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A patient with end-stage renal disease who recovered from coronavirus disease 2019 then received a kidney transplant

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ABSTRACT

Since its emergence in December 2019 many end-stage renal disease (ESRD) patients have been infected with coronavirus disease 2019 (COVID-19). Herein, we describe the case of an ESRD patient who received a kidney transplant after recovering from COVID-19. We described the clinical course of COVID-19 and kidney transplant management, including the patient's symptoms, laboratory results, computed tomography, and antibody profiles. He recovered well, without complications. Chest computed tomography, PCR, and IgG results indicated no recurrence of COVID-19 during the subsequent two weeks. Therefore, kidney transplantation is feasible in an ESRD patient who has recovered from COVID-19, under a normal immunosuppressive regimen.

1. Introduction

As of May 14, more than four million people have confirmed coronavirus disease 2019 (COVID-19) and more than 290,000 patients have died [1]. Patients with end-stage renal disease (ESRD) are susceptible to infection with the virus that causes COVID-19, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) due to frequent hospital visitation for hemodialysis, and their reduced immunity status[2]. Many ESRD patients have reportedly been infected with SARS-CoV-2 in Wuhan [3,4]. Most have recovered well. Because of the transmissibility of the SARS-CoV-2, these patients must not receive a kidney transplant while they have pneumonia [5]. There are also questions about whether it is safe for them to receive a kidney transplant after recovery from COVID-19. There are concerns that immunosuppressants could lead to replication of underlying virus, leading to COVID-19 recurrence after the transplant. Whether different immunosuppression regimens and/or COVID-19 infection prevention measures are required in these patients to enable them to receive kidney transplants is unknown. Currently scant data are available on the management of patients who have received a kidney transplant after recovery from COVID-19. Herein we report the first case of kidney transplantation in a patient who had recently recovered from COVID-19.

2. Case

A 38-year-old man with ESRD was admitted into our hospital for kidney transplant evaluation on 15 December 2020. His medical history indicated that urinary protein had been discovered in a routine physical examination in 2012, but his serum creatinine level was normal. Renal biopsy suggested hepatitis B-related glomerulonephritis, and oral medication was used to control the progression of chronic kidney disease. In 2015 his renal function deteriorated and serum creatinine increased to 150 μmol/L. Regular hemodialysis treatment began in June 2016. Other aspects of his medical history included hypertension for 3 years, psoriasis for 1 year, and hepatitis B for many years.

Extensive laboratory tests and imaging were performed to evaluate the function of various organs, as were iliac vascular testing and tissue matching tests. There was no contraindication for a kidney transplant, so the patient's information was entered into the China Organ Transplant Registration System. He had rented a house in Wuhan and was receiving hemodialysis regularly, while waiting for a kidney transplant.

Unfortunately, he developed a fever, coughing, and analgia from 25

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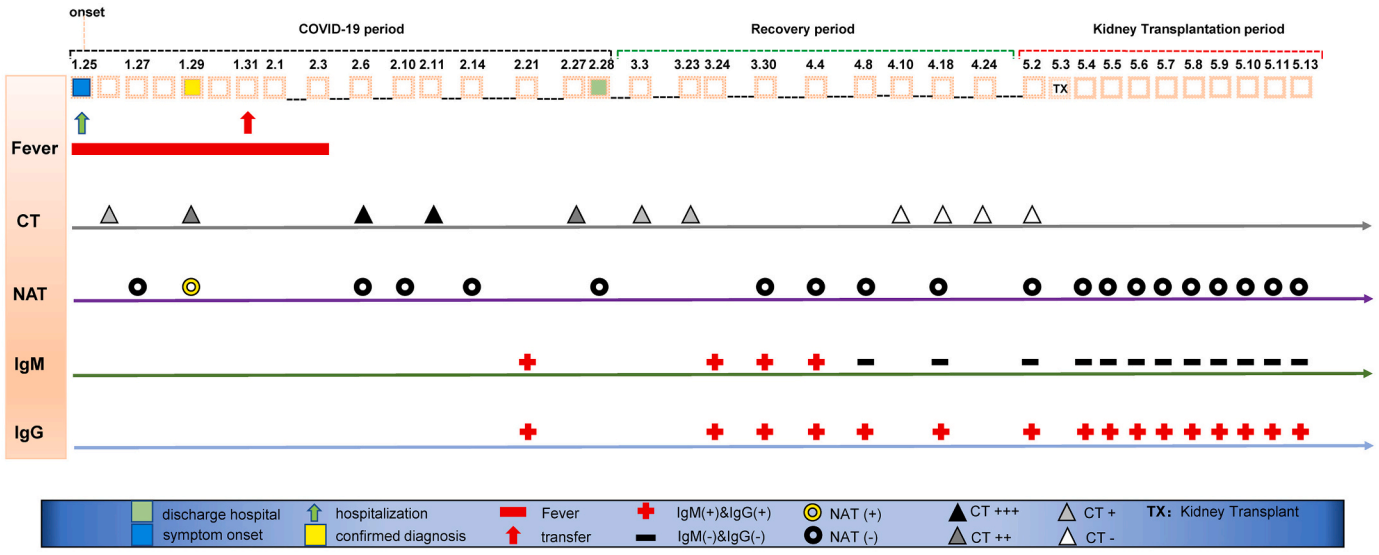

