Received: 30 June 2020 | Accepted: 5 July 2020

DOI: 10.1111/tid.13408

LETTER TO THE EDITOR

WILEY

Persistently positive severe acute respiratory syndrome coronavirus 2 (SARS-COV2) nasopharyngeal PCR in a kidney transplant recipient

To the Editor,

Severe acute respiratory syndrome coronavirus 2 (SARS-COV2) infection is usually diagnosed by a positive PCR test in respiratory samples. While the respiratory PCR may remain positive for 2-3 weeks, in the general population, there have been occasional reports of persistent and recurrent positive SARS-COV2 PCR beyond 4 weeks despite clinical resolution.[1-6] The clinical significance of persistently positive respiratory PCR in asymptomatic patients is not clear but is thought to reflect mere shedding of non-infectious viral RNA. In one study, SARS COV2 could not be cultured in vitro in PCR positive respiratory samples when PCR cycle threshold (Ct) was more than 24 or when the specimens were obtained beyond 8 days after symptom onset.[7] Nonetheless, there is uncertainty regarding transmission dynamics of the virus in persistently PCR positive patients and there is a concern that they may be able to transmit infection to others if discharged to congregate facilities or brought back to the clinic for evaluation. This is particularly relevant in transplant recipients who carry a significant mortality and morbidity associated with SARS COV2 infection.[8] Here, we would like to share our experience of a kidney transplant recipient with intermittently positive nasopharyngeal (NP) PCR for 57 days that eventually converted negative on 2 consecutive samples 65 days after the first positive test.

A 26-year-old female with end-stage renal disease secondary to focal segmental glomerulosclerosis (FSGS) underwent deceased donor kidney transplant. The immediate post-transplant course was complicated by recurrent FSGS requiring -plasmapheresis, intravenous immunoglobulin (IVIG), and a dose of rituximab. She became hypogammaglobulinemic (serum IgG level < 400 mg/dL) following this but did not require further IVIG treatment. She was maintained on azathioprine, tacrolimus, and prednisone 10 mg a day. Her new baseline kidney function remained stable with serum creatinine around 2.5.

Six months after transplant she had a temperature of 100°F of one day duration. She also endorsed minimal cough but no chest pain or shortness of breath. NP SARS-COV2 PCR came back positive, and she was admitted for observation. She did not develop any more fever, and the cough resolved. There was no evidence of pneumonia, and she did not require supplemental oxygen. She was treated with hydroxychloroquine for 5 days and was discharged in a stable condition after 6 days of admission. She was readmitted 3 weeks later with *Klebsiella pneumoniae* bacteremia with left thigh cellulitis. Her clinical course was otherwise uncomplicated except for anasarca as a result of FSGS.

Follow-up NP SARS COV2 PCR, however, remained intermittently positive for 57 days after the first positive test (Table 1). Two consecutive tests finally came back negative on days 64 and 65. She had no fever or respiratory symptoms, and NP PCR was repeated to document clearance of the virus so that she could come back for follow-up clinic visits (two consecutive negative PCRs were required).

The same PCR platform (Roche COBAS 8800) was used except on day 64 when Luminex NxTAG/MagPix was used. The NP PCR was intermittently positive with fluctuating Ct values. On day 29, only the E gene was positive (ORF1 gene negative) with a high Ct value. The subsequent test 7 days later (on day 36) was negative

TABLE 1 SARS COV2 nasopharyngeal PCR with cycle threshold (Ct) values

Test day	Result	Platform	Ct values
0	Positive	Roche COBAS 8800	ORF1 15.93 E GENE 16.19
18	Positive	Roche COBAS 8800	ORF1 23.77 E GENE 24.07
29	E GENE Positive	Roche COBAS 8800	E GENE 38.15
36	Negative	Roche COBAS 8800	Not applicable
37	Positive	Roche COBAS 8800	ORF1 25.6 E GENE 26.33
49	Negative	Roche COBAS 8800	Not applicable
57	E GENE Positive	Roche COBAS 8800	E GENE 36.31
64	Negative	Luminex NxTAG/MagPix	Not applicable
65	Negative	Roche COBAS 8800	Not applicable

providing reassurance but the following day both the E and ORF1 genes were detected at relatively low Ct values (but still above 24). Then, on day 49, the NP PCR came back negative, but on day 57 only the E gene was positive at a high CT value. The subsequent tests on day 64 and 65 with different platforms were negative and further testing was stopped. A commercial serum SARS-2 IgG test done on day 65 also came back negative implying defective immunity.

This case adds to the growing body of literature that NP SARS COV2 can persist longer than the usual 2-3 weeks. In this particular case, the NP PCR remained intermittently positive for more than 8 weeks with fluctuating Ct values. A higher Ct value suggests low viral load and is reassuring, but as illustrated here Ct values can fluctuate thus making it difficult to predict a negative PCR on subsequent tests. Nonetheless our patient consistently had Ct > 24 after day 29 suggesting non-infectious viral shedding. Her immunocompromised status (kidney transplant), receipt of rituximab 6 months prior, and hypogammaglobulinemia with a failure to mount an immune response likely contributed to prolonged shedding.

CONFLICT OF INTEREST

None.

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