

Complications of a Heart Transplanted Patient with COVID-19 Infection

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Abstract

Our knowledge of coronavirus disease-2019 (COVID-19) and its cardiovascular implications is growing every day. The pandemic has raised the question of whether to continue offering heart transplantations due to concerns regarding the risk for exposure to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during hospitalization and challenges in curbing the infection with high levels of immunosuppression. We present the case of a 47-year-old woman who presented with COVID-19 on immunosuppression therapy due to recent heart transplantation four months before admission. The patient's condition worsened, and despite monitoring and treatment updates, she died on day 19 of admission. Although most immunocompromised persons effectively clear a SARS-CoV-2 infection, this case highlights the potential for ongoing and accelerated viral evolution associated with an immunocompromised state. Patients can manifest acute rejection in the months following transplantation surgery, which can ultimately lead to death.

Keywords: COVID 19; Heart transplant; Cardiology; Internal medicine

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Introduction

Health care professionals worldwide are confronted with unprecedented challenges due to the emergence of the novel coronavirus disease-2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus's high infectivity, ability to transmit during the asymptomatic phase and relatively low virulence has resulted in rapid transmission beyond geographic regions, leading to a pandemic. Cardiovascular Disease (CVD) and cardiovascular risk factors enhance vulnerability to COVID-19. Further, COVID-19 can worsen underlying CVD and even precipitate de novo cardiac complications [1]. One area of cardiovascular medicine vulnerable during the pandemic is that of Heart Transplantation (HT). The donors, recipients, and those awaiting HT are at increased risk of infection. The eminent risk for the recipients is more evident given their immunocompromised state. We present the case of a 47-year-old woman who presented with COVID-19 on immunosuppression therapy due to recent heart transplantation four months before admission.

Case Report

A 47-year-old Saudi female patient was referred from a peripheral hospital to our center with a COVID-19 respiratory infection. Her history was significant for long-term diabetes, diabetic nephropathy, and hypertension. Due to cardiomyopathy

and excessive heart failure with an Ejection Fraction (EF) of 15%, she underwent HT at a specialized center in Riyadh four months before her admission with COVID-19. She was on full immunosuppression medication with mycophenolate 1000 mg twice daily, prednisolone 5 mg twice daily, and sirolimus 2 mg daily.

On admission, she reported dry cough concerns but did not have a fever, chest pain, or shortness of breath. She had no diarrhoea, vomiting, or abdominal pain on clinical examination. The patient was conscious, alert, and oriented, with oxygen saturation at 96% on room air (RA). Her chest x-ray showed peripheral bilateral infiltrates (**Figure 1**).

Echocardiography on admission showed left ventricular dysfunction with hypokinesia of the anterior wall and estimated EF of 40% to 45%, dilated left atrium due to the recent transplant, and moderate tricuspid regurgitation. The electrocardiography directly following her HT showed an EF of 55% with no hypokinesia.

We initiated broad-spectrum antibiotics (ceftriaxone 1 g; doxycycline 100 mg every 12 hours) for prophylaxis of hospital-acquired pneumonia and antiviral agents against COVID-19. The transplant team modified her immunosuppressive medications to stop mycophenolate, continue sirolimus and changed prednisolone to dexamethasone 6 mg intravenous (IV) daily.

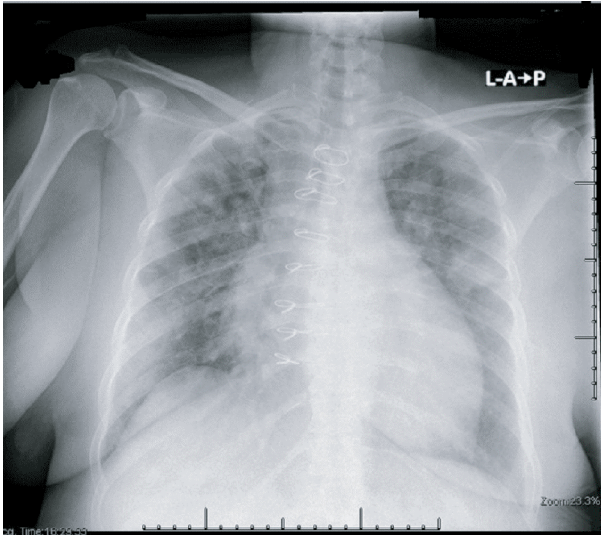


Figure 1 Admission chest x-ray.

On day three, the patient required oxygen because her saturation was 88% to 90% on RA. She was connected to a nasal cannula of 4 L/min flow, and her oxygen saturation increased to 96%. A second chest x-ray showed increased bilateral infiltrations, but the patient was still afebrile with no shortness of breath and was not in respiratory distress. Her antibiotic treatment was upgraded to IV piperacillin/tazobactam. Her transplant center in Riyadh was contacted, and they advised initiating tocilizumab 4 mg/kg, but this medication was not available to our hospital at that time. A second echocardiography study showed only mild improvement of her EF.

