

CASE REPORT AND REVIEW OF THE LITERATURE

COVID-19 in an HIV-positive kidney transplant recipient

Rebecca N. Kumar¹  | Sajal D. Tanna¹ | Aneesha A. Shetty^{2,3} | Valentina Stosor^{1,3}

¹Divisions of Infectious Diseases, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

²Divisions of Nephrology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

³Divisions of Organ Transplantation, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

Correspondence

Rebecca N. Kumar, Division of Infectious Diseases, Northwestern University Feinberg School of Medicine, 645 North Michigan Avenue, Suite 900, Chicago 60611, IL.
Email: Rebecca.Kumar@northwestern.edu

Abstract

We report a case of a 50-year-old male with a history of HIV and kidney transplant who presented with SARS-CoV-2. We also present a review of COVID-19 cases in kidney transplant recipients.

KEYWORDS

COVID-19, human immunodeficiency virus, kidney transplantation, severe acute respiratory syndrome coronavirus-2

1 | INTRODUCTION

Since the first cases of an unusual pneumonia were reported in China in December 2019, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in an ongoing pandemic.¹ By the beginning of May 2020, the Centers for Disease Control and Prevention reported 1 122 486 cases within the United States alone.² Because this is a novel virus, outcomes associated with comorbidities, especially immunosuppressed or compromised states, are still being evaluated. This case describes the clinical course of a symptomatic kidney transplant recipient with HIV who tested positive for SARS-CoV-2.

2 | CASE

A 50-year-old HIV+ (CD4 395 cells/ μ L, CD4% 28%, HIV RNA < 20 copies/mL) African-American male with deceased donor kidney transplantation 14 months earlier for end-stage renal disease secondary to HIV-associated nephropathy (HIVAN)/focal segmental glomerulosclerosis (FSGS) presented to the Emergency Department (ED) complaining of fevers for 2 days, with temperatures to 101°F, chills, nasal congestion, and mild cough. The past medical history also includes hypertension, asthma, steatohepatitis, and resolved hepatitis B infection. The patient denied shortness of breath, chest or abdominal pain, diarrhea, or vomiting. He did not have changes in his urine output, pain over the allograft, or dysuria. The patient reported known exposure to COVID-19 at a family gathering 17 days

prior to symptom onset. His husband, who accompanied him to the event, tested positive for SARS-CoV-2 1 week prior to onset of the patient's illness.

The transplant history was notable for receipt of a PHS-increased risk, HIV antibody-positive, HIV NAT-negative deceased donor kidney allocated through the HIV Organ Policy Equity (HOPE) Act.³ He received induction immunosuppression with basiliximab and steroid-sparing maintenance immunosuppression with tacrolimus (target trough 8-10 mcg/L) and mycophenolate mofetil (1250 mg twice daily orally initially followed by 1000 mg twice daily orally after 6 months post-transplant). Post-transplant course was notable for post-operative perinephric seroma that required drainage. His renal function improved to a baseline serum creatinine of 1.9-2.2 mg/dL range post-transplant. The 6-month and 1-year surveillance allograft biopsies were negative for acute rejection or recurrent HIVAN/FSGS, and he remained without development of donor-specific antibodies (DSA). Two days prior to ED evaluation, when patient first reported fever and COVID-19 exposure to the transplant department, the mycophenolate dose was reduced from 1000 mg twice daily to 250 mg twice daily orally due to suspicion for COVID-19 as cause of the patient's illness.

The patient was diagnosed with HIV infection in 1997, initiated antiretroviral therapy (ART) at that time, and has had long-term viral suppression. At and since time of transplant, the ART regimen consisted of dolutegravir, emtricitabine, and tenofovir alafenamide. He was also receiving maraviroc v. placebo as part of a randomized clinical trial (NCT02741323). There have been no opportunistic infections.

