CASE REPORT

One-year persistence of neutralizing anti-SARS-CoV-2 antibodies in dialysis patients recovered from COVID-19

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Abstract

The immunological mechanisms that modulate immune response to SARS-CoV-2 infection remain elusive. Little is known on the magnitude and the durability of antibody response against COVID-19. There is consensus that patients with immune dysfunction, such as dialysis patients, may be unable to mount a robust and durable humoral immunity after infections. Recent studies showed that dialysis patients seroconverted after COVID-19, but data on the durability of the immune response are missing. We reported the data of a durable anti-spike protein seroconversion after natural SARS-CoV-2 infection in three patients on hemodialysis with a mean age of 67.2 ± 13.8 years. A mean antibody titer of 212.6 ± 174.9 UA/ml (Liaison®, DiaSorin) was found after one year (range, 366-374 days) from the diagnosis of COVID-19. In conclusion, this case series provided evidence that patients

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receiving hemodialysis who recovered from severe COVID-19 were able to mount a long-lasting immune response against SARS-CoV-2. Although the protective capacity of this long-term immunity remains to be determined, these patients did not report signs of reinfection after recovery from COVID-19.

KEYWORDS

antibody, COVID-19, dialysis, immunity, Sars-CoV-2, vaccine

INTRODUCTION

It is still unclear which immune mechanisms modulate magnitude and duration of the humoral response in patients who contract COVID-19. This issue became even more challenging in maintenance dialysis patients who are considered as immunocompromised¹ with lower rates of seroconversion to vaccinations.² Recent evidence shows that most of the hemodialysis patients (95%) are able to seroconvert³ and mount a robust antibody response⁴ but data on the long-term persistence of protecting antibodies are missing.⁵ Here, we report a case series of three patients on dialysis with a durable anti-spike protein seroconversion after natural SARS-CoV-2 infection.

RESULTS

Two patients on hemodialysis and one on peritoneal dialysis contracted COVID-19 during the first wave in March 2020. The diagnosis of COVID-19 was confirmed by a qualitative polymerase-chain-reaction assay. Mean age was 67.2 ± 13.8 years. All three patients need hospitalization for severe symptoms of COVID-19 manifesting principally with fever (100%), dyspnea (66.6%) and hypoxemia (66.6%). Lung involvement was detected in all three patients and multifocal areas of consolidation were found in two of them. The average hospitalization lasted 22.6 ± 14.5 days and nobody required intensive care for worsening of the symptoms associated with COVID-19. One patient on peritoneal dialysis was switched to hemodialysis via a central vein catheter for failure of peritoneal ultrafiltration. After discharge, this group of patients continued to receive appropriate dialysis therapy in a separated room until the detection of two negative nasopharyngeal swabs for SARS-CoV-2. On average, SARS-CoV-2 RNA shedding was measured for 44.6 \pm 26.1 days; in one patient viral genetic material was detected for 74 days from the diagnosis of COVID-19 and 79 from symptoms onset.⁶ After the clearance of the virus, no cases of COVID-19

DISCUSSION

Dialysis patients are known to be susceptible to many major infections, which impact patient survival. There is a prevailing belief that this group of patients has an impaired immune response to foreign antigens. A blunted immune response is indeed seen after some vaccination cycle (e.g., influenza, HBV), especially in elderly subjects. As a result, adapted immunization protocols with larger doses are often required to effectively seroconvert this population.

Because of the aforementioned issues, the nephrology community is uncertain whether hemodialysis patients can maintain a durable seroconversion after SARS-CoV-2 infection.5 This case series showed that SARS-CoV-2 infection provided long-lasting humoral immunity in three patients undergoing maintenance dialysis. Hence, our data confirm the recent encouraging findings on the protective immunity against COVID-19, showing that natural infection induces robust memory B-cell response lasting at least 8 months in the general population. However, work is still needed to ascertain if antibodies against SARS-CoV-2 are able to protect from severe COVID-19. This is issue is particularly relevant for hemodialysis patients that have a low level of antibodies as in our case #2. Emerging evidence suggests that neutralizing antibodies after SARS-CoV-2 infection are associated with protection against reinfection, 8 notably, the presence of anti-spike or anti-nucleocapsid IgG antibodies portends a substantially lower risk of reinfection in the following 6 months from the primary infection.9

TABLE 1 Demographic and clinical characteristics of COVID-19 patients

	Case #1	Case #2	Case #3
Age (year)	72.7	77.5	51.5
Sex	M	F	M
BMI	26.4	27.3	30.1
Dialysis modality	PD/HDF [*]	HDF	HDF
Dialysis vintage (year)	2.2	11.2	5.7
No. of comorbidities	3	2	5
Symptoms			
Fever	Yes	Yes	Yes
Cough	Yes	Yes	No
Dyspnea	Yes	Yes	No
Diarrhea	Yes	No	No
Myalgia	No	No	Yes
Radiological findings of pneumonia	Yes	Yes	Yes
MAP (mmHg)	80	73.3	101.6
PO ₂ (mmHg)	43	63.9	73.5
Nadir PO ₂ (mmHg)	43	60	54.9
Hospitalization	Yes	Yes	Yes
Duration of hospitalization (days)	9	21	38
Days from symptoms to hospitalization	0	3	2
Therapy			
Oxygen therapy	Yes	Yes	Yes
Hydroxychloroquine	No	Yes	Yes
Darunavir/cobicistat	No	Yes	No
Tocilizumab	No	No	Yes
Heparin	No	Yes	No
RNA Shedding from COVID-19 diagnosis (days)	74	24	36
Last Ab titer of IgG anti-Spike (UA/ml)	376	28	234
Time elapsed from COVID-19 to Ab detection (days)	374	369	366

