IS POST-COVID-19 AN IMMUNE DISEASE?

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DEAR EDITOR,

The coronavirus disease 2019 (COVID-19) causes long-term consequences in a large number of patients. Sequels have been identified in several organ systems including pulmonary, cardiac, renal, and central nervous systems. Symptoms can persist after both mild to moderate and severe forms of the disease. According to some studies, about 80% of patients still reported symptoms 12 months after the acute illness (1). An accumulating body of evidence suggests involvement of the immune system in the pathogenesis of this disease. In our unpublished data, two-thirds of acute COVID patients had positive antinuclear (ANA) and anti-neutrophil cytoplasmic (ANCA) antibodies. Patients that tested positive for auto-antibodies had a significantly more severe prognosis. Seeßle *et al*. showed that 43.6% of patients with present post-COVID symptoms had positive ANA titers (1). This phenomenon could be explained by a complex virus-host interaction. It has been shown that there is a homology of primary sequence between humans and components of SARS-CoV-2. Molecular mimicry stimulates the acquired immune system to produce antibodies. Besides, SARS-CoV-2 infection causes immune dysregulation, which may lead to a reduced ability of monocytes/macrophages and dendritic cells to correctly recognize foreign from self-cells, with the possibility of losing self-tolerance towards some self-antigens (2). Autoantibodies previously present in the body at very low levels may be boosted by excessive inflammation. In our opinion, frequently detected ANA and ANCA could be responsible for the pathophysiology of the syndrome. For example, the ANA IIF pattern is often positive in patients with systemic sclerosis (SSc). Lung involvement in SSc has characteristics of interstitial pneumonia, similar to COVID-19 (3). ANCA are associated with the development of small-to-medium-sized vasculitides. As in COVID-19, p*ulmonary vasculitis* is characterized by a reduced diffusion capacity, on computed tomography scans ground-glass opacities and 'crazy paving' patterns could be seen.

Current treatment of post-COVID-19 is based on nonpharmaceutical interventions. Better understanding of the syndrome pathophysiology may enable the application of immunomodulatory drugs.

REFERENCES

1. Seeßle J, Waterboer T, Hippchen T *et al*. Persistent symptoms in adult patients 1 year after coronavirus disease 2019 (COVID-19): a prospective cohort study. Clin Infect Dis 2022; 74: 1191-8.

2. Cañas CA. The triggering of post-COVID-19 autoimmunity phenomena could be associated with both transient immunosuppression and an inappropriate form of immune reconstitution in susceptible individuals. Med Hypotheses 2020; 145: 110345.

3. Orlandi M, Landini N, Sambataro G *et al*. The role of chest CT in deciphering interstitial lung involvement: systemic sclerosis *versus* COVID-19. Rheumatology (Oxford). 2022 Apr 11; 61(4): 1600-9.