Given her severe leukopenia, the patient was also evaluated by a haematologist who suggested her condition was due to immunosuppressive medications augmented with the viral infection, so filgrastim 300 µg daily (subcutaneous) was administered for three days, and her laboratory values were assessed (**Table 1**).

On day five, she developed shortness of breath, and her oxygen saturation dropped to 85% on RA and 97% with the use of 7 L/min flow via a simple face mask. After two hours, she developed a fever and increased dyspnoea. She also developed gastrointestinal symptoms (vomiting and diarrhoea).

The following day (day six), her oxygen requirement increased to 15 L/min flow in a Non-Rebreather Face Mask (NRFM) to keep her oxygen saturation 98%. Piperacillin/tazobactam was stopped, and meropenem with metronidazole was started. The Intensive Care Unit (ICU) team was consulted. On day seven, the patient was moved to the ICU. She did not require intubation or inotropic support, but she was placed on maximum oxygen supply at 15 L/min flow on NRFM and placed in the prone position; her oxygen saturation was 94% to 96%. She had developed acute kidney injury when she moved to the ICU, and her renal function deteriorated, so continuous renal replacement therapy was initiated. Acute rejection of the transplant was suspected, and the team monitoring her was informed. Her medications were

adjusted according to the transplant team's instructions, and that facility accepted the official transfer to their center. However, the medical evacuation team protocol required two negative COVID-19 tests within 48 hours, and the patient was still COVID-19-positive.

On day 13, her oxygen saturation dropped to 60%, she became unconscious, and she was intubated. On day 17, she developed right pneumothorax, for that positive end-expiratory pressure was reduced from 8 cm to 4 cm water and tidal volume from 450 to 350 mL. The cardiothoracic surgeon inserted a chest tube (**Figure 2**). Pneumocystis carinii pneumonia was suspected, and adequate treatment was initiated. However, on day 19, the patient entered cardiac arrest. The care team started cardiopulmonary resuscitation per the advanced cardiac life support protocol, but the patient died.

Discussion

The cardiovascular community faced unprecedented challenges in the COVID-19 pandemic. For HT clinicians, the global pandemic has unique implications for patients, including those on the waiting list and transplant recipients [2]. These populations are at increased risk of both acquiring COVID-19 infection and

Table 1 Laboratory tests.

Analytes	Admission Day to Hospital	Admission Day to ICU	Death Day	Reference Range
WBC Count (×1000/µL)	1.86	3.02	31.6	3.6-11.4
Hb (g/dl)	7.7	7.8	7.7	11.8-17.2
Platelets Count (×1000/µL)	206	212	380	150-400
Neutrophils (%)	83.2	84.9	84	42-77
Lymphocytes (%)	9.8	8.2	7.5	20-44
Ferritin (ng/ml)	697.9	>1650	>1650	10-291
D-Dimer (mg/L)	22.6	23.3	5.36	0.0-0.5
CRP (mg/dl)	2.4			0.0-0.6
BUN (mmol/L)	17	31.7	15.6	2.5-6.4
Creatinine (µmol/L)	187	533	250	49-115
Sodium (mmol/L)	130	133	134	136-145
Potassium (mmol/L)	5.5	4.5	6.79	3.5-5.1
Chloride (mmol/L)	95	97	99	98-107
Calcium (mmol/L)	1.9	1.79	1.89	2.1-2.5
Phosphorous (mmol/L)		2.4	2.1	0.8-1.5
Total Protein (g/L)		50.3	59.7	64-82
Albumin (g/L)		17	28	43-50
ALP (U/L)		113	323	46-116
ALT (U/L)		18	47	14-63
AST (U/L)		35	103	15-37
GGT (U/L)		151	936	5-85
Total Bilirubin (µmol/L)		6.3	19.5	3-17
Conjugated Bilirubin (µmol/L)		2.16	11.19	0.8-3

Abbreviations: ICU: Intensive Care Unit; WBC: White Blood Cell; CRP: C-Reactive Protein; BUN: Blood Urea Nitrogen; ALP: Alkaline Phosphatase; ALT: Alanine Transaminase; AST: Aspartate Transaminase; GGT: Gamma-Glutamyl Transferase

