IDCases 22 (2020) e00943

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case report

COVID-19 in a patient with end-stage renal disease on chronic in-center hemodialysis after evidence of SARS-CoV-2 IgG antibodies. Reinfection or inaccuracy of antibody testing

Jair Munoz Mendoza[a], Maria L. Alcaide[b,*]

[a] 1120 NW 14th St. Suite 809, Katz Family Division of Nephrology, Department of Medicine, University of Miami Miller School of Medicine, Miami, FL, USA
[b] 1120 NW 14th St. Suite 849, Division of Infectious Diseases, Department of Medicine, University of Miami Miller School of Medicine, Miami, FL, 33136, USA

ARTICLE INFO

Article history:
Received 10 August 2020
Received in revised form 25 August 2020
Accepted 29 August 2020

Keywords:
COVID-19
Reinfection
ESRD
SARS-CoV-2 antibodies

ABSTRACT

A patient with end-stage renal disease on hemodialysis with a previous positive SARS-CoV-2 IgG antibody was diagnosed with severe COVID-19. Issues regarding reinfection, the potential lack of antibody protection after asymptomatic infection, the possibility of antibody dependent enhancement and careful interpretation of antibody test results are discussed.

Introduction

The coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has quickly reached pandemic status since the first case was reported in Wuhan, China, and caused over 15 million infections and half a million deaths worldwide [1]. Antibody testing to SARS-CoV-2 either by Enzyme-Linked Immuno-Sorbent Assay (ELISA) or Chemi-Luminescent Immuno Assay (CLIA) are highly sensitive and specific and may indicate prior infection when the clinical suspicious is high [2]. A recent nationwide prevalence study using serological testing, revealed rates as high as 13 % (one third of them asymptomatic) in highly hit areas of Spain [3], and studies in the US showed rates ranging from 1% to 6.9 % [4].

Patients with end-stage renal disease (ESRD) on hemodialysis are at high risk of acquiring SARS-CoV-2, and of developing severe COVID-19 and death [5,6], but whether positive serological testing conveys protection against future infection in this population is unknown. Herein, we report a case of COVID-19 in a patient with a prior detection of SARS-CoV-2 IgG antibodies and discuss issues concerning re-infection with SARS-CoV-2, the potential lack of antibody protection after asymptomatic infection, antibody dependent enhancement and caution for careful interpretation of antibody test results.

Case

A 51-year-old African American male with a history of hypertension and ESRD due to acute tubular necrosis, undergoing chronic hemodialysis thrice weekly, presented to the emergency department in a Hospital in Miami (FL) complaining of fever (38.3 °C) and severe dyspnea for two days. Upon arrival he was in severe respiratory distress, with a respiratory rate of 40 breaths/minute, and an oxygen saturation of 40 %. He was afebrile, and hemodynamically stable (blood pressure of 134/48 mmHg and heart rate 74 beats/minute). On physical examination, his heart had a regular rate and rhythm, and bilateral basal crackles were heard on the lungs. His Chest X-ray revealed diffuse bilateral alveolar opacities. Complete blood count revealed normal white blood cells (6400/mcl: neutrophils 8·9%, lymphocytes 13·1%), anemia with hemoglobin 10·4 g/dL; and platelets 250,000/mcl. Chemistry was consistent with ESRD (creatinine 18·2 mg/dL, and blood urea nitrogen 96 mg/dL). A nasopharyngeal swab for SARS-CoV-2 by real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay was positive, confirming the diagnosis of COVID-19. He was admitted to the medical intensive care unit, placed on non-invasive positive pressure mechanical ventilation, and received emergent hemodialysis. He was started on dexamethasone 6 mg intravenously (IV) daily, and remdesivir 200 mg IV once, followed by 100 mg daily for 5 days. Inflammatory markers were elevated

* Corresponding author.
E-mail addresses: jmmendoza@med.miami.edu (J. Munoz Mendoza), malcaide@med.miami.edu (M.L. Alcaide).

https://doi.org/10.1016/j.idcr.2020.e00943

(C-reactive protein > 45 mg/dL, LDH 1954 units/L and Ferritin 7162 ng/mL), and decreased during hospitalization (at day 7: C-reactive protein 17·5 mg/dL, LDH 835 units/L and Ferritin 2561 ng/mL). He received daily hemodialysis and erythropoietin thrice weekly. He was transferred to a medical ward at day 6 when his clinical status improved and was discharged home on day 10.

