

The use of convalescent plasma, dexamethasone and remdesivir in a renal transplant patient infected with COVID-19

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ABSTRACT

Background: Immunocompromised patients, such as renal transplant recipients, are a high-risk population for coronavirus disease 2019 (COVID-19) infection and complications. The evidence to support specific treatment of COVID-19 in this group of patients remains very limited. We present the first case in West Texas of a renal transplant patient who received combined therapy with convalescent plasma, dexamethasone, and remdesivir for the treatment of COVID-19.

Case summary: We report a female patient who received a deceased donor kidney transplant approximately 2 years prior. She was admitted to our institution with respiratory distress with symptomatic COVID-19 infection. Her baseline renal allograft function per serum creatinine was 0.9 mg/dL, and she was on maintenance immunosuppression with tacrolimus, mycophenolate mofetil, and prednisone. Throughout her hospitalization, her mycophenolate mofetil was maintained, the prednisone was switched for dexamethasone, and her tacrolimus dosage required multiple adjustments secondary to interactions with the azithromycin used to treat an atypical pneumonia upon admission to the hospital. The patient eventually required supplemental oxygen with a venti-mask at 50% FiO₂ and transfer to the medical intensive care unit. She received convalescent plasma from a COVID-19 recovered patient, in addition to dexamethasone and then remdesivir for 5 days, with clinical improvement. She was discharged on 3 L per minute supplemental oxygen by nasal cannula from the hospital on day 17 of hospitalization.

Conclusion: This renal transplant patient in West Texas with symptomatic COVID-19 infection was treated with convalescent plasma, remdesivir, and dexamethasone with a good outcome. This case also shows the common and often missed drug interactions between tacrolimus and azithromycin and describes a safe way of lowering immunosuppression without compromising renal allograft function.

Keywords: COVID-19, coronavirus, renal transplant, immunosuppression, convalescent plasma, dexamethasone, remdesivir, tacrolimus, mycophenolate mofetil

INTRODUCTION

Convalescent plasma has become a therapeutic option during the coronavirus disease 2019 (COVID-19) pandemic. However, evidence remains limited and

controversial when considering the use of this therapeutic modality. Furthermore, the available evidence still lacks definitive outcomes. One study published in *The Journal of the American Medical Association* found that patients with severe symptoms associated with COVID-19 did not show statistically significant improvement in 28-day mortality or discharge with convalescent plasma therapy. However, the group that received convalescent plasma did have a faster negative conversion rate of viral PCR compared to the control group.¹ Furthermore,

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Table 1. Recommendations from Transplant Organizations Regarding Immunosuppression Management

Organization	Recommendation	Date
International Society for Heart and Lung Transplantation	“All prior disease-specific therapy or immunosuppression should be continued unless otherwise instructed” ⁵	08/19/2020
Canadian Society of Transplantation and The Transplantation Society of Canada	“Changes in immunosuppression are also not well studied in the transplant populations. Calibration of dose reduction has to balance consequences of rejection (i.e. easier to do with kidney transplants than heart transplantation).” ⁶	06/08/2020
American Society of Transplantation	“The impact of immunosuppression on COVID-19 is not currently known but decreasing immunosuppression should be considered for infected recipients who have not had recent rejection episodes. Many providers have decreased or discontinued cell cycle inhibitors or reduced calcineurin inhibitor levels, but comparative data regarding these interventions are not yet available.” ⁷	06/18/2020
Organ Procurement and Transplantation Network	No recommendations regarding immunosuppression management. ⁸	02/28/2020
European Renal Association/ European Dialysis and Transplantation Association	<p>–Asymptomatic patients: No change of immunosuppression.</p> <p>–Mild disease (only mild upper respiratory and/or gastrointestinal symptoms, oxygen saturation in room air is >95): Stop mycophenolate/azathioprine/mammalian target of rapamycin inhibitor. Consider calcineurin inhibitor dose if there is no clear improvement over the first 3–5 days.</p> <p>–Severe COVID-19 pneumonia (oxygen saturation <94% in room air, respiratory rate ≥30/min), unstable or deteriorating course (with or without mechanical ventilation): Discontinue all IS drugs, increase/start steroids at 15–25 mg/day (or higher according to local practice). Carefully consider to continue with low dose calcineurin inhibitor in patients with higher risk of rejection.”⁹</p>	06/04/2020
British Transplantation Society	“Levels of immunosuppression should be reviewed but generalised immunosuppression reduction that may jeopardise organ function is not recommended” ¹⁰	08/14/2020

it is important to note that this study was terminated early due to decreased COVID-19 numbers in Wuhan, China, at the time of the investigation. Evidence to support convalescent plasma in renal transplant patients is also lacking and remains controversial at this time. Jiang and colleagues recently published a case report that supported the use of convalescent plasma in renal transplant patients. This report also suggested that immunosuppression agents must be adjusted to manage infection vs. rejection.² Another case report published in *American Journal of Transplantation* showed

that treatment regimens for COVID-19 in renal transplant patients should include reduced immunosuppression and low dose methylprednisolone-based therapy.³ New evidence shows remdesivir may shorten recovery in patients with COVID-19 and respiratory infection.⁴ For patients with special conditions, such as renal transplantation, evidence to support treatment of COVID-19 remains very limited (Table 1).^{5–10} For this reason, we report the first case in West Texas of a renal transplant patient who received convalescent plasma, dexamethasone, and remdesivir for treatment of COVID-19,

recovered, and was successfully discharged home with limited need for oxygen support.

