Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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CASE REPORT

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COVID-19 in posttransplant patients—report of 2 cases

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Coronavirus Disease 2019 (COVID-19) has become a pandemic since March 2020. We describe here 2 cases of COVID-19 infection in a posttransplant setting. First one is a 59-year-old renal transplant recipient; the second is a 51-year-old allogeneic bone marrow transplant recipient. Both patients were on immunosuppressant therapy and had stable graft function before COVID-19 infection. After the diagnosis of COVID-19, immunosuppressive agents were discontinued and methylprednisolone with prophylactic antibiotics were initiated, however, the lung injury progressed. The T cells were extremely low in both patients after infection. Both patients died despite the maximal mechanical ventilatory support. Therefore, the prognosis of COVID-19 pneumonia following transplantation is not optimistic and remains guarded. Lower T cell count may be a surrogate for poor outcome.

KEYWORDS

Coronavirus, COVID-19, transplantation

1 | INTRODUCTION

Coronavirus Disease 2019 (COVID-19) has become a new pandemic with over 190 000 cases and 7800 death reported world-wide as of March 18, 2020 (WHO Coronavirus disease situation reports on March 18, 2020).[1] Due to its high infectivity and pathogenicity, most people are vulnerable to this virus, especially those with comorbidities. According to a previous study, patients with preexisting conditions are more likely to require mechanical ventilation, which may lead to a higher risk of death.[2] Posttransplant patients are usually under immunosuppressive therapy; this immune deficiency status may result in opportunistic infections. For now the experience in the management of COVID-19 in the posttransplant population is limited. Here we report 2 COVID-19 cases with prior history of transplantation.

2 | CASE REPORTS

2.1 | Case 1

On February 14, 2020, a 51-year-old male was admitted with a history of fever, sore throat and runny nose since February 11, 2020. This patient was diagnosed with acute myeloid leukemia (M-2) in September 2018 and underwent allogeneic bone marrow transplantation in a teaching hospital located in Wuhan in June 2019. After transplantation, he was on maintenance immunosuppressive therapy with cyclosporine-A and received regular follow-up in the same hospital every 3 months. On January 20, he travelled to Wuhan city for a 1-day regular checkup and the result showed no evidence of relapse. He denied the exposure to any confirmed case of COVID-19 on that trip. On February 11 (22 days after exposure), he developed a low grade fever,

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sore throat, and runny nose. A computed tomography (CT) of the chest was performed on February 13, which showed multiple patchy ground glass opacities bilaterally. The test for COVID-19 infection by real-time Polymerase Chain Reaction (PCR) assay was performed on February 14 (day 3 of illness) and returned positive. He was admitted to an isolation ward and was given lopinavir/ritonavir (200 mg thrice daily, orally), methylprednisolone (40 mg daily), and immunoglobulin (10 g daily) as recommended by the Chinese COVID-19 Interim Management Guidance. However, on February 21 (10 days after the onset of fever), he developed severe shortness of breath. A repeat CT scan showed the expansion of the lung lesions. Oxygen was administered to the patient at 10 L/min via a nasal cannula; however, the symptom did not improve. The flow cytometry detection showed low counts of T cells in the blood (detailed in Table 1). On day 17, he was transferred to intensive care unit and started on non-invasive ventilation. Cyclosporine A was discontinued and antibiotics were given, including moxifloxacin and cephalosporin, followed by linezolid, meropenem, and caspofungin when nosocomial infection was confirmed by culture. In the following days, this patient's situation deteriorated and was intubated for mechanical ventilation, however the hypoxemia continued and this patient eventually deceased on March 4, 22 days after the onset of symptoms.

2.2 | Case 2

A 58-year-old male with a 12-year history of kidney transplantation was admitted for 4 days of fever and cough on January 30, 2020. This patient had kidney transplantation for end stage renal failure in 2008. He was on mycophenolate mofetil and steroid treatment posttransplant. The renal graft function was stable before this admission. He reported a positive contact with people from Wuhan on January 19.