Abbreviations: Ab, antibody; BMI, body mass index; HDF, hemodiafiltration; MAP, mean arterial pressure; PD, peritoneal dialysis.

However, many variable can affect immune response against SARS-CoV-2 infection. We suppose that multiple determinants including nonmodifiable (sex, age, ethnicity) and clinical (illness severity, dialysis vintage, comorbidities, immune dysfunction) factors and socioeconomic status play a key role in the kinetics of humoral response in dialysis patients and may determine the basis of a heterogeneous antibody production. While awaiting data from ongoing observational studies, durable humoral immunity should be considered a good sign for vaccination policy¹⁰ and the future course of the COVID-19 pandemic in this group of vulnerable patients.

ACKNOWLEDGMENTS

We thank physicians and nurses of the Dialysis Unit of Modena for their praiseworthy work during the COVID-19 pandemic.

CONFLICT OF INTEREST

All the authors declared no competing interest.

ETHICS STATEMENT

This study has been authorized by the local Ethical Committee of Emilia Romagna (protocol number: AOU 0010159/20-0021170/20). The study was conducted in accordance with the Helsinki Declaration.

^{*} The patient switched from PD to HDF 29 days after COVID-19 diagnosis.

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REFERENCES

- Danese MD, Griffiths RI, Dylan M, Yu H-T, Dubois R, Nissenson AR. Mortality differences among organisms causing septicemia in hemodialysis patients. Hemodial Int. 2006;10: 56–62. https://doi.org/10.1111/j.1542-4758.2006.01175.x
- Krueger KM, Ison MG, Ghossein C. Practical guide to vaccination in all stages of CKD, including patients treated by dialysis or kidney transplantation. Am J Kidney Dis Off J Natl Kidney Found. 2020;75:417–25. https://doi.org/10.1053/j.ajkd.2019. 06.014
- 3. McCafferty K, Davari M, Price K, Rajakariar R, Cove-Smith A, Forbes SH. COVID-19 prevalence and seroconversion in an urban hemodialysis unit in the United Kingdom. Hemodial Int. 2021;25:137–9. https://doi.org/10.1111/hdi.12883
- Forbes S, Davari M, Gnanasampanthan S, Roth N, Young G, Rajakariar R, et al. Persistence of antibody response to SARS-CoV-2 in a cohort of haemodialysis patients with COVID-19. Nephrol Dial Transplant. 2021;gfab066https://doi.org/10.1093/ ndt/gfab066
- Alcázar-Arroyo R, Portolés J, López-Sánchez P, Zalamea F, Furaz K, Méndez Á, et al. Rapid decline of anti-SARS-COV-2 antibodies in patients on hemodialysis. The COVID-FRIAT study. Clin Kidney J. 2021;sfab048. https://doi.org/10.1093/ ckj/sfab048
- Alfano G, Perrone R, Fontana F, Mori G, Lucchi L, Guaraldi G, et al. Long-term effects of COVID-19 in a patient

- on maintenance dialysis. Hemodial Int. 2020;24:E50–4. https://doi.org/10.1111/hdi.12859
- Dan JM, Mateus J, Kato Y, Hastie KM, Yu ED, Faliti CE, et al. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science. 2021;6:eabf4063. https://doi. org/10.1126/science.abf4063
- Hanrath AT, Payne BAI, Duncan CJA. Prior SARS-CoV-2 infection is associated with protection against symptomatic reinfection. J Infect. 2020;26:e29–30. https://doi.org/10.1016/j. jinf.2020.12.023
- Lumley SF, O'Donnell D, Stoesser NE, Matthews PC, Howarth A, Hatch SB, et al. Antibody status and incidence of SARS-CoV-2 infection in health care workers. N Engl J Med. 2021;384:533–40. https://doi.org/10.1056/NEJMoa2034545
- Combe C, Kirsch AH, Alfano G, Luyckx VA, Shroff R, Kanbay M, et al. At least 156 reasons to prioritise COVID-19 vaccination in patients receiving in-centre haemodialysis. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2021;20:571–4. https://doi.org/10.1093/ndt/gfab007

How to cite this article: Alfano G, Fontana F, Morisi N, et al. One-year persistence of neutralizing anti-SARS-CoV-2 antibodies in dialysis patients recovered from COVID-19. Hemodialysis International. 2021;25:E53–E56. https://doi.org/10.1111/hdi.12963