Case report

# Uneventful case of COVID-19 in a kidney transplant recipient

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## SUMMARY

Kidney transplant recipients have been reported at a particularly high risk of severe COVID-19 illness due to chronic immunosuppression and coexisting conditions. Yet, here we describe a remarkably mild case of COVID-19 in a 62-year-old female who had a kidney transplantation 10 years earlier due to autosomal dominant polycystic kidney disease. The patient was admitted for 1 day; immunosuppressive therapy with tacrolimus and low-dose prednisolone was continued; and the patient recovered successfully without the use of antiviral agents or oxygen therapy. The case demonstrates that kidney transplant recipients are not necessarily severely affected by COVID-19. Withdrawal of immunosuppressive therapy could be associated with poorer outcomes and should not be implemented thoughtlessly.

## BACKGROUND

As of 1 July 2020, the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing COVID-19 has infected more than 11.4 million individuals, globally spreading across 188 countries.[1] While the numbers of COVID-19 cases and deaths have increased vastly and rapidly, there is sparse evidence about its impact on transplant recipients.

Kidney transplant recipients have been reported at a particularly high risk of severe COVID-19 illness due to chronic immunosuppression and coexisting conditions.[2] Yet, here we describe and discuss a remarkably mild case of COVID-19 in a patient with a kidney transplant.

## CASE PRESENTATION

A 62-year-old female who had a kidney transplantation 10 years earlier due to autosomal dominant polycystic kidney disease was admitted to the department of nephrology with 2 days of dry cough, myalgia, fatigue and fever. She denied other complaints, including chest pain, dyspnoea, palpitations and a sore throat. There was no recent travel history or any known exposures to SARS-CoV-2. However, the husband had similar symptoms for 3 days.

The patient had a medical history of hypertension, hypercholesterolaemia, obesity (body mass index approximately 33.5 kg/m$^2$) and recurring urinary tract infections treated with prophylactic with 400 mg pivmecillinam daily. Kidney graft function was reduced with an estimated glomerular filtration rate of around 30 mL/min/1.73 m$^2$, and she was on a maintenance immunosuppressive regimen with 5 mg prednisolone once a day and tacrolimus 4.5 mg two times per day, with a through level of 2.6–4.8 µg/L at presentation. Mycophenolate mofetil was discontinued 6 months earlier due to the recurrent urinary tract infections. The post-transplantation period was complicated by severe diverticulitis resulting in proctosigmoidectomy and a temporary colostomy.

On admission, the patient had a temperature of 38.6°C; the blood pressure was 147/90 mm Hg; the heart rate was 77 beats/min; the respiratory rate was 18 breaths/min; and the oxygen saturation was 95% while she was breathing ambient air. Physical examination was normal except from sparse peripheral oedemas of both legs. Biochemistry was normal apart from lymphopenia ($1.14\times10^9$/L, reference range 1.30–3.50) and increased creatinine at usual level (174 µmol/L, reference range 45–90). Chest radiograph was without infiltrates. A urinary dipstick showed discrete proteinuria (30–100 mg/dL) and a nasopharyngeal swab tested negative for influenza. Blood cultures were negative, and plasma was negative for cytomegalovirus, Epstein-Barr virus and BK polyomavirus DNA using PCR. Treatment with azathioprine 250 mg once a day for 5 days was initiated, and the patient was discharged the morning after admission with improvement of symptoms.

## OUTCOME AND FOLLOW-UP

Fourteen days after admission, the patient still had discrete coughing and intermittent fever, and was referred to a COVID-19 drive-in test unit for an oropharyngeal swab, which was positive for SARS-CoV-2 RNA using PCR. As this was in the beginning of the pandemic, routine COVID-19 testing was not widely implemented. Subsequently, she was sent in self-isolation with unchanged immunosuppressive therapy. At recurrent phone-based follow-ups, she reported increased well-being and at 37 days after admission, she expressed total recovery.

## DISCUSSION

We present a case of mild COVID-19 in a patient in immunosuppressive therapy due to kidney transplantation. The case demonstrates that kidney transplant recipients are not necessarily severely affected by COVID-19 and warrants future studies



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on the interaction between COVID-19 and the immunocompromised host.

