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Coronavirus disease 2019 (COVID-19) in a kidney transplant recipient; case report

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ABSTRACT

Patients with kidney transplants are at greater risk of contracting COVID-19 because of long-term immunosuppression and may end up with severe disease with adverse outcome. The experiences of COVID-19 management in kidney transplant recipients are limited. This is a case of COVID-19 in a 45-year-old patient with a second renal transplant on triple immunosuppressive therapy who was successfully treated for COVID-19, septic shock, acute kidney injury and was discharged with a stable graft function. The patient presented with mild COVID-19 symptoms but later went into septic shock followed by acute kidney injury due to a secondary bacterial infection. The patient was successfully managed using antivirals, corticosteroids, reducing the dose of immunosuppressants initially, then discontinuing all the immunosuppressants in view of septic shock and finally reinstating the immunosuppression gradually on clinical improvement. This case report may serve as a reference for treating immunocompromised kidney transplant recipients having COVID-19. However, more data and experiences are needed for optimization of treatment of kidney transplant recipients with COVID-19.

Implication for health policy/practice/research/medical education:

This is a case of COVID-19 in a 45-year-old patient with a second renal transplant on triple immunosuppressive therapy who was successfully treated for COVID-19, septic shock, acute kidney injury and was discharged with a stable graft function. This case report may serve as a reference for treating immunocompromised kidney transplant recipients having COVID-19.

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Introduction

COVID-19, the ongoing global pandemic, has over 115 million cases in more than 200 countries and has resulted in over 2.5 million deaths till date (1). Its clinical spectrum varies from asymptomatic presentation to severe disease (2). At present, data on COVID-19 in kidney transplant patients is limited. This group of patients are at greater risk of contracting COVID-19 because of long-term immunosuppression and may end up with severe disease with adverse outcome (3,4). Immunosuppression handling in these patients is very challenging and keeps the clinician in dilemma. Currently, there are no standardized protocols for the use of immunosuppressive therapy in kidney transplant recipients having COVID-19. However, many approaches are being tried and tested in practice, like no change in the baseline immunosuppression,(5)

reducing the number of immunosuppressants,(6) reducing the dose of the immunosuppressants (7) and stopping all immunosuppressants (8). The experiences of COVID-19 management in patients with kidney transplants are limited. Herein, we report one interesting case of COVID-19 in a kidney transplant recipient.

Case Presentation

A 45-year-old male, with morbid obesity, diabetes mellitus, hypertension and chronic kidney disease, received a second living donor kidney transplant from his mother in the year 2010. His immunosuppressive regimen consisted of cyclosporine 125 mg two times a day and mycophenolate mofetil 1 g two times a day. He was initially on oral steroids post-transplant which were gradually tapered and stopped. He presented to the primary healthcare center in

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Ras Al Khaimah, United Arab Emirates, with complaints of fever, cough with whitish sputum since 4 days. He did not report any shortness of breath or breathing difficulty. His reverse transcription–polymerase chain reaction (RT-PCR) test came out to be positive for SARS-CoV-2. He was referred to Ibrahim Bin Hamad Obaidallah Hospital, Ras Al Khaimah, United Arab Emirates on 16th April 2020 for further evaluation and management.

On admission, the patient was febrile with a body temperature of 38.3°C, a regular pulse rate of 100 beats/minute, blood pressure of 152/69 mm Hg, respiratory rate of 18 breaths/minute and supine oxygen saturation of 97%. Physical examination of this morbidly obese patient was unremarkable.

His laboratory investigations revealed total white blood cell (WBC) count of $5.6 \times 10^3/\mu\text{L}$ (reference range: $4-11 \times 10^3/\mu\text{L}$) with a platelet count of $130 \times 10^3/\mu\text{L}$ (reference range: $150-450 \times 10^3/\mu\text{L}$), urea of 6.76 mmol/L (reference range: 2.9 – 9.3 mmol/L), sodium of 132 mmol/L (reference range: 136-144 mmol/L), potassium of 3.8 mmol/L (reference range: 3.6-5.1 mmol/L), serum creatinine of 152 μmol/L (reference range: 53-97 μmol/L), C-reactive protein (CRP) of 17.4 mg/L (reference range: 0-3 mg/L) and lactate dehydrogenase (LDH) of 292 U/L (reference range: 100-190 U/L), D-dimer ($0.49 \mu\text{g}/\text{mL}$), arterial blood gas (ABG) revealed pH of 7.36, pCO_2 of 52.1 mmHg, pO_2 of 55.8 mm Hg, HCO_3 of 29 mmol/L, and HbA1C of 9.3%. The cyclosporine trough level was 173 ng/mL (reference range: 125 to 275 ng/mL). His chest computed tomography (CT) showed bilateral lung lower lobar multifocal patches of consolidations, peripheral subpleural ground glass opacities. Based on the positive RT-PCR test and CT findings, the patient was diagnosed with COVID-19 (Figure 1).