Fig. 1. Timeline of clinical characteristics of the current end-stage renal disease patient who received a kidney transplant after recovering from coronavirus disease 2019. Date of symptom onset was defined as origin point. Symptoms, CT image, nucleic acid test, NAT and antibody level were listed according to the day of illness.

January 2020. Test results included white blood cells 2.6 × 10^9/L, lymphocytes 0.43 × 10^9/L, and C-reactive protein 6 mg/L. Chest computed tomography (CT) on 26 January 2020 depicted one patchy shadow in the right lung near the pleura. PCR testing was then performed using nasal and throat swabs, but it was negative for SARS-CoV-2. From that day onward the patient was treated with oseltamivir and moxifloxacin, but his symptoms worsened, including fever (38.9 °C), sore throat, coughing, and sputum production. On 29 January 2020 he underwent chest CT again, and it depicted rapid progression of the previously observed lesion with multiple patchy ground-glass density shadows in the right lung near the pleura. This time nose and throat swab PCR tests for SARS-CoV-2 were positive, thus he was diagnosis with COVID-19 and transferred to the isolation ward [6].

Arbidol (200 mg three times a day orally), ganciclovir (200 mg two times a day), and immunoglobulin (10 g daily) were administered as antiviral drugs. Continuous renal replacement therapy was administered every 2 days to replace regular hemodialysis. His respiratory symptoms gradually worsened and oxygen therapy was contemplated. Chest CT on 06 February 2020 revealed expansion of the lung lesions with multiple patchy ground-glass density shadows in both lungs, but at this point SARS-CoV-2 PCR tests were negative. Since that timepoint his respiratory symptoms gradually improved, multiple CT scans indicated that the lesion was gradually being absorbed, and multiple SARS-CoV-2 PCR tests were negative. On 21 February 2020 SARS-CoV-2 antibody testing indicated an IgM titer of 392 AU/mL and an IgG titer of 76 AU/mL. After a long period of treatment the patient recovered, and he was discharged from the hospital on 28 February 2020 and recommenced regular hemodialysis. Multiple subsequent CT examinations indicated that the lesions were slowly absorbed. Multiple subsequent SARS-CoV-2 PCR tests conducted at multiple sites were all negative, and serum SARS-CoV-2 IgG remained positive and serum IgM gradually disappeared (Fig. 1).

The patient had recently moved to Wuhan and routinely traveled to the dialysis room and hospital. These risk factors led to susceptibility to SARS-CoV-2 infection, and there were no confirmed cases of SARS-CoV-2 infection in any of his family members. The patient—who had come to Wuhan from far away hoping to receive a kidney transplant—experienced a huge shock, but fortunately he did recover from COVID-19. The next questions were whether to proceed with a kidney transplant, what the best timing for a transplant was, and whether any altered immune suppression regimen would be required.