Two months prior, he was tested for SARS-CoV-2 by RT-PCR on nasopharyngeal swabs, and by serological testing measuring antibodies against the SARS-CoV-2 spike (S) and nucleocapsid proteins (N) using indirect chemiluminescence immunoassay (Diazyme Laboratories, Inc). SARS-CoV-2 IgG antibody was positive (11·87 Arbitrary Units or AU/mL) (a test is considered positive when results are $\geq$ 1·00 AU/mL). SAR-CoV-2 IgM antibody was negative (0·35 AU/mL) and SAR-CoV-2 RT-PCR was negative. At the time of testing, patients attended the same dialysis unit tested positive for SARS-CoV-2 by PCR. He reported not having any COVID-19 related symptoms or known exposure to SARS-CoV-2, but patients attending the same dialysis unit tested positive for SARS-CoV-2 by RT-PCR. During the hospitalization with COVID-19, SARS-CoV-2 IgG antibody was positive (17·9 s/co ratio) and SARS-CoV-2 Total (IgG, IgM and IgA) antibodies were positive (190·0 s/co ratio) (Ortho-Clinical Diagnostics, Inc).

Discussion

We describe a case of severe COVID-19 in a patient with ESRD undergoing chronic in-center hemodialysis, who had previously tested positive for IgG antibody against SARS-CoV-2. A reinfection with SARS-CoV-2 presenting as a severe COVID-19 disease after an asymptomatic primary infection is the most probable explanation. Although the likelihood of an initial false positive antibody testing is a consideration, it is less likely as the patient was at high risk for SARS-CoV-2 acquisition while living in a city experiencing the first surge of COVID-19 cases, getting in-center dialysis prior to implementation of strict infection control measures, and where patients were already diagnosed with COVID-19.

Reinfections with other common human coronaviruses can occur [7], while reinfection with SARS-COV-2 in humans is likely to occur [8], how often would that happen is yet unknown. Some patients have persistent detection of SARS-CoV-2 RNA for over a month [9], and re-appearance of SARS-CoV-2 in nasopharyngeal secretions after negative RT-PCR was reported in patients recovered from COVID-19 in China, but it was considered false negative results [10]. The potential development of protective immunity after a primary infection in monkeys re-infected with the same identical SARS-CoV-2 strain would suggest that reinfections with SARS-CoV-2 do not occur [11]. However, few cases with recurrent COVID-19 suggesting reinfection with SARS-CoV-2 were recently reported [8,12], and recent findings in humans suggests that protective immunity does not occur in all infected individuals [13], supporting the possibility of reinfection in our patient.

Seroconversion of IgM and IgG antibodies occur the first week after onset of symptoms, seroconversion rates rise until the fourth week and decline thereafter, by the seventh week Ig M is not detected in most cases, whereas IgG persists longer for a period of time yet unknown [14]. Development and duration of antibody response to SARS-CoV-2 infection in patients with ESRD undergoing hemodialysis is lacking, and whether it is similar to individuals in the general population or have a different course such as noted in other chronic conditions is unknown [15,16].

For most respiratory viruses, reinfections present with similar or milder symptoms. However, the worse clinical picture seen in this patient with COVID-19 after a prior asymptomatic infection may be the result of developing antibody dependent enhancement (ADE) [17]. ADE is important to consider as re-exposures to SARS-CoV-2 are very likely in future waves, and in evaluating the safety of potential candidate vaccines against SARS-CoV-2.

Although we believe this is a case of re-infection, we cannot rule out with certainty that the first positive serological testing represents a false positive test or cross reactivity with another coronavirus. Common antibody targets such as S and N proteins used in commercially available serological testing have around 30 % similarity with other common coronavirus [18]. We can't neither exclude the possibility of recurrence as recently suggested [19], since we lack data on the strain of the virus. Future longitudinal studies are needed to evaluate potential reinfections, recurrence, and the duration of antibody detection.

In summary, we present a case of an ESRD patient with a positive IgG antibody test against SARS-CoV-2 that subsequently developed severe COVID-19. This case presents the possibility of reinfection with SARS-CoV-2, the potential lack of antibody protection after asymptomatic infection, and the prospect of antibody dependent enhancement. In addition, it highlights the need for careful interpretation of antibody test results until further understanding of the risk of reinfection and antibody responses are available.

Funding

This work was supported by the Miami Center for AIDS Research (CFAR) [Grant number P30AI073961]. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Miami CFAR.

CRediT authorship contribution statement

Jair Munoz Mendoza: Writing - original draft, Writing - review & editing, Conceptualization, Visualization. **Maria L. Alcaide:** Writing - review & editing, Conceptualization, Visualization.

Declaration of Competing Interest

The authors report no declarations of interest.

