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Case Report

Successful deceased donor kidney transplantation to a recipient with a history of COVID-19 treatment

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ABSTRACT

Case presentation.

A 49-year-old Asian male, who had undergone hemodialysis for >16 years, complained of a fever, dysgeusia and dysosmia, and was diagnosed with COVID-19 pneumonia based on severe acute respiratory syndrome coronavirus 2 polymerase chain reaction (SARS-CoV-2 PCR) and computed tomography (CT). Treatment was started with oral favipiravir and ciclesonide inhalation. On the 10th day of treatment, the patient had a persistent high fever and a chest CT showed exacerbation of pneumonia, so dexamethasone was intravenously started. He was discharged after confirming two consecutive negative SARS-CoV-2 PCR tests. Three months after COVID-19 treatment, a SARS-CoV-2 PCR test was negative and he underwent a deceased donor kidney transplantation. Basiliximab induction with triple drug immunosuppression consisting of extended-release tacrolimus, mycophenolate mofetil and prednisolone, which is our regular immunosuppression protocol, was used. He was discharged on postoperative day 18 without the need for postoperative hemodialysis or any complications. The serum creatinine level was 1.72 mg/dL 95 days postoperatively and he had a favorable clinical course that was similar to deceased donor kidney recipients without a history of SARS-CoV-2 infection.

Conclusion.

We report the first case of a kidney transplantation after COVID-19 treatment in Japan and the fourth case globally. We would like to provide information about our successful case due to the anticipated increase in similar candidates in the near future.

1. Introduction

In the midst of the coronavirus disease 2019 (COVID-19) pandemic, the number of infected people continues to increase in the world. There are several reports that patients with end-stage renal disease (ESRD) are at higher risk of severe COVID-19 after

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kidney transplantation [1–3]. Indeed, the first reported case of a successful kidney transplantation was performed on a Hispanic female after COVID-19 treatment in Italy [4].

Herein we present the case of an Asian who underwent a deceased donor kidney transplantation after treatment of COVID-19 pneumonia and has had an uneventful course without any complications related to the infection. We would like to share this information given the anticipated increase in similar cases in the near future.

1.1. Case presentation

The recipient was a 49-year-old Asian male who had been on hemodialysis (HD) for ESRD due to an idiopathic primary disease for 16 years. He had a 13-year history of smoking cigarettes (1 pack per day), but quit smoking when he started HD. He underwent a left and right laparoscopic radical nephrectomy at 47 and 48 years of age, respectively, because of acquired cystic disease-associated renal cell carcinoma.

On July 18, 2020 he had dinner with 9 people, including his family and co-workers, one of whom sitting next to him had a fever. On 19 and 20 July, he developed a low-grade fever, after which he defervesced. On 27 July, however, his temperature was 38.5 °C and he complained of dysgeusia and dysosmia. He sought evaluation at the public health center and underwent severe acute respiratory syndrome coronavirus 2 polymerase chain reaction (SARS-CoV-2 PCR) testing at a designated medical institution for infectious diseases. The result was positive, and he was admitted to our hospital with a diagnosis of COVID-19 on 28 July.

The post-hospital course is shown in Fig. 1, and the computed tomography (CT) findings are displayed in Fig. 2. On admission, the C-reactive protein (CRP) was mildly elevated at 1.14 mg/dL. A chest CT showed scattered ground-glass opacities with a right lung predominance and some of which were accompanied by thickened shadows inside (dashed line circle in Fig. 2), which was consistent with COVID-19 pneumonia. The patient was started on oral favipiravir and ciclesonide inhalation. These medications were administered at the standard therapeutic doses for 1 week.

On the 10th day of treatment, the patient was scheduled for discharge after confirming the SARS-CoV-2 PCR test to be negative, but on the same day he had a fever of 38.2 °C. Because a CT scan showed an exacerbation of known pneumonia or appearance of a new pneumonia, dexamethasone was started intravenously. On the 18th hospital day, the patient was discharged after two SARS-CoV-2 PCR tests were confirmed to be negative. A CT scan showed that the pneumonia had improved on the 52nd hospital day.

