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COVID-19 in post-transplantation patients- report of two cases

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Abbreviations:

COVID-19: Coronavirus Disease 2019

CT: Computed Tomography

PCR: Polymerase Chain Reaction

Disclosure

Conflicts of interest: None

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

Abstract

Coronavirus Disease 2019 (COVID-19) has become a pandemic since March 2020. We describe here, two cases of COVID-19 infection in a post-transplant 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

Introduction

Coronavirus Disease 2019 (COVID-19) has become a new pandemic with over 190000 cases and 7800 death reported world-wide as of 18 March 2020 (WHO Coronavirus disease situation reports on 18 March 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]. Post-transplant 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 post-transplant population is limited. Here we report two COVID-19 cases with prior history of transplantation.

Cases reports

Case 1

On 14th February 2020, a 51-year old male was admitted with a history of fever, sore throat and runny nose since 11th February, 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 20th January he travelled to Wuhan city for a one-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 11th February (22 days after exposure), he developed a low grade fever, sour throat and runny nose. A computed tomography (CT) of the chest was performed on 13th February, 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 14th February (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 (40mg daily) and immunoglobulin (10g daily) as recommended by the Chinese COVID-19 Interim Management Guidance. However, on 21th February (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 10L/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 4th March, 22 days after the onset of symptoms.

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 30th January 2020. This patient had kidney transplantation for end stage renal failure in 2008. He was on mycophenolate mofetil and steroid treatment post-transplant. The renal

graft function was stable before this admission. He reported a positive contact with people from Wuhan on 19th January. Seven days later (26th January) he reported a low grade fever (T 37.6℃) and dry cough. The CT scan was normal on the first day of illness. He received four days of oseltamivir and moxifloxacin treatment, 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 80mg daily and high flow humidification oxygen inhalation therapy were started on day 4, however the hypoxemia continued worsening. COVID-19 infection was confirmed on 3rd February (day 7 of illness) with PCR. Non-invasive ventilation was started on 5th February (day 9) and mechanical ventilation on 16th February (day 20) and later extracorporeal membrane oxygenation on 19th February (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 25th February (Day 29), this patient still developed multiorgan failure (lung, kidney and heart) and eventually died on day 40.

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 two confirmed COVID-19 cases suggested the outcome in post-transplant population might be very poor.

The age of these two post-transplantation 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 two 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 two cases. T cell reduction is common in severe COVID-19 casese[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 two patients developed a nosocomial bacterial infection during hospitalization, which warrants more careful use of steroid in COVID-19 infection.

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

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Table 1 Clinical characteristic of two post-transplant patients with COVID-19 infection

	Case 1	Case 2
Age(year)	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 days	8 days
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/ul)	258	376
Total T cell (955-2860/ul)	233	276
CD4 (550-1440/ul)	73	222
CD8 (320-1250/ul)	160	52
CD4/CD8 (0.64-2.85)	0.45	4.23
T cell count on day 21		
Total lymphocyte (530-3700/ul)	311	499
Total T cell (955-2860/ul)	287	441
CD4 (550-1440/ul)	95	398
CD8 (320-1250/ul)	193	39
CD4/CD8 (0.64-2.85)	0.49	10.23