Recovery From COVID-19 Pneumonia in a Heart Transplant Recipient
A Case Report

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Abstract: Solid-organ transplant patients have a high risk of severe infection related to acute respiratory syndrome coronavirus-2 (SARS-CoV-2). This case represents a 54-year-old woman known as a diabetic, hypothyroidism, and a recent heart transplant recipient who presented with a 1-week history of cough and fatigue. She was hypoxic on presentation to the hospital and progressively declined and required invasive mechanical ventilation. She had respiratory distress and hypoxia and chest X-ray showed progressive bilateral chest infiltrates. She had leukopenia of 3.5 cells × 10^9/L and lymphopenia of 0.2 cells × 10^9/L. The inflammatory markers were increased: C-reactive protein, 25 mg/L; ferritin, 1106 ng/mL; lactate dehydrogenase, 632 U/L; and interleukin-6, 87 pg/mL. She was treated for severe coronavirus disease 2019 (COVID-19) pneumonia. Her treatment involved supportive care with mechanical ventilation, convalescent plasma transfusion, antiviral therapy with favipiravir, intravenous dexamethasone, and reduction of immune suppression medication. This case had a successful recovery through multidisciplinary team management. Solid-organ transplant recipients are a high-risk population who need an individualized care plan for the optimization of immunosuppressive medication and treatment of the COVID-19 infection.

Key Words: coronavirus disease 2019 (COVID-19), severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), solid-organ transplant, heart transplant, immune suppression, convalescent plasma, favipiravir, dexamethasone

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The first case of coronavirus disease 2019 (COVID-19) reported in the Kingdom of Saudi Arabia was on March 2, 2020. There was a nationwide lockdown, which led to an interruption in surveillance of cardiac transplant patients. Many patients remained on a high dose of immune suppression, putting them at a higher risk of attracting COVID-19 infection. Evidence is lacking on the clinical presentation, management, and outcome from COVID-19 infection in solid-organ transplant (SOT) recipients.

CASE PRESENTATION

A 54-year-old woman known to be diabetic, to have hypothyroidism, and to be a heart transplant recipient called her transplant coordinator regarding new symptoms of fatigue and excessive sleepiness for 1 week. She also informed having cough with phlegm for 2 days. She did not report any fever or shortness of breath.

She had a history of dilated cardiomyopathy with recurrent heart failure admissions and end-organ hypoperfusion. The patient underwent a heart transplant 6 months before, which was complicated by acute antibody-mediated rejection within 2 weeks post-transplantation. Her right ventricle biopsy showed moderate lymphocyte infiltrate with myocyte damage and positive precapillary CD4 immune staining. She was treated with plasmapheresis, intravenous (IV) immune globulin, and high-dose methylprednisolone. Her subsequent right ventricle biopsy showed improvement. She remained on a high dose of immune suppressive medication as further scheduled biopsies were not performed because of the COVID-19 hospital lockdown. Her medication included prednisolone 20 mg daily, mycophenolate mofetil (MMF) 1 g twice daily (BID), and tacrolimus 7 mg BID, as well as prophylaxis trimethoprim/sulfamethoxazole, valganciclovir, and nystatin.

On her current presentation to the hospital, she was found to be hypoxic on room air (88%) and to have tachypnea, with a respiratory rate of 28 breaths per minute. Her heart rate was 105 beats per minute in sinus rhythm, and blood pressure was 130/70. Her family gave an additional history of fever and influenza-like symptoms in the patient’s husband and daughter 2 weeks before the onset of the patient’s symptoms. Her family members did not attend any health care facility for their symptoms and did not get tested for COVID-19 infection. Given her clinical presentation and history of contact with febrile family members, she was admitted as a suspected case of COVID-19.

On admission, she was started on oxygen 5 L via a face mask. Her chest X-ray showed bilateral infiltrates. Laboratory investigation was significant for leukopenia and lymphopenia. She had high C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, interleukin 6, and D-dimer levels (Table 1). A nasopharyngeal swab was sent for COVID-19 polymerase chain reaction (PCR), as well as Middle East respiratory syndrome coronavirus influenza viral serology. In addition, bacterial cultures from blood and sputum were sent. She was started empirically on antiviral with oseltamivir and empirical antibiotics with vancomycin and piperacillin/tazobactam. Her trimethoprim/sulfamethoxazole was increased to a therapeutic dose to cover for possible pneumocystis pneumonia. Her cardiac evaluation by echo-cardiography showed a left ventricular ejection fraction of 55% with grade II diastolic dysfunction and mild left ventricular hypertrophy.

