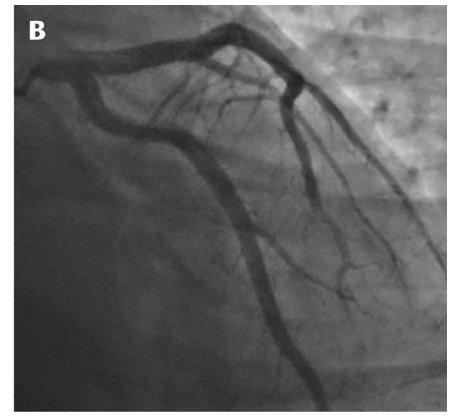
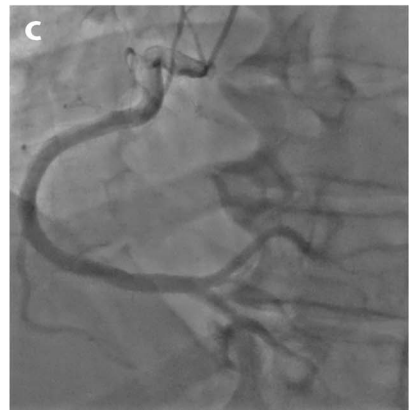


FIGURE 2. A, Initial chest x-ray on admission. Low lung volumes with subsequent prominence of the cardiomediastinal silhouette and interstitial lung markings. Hazy airspace opacities in the lower lungs bilaterally may reflect atelectasis, although findings are concerning for early developing atypical pneumonia/pneumonitis. No pleural effusion or pneumothorax. B, Follow-up chest x-ray after 3 days, with decreased ill-defined hazy bibasilar opacities, which may represent decreased atelectasis, pneumonia, or combination of both. No large pleural effusion or pneumothorax. Stable borderline enlarged cardiac silhouette. Mediastinal contour within normal limits.







D Hemodynamic Measurements

Hemodynamic Parameter	Reference	2LNC
RAP (mmHg)	2-6	15
RV (mmHg)	15-30/2-8	40/13
PAP (mmHg)	15-30/8-15	50/30
Mean PAP (mmHg)	15-30	37
PCWP (mmHg)	12-16	28
CO (L/min)	4-8	7.3
CI (L/min/$m^{2)}$	2.5-4.0	2.85
SVR (Dynes-sec/cm^5)	880-1440	900
PVR (Wood units)	0.5-2	1.2
PA Sat (%)	95-100	99
AO Sat (%)	60-80	62

RAP: Right atrial pressure; **RV**: right ventricle pressure; **PAP**: pulmonary artery pressure; **PCWP**: pulmonary capillary wedge pressure; **CO**: cardiac output; **CI**: cardiac index; **SVR**: Systemic vascular resistance; **PVR**: pulmonary vascular resistance; **PA** sat: pulmonary artery saturation; **AO** sat: aortic saturation

FIGURE 3. Invasive coronary angiogram of (A) left anterior descending artery and (B) left circumflex artery. C, Right coronary artery demonstrating minimal coronary atherosclerotic disease. D, Hemodynamic parameters recorded during right-sided heart catheterization.

mild symptoms of fatigue and dyspnea to cardiogenic shock.[7–9] Differential diagnoses include acute coronary syndrome, sepsis-related cardiomyopathy, and Takotsubo cardiomyopathy. Definitive diagnoses can be difficult because of overlapping disease, and diagnostic methodologies, such as endomyocardial biopsy or invasive angiogram, often carry their own risks of further infection.[10] The American Heart Association guidelines on management of fulminant myocarditis include supportive measures, including inotropic and/or vasopressors; advanced therapies, including mechanical ventilation; mechanical circulatory support, such as extracorporeal membrane oxygenation; ventricular assist device; or intra-aortic balloon pumps.[11] The use of routine immunosuppression including corticosteroids is controversial, and its efficacy in COVID-19 patients even less well-understood because some studies based on SARS-1 (severe acute respiratory syndrome 1) determined it could worsen outcomes and prolong viral load.[12] Although some success has been noted with COVID-19 patients, most glucocorticoids have strong mineralocorticoid activity, which increases sodium reabsorption, water retention, and extracellular fluid volume and may exacerbate fluid overload.[7,13–15]

One unique aspect of this case was the choice of glucocorticoids. A recent multicenter randomized controlled trial investigating dexamethasone 20 mg intravenously administered daily for 5 days in acute respiratory distress syndrome found reduction in ventilator-free days.[16] This could be a reflection of dexamethasone's relatively high glucocorticoid potency and minimal mineralocorticoid activity, an advantage in volume overloaded states such as acute respiratory distress syndrome and decompensated heart failure. Thus, whereas other studies often used high-dose methylprednisolone for the COVID-19–induced myocarditis, our patient may have benefited from the use of dexamethasone to minimize fluid retention. Further studies comparing glucocorticoids with varying degrees of mineralocorticoid activity could illuminate on the viability of dexamethasone as a mainstay of treatment in COVID-19–related myocarditis.

Additionally, we actively used the inflammatory panel to guide treatment. Although the majority of his inflammatory markers such as CRP and ferritin downtrended after dexamethasone, we noted that his D-dimer continued to rise. D-Dimer (biomarker of fibrin formation and degradation) and prothrombin time have been associated with poor prognosis in COVID-19.[17–22] In a retrospective analysis of 191 patients with COVID-19, Zhou et al[23] found that nonsurvivors were more likely to have D-dimer levels of greater than 1 μg/mL than survivors (81% vs 24%). Similarly, in a study of 183 patients, Tang et al[18] noted that nonsurvivors had significantly higher D-dimer values on admission than survivors (2.12 vs 0.61 μg/mL). In a retrospective study, patients with COVID-19 and D-dimer values greater than 6-fold the upper limit of normal had lower 28-day mortality when treated with anticoagulation (32.8% vs 52.4%).[24] Despite the relative novelty of COVID-19, some groups have begun assessing and providing interim guidance on the coagulopathy of COVID-19. This hypercoagulable state is currently being investigated in multiple clinical trials investigating full-dose anticoagulation with tissue plasminogen activator, heparin, or low-molecular-weight heparin.[20,25,26] Knowing the risk of thrombotic complications in COVID-19

prompted the continued anticoagulation in this patient and extended to 30 days after discharge.[27] This highlights the importance of identification of biomarkers and how it portends to clinical treatment. However, the mortality benefit of these biomarkers and impact of treatment must be investigated to identify the best treatment pathways for these patients. Other biomarkers of inflammation such as lactate dehydrogenase, ferritin, CRP, and AST/ALT have also been noted to be elevated in COVID-19 infections, but their role is also unclear. However, their levels may be a better indication of other end points of disease and need to be further studied in longitudinally monitored cohorts.

When considering advanced COVID-19 therapeutics including hydroxychloroquine, lopinavir/ritonavir, remdesivir, or tocilizumab, we refrained from the addition of a second QT-prolonging medication out of an abundance of caution in this patient with tenuous cardiac disease and elected for azithromycin alone for its atypical coverage and pulmonary anti-inflammatory effects. Because the patient rapidly improved on azithromycin alone, the patient did not receive remdesivir or tocilizumab. Supportive measures including dobutamine, diuretics, and medical therapy also likely contributed to the patient's overall recovery. Given the recent negative studies regarding hydroxychloroquine and potential for increased mortality, we are encouraged by the success with a more conservative approach and utilization of glucocorticoids with minimal mineralocorticoid activity.[28] Nevertheless, further studies are needed to detail the therapeutic potential of dexamethasone in COVID-19–related myocarditis.

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