In the ED, the patient was hypertensive with blood pressure 172/95 mm Hg and tachycardic with heart rate 108/min, but he appeared well and had temperature 98.9°F and oxygen saturation 100% on room air. A nasopharyngeal swab was obtained, a respiratory viral panel (FilmArray[®] Respiratory Panel Assay) was negative, and SARS-CoV-2 real-time PCR (Northwestern Memorial CDC COVID-19 SARS-CoV-2 detection assay) was positive. No further lab work or imaging was performed. The patient enrolled in the COVID home monitoring program through our medical center and was discharged to home.

The patient had ongoing symptoms reported through the monitoring program including anosmia and ageusia 1 day after discharge, fatigue, and fevers. Symptoms, including anosmia and ageusia, resolved 10 days after illness onset. On a follow-up telehealth visit 4 weeks later, the patient reported his health was back to baseline. A subsequent laboratory evaluation was notable for white blood cell count $3.7 \times 10^3/\mu\text{L}$ and serum creatinine 1.93 mg/dL. The HIV RNA remained < 20 copies/mL, and the CD4 count was 435 cells/ μL , CD4% 31%, with a CD4/CD8 ratio 0.65 and absolute lymphocyte count of 1413 cells/ μL .

3 | DISCUSSION

There have been reported cases of COVID-19 in HIV-infected patients and cases of COVID-19 in transplant recipients.⁴⁻¹⁵ However, this case is the first detailed report of an HIV-positive kidney transplant recipient who developed and recovered from COVID-19.

Unlike the case series from Spain where HIV patients with COVID-19 changed regimens to include a boosted protease inhibitor, no modifications were made to our patient's ART regimen.⁶ The current regimen was continued due to lack of demonstrated efficacy of lopinavir-ritonavir for COVID-19 in a randomized control trial, as well as avoiding the interactions associated with ritonavir and tacrolimus.^{16,17} Data available on COVID-19 infection in persons with HIV remains limited and further studies are needed to better characterize the disease course and outcomes in this population.^{6,9}

This patient's clinical course appears consistent with other published experiences with HIV-negative renal transplant recipients who developed COVID-19. To date, the largest series of renal transplant recipients with COVID-19 (36 patients) reported a mortality rate of 28% at 3 weeks from initial disease presentation, a striking difference from the mortality rate of 7.5% in COVID-19 patients in New York City in general.^{15,18} However, not all transplant recipients had severe infection or complicated courses. A review of available renal transplant cases can be found in Table 1.^{4,7,10-15}

Overall, our patient did well without experimental antiviral or anti-inflammatory therapies and experienced no serious complications, including need for hospitalization or supplemental oxygenation. In fact, the patient appeared well enough that the ED did not order labs beyond respiratory virus and SARS-CoV-2 testing. Immunosuppression was decreased within 48 hours of symptom onset, but it is unclear if this influenced clinical outcome. As the

pandemic progresses and more data becomes available, the clinical spectrum of COVID-19 infections in the transplant population will be better defined and will better inform the management of immunosuppression in this setting. Concern for a potential immune reconstitution inflammatory syndrome (IRIS)-like reaction has made our center's transplant clinicians hesitant to discontinue immunosuppression altogether in the setting of acute infection; COVID-19 increases this concern because of the potential for the heightened inflammatory state that occurs with critical illness within the non-immunosuppressed patient.¹⁹

Maraviroc is currently FDA-approved for treatment of HIV in patients with R-5 virus, because it blocks the C-C chemokine receptor type 5 (CCR-5) receptor and prevents viral entry into CD4 cells. Because of its importance in immune cell response, CCR5 blockade has been suggested as a potential way to reduce allograft loss recipients.^{20,21} CCR-5 blockade with leronlimab is currently under investigation in a Phase2b/3 for severely ill COVID-19 patients.²² In the case series from New York City, six severely ill patients received leronlimab on compassionate use basis; although there was improvement in interleukin-6 levels noted in five patients, only one patient did not require intubation.¹⁵ Our patient was enrolled in a randomized clinical trial (NCT02741323) evaluating the use of maraviroc after kidney transplantation; due to the blinded nature of the study, we do not know if he was receiving this agent and if this could have modified the severity of COVID-19.

