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Management of COVID-19 in a durable left ventricular assist device recipient: A continuity of care perspective

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ABSTRACT

COVID-19 is impacting the cardiovascular community both here in the United States and globally. The rapidly emerging cardiac complications have heightened implications for those with underlying cardiovascular disease. We describe an early case of COVID-19 in a left ventricular assist device recipient in the United States. We discuss our clinical management during the initial admission, outpatient management, and a unique complication of this disease over a 40-day disease course.

Background

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic originated in Wuhan, Hubei Province, China in December 2019. The enormous strain placed on healthcare systems worldwide by this pandemic emphasizes the importance of prevention and control. Though the severe respiratory clinical manifestations of this disease have been well reported, the data regarding cardiovascular presentations and outcomes of patients infected with coronavirus disease 2019 (COVID-19) are rapidly emerging. While the overall case fatality rate remains low, the groups most at risk include the elderly, the immunocompromised, or those with pre-existing risk factors.[1] Hypertension, diabetes, and cardiovascular disease increase the risk of adverse outcomes with COVID-19 infection.[2] This report describes the clinical course of a left ventricular assist device (LVAD) recipient with acute COVID-19 infection from initial hospital admission to outpatient management.

Case presentation

A 48-year-old woman with HeartMate II LVAD was admitted to a cardiac telemetry unit on March 16th, 2020 with a one-week history of fatigue, myalgias, intermittent productive cough, headache, and subjective fever. Her history was significant for chronic systolic heart failure, hypertension, type 2 diabetes mellitus, chronic kidney disease (stage IIIb), and morbid obesity. She had recently been on a cruise from February 29th to March 5th. The patient was in close contact with a person on the cruise ship who later tested positive for SARS-CoV-2. One week after returning home, she developed rhinorrhea, fever, myalgias, and subjective chills and was subsequently evaluated in the emergency department. Nasopharyngeal and oropharyngeal tests for rapid nucleic acid amplification test (NAAT) for influenza and respiratory syncytial virus (RSV) were negative. NAAT for COVID-

Abbreviations: ACE, angiotensin-converting enzyme; ARBs, angiotensin II type-1 receptor blockers; COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus; LVAD, left ventricular assist device; Lpm, liters per minute; NAAT, nucleic acid amplification test; PA, pulmonary artery; PI, pulsatility index; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

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19 was performed but the turnaround time was >24 hours. As she was clinically stable, she was sent home for self-isolation. Four days later, she developed progressively worsening shortness of breath and was directly admitted to the hospital by her primary care physician.

On admission, the patient's temperature was 98.4°F (36.9°C), mean arterial pressure was 94 mmHg, and she was breathing room air with an oxygen saturation (SpO2) of 93%. Shortly after admission, her SpO2 decreased to 88% and she required supplemental oxygen at 2 liters per minute (Lpm) via nasal cannula. Physical examination revealed diminished breath sounds throughout bilateral lung fields and a mechanical hum. Interrogation of the LVAD demonstrated a flow of 4.4 LPM, pump speed of 9,600 RPM, power of 5.7 watts, pulsatility index (PI) of 7.2, and no alarms, suggesting normal LVAD function. Laboratory tests on presentation revealed leukopenia (3.48 K/μL, ref: 3.99 - 11.19 K/uL) with absolute lymphopenia (0.71 K/μL, ref: 1.16 - 3.51 K/uL), and abnormal international normalized ratio (INR, 4.8). Levels of lactate dehydrogenase (372 U/L, ref: 100 - 190 U/L), D-dimer (0.80 mcg/mL, ref: <0.50 mcg/mL FEU), C-reactive protein (96 mg/L,ref: <10.00 mg/L), interleukin-6 (68 pg/mL, ref: < 6 pg/mL), and haptoglobin (361 mg/dL, ref: 44-215 mg/dL) were elevated. Levels of procalcitonin (0.24 ng/mL, ref: <=0.50 ng/mL) and brain natriuretic peptide (BNP) were within normal range. A nasopharyngeal swab for the detection of viral respiratory pathogens was negative. Chest radiograph demonstrated cardiomegaly, normal mediastinal and hilar findings, and bilateral, peripheral hazy opacities (Fig. 1). Chest computed tomography was deferred due to the potential risk of spreading a presumed infection. While awaiting her test results, the patient required escalating levels of supplemental oxygen as high as 6 Lpm. Her SARS-CoV-2 NAAT was reported as positive on day 2 of admission.

