

Case report: A kidney transplant patient with mild COVID-19

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Abstract

Coronavirus Disease 2019 (COVID-19) is currently a pandemic with a mortality rate of 1%-6% in the general population. However, the mortality rate seems to be significantly higher in elderly patients, especially those hospitalized with comorbidities, such as hypertension, diabetes, or coronary artery diseases. Because viral diseases may have atypical presentations in immunosuppressed patients, the course of the disease in the transplant patient population is unknown. Hence, the management of these patients with COVID-19 is an area of interest, and a unique approach is warranted. Here, we report the clinical features and our treatment approach for a kidney transplant patient with a diagnosis of COVID-19. We believe that screening protocols for SARS-Cov-2 should be re-evaluated in patients with solid-organ transplants.

KEYWORDS

COVID-19, kidney transplantation, SARS-Cov-2

1 | INTRODUCTION

In December 2019, an epidemic of unknown acute respiratory tract infection broke out in Wuhan, China.¹ Shortly after the first pneumonia cases were reported, a novel coronavirus was identified as the culprit.² This newly identified coronavirus was named SARS-Co-2, and the disease caused by this virus was named Coronavirus Disease 2019 (COVID-19). The clinical manifestations of COVID-2019 may vary within a wide spectrum of diseases, including asymptomatic infection, flu-like upper respiratory tract disease with mild symptoms and severe viral pneumonia with respiratory failure on the other end of the spectrum.^{1,3,4} Solid-organ transplant (SOT) recipients are under chronic immunosuppression, and thus, clinical presentations of viral infections could be atypical in this population. Although information regarding the clinical course and risk factors for COVID-2019 has been published, not much data exist regarding the management of SOT patients other than a few case reports of COVID-19 among

SOT recipients. Herein, we present a case of COVID-19 in a kidney transplant recipient.

2 | CASE REPORT

A 28-year-old woman who had undergone living-donor kidney transplantation from her mother 6 months previously presented at our transplant clinic with a history of subfebrile fevers, malaise, sore throat, and rhinorrhea, which began two days after a tourist trip to England. Her husband, who accompanied her during the trip, was also reported to have a high fever and cough.

The patient's previous medical history revealed treatment with cyclophosphamide 500 mg/m²/mo for 7 months between 2006 and 2007, followed by a course of mycophenolate mofetil (MMF) and oral corticosteroids for the treatment of a lupus-like syndrome. Unfortunately, her kidney functions declined during last ten years progressively. Recently, she was diagnosed end-stage renal disease due to chronic glomerulonephritis from Lupus-like syndrome and the patient was referred to our department for a pre-emptive kidney transplant. During the routine evaluation for surgery, no

Abbreviations: COVID-19, Coronavirus Disease 2019; SOT, Solid-Organ Transplant; MMF, Mycophenolate Mofetil; Tac, Tacrolimus; Pred, Prednisone; HUS, Hemolytic Uremic Syndrome; NLR, Neutrophil-Lymphocyte Ratio.

complement deficiencies were detected in the context of her lupus-like syndrome.

She had a kidney transplant with induction therapy of anti-thymocyte globulin and received triple maintenance therapy, which included oral tacrolimus (Tac), MMF, and prednisone (Pred). In the early period after the kidney transplant, she experienced a transient thrombotic microangiopathy induced likely by tacrolimus. She responded well to only two courses of Eculizumab treatment without any relapse.

Since she had experienced intractable leukopenia while she was on triple maintenance, her immunosuppressive protocol was tailored to dual therapy early in the postoperative period, which consisted of tacrolimus and 10 mg Pred daily. The targeted tacrolimus level was determined to be between 6 and 8 ng/mL.

During our first clinical evaluation, the patient's vital signs were within normal limits. The results of a physical examination of the heart, lungs, and abdomen were unremarkable. Only mild hyperemia of the tonsils and pharyngeal mucosa was noted as prominent findings. No other pathological findings were reported. Routine blood tests were run, and nasopharyngeal swab specimens were collected for influenza A/B, respiratory syncytial virus. Since, at our institution, the prerequisites for COVID-19 testing were a reported body temperature over 38°C or cough and/or respiratory distress and an epidemiologic risk of contact, no swabs were collected for COVID-19. According to the blood test results, the patient's creatinine level was 0.92 mg/dL, GFR was 85 mL/min, white blood cell count was 3120/ μ L, total lymphocyte count was 300/ μ L, hemoglobin level was 11.4 gr/dl, platelet count was 211 000/ μ L, and tacrolimus level was 7.23 ng/ml. However, her CRP level was slightly elevated, at 5.7 ng/L. No pathological findings were reported on chest x-ray. Her swabs tests were reported to be negative for influenza A/B. Amoxicillin was started empirically, and the patient was sent home with instructions for isolation.

