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TRANSPLANT INFECTIOUS DISEASE

CLINICAL CORRESPONDENCE

COVID-19 infection in renal transplant recipients in early post-renal transplantation period: Report of three cases

1 | CASE SERIES

All three renal transplant recipients were from living donors and were performed at Shahid Dharmabhakta National Transplant Centre (SDNTC), Bhaktapur, Nepal. All patients provided signed informed consent to perform transplantation surgery at the time of increased epidemiological risk. All patients are required to have a negative SARS-CoV-2 PCR from, nasopharyngeal swabs immediately before the transplant surgery. The demographic and key characteristics of the three patients are summarized in Table 1. Patient 1 required revision of anastomosis twice due to poor reperfusion of graft clinically and assessed by USG Doppler study intraoperatively; patients 2 and 3 had immediate urine output and was adequate immediately after transplantation. All patients received anti-thymocyte globulin induction and prophylactic anticoagulation during hospitalization. All were maintained with tacrolimus (TAC), mycophenolate mofetil (MMF), and steroids as maintenance therapy. The doses of mycophenolate were adjusted based on complete blood counts. The doses of TAC were adjusted with target of 6–8 ng/ml levels. Patient 1 developed delayed graft function, requiring three episodes of in-hospital dialysis, and clinically managed with pulse methylprednisolone therapy (500 mg) on 5th postoperative day (POD) for 3 days; biopsy only showed acute tubular necrosis. Meanwhile, COVID-19 was diagnosed on 7th POD.

All received valganciclovir for cytomegalovirus prophylaxis and trimethoprim-sulfamethoxazole was given for *Pneumocystis carinii* pneumonia prophylaxis. All three patients were stable in terms of respiratory symptoms throughout the initial transplant hospital stay. All patients developed symptoms during the hospital stay, triggering COVID test. We did not identify definitive sick contacts of these cases. After the patient tested positive, they were kept in hospital isolation with close monitoring of symptoms and conservative management.

The early urine output was outstanding in all three patients. On POD 3, C-reactive protein levels and oxygen levels remained normal in patients 2 and 3 and they were discharged from the hospital on 5th and 7th days with improved symptoms. They remained well without complications.

Patient 1 remained hospitalized for 15 days due to delayed graft function (DGF) but was discharged with a serum creatinine (SCr) of 3.9 mg/dl. Oxygen saturation remained normal throughout the initial hospital stay and his symptoms improved prior to discharge. On 24th POD, he was readmitted with severe pneumonia (Figure 1A,B). He was intubated and had a mechanical ventilator initiated on 28th POD for respiratory failure. MMF was held and the dosage of prednisolone was increased. He also received a single dose of 400 mg of tocilizumab. Unfortunately, despite all efforts, he passed away due to COVID pneumonia.

2 | DISCUSSION

These three cases contribute to our understanding of COVID-19 in newly transplanted patients. Kolonko et al.[1] in their study presented their experience with diagnosis in three renal transplants and one liver transplant recipient in the early transplant period. Two patients did well but one died of non-COVID-related complication. Another study by Cheng et al.[2] reported two COVID-19 cases in renal transplant recipients. Both cases were discharged following a treatment regimen with discontinued immunosuppressant and low-dose methylprednisolone-based therapy with no signs of rejection during the management. This study report demonstrates the variability and risk of adverse outcomes with early post-transplant infections.

Will reverse transcription polymerase chain reaction (RT-PCR) remain the best test to diagnose SARS-CoV-2 infection, false negatives do occur. False-negative results can occur because of problems with collection, handling, transport, and storage as well as assay-specific issues of the tests, collecting the test early in the clinical course of infection (i.e., viral recombination, assay quality, harmonization, and instrument performance).[3] Moreover, the utmost likelihood of false-negative results was stated to be 5–7 days before the onset of symptoms. Therefore, the imperfect accuracy of PCR tests was raised as a possible threat, as COVID-19 could not be identified both in donors and waitlisted asymptomatic recipients.[4]