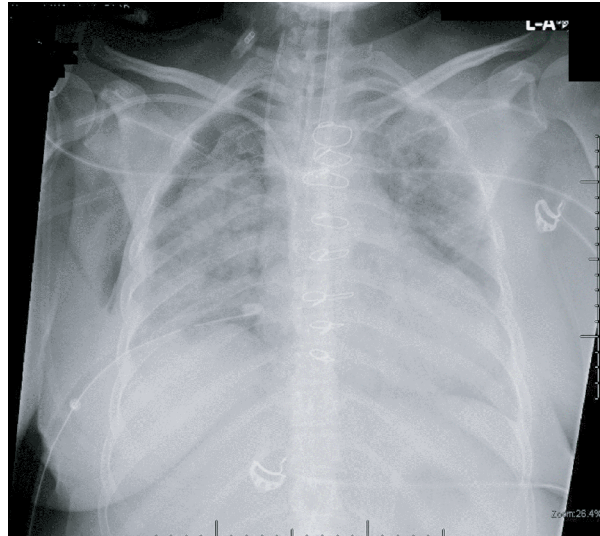


Figure 2 Chest x-ray after intubation.

Table 2 Recommendations regarding heart transplant during the COVID-19 pandemic.

Transplant Area	Recommendations [7]
Donor	COVID-19-focused travel and social history
	Exclusion of donors at risk of other disease transmission (HIV, HPB, HCV)
	Exclusion of marginal donors having mild LVH and/or LV dysfunction
	Donor contract tracing
	Availability and rapid turn-around of PCR assay for donor
	At least two tests to increase sensitivity and specificity
	COVID-19-free interval of 14 days
	Chest CT for exclusion of pneumonia
Recipient	Separate consent for potential COVID-19 donors
	COVID-19-free environment
	Staying away of nurses who attend COVID-19 patients from patients awaiting HT
	Exclusion of hospital-acquired infection by PCR
Post-transplant	Telephonic and/or mail communication regarding expected delay and organizational changes
	Lower threshold for LVAD as a bridge to transplant
	Reduction of overall transplant program activity
	Negative pressure ventilation room with airborne isolation
	Staying away of nurses who attend COVID-19 patients from post-transplant patient
	Reduction of staff contact and outside visitors
	Stress on patient/family hygiene and social distancing
Transplant patients infected with COVID-19	Prompt testing and diagnosis of patients with symptoms related to rejection
	Delaying elective testing, echocardiography, RHC and EMB
	Adherence to local laboratory or home service for the tests
	Reduction of dose of calcineurin inhibitor
	Reduction or withhold of mycophenolate mofetil/azathioprine dose
	Ruling out other bacterial or fungal infection
	Monitoring for viremia
Monitoring for drug-drug interactions	
Continuation of statins unless contraindicated	
IL-6 inhibitors for cytokine storm?	
Monitoring for allograft dysfunction	

Abbreviations: COVID-19: Coronavirus Disease-2019; CT: Computed Tomography; EMB: Endomyocardial Biopsy; HBV: Hepatitis B Virus; HCV: Hepatitis C Virus; HIV: Human Immunodeficiency Virus; HT: Heart Transplant; IL: Interleukin; LVAD: Left Ventricular Assist Device; LV: Left Ventricular; LVH: Left Ventricular Hypertrophy; PCR: Polymerase Chain Reaction; RHC: Right Heart Catheterization

progression to severe disease given their multiple healthcare contacts, underlying health conditions, and immunosuppression; targeted prevention and treatment strategies are needed.

Experience with previous coronavirus epidemics such as severe acute respiratory syndrome and Middle East respiratory syndrome demonstrated that transplant patients have similar presentations to the general population. The first COVID-19 cases reported in two HT recipients were in China in March 2020. Both patients survived, one with a mild form of the illness allowing for treatment and recovery at home, the other with progressive respiratory failure requiring inpatient admission, intravenous immunoglobulin, and methylprednisolone [3].

Experience from other centres suggests that patients with longer post-transplant recovery time and those who did not require intubation during their COVID-19 infection have a better survival ratio [4]. This is unsurprising given the one-year survival rate after HT is approximately 90% [5]. Unfortunately, the patient,

in this case, had undergone her HT procedure only four months before presenting with COVID-19 [6]. Kumar et al. provided new guidelines for managing these patients, especially for patients after transplantation procedures [7]. The new guidelines note the benefits of using interleukin-2 inhibitors such as tocilizumab (Table 2).

Conclusion

An acute cellular rejection triggered by a COVID-19 infection could not be ruled out for this patient. Recent transplantation, insulin resistance, female recipient of a female donor, coronary heart disease, and acute renal injury are factors to be considered. Additional early diagnostics that help prevent acute rejection are usually prohibited due to the high risk of COVID-19 transmission. While considering potential therapies, it is critical to recognize drug-drug interactions and the risk of rejection. Also, the frailty of the patient, her previous condition, and the relatively close transplant date should be considered as factors in her death.

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