Three months after COVID-19 treatment, he underwent a deceased donor kidney transplantation. The donor was a brain-dead male donor in his 60's who had sustained a subarachnoid hemorrhage. SARS-CoV-2 PCR tests performed on the donor and recipient pre-operatively were negative. The recipient had a contrast-enhanced CT of the thoracoabdominal pelvic region that showed no abnormal findings, including pneumonia or a recurrence of the malignancy. Basiliximab induction with triple drug immunosuppression consisting of extended-release tacrolimus, mycophenolate mofetil and prednisolone, which is our regular immunosuppression protocol, was used. The total ischemic time was 385 min and the first urine output was observed 226 min after reperfusion. The serum creatinine (Cr) level decreased immediately and there was no need for HD postoperatively. We performed an allograft biopsy on day 17 postoperatively, the results of which showed mild lymphocytic infiltration in a small portion of the interstitial tissues, suggesting no acute rejection. He was discharged on postoperative day 18 without any complications. As of 1 month postoperatively, the serum Cr level was 1.99 mg/dL and he had a favorable clinical course without any complications related to the COVID-19 infection (Fig. 3).

2. Discussion

We have reported a successful deceased kidney transplantation 3 months after COVID-19 treatment in an Asian male recipient who was on HD. To our knowledge, this is the first report of a kidney transplantation after COVID-19 treatment in Japan and the fourth case globally [4,5].

Post-renal transplant recipients and ESRD patients are at high risk for complications and mortality following COVID-19 because of the high prevalence of co-morbidities or chronic immunosuppression. In a multicenter study involving 144 adult kidney transplant recipients from 12 centers, including the United States, Italy, and Spain, acute kidney injuries occurred in 52% of the cases and the mortality rate was 32% [6]. In Japan, 62 cases of COVID-19 infection in kidney transplant recipients have been reported as of January 11, 2021, with a mortality rate of 3.2% [7]. In the early

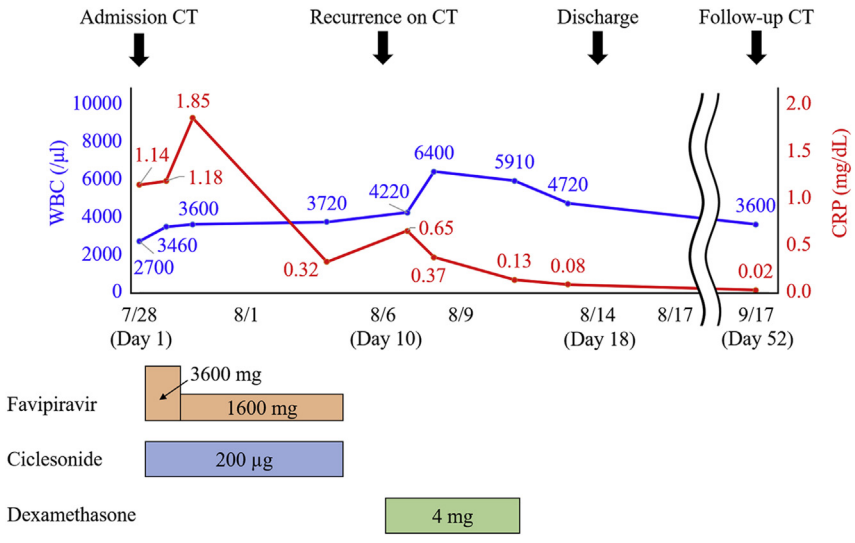

Fig. 1. Inflammation data and therapeutic agents in patients during COVID-19 treatment.