Because this is a singular case report, we are unable to determine what extent immunosuppressant management and/or HIV therapy had an impact on outcome of this infection. We recommend against switching ART in HIV-positive organ recipients, as increased and toxic levels of calcineurin inhibitors can occur if administered concomitantly with protease inhibitors, including ritonavir, and cobicistat therapy, and couple with lack of evidence for efficacy of lopinavir/ritonavir and darunavir/cobicistat against COVID-19.²³ Additionally, there is currently no convincing data to support the use of CCR5 blockade for COVID-19.

It is unknown whether there is a cumulative risk for COVID-19 severity in a person who is HIV-positive and an organ recipient. At present, it is prudent to approach HIV-positive organ recipients with COVID-19 in the same manner as HIV-uninfected persons. Most reported cases of COVID-19 in transplant recipients have been managed with reduction or withdrawal of anti-metabolite agents, which is consistent with our practice of decreasing anti-metabolite therapy to half the patient's dose in the setting of COVID-19. If patients fail to improve or further decline with this adjustment, we recommend discontinuation of anti-metabolite therapy. However, we would discourage the complete discontinuation of all immunosuppression to avoid an IRIS type reaction. Consideration for remdesivir or therapies under investigation can be made on an individual basis for those patients who are critically ill or fail to clinically improve. As data emerges in the US, it is essential to systematically describe outcomes and identify unique features of patients with both HIV and organ transplants. These populations will also be important to include in clinical trials of COVID therapies.

TABLE 1 Summary of reported COVID-19 infection cases among kidney transplant recipients

Patient	Age	Co-morbid Conditions	Clinical Presentation	SARS Co-V-2 Diagnosis	Imaging	Treatment	Immunosuppressive Agent Modifications	Outcome
1	50	HIV HTN Asthma, Steatohepatitis Resolved HBV	Fevers Chills Nasal congestion Cough Anosmia Dysgeusia	NP swab	None	None	MMF reduced	Recovered
2 ⁴	28	Lupus-like syndrome	Low grade fevers Malaise Sore throat Rhinorrhea	NP swab	CT chest: normal	Oseltamivir	None	Recovered
3 ⁷	75	COPD HTN Heart disease	Fevers Dyspnea Myalgias	NP swab	CT chest: extensive bilateral GGO	Hydroxychloroquine Lopinavir/ritonavir	Tacrolimus discontinued MMF discontinued	Expired
4 ⁷	52	HTN	Fevers Dyspnea Diarrhea, Myalgias AKI	NP swab	CT chest: extensive bilateral GGO	Hydroxychloroquine Darunavir/cobicistat Colchicine	Tacrolimus discontinued MMF discontinued	Remained hospitalized
5-40 ¹⁵	32-77	Not available	Fever (58%) Cough (53%) Dyspnea (44%) Myalgias (36%) Diarrhea (22%)	Not available	Imaging consistent with viral pneumonia (96%) ^b	Hydroxychloroquine (86%) Azithromycin (46%) Leronlimab (7%) Tocilizumab (7%) High-dose glucocorticoids (7%)	Anti-metabolite discontinued (86%) Tacrolimus discontinued (21%)	Mechanical ventilation (39%) Remained hospitalized (43%) Expired (28%)
41 ⁸	50	HTN DM	Fever Cough	NP swab	CXR: minimal interstitial lesions	None	None	Recovered
42 ¹⁰	50	Splenectomy ITP PTLD HTN	Fever Vomiting	NP swab	CXR diffuse bilateral infiltrates	Lopinavir/ritonavir Hydroxychloroquine Interferon Beta	Tacrolimus discontinued Everolimus discontinued	Remained in ICU
43 ¹¹	52	Not available	Fatigue Cough Dyspnea Chest pain and tightness Anorexia Nausea Abdominal pain	OP swab	Chest CT: GGO and consolidation	Methylprednisolone IVIG Interferon α	Tacrolimus discontinued MMF discontinued	Recovered Repeat OP swab negative on day 18
44 ¹²	38	Not available	Fever Cough	OP swab	Chest CT: typical signs of viral infection	Oseltamivir or arbidol ⁹	Tacrolimus reduced MMF discontinued	Recovered Repeat OP swab negative on day 26
45 ¹²	64	Bladder cancer	Fever Productive cough Myalgias Fatigue	OP swab	Chest CT: typical signs of viral infection	Oseltamivir or arbidol ⁹	Glucocorticoid discontinued MMF discontinued	Residual dyspnea at time of hospital discharge