The mainstay of this patient's management was supportive care. Given her rapid escalation of supplemental oxygen to maintain SpO2 > 90%, the patient was transferred to a medical intensive care unit (MICU) designated by our medical center for COVID patients for close monitoring with appropriate droplet isolation. Empiric broad-spectrum antibiotics were not initiated due to low suspicion of superimposed bacterial pneumonia. On the recommendation of the infectious disease specialist, a combination protease inhibitor lopinavir-ritonavir was administered for a five-day course due to her cardiac comorbidities and potential for severe infection. The patient remained on supplemental oxygen via nasal cannula during the hospital stay. A repeat SARS-CoV-2 NAAT was reported as negative on day 8 of admission. The patient was discharged home on the same day with instructions for self-quarantine.

The patient was monitored for symptom resolution through routine telephone visits with our LVAD clinic and her primary care physician. She was re-tested for SARS-CoV-2 6 days after discharge (Fig. 2) given the need for a confirmatory negative test to resume home-care services. This test resulted as positive with a detectable viral load. A repeat test one week later, on day 21 of her clinical course, remained positive.

On day 37 of her illness course, the patient-reported symptoms of fatigue, nausea, lower-extremity weakness, and stable dyspnea with an associated 43 lb weight loss since prior discharge. A review of her implanted, wireless pulmonary artery (PA) pressure device data demonstrated a mean PA diastolic pressure of 16-18 mmHg (ref: 10-14 mmHg) since discharge (Table 1). Given her potential for respiratory and hemodynamic compromise, she was subsequently admitted on day 37.

On re-admission, the patient's temperature was 98.5°F (36.9°C), mean arterial pressure was 84 mmHg, and she was breathing room air with an oxygen saturation (SpO2) of 95%. Repeat testing on April 22nd and 23rd (day 37 and 38, respectively) was negative for SARS-CoV-2. Interrogation of her single-chamber implantable cardioverter-defibrillator device demonstrated sinus rhythm with isolated episodes of sinus tachycardia. LVAD interrogation demonstrated a flow of 5.0 LPM, pump speed of 9,600 RPM, power of 6.3 watts, PI of 6.6, and no alarms, again suggesting normal LVAD function. A repeat chest radiograph demonstrated pulmonary venous hypertension with interval improvement in partial hazy opacities (Fig. 1).

Laboratory tests revealed normal serum comprehensive metabolic panel, complete blood count, BNP, CK, interleukin-6, and ferritin with an elevated INR (3.9). C-reactive protein remained elevated (85 mg/dL; ref: 44-215 mg/dL) with a markedly elevated erythrocyte sedimentation rate markedly (>130 mm/hr, ref: <20 mm/hr). Thyroid function tests revealed markedly low thyroid-stimulating hormone (0.015, ref: 0.550-4.780 uIU/mL), elevated free T3 (10.1 pg/mL, ref: 2.3-4.2 pg/mL) and free T4 (5.36 ng/dL, ref: 0.89-1.76 ng/dL). Thyroid-stimulating immunoglobulin and thyrotropic receptor antibody were within normal limits. On the recommendation of the endocrinologist, the patient was started on methimazole therapy on day 38 for subacute thyroiditis as a post-viral complication. The patient was discharged home on day 45.

Discussion

To our knowledge, this is one of the earliest cases of an LVAD recipient in the United States who contracted SARS-CoV-2.[3,4] We discuss our clinical management during the initial admission, outpatient management, and a unique complication of this disease over a 40-day disease course. There are a few key features that distinguish our case and management from the available literature. This includes a relatively benign clinical course in a patient with multiple co-morbidities, probably due to immunomodulatory effect of LVAD support.

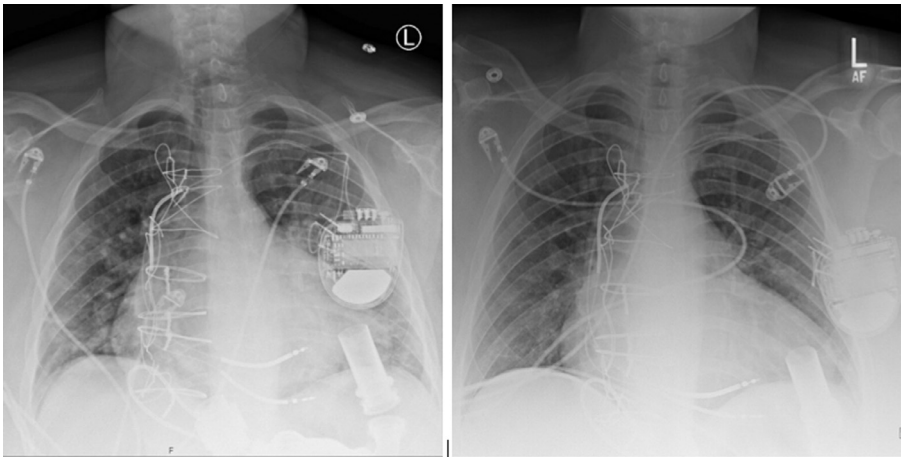

Fig. 1. Posteroanterior chest radiographs obtained on day 1 (LEFT) and day 38 (RIGHT).