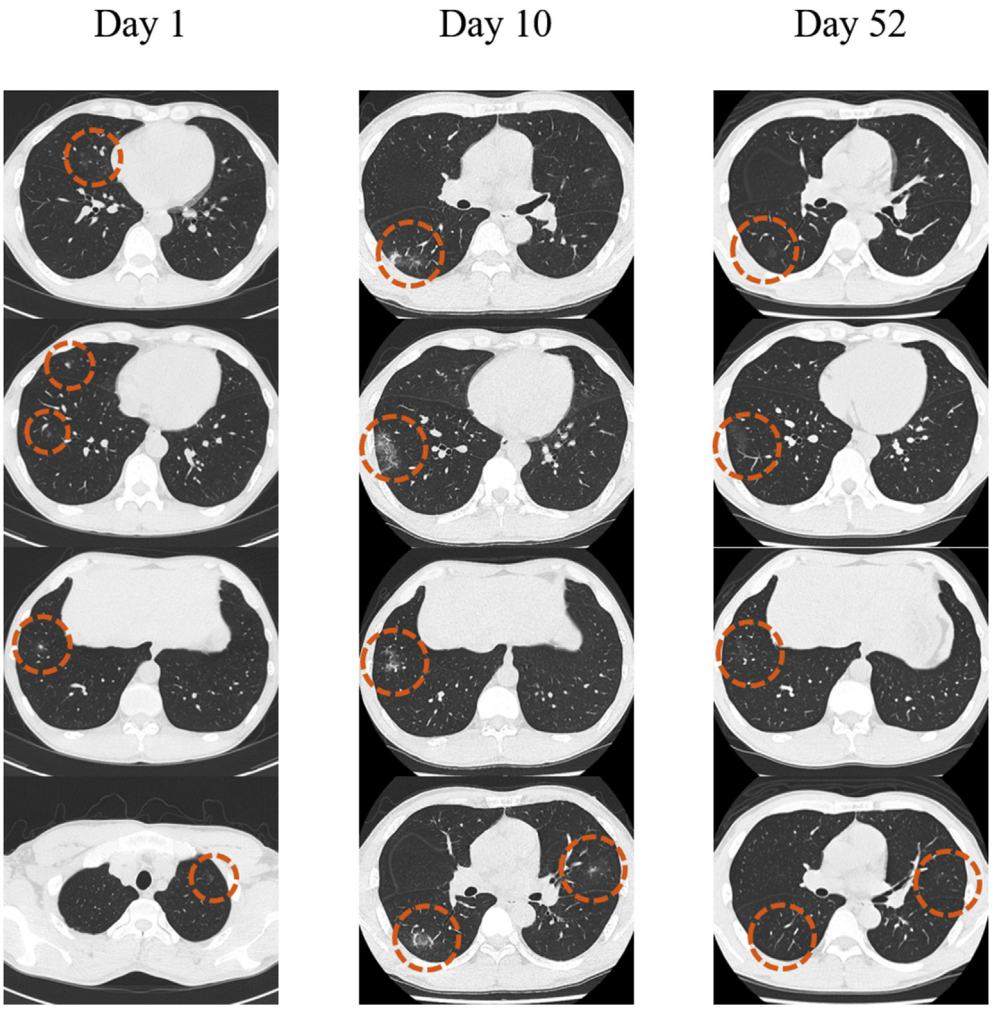

Fig. 2. Clinical change in lung CT during COVID-19 treatment.

