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Case Report

Persistent IgG anticardiolipin autoantibodies are associated with post-COVID syndrome

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A B S T R A C T

Persistence of various symptoms in patients who have recovered from coronavirus disease 2019 (COVID-19) was recently defined as 'long COVID' or 'post-COVID syndrome' (PCS). This article reports a case of a 58-year-old woman who, although recovering from COVID-19, had novel and persistent symptoms including neurological complications that could not be explained by any cause other than PCS. In addition to a low inflammatory response, persistence of immunoglobulin G anticardiolipin autoantibody positivity and eosinopenia were found 1 year after acute COVID-19 infection, both of which have been defined previously as independent factors associated with the severity of COVID-19. The pathophysiological mechanism of PCS is unknown, but the possibility of persistence of the virus, especially in the nervous system, could be suggested with a post-infectious inflammatory or autoimmune reaction.

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Introduction

There is increasing evidence for the persistence of various symptoms in patients who have recovered from coronavirus disease 2019 (COVID-19), defined recently as ‘long COVID’ or ‘post-COVID syndrome’ (PCS) (Tenforde et al., 2020). While markers associated with the severity of COVID-19, such as interleukin-6 (IL-6), immunoglobulin G (IgG) anticardiolipin autoantibodies (aCL), eosinopenia and haemogram-derived ratios, have been described in the acute phase of the disease (Bertin et al., 2020; Liang et al., 2020; Lindsey et al., 2020; Zhou et al., 2020), no biological markers have been proposed to date to predict PCS.

Case presentation

Based on 1 year of follow-up, this article reports a case of a 58-year-old woman who, although recovering from COVID-19, had novel and persistent symptoms including neurological complications. COVID-19 was diagnosed in March 2020 on the basis of a positive SARS-CoV-2 reverse transcriptase polymerase chain reaction assay, and this was followed in June 2020 by positive anti-SARS-CoV-2 serology (Table 1). She had asthma, arterial hypertension, insulin-dependent diabetes and overweight in her medical history (body mass index 35.3kg/m2). During the acute phase of COVID-19, the patient presented febrile hypoaemic pneumonia with dyspnoea and cough, and required hospitalization in an intensive care unit without intubation. She was treated with azithromycin, hydroxychloroquine and ceftriaxone for 1 week. At 1 year follow-up, the patient still complained of asthma, one headache a week with insomnia, memory problems related to dysexecutive syndrome, exertional dyspnoea (stage 2 according to the modified Medical Research Council scale), chest pain and digestive disorders (e.g. intermittent diarrhoea, bloating and belching). Her

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scores on neuropsychological tests were 23/30 on the Mini-Mental Score and 14/18 on the Frontal Assessment Battery, and the Word Memorization Test revealed a deficit of information recall without encoding disorder. Cardiological examination showed minimal left ventricular hypertrophy with preserved ejection fraction. Pertinent laboratory data on admission and during follow-up, summarized in Table 1, showed persistent inflammatory biological syndrome with elevated C-reactive protein and fibrinogen, but not IL-6. Interestingly, among the antiphospholipid autoantibodies tested, only IgG aCL was positive and persistent at 1 year follow-up. Light but persistent eosinopenia was also observed. Other biological data were normal. Apart from the headaches, which persisted without a definite aetiology, the clinical examination did not find any clinical sign of antiphospholipid syndrome (absence of skin lesions, renal or cardiac involvement, or thrombosis). The patient had five children, and no known history of miscarriage or thrombosis.

Due to the persistent neurological complaints, the patient’s cerebrospinal fluid (CSF) was analysed and showed normal CSF protein without oligoclonal band or pleocytosis. Cerebral magnetic resonance imaging showed isolated temporal lacunar stroke of old
appearance. Cerebral 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET) scan showed moderate hypometabolism of the amygdala, and mild hypometabolism of the fronto-mesial lobe, insula, brainstem and cerebellum, as described previously in patients with long COVID (Guedj et al., 2021). Whole-body 18F-FDG-PET scan did not show any systemic pathological hypermetabolism.

**Discussion**

To date, most clinical studies of COVID-19 have focused on symptoms during the acute phase of disease. Patients mainly present with fever (≥38°C), cough, chest pain, dyspnoea, diarrhoea, fatigue or myalgia, and approximately 15% of cases develop acute respiratory distress syndrome or end-organ failure. Recently, PCS has been described in patients who exhibit at least one persistent symptom, 12 weeks after disease onset, which cannot be explained by another cause (Tenforde et al., 2020). This syndrome seems to be common after acute COVID-19 infection, and not only among severe cases. The most common signs of this clinical picture are persistent fatigue, dyspnoea, anosmia and memory complaints. In the study case, neurological complications have been evidenced that cannot be explained by any cause other than PCS. In addition to a low-grade inflammatory process, the persistence of IgG aCL positivity and eosinopenia 1 year after acute COVID-19 infection were noted, and both have been defined previously as independent factors associated with disease severity. As such, they could be biological predictors of PCS. Positive aCL has been reported in 13.9% of patients with COVID-19 (Taha et al., 2021) and >50% of cases with severe COVID-19, whereas the prevalence of aCL was only 1.5% in the general population (Selmi et al., 2020). At present, the prevalence of aCL in patients post-COVID and the pathophysiological mechanism involved in PCS remain unknown, but the following hypotheses have been suggested: (1) persistence of the virus, especially in the nervous system; (2) a post-infectious inflammatory or autoimmune reaction; or (3) microglial involvement (Matschke et al., 2020). aCL could be associated with viral infections and may have persistent pro-inflammatory effects in this context, as described recently (Müller-Calleja et al., 2021).

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