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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
INTRODUCTION

Coronavirus Disease 2019 (COVID-19) has become a new pandemic with over 190,000 cases and 7,800 deaths reported worldwide as of March 18, 2020 (WHO Coronavirus disease situation reports on March 18, 2020). Due to its high infectivity and pathogenicity, most people are vulnerable to this virus, especially those with co-morbidities. 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. 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.

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 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
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.

|                       | 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 (950-2860/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 (950-2860/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.

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.

ORCID
Su Lin https://orcid.org/0000-0001-7517-9859

REFERENCES
1. World Health Organization. Coronavirus disease situation reports, 18 March 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports. Accessed March 19, 2020.
2. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of Coronavirus disease 2019 in China [published online ahead of print 2020]. N Engl J Med. 2020; https://doi.org/10.1056/NEJMoa2002032
3. Matsuda S, Koyasu S. Mechanisms of action of cyclosporine. Immunopharmacology. 2000;47(2):119-125.
4. McMurray RW, Harisdangkul V, Mycophenolate mofetil: selective T cell inhibition. Am J Med Sci. 2002;323(4):194-196.
5. Knight SR, Morris PJ. Does the evidence support the use of mycophenolate mofetil therapeutic drug monitoring in clinical practice? A systematic review. Transplantation. 2008;85(12):1675-1685.
6. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China [published online ahead of print 2020]. Clin Infect Dis. 2020; https://doi.org/10.1093/cid/ciaa248
7. Zhu L, Xu X, Ma KE, et al. Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression [published online ahead of print 2020]. Am J Transplant. 2020; https://doi.org/10.1111/ajt.15869 [Epub ahead of print]

How to cite this article: Huang J, Lin H, Wu Y, et al. COVID-19 in posttransplant patients—report of 2 cases. Am J Transplant. 2020;20:1879-1881. https://doi.org/10.1111/ajt.15896