On the second day, her oxygen saturation continued to drop despite the oxygen supply. She was started on noninvasive ventilation by noninvasive ventilation. Her COVID-19 PCR result was positive. She had progressive shortness of breath, tachypnea, and hypoxia. The patient was unstable for computed tomography of the chest. Serial investigations were requested, including CRP, D-dimer, serum ferritin, and LDH (Table 2). Subsequently, she was started on favipiravir loading of 1600 mg for 2 doses and a...
maintenance dose of 600 mg BID for 7 days. Immune suppressive therapy was reduced. The MMF and tacrolimus were discontinued. The prednisone was continued at 20 mg daily then switched to hydrocortisone 50 mg IV every 6 hours. Tocilizumab was not given as the inflammatory markers did not rise further. The patient remained hemodynamically stable with no renal or liver failure.

On the fourth day, she had a reduced level of consciousness, and a chest x-ray showed progressed bilateral lungs infiltrate; thus, she was intubated and started on a mechanical ventilator (MV). The multidisciplinary team discussed enrolling the patient in the convalescent plasma study. The patient's family was informed and agreed and consented to proceed with plasma therapy. Two units of compatible ABO plasma therapy were given for 2 consecutive days. Of note, the patient is blood group A. While the patient was on MV, she was shifted from IV hydrocortisone to an equivalent dose of IV dexamethasone as per the recent update on COVID-19 management guidelines by the Ministry of Health.

Her immune suppression was monitored closely. The MMF and tacrolimus were discontinued. 10 of 14 patients (71%). In the Spanish series of SOT, calcineurin inhibitors and sirolimus were discontinued because of drug interaction with lopinavir/ritonavir. The dose of prednisolone was reduced by 50% and MMF was also discontinued. In addition, a renal transplant cohort from Spain with COVID-19 respiratory failure had more than 1 immune inflammatory markers started to decline. The dexamethasone was tapered gradually by 2 mg every 2 days.

She had a successful trial of weaning and was extubated after 10 days. She required minimal oxygen post extubation. She had repeated COVID-19 PCR, which remained positive. Given her marked clinical improvement, she was started on prednisolone 15 mg, MMF 1 g BID, and tacrolimus adjusted to a serum target level of 5. The patient was followed by echocardiography and biomarkers. There was no deterioration in cardiac function. The biopsy was deferred because of isolation protocols. On discharge, she was given instructions on home isolation by the infection control department. The patient was discharged home after 3 weeks of admission.

**DISCUSSION**

The clinical presentation of COVID-19 in SOT recipients has variable presenting symptoms. There are limited data on COVID-19 presentation and clinical outcome in a cardiac transplant recipient. In a series of 15 kidney transplant recipients in the United States, fever was reported in 87% of patients, whereas cough was found in 60%, fatigue and malaise were found in 27%, and shortness of breath was in 27%. Less frequent symptoms were diarrhea (20%) and myalgia (13%). Severe respiratory distress with MV occurred in 4 patients (27%). Patients presented to the hospital between 1 day and 3 weeks from the onset of symptoms. Moreover, in a series of 18 patients with SOT in Spain, including kidney (8/18, 44.4%), liver (6/18, 33.3%), and heart (4/18, 22.2%), the most common presentation was fever (83.3%), and severe respiratory failure occurred in 4 of the 18 patients (30.8%) in the cohort. Our patient did not have fever throughout her course of illness. Her main presenting symptoms were fatigue and cough and she developed respiratory distress during hospital admission. She had a hypoxic respiratory failure with bilateral interstitial pneumonia requiring MV.

The management of immune suppression in COVID-19 pneumonia is limited to expert opinion, case reports, and case series. The International Society of Heart and Lung Transplant provided guidance on decreasing immune suppression in heart and lung transplant recipients based on the severity of COVID-19-related infection. The International Society of Heart and Lung Transplant provided guidance on decreasing immune suppression in heart and lung transplant recipients based on the severity of COVID-19-related infection. In the case series of renal transplant patients with COVID-19, MMF and azathioprine were held in 10 of 14 patients (71%). In the Spanish series of SOT, calcineurin inhibitors and sirolimus were discontinued because of drug interaction with lopinavir/ritonavir. The dose of prednisolone was reduced by 50% and MMF was also discontinued. In addition, a renal transplant cohort from Spain with COVID-19 respiratory failure had more than 1 immune

**TABLE 1. Laboratory Test and Inflammatory Markers on Admission**

|          | Results                  | Reference   |
|----------|--------------------------|-------------|
| WBC      | 3.5 cells *10⁹/L         | 4.0–11 cells *10⁹/L |
| Lymphocyte | 0.2 cells *10⁹/L     | 1.5–4 cells *10⁹/L |
| Hb       | 13 g/dL                  | 11.5–16.5 g/dL   |
| PLT      | 185 cells *10⁹/L         | 150–450 cells *10⁹/L |
| Urea     | 30.6 mmol/L              | 2.8–8.1 mmol/L   |
| Creatinine | 209 mmol/L          | 45–84 mmol/L    |
| Na⁺      | 136 mmol/L               | 136–145 mmol/L   |
| K⁺       | 4.1 mmol/L               | 3.5–5.5 mmol/L   |
| LDH      | 632 U/L                  | 135–214 U/L     |
| Ferritin | 1106 ng/mL               | 13–150 ng/mL     |
| D-dimer  | 0.600 μg/mL              | 0.0–0.5 μg/mL    |
| Procalcitonin | 0.18 ng/mL           | <0.05 ng/mL     |
| ESR      | 31 mm/h                  | 0–15 mm/h       |
| CRP      | 25 mg/L                  | 0–6 mg/L        |
| IL-6     | 87 pg/mL                 | 7 pg/mL         |