(Continues)

TABLE 1 (Continued)

Patient	Age	Co-morbid Conditions	Clinical Presentation	SARS Co-V-2 Diagnosis	Imaging	Treatment	Immunosuppressive Agent Modifications	Outcome
46 ¹²	37	HTN	Fever Cough	OP swab	Chest CT: typical signs of viral infection	Oseltamivir or arbidol ^a IVIG	Tacrolimus discontinued MMF discontinued	Recovered Repeat OP swab negative on day 22
47 ¹²	47	Not available	Fever Productive cough Myalgias Fatigue	OP swab	Chest CT with typical signs of viral infection	Oseltamivir or arbidol ^a	Tacrolimus discontinued MMF discontinued Glucocorticoid discontinued	Resolved Repeat OP swab positive on day 18
48 ¹²	38	HTN DM	Fever Productive cough Myalgias Fatigue	OP swab	Chest CT with typical signs of viral infection	Oseltamivir or arbidol ^a	None	Resolved Repeat OP swab negative on day 18
49 ¹³	49	Not available	Fever Respiratory symptoms	NP swab	Chest CT with multifocal GGO	Lopinavir/ritonavir Ribavirin Interferon-alpha-2b Methylprednisolone	None	Resolved
50 ¹⁴	58	Testicular cancer	Fever Dyspnea Cough	NP swab	Chest CT peripheral GGO	None	Belatacept discontinued MMF discontinued	Resolved

Abbreviations: AKI, acute kidney injury; COPD, chronic obstructive pulmonary disease; CXR, chest radiograph; DM, diabetes mellitus; GGO, ground-glass opacity; HBV, hepatitis B virus; HTN, hypertension; ITP, idiopathic thrombocytopenic purpura; IVIG, intravenous immunoglobulin; MMF, mycophenolate mofetil; NP, nasopharyngeal; OP, oropharyngeal; PTLN, post-transplant lymphoproliferative disorder.

^aNot specified which of the two medications (oseltamivir or arbidol) the patient received.

^bImaging modality not specified.

AUTHORS' CONTRIBUTIONS

RNK, SDJ, AAS, and VS contributed to the designing, acquisition of data, analysis, and writing of the manuscript. All four authors contributed to the editing of the manuscript and approved the final version submitted.