Furthermore, the transmission of SARS-CoV-2 by presymptomatic or asymptomatic staff has been repeatedly demonstrated.[5] The main problem is how to prevent transmission from asymptomatic medical staff working in the hospitals. If testing is limited to patients with symptoms, asymptomatic cases may not be detected. Other approaches, such as temperature screening and mandatory use of facial mask can be utilized and was implemented by our team to prevent future transmissions. Visitors are no longer allowed in the ward to prevent nosocomial transmission. Due to potential concentration of infected patients in the hospital, risk of exposure may be higher in the hospital than in the home, particularly when rates are high in the community. Asymptomatic persons are possible sources of COVID-19 infection

TABLE 1 Patient's demographics and perioperative data

Variables	Patient 1	Patient 2	Patient 3
Recipient's age (years)	32	43	47
Recipient's sex	Male	Male	Male
Recipient's weight (kg)	62	50	68
History of COVID-19 vaccination	Yes	Yes	Yes
History of prior dialysis	Yes	Yes	Yes
HLA mismatch	2/6	2/6	3/6
Infectious complication	Urinary tract infection	None	Urinary tract infection
COVID positive on POD	7	1	1
COVID symptoms in early days of infection	Sore throat, mild cough, no fever	Cold like illness, no cough, no fever	Cold like illness, no cough, no fever
Readmission	For COVID pneumonia on 23rd POD	No	No
Intubation/mechanical ventilatory support	For severe respiratory distress on 28th POD	No	No

Abbreviation: POD, postoperative day; HLA, human leukocyte antigen.

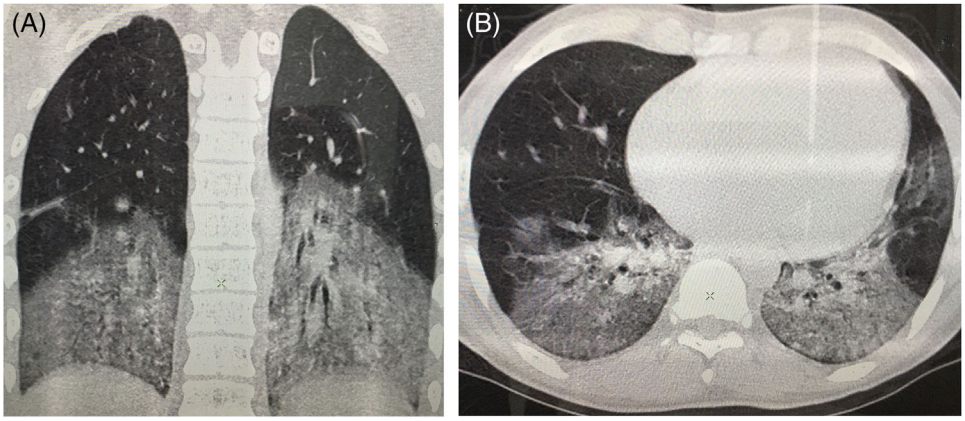

FIGURE 1 (A and B) High-resolution computerized tomography (HRCT) of patient 1 showing COVID-19 pneumonia in bilateral lung

may deserve a reassessment of transmission mechanism of the present pandemic.

After the second wave of COVID, renal transplant services have continued in our center. Meanwhile, the third wave of Omicron hit so quickly that despite all the safety measures, three patients were tested positive in the early postoperative period. The consequent screening showed further cases of COVID-19 infection affecting a few staff members. Though the definitive source was not identified, exposure to presymptomatic hospital staff or other prospective kidney transplant recipient patients is possible since we identified a large number of staff and potential kidney transplant recipients with COVID-19 at the time. To prevent further exposure of other patients, we aggressively used contract tracing for all staff testing positive. Meanwhile, precautions like social distancing and, the use of personal protective equipment (PPE) was made mandatory while patient management.

According to some literature, it is essential to adjust the post-transplant immunosuppression regimens, depending upon the clinical scenario of the virus-infected patients.[6] In all three patients, the level of TAC was different and tried to maintain around 6–8 ng/ml. Initially, the doses of prednisone had been decreased in all three patients to prevent further escalation of symptoms, however, the doses of prednisone increased to 40 mg/day in patient 1 when he developed severe pneumonia. Despite holding MMF and giving tocilizumab the patient progressed and died.[6,7]

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

AUTHOR CONTRIBUTIONS

Tika Ram Bhandari participated in the study concept, data collection, and writing of the original manuscript. Kalpana Kumari Shrestha and Pukar Chandra Shrestha participated in the study concept and critically revised the manuscript.

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