




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.

CASE REPORT

Immunosuppressive therapy maintenance in a kidney transplant recipient with SARS-CoV-2 pneumonia: A case report

Elisabetta Bussalino¹ | Andrea De Maria² | Rodolfo Russo¹ | Ernesto Paoletti¹ 

¹Nephrology, Dialysis and Transplantation, University of Genoa and Policlinico San Martino, Genoa, Italy

²Infectious Diseases Unit, University of Genoa and Policlinico San Martino, Genoa, Italy

Correspondence

Ernesto Paoletti

Email: ernesto.paoletti@hsanmartino.it

The role of systemic inflammation is proving crucial in determining unfavorable outcome in SARS-CoV-2-infected patients. Limited data are available regarding immunosuppression management in kidney transplant recipients (KTRs) with SARS-CoV-2 pneumonia. We report a case of a 32-year-old KTR who developed SARS-CoV-2 infection and fully recovered in 15 days while maintaining standard immunosuppressive therapy.

KEYWORDS

clinical research/practice, immunosuppressive regimens, infection and infectious agents—viral, kidney transplantation/nephrology

1 | INTRODUCTION

The novel coronavirus outbreak has startled the world due to its widespread diffusion and socioeconomic burden. Kidney transplant recipients (KTRs) are perceived to be at high risk of infection, and immunosuppressive therapy management during this global emergency can be a challenge. Herein, we report the case of a KTR who developed SARS-CoV-2 pneumonia and recovered in 15 days while continuing administration of his usual immunosuppressive treatment.

2 | CASE REPORT

The patient is a 32-year-old man who underwent kidney transplantation in September 2017 from a deceased donor; ESRD etiology was unknown. Prior to admission, February 3, 2020, his most recently measured creatinine level was 1.9 mg/dL (eGFR 46 mL/min/1.73 m²). Immunosuppressive therapy consisted in tacrolimus (trough levels 6–8 ng/mL), mycophenolic acid (360 mg BID), and prednisone (5 mg). Induction therapy included ATG and basiliximab.

Previous medical history was irrelevant except for hypertension and pericarditis treated with colchicine in February, 2017.

On March 12, 2020, the patient was admitted to our emergency room after a fever lasting 3 days, dyspnea and non-productive cough, unsuccessfully treated with amoxicillin-clavulanate 1 g TID.

Physical evaluation was normal: body temperature was 38°C and oxygen saturation was 97% in ambient air, blood pressure was 130/70 mm Hg, and respiratory rate was 25 breaths per minute. Laboratory results demonstrated a low percentage of lymphocytes (17.8%), absolute and relative monocytosis (1000/mm³; 16.7%), C-reactive protein (CRP) elevation (47.9 mg/L), and slightly elevated levels of procalcitonin (PCT) (0.33 µg/L). Renal function impairment was observed (creatinine 2.6 mg/dL, eGFR 31 mL/min/1.73 m²). Pneumococcus and *Legionella* infections were ruled out by negative urinary antigens. Arterial blood gas analysis was suggestive of respiratory alkalosis.

Chest X-ray demonstrated diffuse septal thickening in the absence of areas of consolidation.

On March 13, nasopharyngeal swab testing was performed and SARS-COV-2 was identified by rRT-PCR (Day 0).

The patient was then transferred to the Infectious Disease Unit. In agreement with the nephrologist, his prednisone dose was increased to 15 mg/d, while the remaining immunosuppressive therapy was left unchanged.

Abbreviations: ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 19; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; IL-6, interleukin 6; KTRs, kidney transplant recipients; PCT, procalcitonin; SARS-CoV-2, severe acute respiratory syndrome coronavirus – 2.

On Day 0, according to the local protocol, hydroxychloroquine 200 mg BID and oseltamivir 30 mg OD were started. The patient was febrile (TA 38°C), respiratory rate increased to 30 breaths per minute, oxygen saturation decreased to 94%, and oxygen administration was started at 4 mL/min by nasal cannula. Due to the concomitant increase in CRP (97 mg/L) and PCT (2.33 µg/L), antibiotic therapy with ceftaroline was started. On Day 2, laboratory results showed a decrease in platelets (minimum 108 000/mm³) and a reduction of prothrombin time (PT 78%). Moreover, a high IL-6 concentration was detected (86.3 ng/L) and lower CD4⁺, CD8⁺, CD3⁺ count was found in the peripheral blood, although with a normal CD4/CD8 ratio (respectively, 131/cmm, 80/cmm, 227/cmm, CD4/CD8:1,7). Increased levels of ferritin, transaminases, and lactic dehydrogenase (LDH) were found. The patient remained febrile until Day 5; on Day 8, oxygen saturation in ambient air reached 96%; on Day 11, the patient was released with indication to solitary confinement. At discharge, CRP and IL-6 levels were significantly decreased (respectively, 18 mg/L and 6.9 ng/L). Renal function was comparable to what it was at admission

(creatinine 2.8 mg/dL, eGFR 29 mL/min/1.73 m²) and proteinuria had significantly increased (Day 0:1 g/L; Day 11:3 g/L). Symptoms, laboratory results, and treatments are described in Table 1.

3 | DISCUSSION

In December 2019, SARS-CoV-2 was identified in Wuhan, China. In February 2020, the first case was diagnosed in Italy, and within a few weeks, the COVID-19 infection has taken on the characteristics of a “pandemic.”