To the best of our knowledge 6 lung transplants have been performed to save the lives of critical COVID-19 patients in China, and there were no recurrences of COVID-19 in these patients despite the administration of immunosuppressant drugs [7,8]. After immunosuppressant drug withdrawal and treatment with antiviral drugs many organ transplant patients have also recovered from COVID-19, and there was no recurrence of COVID-19 associated with restarting immunosuppressants to prevent rejection [9,10]. The traditional immunological view is that IgG antibody is the main protective isotype, and it may have been helpful in preventing late COVID-19 in the current patient. After detailed

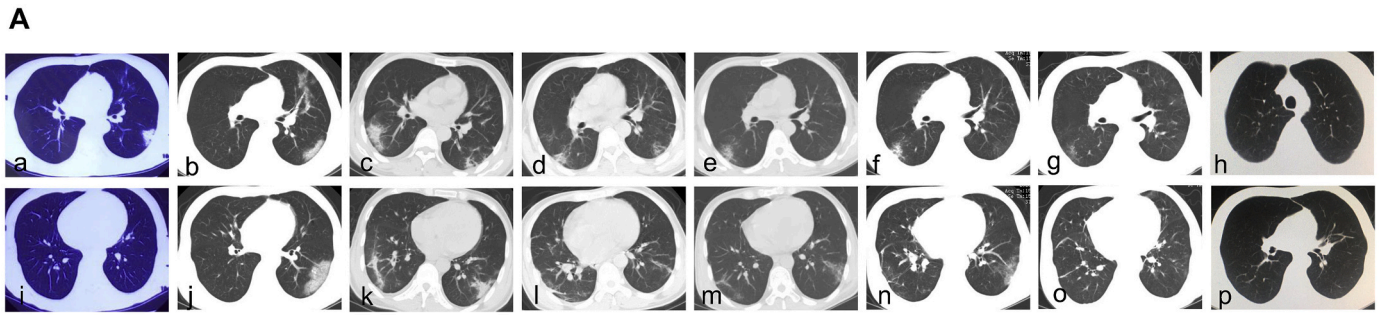

Fig. 2. Changes in the patient depicted via chest computed tomography imaging. (a and i)symptom onset, single subpleural patchy ground-glass opacities(GGO); (b and j)On illness day 4, multiple subpleural patchy GGO; (c and k)On illness day 12,the worst CT image with multiple subpleural patchy GGO in bilateral lung; (d and l) and (e and m) on illness day 17 and 33, the lesion was gradually absorbed; (f and n) and (g and o) on illness day 38 and 58,the lesion was almost absorbed at a low speed; (h and p)CT image on pre transplant day, the lesion was absorbed without fibrotic shadow.

Table 1
Clinical laboratory results.

		On Waitlist	COVID-19 period						Recovery period					Kidney transplant period								
														pTx	Tx1	Tx2	Tx3	Tx4	Tx5	Tx6	Tx7	Tx8	Tx10
Measures	Date Reference	12.16	1.26	2.1	2.10	2.24	2.26	2.29	3.1	3.23	3.26	4.2	4.10	5.2	5.4	5.5	5.6	5.7	5.8	5.9	5.10	5.11	5.13
WBC ($\times10^9$/L)	4–10	4.43	2.60	2.54	1.23	0.94	3.10	2.84	2.02	3.31	3.15	4.43	2.33	4.65	6.83	6.81	3.95	2.75	5.07	4.19	3.84	5.49	5.81
Lym ($\times10^9$/L)	0.8–3.5	1.11	0.43	0.30	0.35	0.44	0.57	0.67	0.23	0.77	0.74	0.72	0.41	0.63	0.27	0.22	0.17	0.13	0.28	0.65	0.64	0.44	0.79
Neu ($\times10^9$/L)	1.8–6.3	2.92	2.03	2.12	0.80	0.17	1.74	1.64	1.74	2.13	2.09	3.36	1.74	3.72	6.11	6.29	3.62	2.53	4.40	3.07	2.80	4.68	4.6
RBC ($\times10^{12}$/L)	4.0–5.5	2.88	3.4	3.07	2.86	1.89	1.85	1.75	2.13	2.06	1.88	2.33	2.24	2.68	2.88	2.92	2.77	2.82	3.14	2.83	2.80	2.67	2.61
Hb (g/L)	120–160	89	105	94	84	56	54	51	62	66	60	78	74	89	94	98	91	91	103	94	92	90	86
PLT ($\times10^9$/L)	150–400	214	127	132	88	86	97	116	102	97	59	167	74	115	133	101	88	80	99	112	111	144	180
CRP (mg/L)	0–10	/	6.0	58.5	9.3	<0.5	<0.5	<0.5	<0.5	0.8	2.3	4.8	<0.5	<0.5	13.3	/	99.0	6.7	0.8	1.4	1.1	<0.5	<0.5
PCT (ng/mL)	<0.05	/	/	1.60	2.94	1.66	/	0.93	/	0.62	/	0.74	0.73	/	0.93	1.04	0.81	/	/	/	/	/	0.08
Urea (mmol/L)	3.1–8.0	18.24	/	27.70	39.92	45.83	43.80	33.24	/	41.95	/	51.40	39.59	28.93	30.91	32.00	32.63	34.72	30.89	26.34	17.54	12.81	10.72
Cr (μmoI/L)	54–106	963	/	1168	1410	1527	1609	1496	1148	1301	/	1460	1212	1089	497	222	155	153	106	88	72	82	66
UA (μmoI/L)	149–416	430	/	420	490	528	497	345	/	594	/	534	494	375	481	434	357	334	290	397	282	183	176
ALT (U/L)	0–40	11	/	3	/	4	5	6	/	21	/	13	/	18	16	9	8	/	7	8	9	14	12
AST (U/L)	0–40	13	/	12	/	12	11	11	/	20	/	12	/	16	13	12	10	/	10	13	15	11	14

