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Commentary

Post–COVID-19 chronic symptoms: a postinfectious entity?

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As clinicians working for the Assistance Publique–Hôpitaux de Paris (39 hospitals, 20 000 beds), we admitted numerous patients for a severe coronavirus disease 2019 (COVID-19) during the first wave of the epidemic. On 18 May 2020, Santé Publique France confirmed 142 903 cases of COVID-19, including 61 728 patients who had returned home since 1 March 2020 [1]. In the Paris–Île-de-France area, more than 50 000 outpatients were monitored during 30 days using the Covidom telemedicine platform [2]. During the lockdown from 16 March 2020 until 11 May 2020, numerous symptomatic outpatients could not be tested by PCR and stayed home in compliance with the laws in force.

Surprisingly, today, while we are fearing a second wave, we find ourselves receiving more and more of those outpatients who experienced mild symptoms attributable to COVID-19 such as anosmia and ageusia [3], followed by a short period of convalescence (on the order of few days). Subsequently they complained of a relapse with persistent symptoms, especially myalgia, intense fatigue, sensation of fever, shortness of breath, chest tightness, tachycardia, headaches and anxiety.

Since mid-May (right after the lockdown ended), we now evaluate an average of 30 individuals per week for whom symptoms have not completely subsided, essentially young women (sex ratio 4:1) around 40 years old with no relevant medical history. Interestingly, few of them present biological abnormalities (especially no lymphocytopenia or increased C-reactive protein) and in rare case traces of infection on chest computed tomographic scan. While nasopharyngeal PCR can be still positive even after 30 days of onset symptoms [4], we found no argument for a reinfection when repeating PCR testing. It is more likely a postviral syndrome that requires no specific treatment, as described in Epstein-Barr virus infection [5]. Up to today, and based on preliminary data, only a small proportion of patients who sought care (up to 30%) had a proven history of COVID-19 by PCR amplifying the betacoronavirus E gene and the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) *RdRp* gene on nasopharyngeal swab. By repeating in-hospital serology using the Abbott Architect platform (Abbott Diagnostics, Chicago, IL, USA), the rate can reach up to 50%. Indeed, it has been recently established that serodiagnosis of SARS-CoV-2 using IgG enzyme-linked immunosorbent assay antibodies on the Abbott Architect like the one performed in our centres had a sensitivity of 84.5% (95% confidence interval, 66.5–94.1) 21 days after the onset of symptoms [6], making large-scale screening of patients feasible.

This post–COVID-19 entity is worth addressing because we are facing an unprecedented pandemic, which explains why suddenly patients are all at the same time seeking care for what might otherwise be a banal chronic fatigue syndrome. Although there are discrepancies between the results of the clinical examination and the patients' complaints, the symptoms are compatible with dysautonomia, as previously described in the ALBACOVID registry (2.5%) [7], and should be considered as such. Such a neurologic disorder might be related to microangiopathy and endothelial injury, as already reported in brain biopsy samples of severe COVID-19 [8], and look like a recent late Kawasaki syndrome described after COVID-19 in children [9].

Close to this so-called post–COVID-19 syndrome, a post-chikungunya syndrome was described after the Reunion Island outbreak in 2006, possibly related to an inadequate inflammatory disorder, sometimes with no seroconversion [10]. SARS-CoV-2 could probably play the same role of an immune trigger, as already known in Guillain-Barré syndrome and other autoimmune diseases. Therefore, patients should be tested for antinuclear antibodies and the tests repeated over time after 6 weeks, especially if they are young women with rheumatologic pain, in order to rule out a possible dormant underlying autoimmune disease.

Overall, we believe patients with persistent symptoms (beyond 8 weeks after the onset of COVID-19) should consult their general

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practitioner for a first evaluation, including biological tests with COVID-19 serology, antinuclear antibodies and transthoracic echocardiography to rule out other diagnosis, especially myopericarditis, with a chest computed tomographic scan to assess precisely whether there is any sequelae of COVID-19 and offer reassurance. In case of persistent symptoms beyond 3 months, it could be relevant to investigate deeply the possible relationship between those chronic inflammatory symptoms and COVID-19, and to work hand in hand with other specialists, including a psychologist, a pneumologist, a neurologist and a specialist in physical medicine and rehabilitation. Thereafter, a better understanding of this entity might help the medical community propose an adequate treatment that depends on the acknowledged physiopathology.

Transparency declaration

All authors report no conflicts of interest relevant to this article.

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