On 17 March 2020, the first case of post-transplant COVID-19 was reported in a 52-year-old Chinese male kidney transplant recipient who recovered successfully.[3] The patient was discontinued on tacrolimus and mycophenolate mofetil, was reduced in dose of methylprednisolone (40 mg once a day), and treated with nebulised interferon-α and polyclonal intravenous immunoglobulin therapy. At day 9 of illness, oxygen therapy of 2 L/min was administered. Throughout the course of disease, biochemistry showed more evident signs of infection although still discrete with C reactive protein of 54 mg/L (day 2) and white blood cell count $11.68\times10^9$/L (day 11). In comparison, this patient was hospitalised for 13 days, while the patient in our case was only admitted for a night. To our knowledge, the patient was in good health at home a week after admission, similar to the patient in our case story. Tacrolimus and prednisolone were continued in our patient, although recently published data show that immunosuppressive therapy is often discontinued in kidney transplant recipients.[4] In this study, immunosuppressive management included withdrawal of an antimetabolite among 86% (n=24/28) and of tacrolimus among 21% (n=6/28). The authors suggest that low levels of CD3, CD4 and CD8 could justify this withdrawal strategy. Unfortunately, in our case, an extensive analysis of inflammatory biomarkers was not conducted.

In addition, the data (n=36) suggest a very high early mortality among kidney transplant recipients with COVID-19 of 28% at 3 weeks compared with 1%–5% in the overall population in the USA.[4] A similar case fatality rate of 27.8% has been reported for a heterogenous group of solid-organ transplant recipients with COVID-19 in Spain, also much higher than the overall population.[5] Most patients in this study underwent temporary discontinuation or dose reduction of calcineurin inhibitors (55.6%, n=10/18), while 50% (n=9/18) had their antimetabolites reduced or withdrawn. An ongoing study identified 10 kidney transplant recipients with COVID-19, of which 9 were hospitalised.[6] Five were admitted to the intensive care unit and three patients, who required intubation, died. All hospitalised patients had their antimetabolite agent stopped. Tacrolimus/sirolimus was discontinued in 30% (n=3/10). For comparison, 4% of 237 patients, in a large multicentre study, with any solid-organ transplant (n=87, kidney) and microbiologically confirmed influenza A, died at a median of 15 days after onset of symptoms.[7]

As demonstrated by our case and preliminary data, COVID-19 presents with a wide clinical spectrum, ranging from asymptomatic and subclinical to severe, life-threatening infection. Similarly, the prognosis seems to vary considerable among the overall population and individual kidney transplant recipients, although data imply an overall high mortality in transplant recipients.[4–6]

A cytokine storm triggered by SARS-CoV-2 has been proposed responsible for the high morbidity in COVID-19,[8] and it could be speculated that withdrawal of antirejection therapy could be associated with an exacerbated systemic inflammatory response to viral infection.[4] Immunosuppressive therapy was relatively modest in this case, while other risk factors favouring a severe course of COVID-19, such as hypertension, chronic kidney disease and obesity, were present.[9 10] Regardless, the importance of addressing SARS-CoV-2 infection in transplant recipients and management of immunosuppressive therapy in relation to ongoing infection seems evident.[11]

So far, no significant differences between baseline immunosuppression in solid-organ transplants and COVID-19 severity have been reported.[12]

Despite the massive quantity of COVID-19 data and research worldwide, more and improved information to guide clinical management is urgently needed. Larger studies should be conducted to clarify whether solid-organ transplant recipients are in fact at a higher risk of severe disease compared with immunocompetent hosts, to determine the interaction between COVID-19 and the graft and to elucidate the impact of immunomodulatory therapy and antiviral agents. For now, a prudence concept should be applied with utmost precaution advised in terms of infection prevention and clinical management of solid-organ transplant recipients. Case by case must be evaluated carefully and managed according to age, risk factors, severity of infection, immunosuppressive regimen, immune status and side effects.

## Patient's perspective

Thoughts about my meeting with COVID-19. One day, I had a high fever and contacted the nephrologist on duty. I was admitted and had blood samples taken among others. Actually, I was okay… just a fever. The nephrologist did not see any reason to test for COVID-19 as it was so early in the course, and also my temperature decreased the next morning. I was discharged!

Having a fluctuating fever, nausea, vomiting and immense fatigue is not the most interesting. I did not have trouble breathing or pneumonia at any point. I did, however, cough a lot and I just could not believe it kept on. I often thought, have I been infected with the virus after all? It disturbed me that my temperature remained high.

As days went by, the nausea gradually disappeared, and the appetite returned. The fever stabilised. Only first at this point, after 14 days of illness, I was tested positive. For weeks after COVID-19, I was very fatigued, but now finally, I have again regained my strength.

## Learning points

- There is sparse evidence about the impact of severe acute respiratory syndrome coronavirus 2 on kidney transplant recipients.
- Limited data suggest a very high early mortality in these patients.
- Withdrawal of immunosuppressive therapy could be associated with poorer outcomes and should not be implemented thoughtlessly.
- Each case must be evaluated and managed carefully by experts.

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