NOTE:WBC = white blood cell ; Lym = lymphocyte; Neu = neutrophil ; RBC = red blood cell ; Hb = Hemoglobin ; PLT = platelet ; CRP = C-reactive protein ; PCT = procalcitonin ; Urea = blood urea nitrogen; Cr = serum creatinine; UA = uric acid; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase ; pTx = pre-kidney transplantation;Tx = Kidney transplantation.

Table 2
The NAT result of SARS-CoV2.

Stage	COVID-19 period					Recovery period				Kidney transplantation period									
										pTx	Tx	Tx1	Tx2	Tx3	Tx4	Tx5	Tx6	Tx7	Tx8	Tx10
Date	1.27	1.29	2.6	2.10	2.14	2.28	3.23	3.30	4.4	4.8	4.18	5.2	5.3	5.4	5.5	5.6	5.7	5.8	5.9	5.10	5.11	5.13
Specimen																						
Nasopharyngeal swab	–	+	–	–	–	–	–	–	–	–	–	–	/	–	–	–	–	–	–	–	–	–
Oropharyngeal swab	–	+	/	/	/	/	/	/	–	–	–	–	/	–	–	–	–	–	/	–	/	–
Anal swab	/	/	/	/	/	/	/	/	–	–	–	/	/	–	–	–	–	–	–	–	–	–
Serum	/	/	/	/	/	/	/	/	/	/	/	/	/	–	–	–	–	–	–	–	–	–
Urine	/	/	/	/	/	/	/	/	/	/	/	/	/	–	–	–	–	–	–	–	–	–

Notes: NAT = nucleic acid testing; - = negative; + = positive;/=no test;pTx = pre-kidney transplantation;Tx = Kidney transplantation.

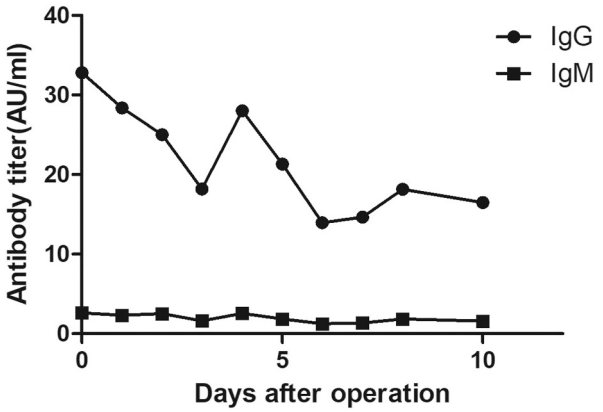

Fig. 3. Severe acute respiratory syndrome coronavirus 2 IgG and IgM antibody titer changes in the patient from the time of pre-transplant to the time post 10 days of kidney transplant.

discussion and literature review we surmised that a kidney transplant was feasible. Clinical symptoms, CT imaging, PCR testing, and antibody levels all indicated a complete recovery. The patient was effectively no different from a normal person. CT imaging is shown in Fig. 2. The complete timeline of the patient's clinical test results and treatment is shown in Fig. 1.