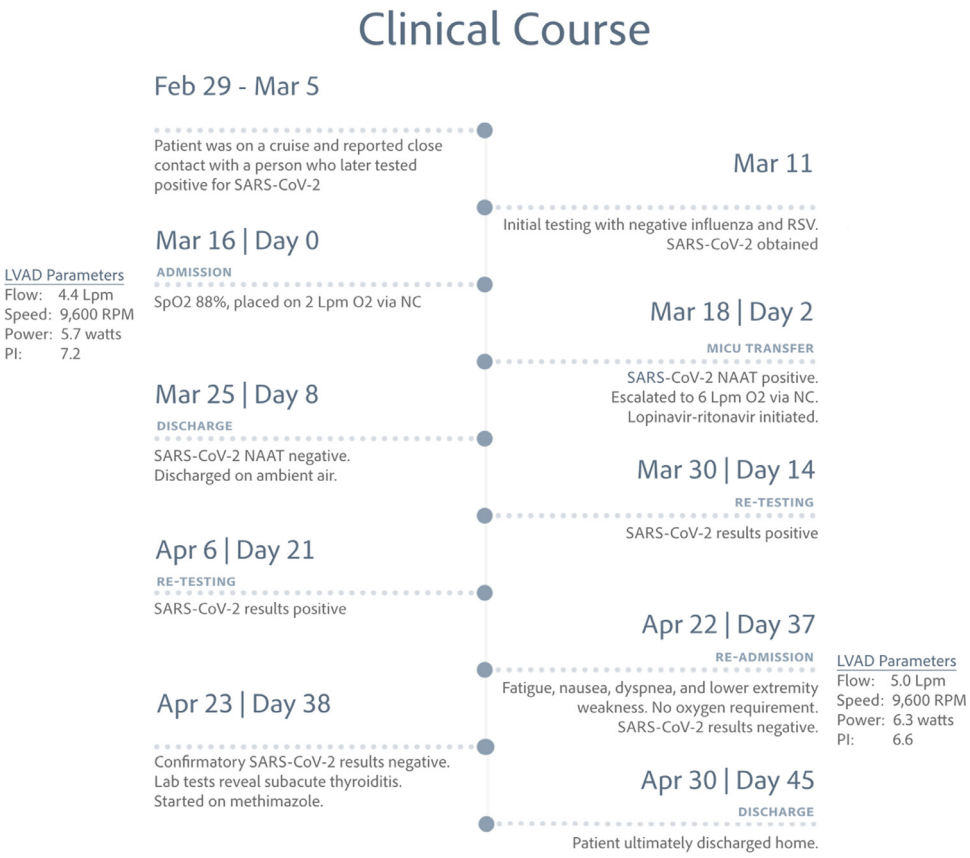

Fig. 2. A clinical course of events referenced in the article.

Table 1
Trend of pulmonary artery pressures measured by CardioMEMS™ remote sensor.

Day of illness course	Date	PA systolic	PA diastolic	PA mean	Heart rate
Day 9	3-25-20	44 mmHg	19 mmHg	28 mmHg	88 bpm
Day 25	4-10-20	42 mmHg	18 mmHg	27 mmHg	102 bpm
Day 39	4-24-20	46 mmHg	18 mmHg	28 mmHg	89 bpm
Day 39	4-24-20	44 mmHg	16 mmHg	27 mmHg	84 bpm
Day 44	4-29-20	42 mmHg	16 mmHg	25 mmHg	81 bpm
Day 44	4-29-20	41 mmHg	16 mmHg	25 mmHg	82 bpm

This case report also presents the utility of PA sensor and LVAD parameters for remote monitoring.