TABLE 1 Clinical characteristic of 2 posttransplant patients with COVID-19 infection

	Case 1	Case 2
Age (y)	51	58
Sex	Male	Male
Symptoms	Fever, cough, runny nose	Fever, cough, shortness of breath
History	Allogeneic bone marrow transplantation in 2018	Kidney transplantation in 2008
Immunosuppressant	Cyclosporine A	Mycophenolate mofetil and steroid
Cessation of immunosuppressant (days from symptoms)	Day 17	Day 3
Incubation period	22 d	8 d
COVID-19 RNA negative time	Day 11	Day 26
Methylprednisolone	Day 6-21	Day 3-39
Lopinavir/ritonavir	Yes	Yes
Mechanical ventilation	Yes	Yes
Extracorporeal membrane oxygenation	No	Yes
Nosocomial bacterial infection	Yes	Yes
Organ failure	Respiratory	Respiratory; kidney; heart
Death time	Day 22	Day 40
T cell count on day 14		
Total lymphocyte (530-3700/μL)	258	376
Total T cell (955-2860/μL)	233	276
CD4 (550-1440/μL)	73	222
CD8 (320-1250/μL)	160	52
CD4/CD8 (0.64-2.85)	0.45	4.23
T cell count on day 21		
Total lymphocyte (530-3700/μL)	311	499
Total T cell (955-2860/μL)	287	441
CD4 (550-1440/μL)	95	398
CD8 (320-1250/μL)	193	39
CD4/CD8 (0.64-2.85)	0.49	10.23

Seven days later (January 26), he reported a low grade fever (T 37.6°C) and dry cough. The CT scan was normal on the first day of illness. He received oseltamivir and moxifloxacin treatment for 4 days, but the symptoms did not improve. This patient continued to report shortness of breath. A repeated CT scan revealed typical signs of COVID-19 pneumonia. Methylprednisolone 80 mg daily and high flow humidification oxygen inhalation therapy were started on day 4; however, the hypoxemia continued worsening. COVID-19 infection was confirmed on February 3 (day 7 of illness) with PCR. Non-invasive ventilation was started on February 5 (day 9) and mechanical ventilation on February 16 (day 20) and later extracorporeal membrane oxygenation on February 19 (day 23). The results of flow cytometry detection revealed continuous low T cell count during the hospitalization. Although the coronavirus RNA detection turned negative after February 25 (day 29), this patient still developed multiorgan failure (lung, kidney, and heart) and eventually died on day 40.

3 | DISCUSSION

The management of COVID-19 in transplant population remains unclear. According to previous reports, the comorbidities increase the risk of severe pneumonia in COVID-19 infected population,[2] yet the history of transplantation has never been reported as a risk factor. Our report of 2 confirmed COVID-19 cases suggested the outcome in posttransplant population might be very poor.

The age of these 2 posttransplantation patients was relatively younger than the age of patients (median 63 years old) with poor outcome documented in liturature,[2] thus it is reasonable to speculate that the history of transplantation might play a role in the progress of COVID-19 pneumonia. Since the grafts function was well controlled in these 2 cases, the immunosuppressants could be the crux of the problem. The immunosuppressive agents they took, including cyclosporin-A and mycphenolate mofetil, have been reported to increase the risk of opportunistic infection, including viral infection.[3-5] Whether or not these drugs could also increase the chances of COVID-19 infection, as an additional opportunistic infection, remains unknown. Both cyclosporin-A and mycphenolate mofetil work by targeting the proliferation and differentiation of T cells.[3-5] It is notable that the number of T cells was significantly decreased in these 2 cases. T cell reduction is common in severe COVID-19 cases,[6] indicating coronavirus might mainly act on lymphocytes, especially T lymphocytes. The pre-exposure to the immunology impairment may exacerbate the severity of COVID-19 infection and thus deteriorate the course of the disease. A latest report suggests that discontinuation of immunosuppressants and steroid treatment might help faster recovery from COVID-19 pneumonia.[7] However, the same strategy did not work in the second case of our report. Additionally, both of the 2 patients developed a nosocomial bacterial infection during hospitalization, which warrants more careful use of steroid in COVID-19 infection.

In conclusion, we reported 2 COVID-19 cases after transplantation with poor outcome. The management of COVID-19 infection in the posttransplant population is more complicated than expected. Strong efforts must be carried out to control coronavirus spread and avoid posttransplant infections, especially when the vaccine is not available.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

ETHICS

Study procedures were approved by the institutional review board (IRB) at Fujian Medical University. The clinical activities being reported are consistent with the principles of the declaration of Istanbul as outlined in the "Declaration of Istanbul on Organ Trafficking and Transplant Tourism."

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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