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Case Report of COVID-19 Infection After Kidney Transplant Treated With Casirivimab-Imdevimab and Mycophenolate Mofetil Changed to Everolimus

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ABSTRACT

Background. Casirivimab-imdevimab is a cocktail of 2 monoclonal antibodies designed to prevent infection by SARS-CoV-2, the virus that causes COVID-19. Casirivimab-imdevimab has been approved in Japan for treating mild to moderate COVID-19; however, to our knowledge, there are no reports of its use after kidney transplant from a live donor. Everolimus, an antineoplastic chemotherapy drug, is expected to be effective in inhibiting the spread of SARS-CoV-2 and preventing its replication, which may facilitate treatment. Here, we report a case of COVID-19 infection after kidney transplant that was initially treated with casirivimab-imdevimab and mycophenolate mofetil but was later changed to everolimus.

Case Report. A 47-year-old man underwent living donor kidney transplant from his mother in 2017. Immunosuppression therapy was underway through the administration of tacrolimus, mycophenolate mofetil, and methylprednisolone. In early September 2021, he was diagnosed as having COVID-19 and was hospitalized on day 3. On hospitalization, mycophenolate mofetil was discontinued and casirivimab-imdevimab and heparin were started. The patient started an everolimus regimen on day 5. The clinical course was successful without rejection. There was no exacerbation of COVID-19; the patient's serum creatinine levels and renal function had otherwise remained stable.

Conclusions. We could safely treat a patient with casirivimab-imdevimab after kidney transplant. It is suggested that casirivimab-imdevimab can prevent COVID-19 from becoming severe and can be administered without worsening renal function. In addition, everolimus may have inhibited the spread of the virus and prevented it from replicating.

CASIRIVIMAB-IMDEVIMAB has been approved in Japan for treating mild to moderate COVID-19; however, to our knowledge, there are no reports of its use after living kidney transplant. Everolimus, an antineoplastic chemotherapy drug, is expected to be effective in inhibiting the spread of SARS-CoV-2 and preventing its replication, which may facilitate treatment.

Here, we report a case of COVID-19 infection after kidney transplant; the patient was initially treated with casirivimab-imdevimab and mycophenolate mofetil, but the treatment was later changed to everolimus.

CASE PRESENTATION

A 47-year-old man with end-stage renal disease caused by chronic glomerulonephritis received a living related kidney transplant from his mother in January 2017. The patient had a

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Table 1. Blood Examination Results

WBC 5.280/ μ L	TP 6.9 g/dL	Na 137 mEq/L
Neut 77%	Alb 4.3 g/dL	K 4.4 mEq/L
EOSI 0%	T-Bil 0.6 mg/dL	Cl 103 mEq/L
MONO 13%	AST 18 IU/L	
LYMPH 10%	ALT 13 IU/L	PT 11.9 s
RBC 4.84×10^6 / μ L	Cr 1.45 mg/dL	APTT 48.1 s
Hb 14.7 g/dL	BUN 15.7 mg/dL	FDP 2.0 μ g/mL
Ht 44.5%	LDH 197 IU/L	
PLT 3.30×10^5 / μ L	CRP 1.66 mg/dL	

Alb, albumin; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, asparagine aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; CRP, C-reactive protein; Cl, chloride; EOSI, eosinophil; FDP, fibrinogen degradation products; Hb, hemoglobin; Ht, hematocrit; K, potassium; LDH, lactate dehydrogenase; LYMPH, lymphocyte; MONO, monocyte; Na, sodium; Neut, neutrophil; PLT, platelets; PT, prothrombin time; RBC, red blood cells; TP, total protein; T-Bil, total bilirubin; WBC, white blood cell count.

history of hypertension, peritoneal dialysis-related peritonitis, umbilical hernia repair, and sleep apnea syndrome. After surgery, he was receiving immunosuppressive treatment comprising tacrolimus, mycophenolate mofetil, and methylprednisolone. On September 6, 2021, the patient presented with fever, cough, sputum, and a sore throat. Computed tomography results showed no pneumonia. He tested positive for COVID-19 and was hospitalized on day 3. Physical examination revealed a body temperature, 38.6°C; blood pressure, 120/74 mm Hg; pulse, 89 beats/min; and blood oxygen saturation, 97% (in

room air). Laboratory data showed an increased C-reactive protein level (1.66 mg/dL) and serum creatinine level (1.45 mg/dL) (Table 1).

On hospitalization, mycophenolate mofetil was discontinued, and casirivimab-imdevimab and heparin were started. On day 5, the patient started an everolimus regimen. The clinical course was successful without any evidence of organ rejection (Fig 1). There was no exacerbation of COVID-19; the patient's serum creatinine levels and renal function had otherwise remained stable. The patient was discharged on the 11th day after hospitalization.

DISCUSSION

We present a case of COVID-19 treated with antibody cocktail therapy after kidney transplant. Casirivimab-imdevimab and bamlanivimab are COVID-19 monoclonal antibodies that have received emergency use authorization from the United States Food and Drug Administration for the treatment of patients with mild to moderate COVID-19 who are at high risk for progression to severe disease [1]. Dhand et al reported casirivimab-imdevimab for treatment of COVID-19 in solid-organ transplant recipients [2]. In their study, none of the 25 solid organ transplant recipients with mild to moderate COVID-19 who were treated with casirivimab-imdevimab had worsening symptoms or required hospitalization because of COVID-19 [2].