WBC indicates white blood cell; Hb, hemoglobin; ESR, erythrocyte sedimentation rate; IL-6, interleukin 6; PLT, platelet.

**TABLE 2. Serial White Blood Count, Lymphocyte, and Inflammatory Markers**

|          | D1          | D8          | D24         | Reference   |
|----------|-------------|-------------|-------------|-------------|
| WBC      | 3.5 cells *10⁹/L         | 3.4 cells *10⁹/L   | 3.6 cells *10⁹/L | 4.0–11 cells *10⁹/L |
| Lymphocyte | 0.2 cells *10⁹/L     | 0.2 cells *10⁹/L   | 0.1 cells *10⁹/L | 1.5–4 cells *10⁹/L  |
| LDH      | 632 U/L                  | 742 U/L         | 680 U/L     | 135–214 U/L     |
| Ferritin | 1106 ng/mL               | 1540 ng/mL      | 923 ng/mL   | 13–150 ng/mL     |
| D-dimer  | 0.600 μg/mL              | 1.500 μg/mL     | 0.920 μg/mL | 0.0–0.5 μg/mL    |
| Procalcitonin | 0.18 ng/mL         | –             | –           | <0.05 ng/mL     |
| ESR      | 31 mm/h                  | –             | –           | 0–15 mm/h       |
| CRP      | 25 mg/L                  | –             | 2 mg/L      | 0–6 mg/L        |

WBC indicates white blood cell; ESR, erythrocyte sedimentation rate.
suppressive medication discontinued in 91.3% of the cohort. In 1 case, a 77-year-old man, a heart transplant recipient, presented with shortness of breath, dry cough, and fatigue without fever. He had interstitial pneumonia but no respiratory distress or MV. He was treated successfully with hydroxychloroquine and the immune-suppressive treatments were modified to tacrolimus instead of sirolimus and MMF was held. In another case, a 52-year-old heart transplant recipient had COVID-19-related acute respiratory syndrome 24 days posttransplantation, who recovered with high-dose steroid and tocilizumab therapy. Also, the MMF was discontinued while the tacrolimus was given intravenously.

The use of steroids has shown benefit in COVID-19 respiratory failure. Dexamethasone was used in 2104 COVID-19 patients with hypoxia in a randomized clinical trial in the United Kingdom. The treatment showed a one-third reduction in mortality in ventilated patients in the RECOVERY trial.

In the general population, patients with SARS-CoV-2 infection have the highest viral load around the time of hospital admission. This is not well studied in SOT patients. Early use of potent antiviral agents might be beneficial in controlling disease severity. To date, there are no antivirals with a mortality benefit. Favipiravir, originally approved for oseltamivir-resistant influenza, works by inhibiting RNA-dependent RNA polymerase. The use of favipiravir in COVID-19 patients is based on small studies. An open-label nonrandomized trial of 80 patients in China identified a significant reduction in the time to SARS-CoV-2 viral clearance in patients treated with favipiravir compared with historical controls treated with lopinavir/ritonavir. In the pilot stage of phase II/III clinical trial conducted in Russia, favipiravir enabled rapid clearance of the virus in 62.5% of patients within 4 days and was safe and well tolerated.

Convalescent plasma is an emerging therapy for COVID-19. The treatment is under clinical trial, but a review of the published case series has shown a reduction in mortality, reduction in the level of respiratory support, and a decrease in the length of hospitalization. Our patient received 2 units of convalescent plasma after 4 days on the MV, and she had a reduction in her fraction of inspired oxygen requirement.

Survival from COVID-19 in SOT was studied in a renal transplant cohort in Spain. The study showed that mortality was strongly associated with age, baseline LDH, and acute respiratory distress syndrome. Survival was not associated with time from transplantation, type of immune suppression used or type of antiviral used, baseline graft function, or presence of acute kidney injury in the renal transplant recipients.

**CONCLUSIONS**

Our patient had multifaceted management for severe COVID-19 pneumonia, including enrolment in the clinical trial for convalescent plasma therapy. Withholding immune suppression in a recent heart transplant patient with a history of antibody-mediated rejection was addressed cautiously. This case shows that SOT patients with COVID-19 pneumonia can have a favorable prognosis.

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