Fortunately, a matched kidney was allocated to the patient in early May 2020. A 45-year-old man donated an organ after brain death caused by cerebral hemorrhage. Creatine was 51 μmol/L and the estimated glomerular filtration rate was 123 mL/min. Ultrasound of the kidney was normal, and a urine sediment test was negative. Procalcitonin and other infection markers were also negative. A rigorous evaluation of the donor was conducted to exclude COVID-19, including routine blood tests, CT, nasal, throat, and anal swab PCR tests, and SARS-CoV-2 antibody testing.

Basiliximab (20 mg on day 0 and 20 mg on day 4) and methylprednisolone (500 mg per day on days 0–3) were used as induction drugs, and mycophenolic acid + Tacrolimus + prednisone triple maintenance immunosuppressive therapy was administered. A routine operation was performed under strict protective measures. A series of PCR tests and antibody titer determinations were conducted after the transplant. As shown in in Table 1, renal function was restored quickly, other indicators were similar to those of normal transplant patients (Table 1). After transplantation, we continuously took the blood, urine, nasopharyngeal swab, oropharyngeal swab and anal swab every day for SARS-CoV-2 detection. There were no post-transplant SARS-CoV-2-positive PCR results (Table 2).The SARS-CoV-2 IgM titer was very low and considered as negative level. Although the IgM titer value was positive, the titer gradually decreased comparable to post-COVID-19 recovery pre-transplant levels (Fig. 3). Tests for liver function and other inflammatory markers were also normal 2 weeks post-transplant (Table 1).

3. Discussion

Kidney transplantation is an important therapy for end-stage renal disease. It is used to improve quality of life in ESRD patients, in which cases it is not regarded as an urgently needed salvage therapy. To our knowledge to date there have been no reports of ESRD patients recovering from COVID-19 then receiving a kidney transplant. 6 cases lung transplants have been performed to save patients with pulmonary fibrosis and respiratory failure caused by COVID-19 infection [7,8]. No recurrence of COVID-19 was detected in those pulmonary transplant patients, and there were no subsequent cases of COVID-19 in associated medical staff.

In the present patient it was concluded that a kidney transplant was

appropriate, thus only the correct timing of it remained to be decided. There is currently no guideline for kidney transplants in ESRD patients who have recovered from COVID-19 pneumonia. In lung transplant waiting-list patients infected with SARS-CoV-2 it is recommended that the results of two viral RNA tests performed at least 24 h apart should be negative prior to proceeding with a transplant. Test specimens should include sputum and bronchoalveolar lavage [7]. We recommend performing a kidney transplant in COVID-19 patients when the COVID-19 has resolved.

Although the current patient had ESRD he recovered quickly after critical COVID-19, SARS-CoV-2 PCR tests quickly became negative, and IgM and IgG antibodies were produced. Notably absorption of the lesions in his lungs took approximately 2 months as determined via CT, but after that time no fibrotic lesions remained. The timing of kidney transplants in patients with COVID-19 on waiting-lists requires further investigation. We believed that prior to a transplant symptom should completely resolved, chest CT should depict full absorption of pulmonary lesions, and negative virology status should be confirmed by at least two consecutive nucleic acid-based tests performed using samples derived from multiple sites.

After infection the current patient's IgG antibody was always positive, whereas IgM positivity lasted for 2 months. If calculated based on the time since symptom onset, IgM antibody production continued for nearly 3 months. Performing a transplant during this 3 months is not suggested. Notably however, whether patients with IgM antibody positivity can undergo a transplant when other conditions are met requires further investigation.