The following day, the patient presented to our transplant clinic with a high fever, which she measured as 38°C at home. The patient was transferred to the emergency department, and an infectious disease consultation was requested for COVID-19 testing. During this admission, the physical examination revealed a body temperature of 36.8°C, pulse rate of 70/min, respiratory rate of 14/min, blood pressure of 120/60 mm Hg, and oxygen saturation of 98% on room air. Physical examination findings were unremarkable, including breath sounds on chest auscultation. The blood test results were similar to those from the previous day. Swab tests for COVID-19 were collected, oseltamivir treatment was started empirically by the Infectious disease consultant, and she was discharged from the emergency department on the same day with very strict isolation instructions for home.

Six days later, her swabs tests were reported to be positive for COVID-19. In the meantime, although she reported no high fevers or additional symptoms, the patient was admitted to the hospital for close monitoring and further testing. At the time of this admission, the patient had no complaints, and there were no positive physical examination findings suggesting a respiratory tract infection. A CT

scan of the chest showed no pathological changes. All laboratory tests evaluating liver enzymes, kidney function, and acute phase reactants, including CRP, were within normal range except her total lymphocyte count, which was 800/ μ L. No change in vital signs or respiratory functions were observed during the 24-hour hospitalization for monitoring. She was discharged after 24 hours. Seven days after the discharge from the hospital she was seen in the clinic and swab tests were collected for COVID-19, which were reported to be negative afterward. To date, she has been healthy with no complaints at home for 14 days.

3 | DISCUSSION

COVID-19 is a respiratory disease caused by SARS-CoV-2. The clinical manifestations are quite variable, which include asymptomatic carrier status, mild flu-like disease, acute respiratory disease, and severe disease, which necessitates intubation and mechanical ventilator support. Most of the patients with COVID-19 are reported to present with similar symptoms, such as fever, malaise, and cough.^{5,6} Nausea, vomiting, and diarrhea are uncommon symptoms associated with this disease. Based on current epidemiological studies, the incubation period is between 1 and 14 days. No data have been published regarding the incidence and fate of asymptomatic carriers. According to analyses from China, 16%-18% of confirmed cases were severely ill patients.^{5,7} The mortality rate of hospitalized patients could be as high as 28%, depending on different series.^{1,4,5,8} So far, many potential drugs have been tested for the treatment of COVID-19. However, only remdesivir and chloroquine seem to be effective.^{9,10} Older age, accompanying chronic illnesses, lymphopenia, and elevated procalcitonin and d-dimer levels were found to be related to severe disease and mortality.⁸

Theoretically, renal transplant patients under immunosuppression may have deficiencies in clearing the SARS-CoV-2 virus and may exhibit more atypical clinical presentations than do the general population. Reports on the clinical course and treatment of renal transplant patients with COVID-19 are scarce, and currently, only a few case reports exist in the literature.¹¹⁻¹⁴

All patients from these case reports presented with overt manifestations of COVID-19 symptoms. The most prominent symptoms were high fever and cough, both of which were reported in all patients. Table 1 highlights the clinical manifestations, treatment choices, and clinical courses of the patients.

Discontinuing immunosuppressive agents and starting wide-spectrum antibiotics were the initial treatment approaches for most of the patients. Zhu et al reported that they administered IVIG, steroids, and interferon α in the treatment of their patient after the COVID-19 diagnosis was confirmed. Guillen et al initiated hydroxychloroquine treatment in the following phase. Gandolfini et al also used hydroxychloroquine in addition to "lopinavir + ritonavir" or "darunavir + cobicistat" treatment. They mentioned that the administration of colchicine may reduce the exaggerated

TABLE 1 Demographic data, clinical manifestations, treatment choices, and clinical courses of the transplant patient with COVID-19