The patient was managed as per the then National Guidelines for Clinical Management and Treatment of COVID-19 and current best practice.

On day 1 of the admission (16th April 2020), the patient was started with antiviral therapy with combination of lopinavir/ritonavir (400 mg/100 mg two times a day) and hydroxychloroquine (400 mg two times a day). The dose

of mycophenolate mofetil was reduced to 500 mg two times a day; cyclosporine was continued in the same dose of 125 mg two times a day.

Next 7 days were uneventful; patient was stable with improvement in clinical condition. However, on 24th April 2020, patient reported shortness of breath, difficulty in breathing and increase in cough with oxygen saturation of 97% at 5 L/min via nasal cannula. Laboratory results showed elevated CRP (99.1 mg/L), elevated D-dimer ($1.76 \mu\text{g}/\text{mL}$), hyponatremia (128 mmol/L), hypomagnesemia (0.69 mmol/L) and elevated serum creatinine (134 μmol/L). A follow-up CT scan showed progression of pneumonia (Figure 1). Lopinavir/ritonavir was stopped and favipiravir 1600 mg per oral two times a day (2 doses) then 600 mg per oral two times was initiated. Methylprednisolone 40 mg once daily intravenously was also started. The patient showed improvement over the next few days. Repeat RT-PCR test conducted on 28th April 2020 turned out positive for COVID-19.

On 2nd May 2020, day 17 of admission, the patient developed secondary bacterial infection. He had fever with chills, localized fluctuant swelling, pain and erythema in the left anterior chest wall. Ultrasound findings confirmed the presence of an abscess. The abscess was incised and drained under appropriate intravenous antibiotic coverage.

The patient went into septic shock on 6th May 2020 (Day 21 of hospitalization). He was tachypneic, distressed, had high-grade fever (40°C) with a blood pressure of 80/50 mmHg. The patient was shifted to intensive care unit and subsequently intubated with ventilatory supportive care on 7th May 2020 and was initiated on adequate intravenous fluids, vasopressor support and hydrocortisone intravenously. The patient's renal functions deteriorated significantly (eGFR 18 mL/min/1.73 m², serum creatinine 337 μmol/L, urea 15.45 mmol/L, sodium 116 mmol/L, potassium 5.02 mmol/L). In view of rapidly worsening renal functions and oliguria, the patient was initiated on continuous renal replacement therapy (CRRT). Cyclosporine and mycophenolate mofetil were discontinued with the exception of steroids. The patient was in septic shock and it was decided to

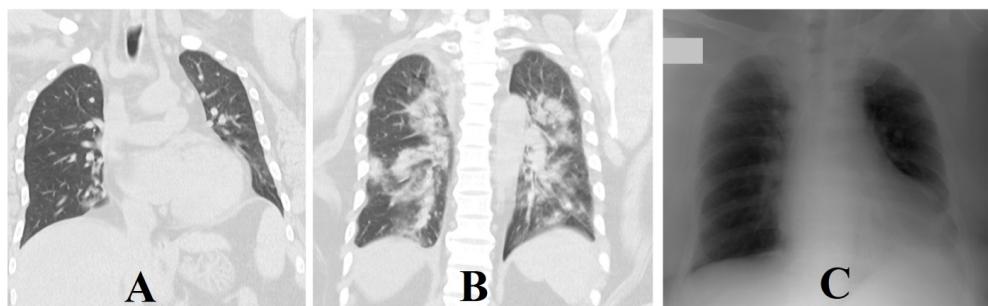


Figure 1. Radiological findings; A. CT chest on admission B. CT chest on Day 9 of admission C. X-ray chest on discharge.

discontinue immunosuppression as a life saving measure. The potential of renal graft rejection in the absence of immunosuppression was also considered and the implications were discussed with his relatives.