Because there were no existing guidelines to refer to we chose basiliximab and methylprednisolone for immunoinduction and tacrolimus/mycophenolate mofetil/prednisone for maintenance immunosuppression. The patient did not experience recurrence of COVID-19 due to heavy immunosuppressant use. His recovery was similar to that of an ordinary patient. The titer of IgG antibody decreased gradually after transplantation, though further observational studies are certainly required.

After nearly one year's follow-up, the patient's renal function is stable, blood creatinine is maintained between 110 and 130 mmol/L, WBC is maintained between 6.1 and 6.5 mmol/L, Hb is maintained between 130 and 145 g/L, erythropoietin is not used, and 24h urine volume is maintained between 2000 and 3000 mL. Furosemide was not administered orally. The current immunosuppressive regimen for the patient was FK506 + MMF + Pred. The dose of FK506 was 1.75 mg in the morning and evening, MMF 3 mg in the morning and 2 mg in the evening, hormone 10 mg, and WUZHIDIWAN pills 3 pills in the morning and evening. The concentration of FK506 was kept at about 7 ng/mL. The color ultrasound of the transplanted kidney showed that the size of the transplanted kidney did not change significantly compared with that after surgery. The blood flow signal was rich, the blood flow resistance index of all levels of arteries was normal, and there was no rejection reaction or other infectious diseases after kidney transplantation. The patient is now living a normal life, eating a normal diet and returning to work.

In summary, this report is the first description of a kidney transplant in an ESRD patient after recovery from COVID-19. We suggest that a kidney transplant could be considered when a patient's symptoms have completely resolved, chest CT depicts lesion absorption, and repeated nucleic acid-based tests and IgM antibody tests are negative.

Declarations

Information on the donor: The donor is a brain-dead painent with no kinship with the recipient. And the donor was deceased.

Ethics approval and consent to participate

The transplant operation and publication of this case report were proved by the Ethics Committee of Wuhan University Renmin Hospital, Wuhan, China.

The patient whose case is described in the report has provided written informed consent for its publication.

Consent for publication

All authors agreement with the publication of this report.

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Declaration of Competing Interest

All authors declare that there are no conflicts of interest.

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References

[1] M. Haberal, Covid-19 update [J], Exp. Clin. Transplant. 18 (2) (2020) 139–140.
[2] J. Li, G. Xu, Lessons from the experience in Wuhan to reduce risk of COVID-19 infection in patients undergoing long-term hemodialysis [J], Clin. J. Am. Soc. Nephrol. 15 (5) (2020) 717–719.
[3] D. Fu, B. Yang, J. Xu, et al., COVID-19 infection in a patient with end-stage kidney disease [J], Nephron 144 (5) (2020) 245–247.
[4] K. Su, Y. Ma, Y. Wang, et al., How we mitigated and contained the COVID-19 outbreak in a hemodialysis center: lessons and experience [J], Infect. Control Hosp. Epidemiol. 41 (10) (2020) 1240–1242.
[5] F. Martino, M. Plebani, C. Ronco, Kidney transplant programmes during the COVID-19 pandemic [J], Lancet Respir. Med. 8 (5) (2020), e39.
[6] L.X. Xie, Interpretation of the 7th edition of the "diagnosis and treatment guidelines of coronavirus disease 2019 in China": Progress and challenges [J], Chronic Dis Transl Med 6 (2) (2020) 75–78.
[7] W. Han, M. Zhu, J. Chen, et al., Lung transplantation for elderly patients with end-stage COVID-19 pneumonia [J], Ann. Surg. 272 (1) (2020) e33-e4.
[8] J.Y. Chen, K. Qiao, F. Liu, et al., Lung transplantation as therapeutic option in acute respiratory distress syndrome for coronavirus disease 2019-related pulmonary fibrosis [J], Chin. Med. J. 133 (12) (2020) 1390–1396.
[9] L. Zhu, N. Gong, B. Liu, et al., Coronavirus disease 2019 pneumonia in immunosuppressed renal transplant recipients: a summary of 10 confirmed cases in Wuhan, China [J], Eur. Urol. 77 (6) (2020) 748–754.
[10] E. Akalin, Y. Azzi, R. Bartash, et al., Covid-19 and kidney transplantation [J], N. Engl. J. Med. 382 (25) (2020) 2475–2477.