	Age	Gender	Tx date	Comorbidities	Manifestation	Anti-viral Management	Intubation	Clinical Outcome
Our Pt	28	Female	6 mo ago	None	Mild Flu-like symptoms	Oseltamivir	No	Recovered
Pt-1 ¹²	52	Male	12 y ago	N/A	Viral Pneumonia	IVIG, Interferon α	No	Recovered
Pt-2 ¹¹	50	Male	N/A	3rd kidney Tx, History of PTLD	Viral Pneumonia, Gastroenteritis	Lopinavir/Ritonavir, hydroxychloroquine, Interferon β	Yes	Stabilized
Pt-3 ¹³	75	Male	N/A	N/A	Viral Pneumonia	Lopinavir/Ritonavir, hydroxychloroquine	No	Exitus
Pt-4 ¹³	52	Female	N/A	N/A	Viral Pneumonia	Lopinavir/Ritonavir, hydroxychloroquine, colchicine	No	Stabilized
Pt-5 ¹⁴	38	Male	N/A	None	Viral Pneumonia	Oseltamivir	No	Recovered
Pt-6 ¹⁴	64	Male	N/A	History of Bladder Cancer	Viral Pneumonia	Oseltamivir, IVIG	No	Respiratory Symptoms worsened
Pt-7 ¹⁴	37	Female	N/A	Hypertension	Viral Pneumonia	Oseltamivir, IVIG	No	Symptoms Resolved
Pt-8 ¹⁴	47	Male	N/A	None	Viral Pneumonia	Oseltamivir	No	Symptoms Resolved
Pt-9 ¹⁴	38	Male	N/A	Hypertension, Diabetes	Viral Pneumonia	Oseltamivir	No	Recovered

inflammatory response observed in these patients. Unlike these previous cases, none of the five patients reported by Zhang et al were treated with hydroxychloroquine. Instead, their approach included supportive care and antiviral treatment of oseltamivir or arbidol. In addition, they did not reduce the immunosuppression in one of their patients.¹⁴

Our review of the clinical courses revealed that most of the transplant patients were managed successfully without any progression of the disease. Only one transplant patient was lost due to quick respiratory deterioration before intubation.¹³

We did not discontinue our patient's immunosuppressive medication, because she was clinically stable and not critically ill. Fortunately, she did not require either a specific treatment or placement in the intensive care unit during the disease. Our treatment strategy was to monitor the patient closely and intervene immediately if needed.

We agree with the general principle that viral infections may have a fatal course in transplant patients. Nevertheless, the risk factors defined for severe COVID-19, such as age, gender, and comorbidities, are also important in defining the course of COVID-19 in transplant patients. Our patient was a young woman without any accompanying disease. She appeared to have more favorable prognostic factors compared with the patients presented in the previous reports. The only possible negative prognostic factor for our patient was her high neutrophil-lymphocyte ratio (NLR). However, the patient has had some degree of chronic lymphopenia for a long time, similar to many other transplant patients, and we think the validity of the NLR for these patients should be questioned.¹⁵

When all these cases are taken into consideration, we can easily see the two extreme aspects of COVID-19: mild disease at one end of the spectrum and life-threatening, very severe respiratory disease at the other end of the spectrum. Our patient likely experienced the most common and mild form of the disease, as expected in the general population. However, extrapolating from such a small group of patients is impossible. Large-scale, multicentric studies with a high number of transplant patients are necessary to determine the percentages of different clinical manifestations of COVID-19.

It is postulated that the over-activation of complement system or discordant expressions of type I and type II cytokines might lead to deficient viral clearance and exaggerated, prolonged inflammatory responses, which could result in a cytokine storm and the grave clinical course observed in coronavirus infections.^{16,17} Corticosteroids facilitate a reduction in systemic symptoms, such as fever or fatigue, and decrease alveolar exudation caused by the cytokine storm.¹⁸ Colchicine may also alleviate this cytokine storm through a distinct pathway.¹⁹ Thus, chronically immunosuppressed patients, such as kidney transplant patients, can have unpredictable, different clinical courses resulting from coronavirus infection.

In conclusion, we presented a kidney transplant patient with a mild form of SARS-CoV-2 infection. We think that the general risk factors for severe illness are also applicable to transplant patients. However, large-scale studies are needed to define or confirm the

risk factors for the prognosis of COVID-19 in transplant patients. Patients who are immunocompromised can present with an atypical form of the disease. Hence, all transplant patients presenting with any respiratory tract signs or symptoms, even in very mild forms, or with high fever should be tested for COVID-19. Oligosymptomatic organ recipients as possible carriers can likewise be extremely dangerous for other transplant patients, they meet in transplant centers. Therefore, we believe that strict precautions are necessary for contact isolation in transplant centers.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Authors whose names are written above meet all of the four listed criteria for authorship. These criteria are mentioned below. (1) Substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data. (2) Drafting the article or revising it critically for important intellectual content. (3) Final approval of the version to be published. (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Contributions of each author can be summarized as follows: EA involved in the conceptual development, writing the paper, analysis, and editing; BA, AT, and ST involved in the analysis and editing; BY involved in writing the paper and analysis; BK involved in conceptual development, analysis, and editing.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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