After 6 days, the patient was weaned off mechanical ventilation and CRRT was stopped. His renal functions improved [estimated glomerular filtration rate (eGFR) 88 mL/min/1.73m², serum creatinine 90 µmol/L, urea 9 mmol/L, sodium 139 mmol/L, potassium 4.62 mmol/L]. The patient had recovered from sepsis and immunosuppression was gradually restarted in stages. Cyclosporine was re-initiated at 50 mg bid and then gradually increased to 125 mg bid and oral prednisolone was started at 20 mg daily. He was resumed on mycophenolate mofetil at the time of discharge. The plan was to rapidly taper and stop steroids with regular follow up of the patient after discharge.

After 39 days of admission, on 25th May 2020, the patient was COVID-19 free, recovered from septic shock secondary to bacterial abscess, recovered from dialysis dependent acute kidney injury, had a baseline functioning graft kidney and was discharged home in a stable clinical condition (Figure 1).

Discussion

There is an increased risk of infections to kidney transplant recipients, owing to several factors like associated comorbid conditions, especially diabetes mellitus and hypertension, underlying chronic kidney disease and long-term maintenance immunosuppression (9). It is expected that because of the long-term immunosuppression in these patients, the presentation of COVID-19 infection may be more distinct and may require special considerations for the management of the same (3). COVID-19 management is quite challenging in kidney transplant recipients, particularly in the absence of a specific antiviral therapy for it.

In this case, clinical presentation, laboratory investigations, and radiology findings were comparable to COVID-19 patients without kidney transplants. The patient was admitted with mild COVID-19 symptoms without any shortness of breath or breathing difficulty. However, it was complicated by secondary bacterial infection in the left anterior chest wall following which the patient went into septic shock and acute kidney injury.

Management of COVID-19 patients with kidney transplants presents the clinician with the challenge of adjusting, reducing or stopping the immunosuppressive agents while guarding the graft function. In this patient also, at the initial diagnosis of COVID-19, the dose of mycophenolate mofetil was reduced to half. Similar management strategy has been employed in previous reported cases (7,10). Later, in view of progression of

COVID-19 pneumonia and septic shock owing to the secondary bacterial infection, both cyclosporine and mycophenolate mofetil were discontinued with the exception of steroids. Withdrawal of immunosuppressants can promote recovery from the infection but it may increase the chance of renal graft rejection and make the management more complex. Discontinuation of immunosuppressants has previously been reported in kidney transplant receipts with severe COVID-19 (7,11). In our patient, we were left with no choice but to withdraw the immunosuppressants as the patient went into septic shock and as a life saving measure we had to take that decision.

However, we continued intravenous corticosteroids, which might have offered protection to renal graft from acute rejection, prevented Addisonian crisis and dampened the cytokine storm. Use of corticosteroids in the management of COVID-19 is still controversial. However, recent randomized controlled clinical trial has shown that corticosteroid use decreased mortality in mechanically ventilated severe COVID-19 patients (12). As our patient recovered from sepsis, immunosuppression was gradually reinstated. He was resumed on a lower dose of cyclosporine which was gradually increased to the normal dose along with oral corticosteroids. Mycophenolate mofetil was re-started at the time of discharge.

Conclusion

In conclusion, we report a case of COVID-19 in a 45-year-old patient with a second renal transplant on triple immunosuppressive therapy who was successfully treated for COVID-19, septic shock, acute kidney injury and was discharged with a stable graft function. The patient presented with mild COVID-19 symptoms but later went into septic shock followed by acute kidney injury due to a secondary bacterial infection. The patient was successfully managed initially by reducing the dose of immunosuppressants, then discontinuing all the immunosuppressants in view of septic shock and finally reinstating the immunosuppression gradually on clinical improvement. This case report may serve as a reference for treating immunocompromised kidney transplant recipients having COVID-19. However, more data and experiences are needed for optimization of treatment of kidney transplant recipients with COVID-19.

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Authors' contribution

MTK: Conceptualization, formal analysis, data curation,

Writing - review and editing. SAR: Conceptualization, Data curation, writing - review and editing. ACT: Conceptualization, formal analysis, data curation, writing - review and editing. NJ: Conceptualization, formal analysis, data curation, writing - review and editing.

Conflicts of interests

The authors declared no conflict of interest.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patient gave the consent to publish as a case report.

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