Management of COVID-19 infection has largely been guided by standard respiratory care, case reports, expert opinion, small randomized clinical trials, and prior experience with SARS-CoV-1, MERS, and H1N1. No proven, effective therapies currently exist to treat SARS-CoV-2 infection.[5] Conflicting data casts doubt on the efficacy of hydroxychloroquine use in COVID-19.[6] Furthermore, the potential risk of fatal cardiac arrhythmia cannot be easily overlooked. A recent study showed that combination protease inhibitor lopinavir-ritonavir did not offer any benefit beyond standard care.[7] Further research of remdesivir, corticosteroids, immunomodulatory therapies, and vaccines is underway.[5]

The cardiovascular manifestations of this disease are rapidly emerging. Proposed mechanisms include angiotensin-converting enzyme 2 (ACE) mediated damage, hypoxia-induced myocardial damage, microvascular insult, and systemic pro-inflammatory cytokine storm.[8] Despite the virus gaining entry using the ACE2 receptor, in-hospital use of renin-angiotensin-aldosterone system inhibitors was associated with a lower risk of all-cause mortality. [9] Our patient was not on an ACE-inhibitor at the time of initial admission due to previous intolerance. Major cardiology societies strongly recommend continuing treatment with these medications in stable patients with COVID-19.[5,7]

There are case reports of suspected cytokine-release mediated fulminant myocarditis in patients with COVID-19.[4] Additionally, there are reports of presumed ST-elevation myocardial infarction (STEMI) with no or minimally-occlusive coronary disease on coronary angiography.[10] In patients with COVID-19, elevated d-dimer levels are associated with adverse outcomes. This may be related to the activation of coagulation cascade which can predispose to ischemia and thrombosis.[8] In a joint webinar between the Chinese Cardiology Association and the American College of Cardiology on March 28, 2020, Chinese physicians presented autopsy data of COVID-19 non-survivors describing diffuse microvascular thrombi in multiple organs. Based on these findings, the Chinese cardiologists suggested systemic anticoagulation in patients with severe COVID-19 infection. However, there is no concrete evidence to support this strategy. Laboratory studies including lactate dehydrogenase, haptoglobin, liver function tests, and plasma free hemoglobin levels may further indicate pump thrombosis or mechanical hemolysis. It is conceivable that coagulation dysfunction, in LVAD recipients with COVID-19 infection, may increase the risk of pump thrombosis. Therefore, ensuring therapeutic anticoagulation is essential to prevent pump thrombosis. It is not

known whether higher intensity anticoagulation targeting an INR between 2.5 and 3.5 is needed in critically ill LVAD recipients with severe COVID-19 infection. In our patient, drug interaction between lopinavir-ritonavir and warfarin probably contributed to an elevated INR around 4.

In contrast to cases published by Chau et al. and Singh et al., our patient experienced a far less severe COVID-19 illness.[3,4] Despite escalation to intensive care monitoring given her initial tenuous presentation, our patient ultimately avoided mechanical ventilation. This suggests that LVAD recipients may have varying severity of illness dependent on predisposing inflammatory risk factors. Singh et al. describe a potential "functionally immunocompromised state" with prior literature demonstrating impaired cellular immunity in long-term LVAD recipients.[3] However, Mahmood et al. describe a net effect of LVAD support which decreases inflammatory cytokines compared to pre-implant levels.[11] Significantly elevated inflammatory markers including C-reactive protein, interleukin-6, and ferritin may suggest a hyperinflammatory state due to COVID-19. The trends of these laboratory studies may identify a need for additional medical intervention. Further analysis is required to understand if long-standing durable mechanical circulatory support devices, such as an LVAD, provide a protective effect or predispose to a hyperinflammatory state.

When available, daily interrogation of LVAD parameters is a useful tool in the management of LVAD recipients with COVID-19 infection. Abnormal parameters may signal early signs of hemodynamic compromise, pump thrombosis, right ventricular failure, vasoplegia associated with secondary infection, or innate device malfunction.[12] Furthermore, remotely-available PA pressure data in our patient allowed accurate assessment of volume status throughout her acute illness and recovery course (Table 1). In close coordination with the ventricular assist device clinic, the patient was readmitted due to generalized, systemic symptoms. Her baseline PA pressures, negative COVID-19 testing, and lack of clinical findings to suggest either a heart failure exacerbation or repeat COVID-19 infection prompted further workup resulting in a diagnosis of subacute thyroiditis, likely as a post-viral complication of her initial infection.

Conclusions

We describe a unique case of a patient mild COVID-19 infection on LVAD support. Whether the cardiovascular outcomes of LVAD recipients differ from other populations requires further investigation. However, prompt diagnosis, supportive care, and close follow-up are vital in the management of LVAD recipients with COVID-19 infection.

Disclosures

Dr. Mokadam is a consultant for Abbott, Medtronic, SynCardia, and Carmat. The other authors have no conflicts of interest to disclose.

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