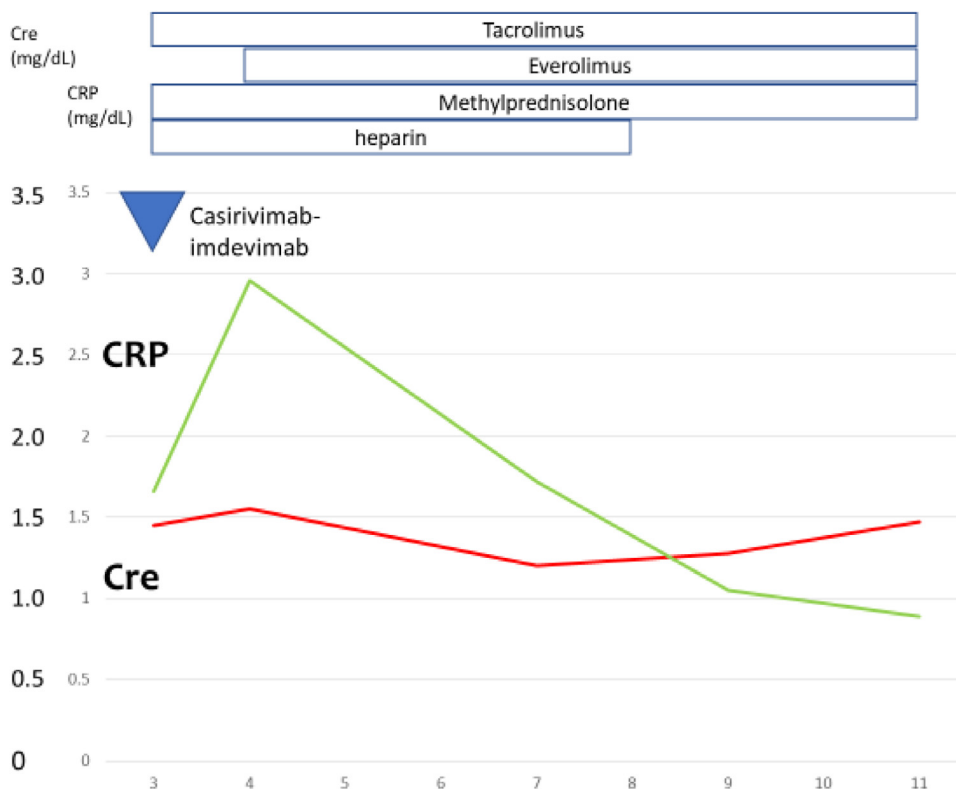


Fig 1. Successful Clinical Course After Antibody Cocktail Therapy. Tacrolimus target through 4-6 ng/mL (dose of tacrolimus is 2 mg). Cre, serum creatinine level; CRP, C-reactive protein level.

Additionally, a retrospective study in the United States reported 707 confirmed COVID-19 cases treated with neutralizing monoclonal antibodies (bamlanivimab or casirivimab and imdevimab) [3]. In this report, the use of neutralizing monoclonal antibodies reduced the need for hospitalization in mild and moderate cases of COVID-19 [3]. In our case, there was no exacerbation during hospitalization and no need to extend hospital stay. Currently, casirivimab-imdevimab (suitable for mild to moderate disease I), remdesivir, dexamethasone, and baricitinib (suitable for moderate disease II and above) have been approved for use in Japan. Heparin is recommended in patients with moderate disease II and above [4]. We selected casirivimab-imdevimab and heparin for our patient with COVID-19 pneumonia.

COVID-19 after living donor kidney transplant has a higher mortality rate (28%) than in the general population [5]. Treatment with mycophenolic acid and everolimus has been reportedly reduced or discontinued (68%), and that with calcineurin inhibitors has been discontinued (32%) [6]. However, we subsequently changed the treatment to everolimus. In SARS-CoV2 infection, everolimus is also expected to be effective in preventing replication by inhibiting the spread of the virus [7]. Also, mammalian target of rapamycin inhibitors such as everolimus suppress the early production of B cells and decrease the populations of antigen-specific memory B cells [8]. Therefore, patients with COVID-19 treated with mammalian target of rapamycin inhibitors would be expected to have reduced cross-reactive antibody production, resulting in reduced antibody-dependent potentiation [9].

Everolimus has been reported to reduce the risk of COVID-19-associated death in kidney transplant recipients [10]. Everolimus may also have modulated the immune response in SARS-CoV2 infection by acting as a key molecule in immune regulation.

CONCLUSIONS

We could safely treat a patient with COVID-19 with casirivimab-imdevimab after kidney transplant. It is suggested that casirivimab-imdevimab can prevent COVID-19 from becoming

severe and can be administered without worsening renal function. In addition, everolimus may have inhibited the spread of the virus and prevented it from replicating.

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