Immunosuppressed patients are, by definition, at high risk of infections. However, COVID-19 does not appear to cause more severe disease in liver transplant recipients.¹

Systemic inflammatory response plays a main role in provoking viral-induced lung injury and could be largely responsible for the poor respiratory outcome in most patients, thus favoring transition to acute respiratory distress syndrome (ARDS).² Moreover, a study

TABLE 1 Symptoms, laboratory results, and treatments according to day of illness

	Day -3	Day -1	Day 0	Day 1	Day 2	Day 4	Day 6	Day 7	Day 11	
Body temperature	38.5	38	38	38.5	37	37.8	37	36.5	36.5	
FiO ₂	AA	AA	AA	35	35	AA	24	AA	AA	
SpO ₂	97	94	94	94	96	97	95	96	99	
Respiratory rate	25	30					30			
Arterial pCO ₂	32.2					24.8	32.3			
WBC	6210	4930			7170	6290	5960			
Lymphocytes	1100				1100	830	900			
Monocytes	1000				500	520	800			
PLTs	137 000				108 000	156 000	245 000			
Hgb	11.4	11.1			11.0	10.3	10.6			
Creatinine	2.6	2.6			2.7	3	2.9		2.8	
LDH	178				249	337			218	
Ferritin					504				664	
IL-6					86.3				6.9	
CRP	47.9	97			69.8				18	
PCT	0.33	2.33			2.33	1.14			0.08	
ALT	40	35			42	62			18	
AST					45	80			24	
PT	70	65			78				75	
TL TAC	6.6						12			
Cough and dyspnea										
Therapy	Chest X-ray		Hydroxychloroquine							
	Chest X-ray		Oseltamivir					Ceftaroline		
	Chest X-ray		Ceftaroline							

Abbreviations: AA, ambient air; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; FiO₂, fraction of inspired oxygen; Hgb, hemoglobin; IL-6, interleukin 6; LDH, lactate dehydrogenase; pCO₂, partial pressure of carbon dioxide; PCT, procalcitonin; PLTs, platelets; PT, prothrombin time; SpO₂, peripheral capillary oxygen saturation; TAC, tacrolimus; TL, trough levels; WBC, white blood cells. [Color table can be viewed at wileyonlinelibrary.com]

performed in Wuhan identified IL-6 and ferritin as predictors of mortality in COVID-19 patients³ thereby paving the way to experimentation with tocilizumab, an IL-6 receptor blocker.

In their work, Shi et al⁴ suggest the presence of two phases in the COVID-19 infection; in the first, which occurs during incubation and in the non-severe disease period, virus replication activates immune response. Thus, boosting the immune system at this exact moment could be the winning strategy to obtain complete virus clearance. At later stages, when severe disease develops, lung damage is induced by the systemic inflammation itself.

Based on this rationale and on laboratory results demonstrating hyperinflammation,⁵ immunosuppressive therapy was left unchanged and therefore lopinavir/ritonavir was not administered due to proven drug interaction with calcineurin inhibitors.

Even though corticosteroid use in COVID-19 pneumonia remains controversial,^{6,7} we increased our patient's prednisone dose to 15 mg for 9 days as an anti-inflammatory agent.

Interestingly, we did not observe complete recovery of graft function, and moreover, proteinuria developed. Further investigation into these findings is needed. Since discharge, the patient's clinical condition has been closely monitored via telephone.

Immunosuppression in critically ill patients is still a matter of debate. As recently highlighted by Ritchie and Singanayagam in their letter,⁸ the relationship between virus replication and systemic inflammation may be consequential and directly related rather than an excessive response by the immune system. Therefore, the impact of immunosuppressive therapy is crucial in transplant recipients.

In conclusion, although our evidence is anecdotal, it may provide some clinical insight into therapeutic management. Maintaining immunosuppression could be beneficial in stopping, or at least mitigating the "cytokine storm" that usually leads to poor outcome in these patients and, only secondarily, in preventing graft rejection. Further studies are warranted to confirm these findings and to evaluate the clinical and laboratory characteristics of the KTRs who might benefit from this therapeutic strategy.

DISCLOSURE

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

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author, [EP] and with permission from Policlinico San Martino. The data are not publicly available due to their containing information that could compromise the privacy of research participant.

ORCID

Ernesto Paoletti  <https://orcid.org/0000-0002-5509-6252>

REFERENCES

1. D'Antiga L. Coronaviruses and immunosuppressed patients. The facts during the third epidemic [published online ahead of print 2020]. *Liver Transpl*. 2020. <https://doi.org/10.1002/lt.25756>
2. Li LQ, Huang T, Wang YQ, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. *J Med Virol*. 2020;92:577-583.
3. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China [published online ahead of print 2020]. *Intensive Care Med*. 2020; <https://doi.org/10.1007/s00134-020-05991-x>
4. Shi Y, Wang Y, Shao C, et al. COVID-19 infection: the perspectives on immune responses [published online ahead of print 2020]. *Cell Death Differ*. <https://doi.org/10.1038/s41418-020-0530-3>
5. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395(10229):1033-1034.
6. Shang L, Zhao J, Hu Y, Du R, Cao B. On the use of corticosteroids for 2019-nCoV pneumonia. *Lancet*. 2020;395(10225):683-684.
7. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet*. 2020;395(10223):473-475.
8. Ritchie AI, Singanayagam A. Immunosuppression for hyperinflammation in COVID-19: a double-edged sword. *Lancet*. 2020;395(10230):1111.

How to cite this article: Bussalino E, De Maria A, Russo R, Paoletti E. Immunosuppressive therapy maintenance in a kidney transplant recipient with SARS-CoV-2 pneumonia: A case report. *Am J Transplant*. 2020;20:1922-1924. <https://doi.org/10.1111/ajt.15920>