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.

Medicina Intensiva 45 (2021) 375–380

medicina intensiva

http://www.medintensiva.org/en/

SCIENTIFIC LETTER

SARS-CoV-2 reinfection☆

Reinfección por SARS-CoV-2

To the Editor,

Every new SARS-CoV-2 infection opens a whole new world of doubts and questions on possible reinfections and possible clinical signs.

We present the case of a 78-year-old male with diabetes mellitus type II, dyslipidemia, hyperuricemia, and a pulmonary node under periodic monitoring treated in his home with atorvastatin, alopurinol, and tamsulosin. By the end of 2020 the patient was showing signs of low-grade fever, rhinorrhea, unproductive cough, and general discomfort. No signs of ageusia, anosmia or diarrhea were found. A serologic test was run on May 15, 2020 using the enzyme-linked immunoassay ELISA for SARS-CoV-2 with the following results: IgM < 2.3 AU/mL (10—12 AU/mL), and IgG 26.67 AU /mL (10—12 AU/mL).

On October 17th, 2020 the patient started showing signs of odynophagia, diarrhea, and poor health complicated with respiratory failure 1 week later. The thoracic X-ray performed confirmed the presence of peripheral bilateral infiltrates compatible with bilateral pneumonia due to COVID-19. The blood test results revealed D-dimer levels of 741 ng/mL (0—250 ng/mL), serum ferritin levels >2000 ng/mL (25—360 ng/mL), IL-6 levels of 21.87 pg/mL (0.01—7 pg/mL), PCR levels of 130 mg/L (0—3 mg/l), procalcitonin levels of 0.21 pg/mL (0.01—0.5 pg/mL), and troponin-I levels of 44 pg/mL (0—39.2 pg/mL). The antigen and PCR tests run for SARS-CoV-2 with nasopharyngeal swabs tested positive, but the Chemiluminescent Microparticle Immuno Assay (CMIA) found no antibodies (index IgM levels of 0.13 (positive if > 1.0); index IgG levels of 0.40 (positive if > 1.4). The patients required ICU admission for ventilatory support combining non-invasive mechanical ventilation and high-flow oxygen therapy. The patient's progression was slow, but he met no criteria for orotracheal intubation. The patient received a 5-day course of remdesivir, 2 doses of 600 mg of tocilizumab followed by methylprednisolone at 1 mg/kg/day. The patient was discharged from the ICU 12 days after admission and then received home discharge. The new serologic test performed tested positive for the following antibodies: index IgM levels of 27.63 (positive if > 1.0), and index IgG levels of 3.30 (positive if > 1.4).

We still have much to learn about SARS-CoV-2 reinfections. As a matter of fact, we don't even have an established definition. The medical literature includes case reports and the experience of different centers across the world with series showing rates of reinfection that go from 3% to 31%.[1] Most studies define reinfection as the findings of viral RNA after testing negative to 2 PCR consecutive tests. This definition implies not knowing what the level of protection against the virus from the immune system really is; what is the duration of prophylactic immunity; and how difficult it is to distinguish the detection of nonviable virus from viral reactivation and from reinfection by a different variant of the virus.

Seasonal coronaviruses like SARS-CoV and MERS-CoV share clinical, genetic, and epidemiological characteristics with SARS-CoV-2. Therefore, their study should help understand better what our immune response against this virus will be.[2] We do know that seasonal coronaviruses create a short protective immunity, above all, in cases of mild or asymptomatic disease,[3,4] with progressive reduction of antibody titers during convalescence (an average 39 days since symptom onset).[5] However, some studies published have found active antibodies against SARS-CoV 2 years after infection and even neutralizing antibodies 17 years after infection in a patient from Singapor.[1]

The level of protection of the immune system against SARS-CoV-2 reinfection is unknown too. According to several studies, most antibodies produced against SARS-CoV-2 are not neutralizing. However, after SARS-CoV-2 reinfection the antibody response is faster and, in this case, actually neutralizing.[6] It has been suggested that the presence of IgM has a diagnostic use in the acute phase of reinfection, but its absence does not exclude it.[6] Regarding severity, our patient experienced a second episode that was more severe. This has also been described by other authors.[1] However, the factors that determine the severity of reinfections is still unknown.[7,8]

On the other hand, it is striking to see that there are 2 key factors in the development of new SARS-CoV-2 reinfections: the circulation of different variants, and the mutant capabilities of the virus. To this date, several cases of infection due to different SARS-CoV-2 variants have been reported. Genome sequencing is essential here to distinguish viral reinfection from viral reactivation.[5] However, the fast evolution of the pandemic and the lack of protocolized genome sequencing of positive cases not only limits health monitoring but also the definition and detection of the cases of reinfection.[7] In this sense, animal models are being developed[9] to know the mechanism of primary infection, reactivation, and reinfection due to SARS-CoV-2.

Consequently, we should mention the importance of learning about the pathophysiology of reinfection in the development and applicability of vaccines. Therefore, it will be necessary to distinguish different epitopes to optimize the antibody effector function or improve the cellular response,[5,8,10] and the possibility of administering several doses of the vaccines.[11]

In conclusion, the SARS-CoV-2 pandemic has been surrounded by a shroud of uncertainty from day one. Reinfections may be more common than we think taking into account how difficult they are to define and diagnose. As more studies become available, we will have more solid evidence on the duration of immunity, cross-protection against seasonal coronaviruses, and the potential risk of reinfection.

☆ Please cite this article as: Romera I, Núñez K, Calizaya M, Baeza I, Molina R, Morillas J. Reinfección por SARS-CoV-2. Med Intensiva. 2021;45:375–376.

Funding

None.