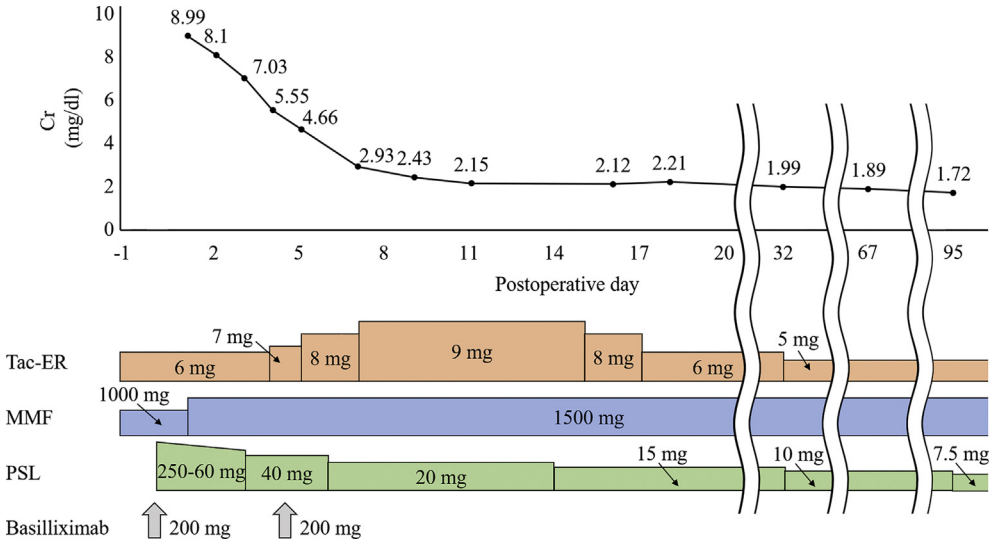

Fig. 3. Clinical course of deceased donor kidney transplantation, including immunosuppressive therapy.

Japanese report, the mortality rate among dialysis patients was 16.2%, which was much higher than the general population (5.3%), even though there was an age bias with dialysis patients primarily in the 70–90 year age group, while the general population was 20–60 years of age [8]. In the latest report, as of 7 January, 83 of 700 patients infected with COVID-19 on dialysis had succumbed, for a mortality rate of 11.9% [9].

It is important to diagnose and intervene early to prevent organ failure caused by cytokine storm for immunosuppressed patients [7]. A report from China showed that HD patients with COVID-19 infections were less likely to have lymphopenia, lower serum levels of inflammatory cytokines, and milder clinical symptoms than other COVID-19-infected patients, but were more likely to die from cardiovascular diseases [10]. Patients on HD are at high risk for COVID-19 infection because they have various co-morbidities and are required to visit the hospital three times a week. According to the Japanese Society for Dialysis Therapy, a patient on HD who is positive for COVID-19 based on antigen or SARS-CoV-2 PCR testing must be hospitalized whether or not they have symptoms [11]. The number of patients on HD who are diagnosed with COVID-19 is rapidly increasing, and it is assumed that this regulation will be unavoidably changed in the near future.

As shown in Table 1, our case report was compared to the world's previous reports [4,5]. When compared to the first report which had more detailed data, our patient was older (28 vs. 49 years) and the duration of ESRD was much longer (8 vs. 201 months), suggesting that our patient was more fragile. In our patient the usual therapeutic doses of favipiravir and ciclesonide inhalation were administered because the drugs are metabolized in the liver. Lemdesivir was not administered due to renal dysfunction. No liver dysfunction was observed during treatment. Although our patient was more severe than the previously reported patient, the IgM titer was negative on hospital day 8, the IgG titer was positive on hospital day 11, and the pneumonitis showed objective CT findings of improvement on hospital day 52. It has been reported that COVID-19 infectivity decreases from day 8–20 after the onset of disease; however, the virus excretion time lasts longer in HD patients than in healthy subjects [12]. Therefore, in our patient we delayed the transplantation for >4 weeks. Varotti et al. concluded that it would be safer to wait 4 weeks before considering kidney transplantation rather than 2 weeks that is recommended for general patients [4]. Thus, it is our opinion that a 1-month interval should elapse between COVID-19 treatment and kidney transplantation for dialysis patients. Longer interval might be needed when the symptoms of COVID-19 are relatively severe. In some HD patients, however, kidney disease may be more critical than COVID-19 itself [5]. The timing of kidney transplantation after COVID-19 treatment must be carefully considered, taking into

Table 1
Comparison between the previous cases and our report.