CASE REPORT

A 62-year-old woman with a past medical history of diabetes mellitus type 2, hypertension, coronary artery disease status-post CABG seven years ago, hypothyroidism, and renal failure status-post deceased donor kidney transplantation approximately 2 years prior to admission. Prior to her transplantation, the patient was on peritoneal dialysis for five years. Her serum creatinine was 0.9 mg/dL at baseline before presentation to the hospital for symptoms related to COVID-19 infection. She was on maintenance immunosuppression with tacrolimus, mycophenolate mofetil, and prednisone prior to admission.

On day 1, the patient presented to the emergency department (ED) for symptoms of fever, cough, dyspnea, chest pain, and nausea that had progressively worsened over the previous four days before admission. She had been tested for COVID-19 at an outlying community clinic the day prior and was found to be positive. The patient had been exposed to the virus by her son who also tested positive prior to her diagnosis. Of note, she also tested positive for a Streptococcal infection four days prior to admission and was being treated with amoxicillin.

Initial presentation vital signs revealed a temperature of 100.9° F, blood pressure 142/71 mmHg, heart rate 66 beats per minute, respiratory rate 24 breaths/minute, and oxygen saturation of 82% on room air. The patient was placed on 4 liters oxygen per minute by nasal cannula (4L NC) and oxygen saturation increased to 94%. Laboratory testing in the ED revealed a positive nasopharyngeal swab for SARS-CoV2 by polymerase chain reaction (PCR), white blood cells 5.6 k/ μ L, hemoglobin 14.2 g/dL, platelets 141 k/ μ L, troponin 29.5 ng/L, lactate dehydrogenase 263 units/L, lactic acid 0.9 mmol/L, and ferritin level >2000 ng/ml. A chest x-ray done on admission showed patchy bibasilar opacities. Computed tomography of the chest revealed multiple small areas of ground-glass opacities in both lungs. An electrocardiogram done in the ED did not demonstrate ischemic changes.

The findings on presentation were consistent with acute hypoxic respiratory failure secondary to pneumonia in the setting of confirmed SARS-CoV2 infection. The patient was admitted to the hospital's COVID-designated ward. Heparin was started for DVT prophylaxis at 5000 units SQ BID. Amoxicillin was discontinued, and she was started on ceftriaxone and azithromycin for empiric treatment of community-acquired pneumonia, which would also cover the concurrent strep pharyngitis. The patient had a left heart angiogram done recently, which revealed patent graft at that time. Although her troponin was initially elevated, it remained stable on subsequent testing throughout her hospitalization. Chest pain resolved upon oxygen supplementation in the ED. Supportive care continued with 4L NC to maintain oxygen level above 90%.

On hospital day 2, prednisone was stopped, and dexamethasone (6 mg daily) was started. Ceftriaxone and azithromycin were continued. Patient remained stable on 5L NC. On hospital day 3, mycophenolate mofetil and azithromycin were stopped. Azithromycin was discontinued due to supratherapeutic tacrolimus levels. Because of the elevated levels, tacrolimus dose was held on the evening of hospital day 3 and on the morning and evening of hospital day 4. On hospital day 5, the patient received convalescent plasma. Attempts were made to decrease the oxygen supplementation but were not successful. On hospital day 8, she became hypoxic and tachypneic with labored respirations. She was placed on a Venturi-mask at 50% FiO₂ and transferred to the Medical Intensive Care Unit for closer monitoring. She was also started on remdesivir IV and completed a five-day course. She received dexamethasone for a total of 10 days. Patient was transitioned to floor status on day 16 and was discharged on 3L NC from the hospital on day 17.

Throughout her 17-day hospitalization the patient maintained stable kidney function. The mycophenolate mofetil was held as part of the management of an active infection. Her tacrolimus regimen required multiple adjustments secondary to interactions with azithromycin and in an attempt to maintain serum trough levels around 6 ng/ml (Table 2). Prednisone was held after starting dexamethasone for 10 days as part of the COVID-19 management (Table 2) and then restarted at 5 mg daily.

Table 2. Oxygen and Medication Provided During Hospitalization

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17
Max. O ₂ req./day	5L NC	5L NC	5L NC	5L NC	5L NC	5L NC	5L NC	V mask	V mask	V mask	V mask	4L NC	4L NC	4L NC	4L NC	3L NC	3L NC
Immuno-suppressants	P, M, T	P, M, T	T	none	T	T	T	T	T	T	T	T	T	T	T	T	T
Dexamethasone		x	x	x	x	x	x	x	x	x	x						
Antibiotics	A, C	A, C	C	C	C	C											
Remdesivir								x	x	x	x	x					
Convalescent Plasma					x												
Anticoagulation	H	H	H	H	E	E	E	E	E	E	E	E	E	E	E	E	E

P = prednisone, M = mycophenolate mofetil, T = Tacrolimus, A = azithromycin, C = ceftriaxone, H = heparin, E = Eliquis, Vmask = Venti-Mask

DISCUSSION

Although the patient still required oxygen therapy at discharge, she was continuing to improve and was expected to wean off oxygen. During this pandemic, evidence continues to be limited and controversial in regard to treatment of COVID-19 infection, especially in immunocompromised patients. This case report provides a data point demonstrating safety in the use of convalescent plasma, remdesivir, and dexamethasone in renal transplant patients infected with COVID-19. It also supports the strategy of reducing chronic immunosuppression therapies when treating COVID-19 in renal transplant patients, but more clinical studies are needed on the topic.

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