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Acute Biventricular Heart Failure After COVID-19 Infection in an Orthotropic Heart Transplant Patient: A Case Report

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ABSTRACT

The cardiac effects of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) include myocarditis, takotsubo cardiomyopathy, pericardial effusion, and cardioembolic events in the general population. The effects of SARS-CoV-2 in heart transplant patients are unclear. We describe a case of myocarditis in the transplanted heart that responded to methylprednisolone.

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CASE PRESENTATION

The patient was a 66-year-old man with a history of orthotropic heart transplant in 2013 and dystonic muscular dystrophy type 2 who presented with shortness of breath and fatigue and was found to have biventricular systolic dysfunction. He incidentally tested positive for coronavirus disease 2019 (COVID-19) without having respiratory symptoms other than dyspnea on exertion.

His other comorbidities included recent diagnosis of prostate cancer, hypertension, and chronic kidney disease stage 3. At presentation, his blood pressure was 128/94 mm Hg, heart rate was 108 beats per minute, respiratory rate was 24, temperature was 37°C, and his oxygen saturation was 97%. He also reported nausea at home and missed taking his immunosuppressive drugs 2 days before presentation. On admission, his troponin-I was 0.04 ng/mL on 2 blood draws, slightly elevated above the lab cutoff of 0.03, then down trended to 0.03. Brain natriuretic peptide was within normal limits at 47 pg/mL. His electrocardiogram showed diffuse T wave inversions, including new inversions in leads II, III, and V4-V6. His echocardiogram on presentation showed left ventricular ejection fraction of 37% and right ventricle that was dilated with at least moderately reduced systolic function, both changes from a normal echo 5 months prior. Because of his history of shortness of breath, he was tested for SARS-CoV-2, which came back positive.

Endomyocardial biopsy was performed because of new biventricular failure due to not taking immunosuppression medications. The endomyocardial biopsy showed no evidence of acute cellular rejection (Grade 0R) or antibody mediated rejection with negative immunofluorescence. There was subendocardial fibrosis and Quilty lesion. He was treated with high-dose steroids at 1 g/d of methylprednisolone for 3 days for presumed rejection until the biopsy results were completed. Follow-up echocardiogram at the end of 3 days showed improvement of left ventricular ejection fraction to 66% and grossly normal right ventricular function. Discussion

Since the advent of SARS-CoV-2 from COVID-2019 infection, immunocompromised and solid organ transplant recipients have been recognized as a vulnerable population with potentially worse outcomes. Currently available data on presentation, management, and outcomes are limited to case reports and case series [1]. There is only one other case of cardiac allograft dysfunction reported in a patient with COVID-19 infection who had undergone heart and kidney transplantation [2].

The index patient underwent heart transplant 7 years ago with no significant rejection history and had no nosocomial COVID-19 exposure. Our patient had a very vague and nonspecific presentation with fatigue and dyspnea on exertion but notably no fever, anosmia, or typical viral prodrome typically associated with SARS-CoV-2. The concomitant allograft dysfunction in

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the presence of a nonsignificant troponin elevation and no arrhythmia presented a diagnostic and therapeutic dilemma. The differential diagnosis included nonrejection mechanisms—myocarditis, or stress cardiomyopathy that has been described in COVID-19 [3,4], cardiac allograft vasculopathy, and possibly allograft rejection. The probability of transplant rejection was low because he was 7 years posttransplant and his endomyocardial biopsy was negative for cellular and antibody-mediated rejection with normal filling pressures and cardiac output. He had a coronary angiogram 3 months before presentation that showed no coronary artery disease or cardiac allograft vasculopathy. The optimal management especially of immunosuppression would depend greatly on the leading differential diagnosis because treatment for rejection may be contradictory to that of a severe viral infection.