ORCID

Rebecca N. Kumar  <https://orcid.org/0000-0001-6650-0612>

REFERENCES

1. CHP closely monitors cluster of pneumonia cases on Mainland. The Government of the Hong Kong Special Administrative Region. <https://www.info.gov.hk/gia/general/201912/31/P2019123100667.htm>. Published 2019. Updated 31 December 2019. Accessed 21 April, 2020.
2. CDC. Cases of Coronavirus Disease (COVID-19) in the U.S. <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html>. Published 2020. Updated 4 May 2020. Accessed 4 May, 2020.
3. Health Resources and Services Administration (HRSA), Department of Health and Human Services (HHS). Organ procurement and transplantation: implementation of the HIV Organ Policy Equity Act. Final rule. *Fed Regist*. 2015;80(89):26464-26467.
4. Arpali E, Akyollu B, Yelken B, Tekin S, Turkmen A, Case KB. Report: a kidney transplant patient with mild COVID-19. *Transpl Infect Dis*. 2020;e13296.1399-3062. <https://doi.org/10.1111/tid.13296>.
5. Bhoori S, Rossi RE, Citterio D, Mazzaferro V. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy. *Lancet Gastroenterol Hepatol*. 2020;5(6):532-533.
6. Blanco JL, Ambrosioni J, Garcia F, et al. COVID-19 in patients with HIV: clinical case series. *Lancet HIV*. 2020;7(5):e314-e316.
7. Gandolfini I, Delsante M, Fiaccadori E, et al. COVID-19 in kidney transplant recipients. *Am J Transplant*. 2020;20(7):1941-1943.
8. Seminari E, Colaneri M, Sambo M, et al. SARS Cov2 infection in a renal transplanted patients. A case report. *Am J Transplant*. 2020;20(7):1882-1884.
9. Zhao J, Liao X, Wang H, et al. Early virus clearance and delayed antibody response in a case of COVID-19 with a history of co-infection with HIV-1 and HCV. *Clin Infect Dis*. 2020. <https://doi.org/10.1093/cid/ciaa408>.
10. Guillen E, Pineiro GJ, Revuelta I, et al. Case report of COVID-19 in a kidney transplant recipient: Does immunosuppression alter the clinical presentation? *Am J Transplant*. 2020;20(7):1875-1878.
11. Zhu L, Xu X, Ma K, et al. Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression. *Am J Transplant*. 2020;20(7):1859-1863.
12. Zhang H, Chen Y, Yuan Q, et al. Identification of Kidney Transplant Recipients with Coronavirus Disease 2019. *Eur Urol*. 2020;77(6):748-747. <https://doi.org/10.1016/j.eururo.2020.03.030>.
13. Wang J, Li X, Cao G, Wu X, Wang Z, Yan T. COVID-19 in a Kidney Transplant Patient. *Eur Urol*. 2020;77(6):769-770.
14. Marx D, Moulin B, Fafi-Kremer S, et al. First case of COVID-19 in a kidney transplant recipient treated with belatacept. *Am J Transplant*. 2020;20(7):1944-1946.

15. Akalin E, Azzi Y, Bartash R, et al. Covid-19 and kidney transplantation. *N Engl J Med*. 2020;382:2475–2477. <https://doi.org/10.1056/NEJMc2011117>.
16. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *N Engl J Med*. 2020;382:1787–1799. <https://doi.org/10.1056/NEJMoa2001282>.
17. Blumberg EA, Rogers CC, American Society of Transplantation Infectious Diseases Community of P. Solid organ transplantation in the HIV-infected patient: guidelines from the American society of transplantation infectious diseases community of practice. *Clin Transplant*. 2019;33(9):e13499.
18. Cases, Hospitalizations and Deaths. NYC Health. COVID-2019: data web site. <https://www1.nyc.gov/site/doh/covid/covid-19-data.page>. Updated 27 April 2020. Accessed 27 April, 2020.
19. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497–506.
20. Fischereder M, Luckow B, Hocher B, et al. CC chemokine receptor 5 and renal-transplant survival. *Lancet*. 2001;357(9270):1758–1761.
21. Akashi S, Sho M, Kashizuka H, et al. A novel small-molecule compound targeting CCR5 and CXCR3 prevents acute and chronic allograft rejection. *Transplantation*. 2005;80(3):378–384.
22. First two patients enrolled in randomized phase 2, COVID-19 trial with leronlimab; Five more severely ill COVID-19 patients treated under emergency IND and two patients have already extubated [press release]. 6 April 2020 2020.
23. Han Z, Kane BM, Petty LA, Josephson MA, Sutor J, Pursell KJ. Cobicistat significantly increases tacrolimus serum concentrations in a renal transplant recipient with human immunodeficiency virus infection. *Pharmacotherapy*. 2016;36(6):e50–e53.

How to cite this article: Kumar RN, Tanna SD, Shetty AA, Stosor V. COVID-19 in an HIV-positive kidney transplant recipient. *Transpl Infect Dis*. 2020;22:e13338. <https://doi.org/10.1111/tid.13338>