References

[1] Johns Hopkins University Center for Systems Science and Engineering. Coronavirus COVID-19 global cases. 2020 Available from: https://coronavirus.jhu.edu/us-map. (Accessed 2 July 2020).
[2] Caturegli G, Materi J, Howard BM, Caturegli P. Clinical validity of serum antibodies to SARS-CoV-2: a case-control study. Ann Intern Med 2020, doi:http://dx.doi.org/10.7326/M20-2889 Online ahead of print.
[3] Pollan M, Perez-Gomez B, Pastor-Barriuso R, Oteo J, Hernan MA, Perez-Olmeda M, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet 2020;535–44.
[4] Havers FP, Reed C, Lim T, Montgomery JM, Klena JD, Hall AJ, et al. Seroprevalence of antibodies to SARS-CoV-2 in 10 sites in the United States, March 23-May 12, 2020. JAMA Intern Med 2020, doi:http://dx.doi.org/10.1001/jamainternmed.2020.4130 Online ahead of print.
[5] Valeri AM, Robbins-Juarez SY, Stevens JS, Ahn W, Rao MK, Radhakrishnan J, et al. Presentation and outcomes of patients with ESKD and COVID-19. J Am Soc Nephrol 2020;31(7):1409–15, doi:http://dx.doi.org/10.1681/ASN.2020040470.
[6] Corbett RW, Blakey S, Nitsch D, Loucaidou M, McLean A, Duncan N, et al. Epidemiology of COVID-19 in an urban dialysis center. J Am Soc Nephrol 2020;1815–23, doi:http://dx.doi.org/10.1681/ASN.2020040534.
[7] Brooks JT. COVID-19 and postinfection immunity: limited evidence, many remaining questions. JAMA 2020;2245–6.
[8] Batisse D, Benech N, Botelho-Nevers E, Bouiller K, Collarino R, Conrad A, et al. Clinical recurrences of COVID-19 symptoms after recovery: viral relapse, reinfection or inflammatory rebound? J Infect 2020, doi:http://dx.doi.org/10.1016/j.jinf.2020.06.073.
[9] Gombar S, Chang M, Hogan CA, Zehnder J, Boyd S, Pinsky BA, et al. Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19. J Clin Virol 2020104477.
[10] Xiao AT, Tong YX, Zhang S. False negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: rather than recurrence. J Med Virol 2020, doi:http://dx.doi.org/10.1002/jmv.25855.

[11] Bao L, Deng W, Gao H, Xiao C, Liu J, Xue J, et al. Reinfection could not occur in SARS-CoV-2 infected rhesus macaques. 2020 2020.03.13.990226.
[12] Duggan NM, Ludy SM, Shannon BC, Reisner AT, Wilcox SR. A case report of possible novel coronavirus 2019 reinfection. Am J Emerg Med 2020, doi:http://dx.doi.org/10.1016/j.ajem.2020.06.079 [Epub ahead of print].
[13] Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clin Infect Dis 2020, doi:http://dx.doi.org/10.1093/cid/ciaa344 Online ahead of print.
[14] Sethuraman N, Jeremiah SS, Ryo A. Interpreting diagnostic tests for SARS-CoV-2. JAMA 2020;2249–51, doi:http://dx.doi.org/10.1001/jama.2020.8259.
[15] Zhao J, Liao X, Wang H, Wei L, Xing M, Liu L, et al. Early virus clearance and delayed antibody response in a case of COVID-19 with a history of co-infection with HIV-1 and HCV. Clin Infect Dis 2020, doi:http://dx.doi.org/10.1093/cid/ciaa408 Online ahead of print.
[16] Ibarrondo FJ, Fulcher JA, Goodman-Meza D, Elliott J, Hofmann C, Hausner MA, et al. Rapid decay of anti-SARS-CoV-2 antibodies in persons with mild Covid-19. N Engl J Med 2020;1085–7, doi:http://dx.doi.org/10.1056/NEJMc2025179.
[17] Ulrich H, Pillat MM, Tarnok A. Dengue fever, COVID-19 (SARS-CoV-2), and antibody-dependent enhancement (ADE): a perspective. Cytometry A 2020;(10):1002, doi:http://dx.doi.org/10.1002/cyto.a.24047.
[18] Theel ES, Slev P, Wheeler S, Couturier MR, Wong SJ, Kadkhoda K. The role of antibody testing for SARS-CoV-2: is there one? J Clin Microbiol 2020, doi:http://dx.doi.org/10.1128/JCM.00797-20.
[19] Lafaie L, Célarier T, Goethals L, Pozzetto B, Sylvain G, Ojardias E, et al. Recurrence or relapse of COVID-19 in older patients: a description of three cases. J Am Geriatr Soc 2020, doi:http://dx.doi.org/10.1111/jgs.16728 Online ahead of print.