Post-COVID-19 Syndrome (PC19S): Chronic Reactive Endotheliitis and Disseminated Vascular Disease

Síndrome Pós-COVID-19 (PC19S): Endotelite Reactiva Crónica e Doença Vascular Disseminada

Keywords: Coronavirus Infections/complications; COVID-19; Pneumonia, Viral; SARS-CoV-2
Palavras-chave: COVID-19; Infecções por Coronavírus/complicações; Pneumonia Viral; SARS-CoV-2

To the Editor:

From SARS-CoV-2 there is sufficient evidence to affirm that it is a proinflammatory and prothrombogenic virus which produces active infection of variable duration in various organs and systems (lung, digestive system, central nervous system, skin, etc.).[1] The period of acute infection is estimated between 15 and 30 days, after which immunity of indeterminate duration is generated, and cases of early reinfection cannot be ruled out. However, with increasing frequency, it is observed that patients who have already suffered from the disease, especially in its most severe forms such as bilateral pneumonia or respiratory distress, present symptoms and signs of chronic involvement. The first complete necropsy studies performed show multiple and severe vascular involvement in the lungs, heart (myocarditis, vasculitis, and myocardial cell necrosis), hepatic focal necrosis and infiltrates with neutrophils, and the same occurs in the kidney, with microthrombi and fibrotic areas being observed in the renal interstitium.[2] The degree of endotheliitis is almost imperceptible in light microscopy but sufficiently relevant to produce the well-known symptoms in the various organs and systems. It is also already known that the cytoplasm of endothelial cells, which have AT2 receptors for ACE2 (angiotensin-converting enzyme) is loaded with viral particles that appear as dense circles with a clear center. Both pneumocytes and the vascular endothelium have ACE2 receptors in abundance, which makes these cells particularly vulnerable to the entry of SARS-CoV-2,[3] producing a proinflammatory state (endotheliitis) that would promote the quick appearance of bilateral pulmonary infiltrates that favor adhesion and subsequent platelet aggregation. Ultimately, this leads to a subsequent prothrombotic state in the microcirculation, especially in the lung.

This explains why pulmonary hyperoxygenation with invasive mechanical ventilation (IMV) has so little success in these patients (it is useless to ventilate a poorly perfused lung) and yet extracorporeal membrane oxygenation (ECMO) does manage to improve pulmonary ventilation on many occasions.[4] In those patients who had severe disease but manage to overcome the acute infection, recovery is usually satisfactory and resolves completely without sequelae in most cases. However, in a still unknown but not negligible percentage of cases (estimated around 15%), symptoms suggestive of residual pulmonary fibrosis and even cases of fulminant myocarditis with a severe prognosis have been described. Although the virus has already been eliminated from the body (and that can be demonstrated by repeated negative polymerase chain reaction tests), the proinflammatory and prothrombotic state at the endothelial level in the microvasculature remains in some patients for reasons that are not well known, leading to reactive chronic endotheliitis with disseminated vascular involvement. In turn, this leads, within approximately two months, to pulmonary disease that mimics fibrotic interstitial lung disease but is clearly distinct from classic pulmonary fibrosis,[5] causing autoimmune hyperexcitability of the endothelium that continues after the acute clinical manifestation of the disease and favors a progressive decrease in pulmonary compliance. There is thus an urgent need to prolong immunomodulatory treatment (corticotherapy or tocilizumab) and anticoagulant (with low molecular weight heparin) treatment, at least in the medium term in patients who have suffered severe SARS-CoV-2 infection.

REFERENCES

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054-62.
2. Wichmann D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A, et al. Autopsy findings and venous thromboembolism in patients with COVID-19: a prospective cohort study. Ann Intern Med. 2020;173:268-77.
3. Hussain M, Jabeen N, Raza F, Shabbir S, Baig AA, Amanullah A, et al. Structural variations in human ACE2 may influence its binding with SARS-CoV-2 spike protein. J Med Virol. 2020 (in press). doi: 10.1002/jmv.25832.
4. Matthay MA, Aldrich JM, Gotts JE. Treatment for severe acute respiratory distress syndrome from COVID-19. Lancet Respir Med. 2020;8:433-4.
5. George P, Wells A, Jenkins R. Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy. Lancet Respir Med. 2020;8:807-15.

José LÓPEZ CASTRO✉[1]
1. Internal Medicine Department. Public Hospital of Monforte. Lugo. Spain.
Autor correspondente: José López Castro. jlcastro126@hotmail.com
Recebido: 23 de julho de 2020 - Aceite: 11 de novembro de 2020 | Copyright © Ordem dos Médicos 2020
https://doi.org/10.20344/amp.14612