References

1. Murchu EO, Byrne P, Walsh KA, Carty PG, Connolly M, de Gascun C, et al. Immune response following infection with SARS-CoV -2 and other coronaviruses: a rapid review. Rev Med Virol. 2020. Available from: https://onlinelibrary.wiley.com/doi/10.1002/rmv.2162. [Accessed 7 November 2020].
2. González-Castro A, Escudero-Acha P, Peñasco Y, Leizaola O, Martínez de Pinillos Sánchez V, García de Lorenzo A. Cuidados intensivos durante la epidemia de coronavirus 2019. Med Intensiva. 2020;44:351–62.
3. Edridge AWD, Kaczorowska J, Hoste ACR, Bakker M, Klein M, Loens K, et al. Seasonal coronavirus protective immunity is short-lasting. Nat Med. 2020. Available from: http://www.nature.com/articles/s41591-020-1083-1. [Accessed 7 November 2020].
4. Long Q-X, Tang X-J, Shi Q-L, Li Q, Deng H-J, Yuan J, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med. 2020;26:1200–4.
5. To KK, Hung IF, Ip JD, Chu WH, Chan WM, Tam AR, et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. Clin Infect Dis. 2020, http://dx.doi.org/10.1093/cid/ciaa1275.
6. Seydoux E, Homad LJ, MacCamy AJ, Parks KR, Hurlburt NK, Jennewein MF, et al. Analysis of a SARS-CoV-2-infected individual reveals development of potent neutralizing antibodies with limited somatic mutation. Immunity. 2020;53, 98.e5–105.e5.
7. Tillett RL, Sevinsky JR, Hartley PD, Kerwin H, Crawford N, Gorzalski A, et al. Genomic evidence for reinfection with SARS-CoV-2: a case study. Lancet Infect Dis. 2020. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1473309920307647. [Accessed 7 November 2020].
8. Velikova TV, Kotsev SV, Georgiev DS, Batselova HM. Immunological aspects of COVID-19: what do we know? World J Biol Chem. 2020;11:14–29.
9. Chandrashekar A, Liu J, Martinot AJ, McMahan K, Mercado NB, Peter L, et al. SARS-CoV-2 infection protects against rechallenge in rhesus macaques. Science. 2020;369:812–7.
10. Overbaugh J. Understanding protection from SARS-CoV-2 by studying reinfection. Nat Med. 2020:1–2.
11. To KKW, Hung IFN, Chan KH, Yuan S, To WK, Tsang DNC, et al. Serum antibody profile of a patient with coronavirus disease 2019 reinfection. Clin Infect Dis. 2020, http://dx.doi.org/10.1093/cid/ciaa1368.

I. Romera*, K. Núñez, M. Calizaya, I. Baeza, R. Molina, J. Morillas

Servicio de Medicina Intensiva, SCIAS Hospital de Barcelona, Barcelona, Spain

* Corresponding author.
E-mail address: irene.r.s@outlook.com (I. Romera).

Combination of airway pressure release ventilation with inverted inspiration-exhalation ratio and low-flow CO_2 removal devices with renal replacement therapy in refractory hypoxemia☆

Combinación de la ventilación con liberación de presión con la relación inspiración-espiración invertida y los dispositivos de eliminación de CO_2 de bajo flujo con terapia de sustitución renal en la hipoxemia refractaria

Dear Editor,

Acute respiratory failure which under pneumoprotective measures persistently maintains PaO_2/FiO_2 < 100 or a plateau P > 30 cmH_2O can be classified as refractory hypoxemia. The different therapeutic strategies under such circumstances include the combination of pressure-controlled ventilation and the inverted inspiration-exhalation ratio (inverted I:E): airway pressure release ventilation (APRV).[1]

We present a series of three cases of refractory hypoxemia in which APRV was applied in combination with a low-flow CO_2 removal device with renal replacement therapy ($ECCO_2R$-RRT). Table 1 details the clinical-epidemiological and evolutive characteristics of the three cases.

The first case in which both therapies were combined corresponded to a 75-year-old male admitted to the Intensive Care Unit (ICU) due to sepsis of respiratory origin. The patient developed severe acute respiratory distress syndrome (ARDS) secondary to nosocomial pneumonia, and mechanical ventilation was started. Anuric renal failure was diagnosed and renal replacement therapy (RRT) was decided. After 9 h of protective ventilation, and due to the persistence of refractory hypoxemia, we introduced APRV followed by $ECCO_2R$-RRT. The patient was discharged after 40 days in the ICU.

The second case corresponded to a patient admitted to the ICU with a diagnosis of possibly progressing multiple myeloma with established renal failure and severe respiratory failure secondary to community-acquired pneumonia. Upon admission to intensive care, mechanical ventilation was started and pneumoprotective measures were adopted, together with RRT. In view of the failure of these measures and the rapid progression of the clinical condition, combined therapy with APRV and $ECCO_2R$-RRT was started. Despite initial improvement, however, the patient died of hypoxia in the following 12 h.

The third case corresponded to an episode of respiratory failure of uncertain origin in a woman who had been treated with cetuximab due to a tumor of the floor of the mouth. She had undergone blood product transfusion 24 h before developing rapidly evolving severe ARDS. The patient was admitted to the ICU due to respiratory failure that progressed with multiorgan failure and anuric acute respiratory failure. In this case, $ECCO_2R$ was started 24 h before switching the ventilatory mode

☆ Please cite this article as: González-Castro A, Escudero Acha P, Rodríguez Borregán JC, Peñasco Y, Blanco Huelga C, Cuenca Fito E. Combinación de la ventilación con liberación de presión con la relación inspiración-espiración invertida y los dispositivos de eliminación de CO_2 de bajo flujo con terapia de sustitución renal en la hipoxemia refractaria. Med Intensiva. 2021;45:376–379.