Reported order	First case	Second case	Third case	Present case
Authors	Varotti G et al.	Kanch P et al.	Kanch P et al.	Yoshinaga K et al.
Age	28	44	35	49
Race	Hispanic	Asian	Asian	Asian
Country	Italy	India	India	Japan
Gender	Female	Male	Female	Male
Duration of ESRD (months)	8	Not documented	Not documented	201
Type of dialysis	Hemodialysis	Hemodialysis	Hemodialysis	Hemodialysis
Origin of ESRD	Membranous glomerulonephropathy	Diabetic nephropathy	Not documented	Chronic glomerulonephropathy
Onset of COVID-19	28th March 2020	Not documented	Not documented	27th July 2020
Reasons for SARS-CoV-2 PCR test	Close contact with her partner who developed COVID-19	With symptoms	With symptoms	With symptoms
Location of swab	Nasopharyngeal	Not documented	Not documented	Nasopharyngeal
Symptoms	Mild cry cough	Myalgias	Fever, sore throat and myalgia	Fever, dysgeusia and dysosmia
Chest X-ray at diagnosis	Unremarkable	Not documented	Not documented	Unremarkable
Isolation quarantine	Home	Hospitalized	Not documented	Admitted to our hospital
Treatment	Hydrocychloroquine, clarithromycin, prednisone	Dexamethasone, oxygen support and other symptomatic treatment	Only symptomatic treatment	Favipiravir, ciclesonide, dexamethasone
Duration of treatment (days)	7	Not documented	Not documented	16
Date of 2 consecutive negative nasopharyngeal SARS-CoV-2 PCR	12th and 14th April 2020	Two weeks after the start of treatment	Three weeks after the start of treatment	13th and 14th August 2020
Date of KTx	11th May 2020	Not documented	Not documented	23rd November 2020
Type of KTx	Deceased	Deceased	Living (from her sister)	Deceased
RT-PCR of BALF before KTx of donor	Negative	Not documented	Not applicable	Not applicable
RT-PCR of nasopharyngeal swab before KTx	Negative	Negative	Negative	Negative
Immunosuppression	Tac, MMF, PSL, Basilliximab	Tac, MMF, PSL, Basilliximab	Tac, MMF, PSL	Tac, MMF, PSL, Basilliximab
Complication after KTx	Blood stream infection due to *E.coli* which resolved after 10 days of ceftriaxone	None	None	None
Discharge (PostTx day)	15	Not documented	Not documented	20
Follow up after KTx (days)	60	107	100	95
SARS-CoV-2 IgG	Positive at 4 days after kidney transplant	Positive at 14 days after COVID-19 treatment	Positive at 6 weeks after COVID-19 treatment	Positive at 11 days after COVID-19 treatment
SARS-CoV-2 IgM	Negative at 20 days after kidney transplant	Not documented	Not documented	Negative at 52 days after COVID-19 treatment

ESRD, end-stage renal disease; SARS-CoV-2 PCR, severe acute respiratory syndrome coronavirus 2 polymerase chain reaction; BALF, Bronchoalveolar Lavage Fluid; KTx, kidney transplantation; RT-PCR, reverse transcription polymerase chain reaction; Tac, tacrolimus; MMF, mycophenolate mofetil; PSL, prednisolone; *E. coli*, *Escherichia coli*. COVID-19, coronavirus disease 2019.

account these precise factors. We actually performed the kidney transplantation 3 months after treatment for COVID-19. Further study is needed to evaluate how this time difference affects the allograft compared with the previously reported case and the appropriate adjustment of postoperative immunosuppression.

3. Conclusion

We report the first case of a kidney transplantation after COVID-19 treatment in Japan and the fourth case globally. Our case suggests that kidney transplantation with regular immunosuppressive therapy can be performed safely among recipients with a history of COVID-19 as well.

ICMJE statement

Contributors K. Yoshinaga was responsible for the organization and data analysis. M. Araki were responsible for coordination, submission and corresponding of the report. K. Yoshinaga, M. Araki, K. Wada, K. Hasegawa, T. Sekito, S. Miyake, S. Watari, S. Nishimura, K. Tanabe, H. Takeuchi, Y. Nakashima, M. Kinomura and K. Edamura treated the patient. K. Yoshinaga, K. Hasegawa collected clinical data. K. Yoshinaga and H. Acosta wrote the draft and M. Araki, K. Wada and H. Nakajima proofread the manuscript. All authors confirmed the draft and contributed to the writing of the final manuscript.

Declaration of competing interest

None declared.

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