The recent International Society for Heart and Lung Transplantation recommendations to centers treating cases of severe COVID-19 in cardiothoracic transplantation recipients advise reducing or holding the antimetabolites [5]. Our patient was treated with 3 days of high dose intravenous methylprednisolone, and because our patient did not have any significant hypoxia, pneumonia, or marker of severe inflammatory disease, we decided to continue his baseline immunosuppression with cyclosporine and azathioprine and maintain therapeutic levels.

We postulate that without any specific evidence for rejection or myocarditis, the patient most likely experienced transient stress injury to the allograft from critical illness that resolved as his condition improved within 5 days of admission.

Some additional proof of cardiac damage is revealed by a study involving cardiac magnetic resonance imaging on patients after recovering from a polymerase chain reaction−diagnosed COVID-19 infection. New data reveal that myocarditis may be present even in healthy, young patients with minimal symptoms. This is further supported by a study on 100 patients in Germany in which one-third of patients required hospitalization. Seventy-eight were shown to have cardiac involvement and 60 still showed inflammation on cardiac magnetic resonance imaging [6].

Developing data also show some cases of myocarditis in patients who contract SARS-CoV-2. The incidence of myocarditis in patients with COVID-19 is unknown, but there are numerous case reports and reviews. One such study took place in China and involved 416 patients. Eighty-two of these patients showed cardiac injury. The patients with cardiac involvement had a much higher mortality rate. These symptoms vary anywhere from mild, with fatigue, dyspnea, chest pain, and palpitations, to severe, with patients presenting in cardiogenic shock or sudden death due to arrythmias. [7] Overall, the early data from China suggested the myocardial injury was fairly common with an estimated incidence of 7% to 23% of reported cases [1,8,9].

Our case adds to the growing body of literature documenting the potential cardiotoxic effects of the coronavirus. The exact pathogenesis of myocardial injury in the SARS-CoV-2 syndrome is unclear. Some studies have suggested cytokine release syndrome is the core pathophysiology of SARS-CoV-2 fulminant myocarditis. Chen et al [10] reported that patients who are infected with SARS-CoV-2 had high levels of interleukin 1 beta, interleukin 6, interferon gamma, interferon inducible protein-10, and monocyte chemoattractant protein-1, which likely leads to massive activation of T-helper-1 cell response [10]. Higher granulocyte colony-stimulating factor, interferon inducible protein-10, monocyte chemoattractant protein-1, macrophage inflammatory protein-1A, and tumor necrosis factor alpha also have been reported, suggesting that the cytokine storm might affect disease severity [10]. Zheng et al. proposed that the mechanism of injury might be related to angiotensin-converting enzyme 2 (ACE2), which is widely expressed not only in the lungs but also in the cardiovascular system, so ACE2-related signaling pathways might also have a role in heart injury [11]. ACE2 is a membrane-bound aminopeptidase that has been identified as a functional receptor for coronaviruses. SARS-CoV-2 infection is triggered by the spike protein of the virus binding to ACE2, which is highly expressed in the heart and lungs resulting in acute respiratory distress syndrome and fulminant myocarditis. In a less-adopted hypothesis, several authors have speculated that SARS-CoV-2−induced severe acute respiratory distress syndrome results in persistent hypoxemia leading to myocardial cell damage [11].

Great interest is invested in the care for immunosuppressed patients infected with COVID-19. Studies are beginning to provide data to guide treatment for these patients with organ transplants and how to adjust the medications used. Two studies in particular, the COVID-LT and SETH, suggest that certain immunosuppressants may be protective and that complete pause of these drugs may be unwise [12,13]. In the COVID-LT study, there was a mortality reduction in patients who continued taking calcineurin inhibitors. The SETH study showed a trend toward reduced severity of COVID-19 pneumonia in patients taking tacrolimus, but it was not statistically significant [12,13] Both studies demonstrated that stopping immunosuppressive therapies had no survival benefit. This data supports continued use of immune modulating medications in patients with solid organ transplants despite concerns for severe viral infections in these patients.

This case demonstrates the importance of further investigation into the effects of SARS-CoV-2 on the human body, especially the cardiovascular system.

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