To the Editor,

Post-acute Coronavirus Disease of 2019 (COVID-19) syndrome is defined as the appearance of symptoms or an organ dysfunction, which occurs at least 4 weeks after the first COVID-19 manifestations and cannot be explained by any alternative diagnosis [1]. Neurological complications are also well recognized, and include acute cerebrovascular events, encephalopathy, meningoencephalitis, Guillain–Barre syndrome, demyelination, dementia, parkinsonism, and others [2]. On the other hand, cerebral vasculitis is one of the causes which can lead to brain damage related to COVID-19 infection [3]. We present a 69-year-old male with systemic vasculitis and central nervous system (CNS) involvement as a manifestation of post-acute COVID-19 syndrome.

Our patient is a 69-year-old male, with a history for arterial hypertension and type 2 diabetes mellitus. In November 2020, he had a mild COVID-19 infection, presented with fever, without pneumonia. The ambulant treatment was conducted, with complete recovery. Six weeks after the infection onset, on January 18th, 2021, he experienced a temporo-occipital tension headache, with moderate intensity, and exaggeration during coughing. Headache was occurring daily and required the repeating utilization of numerous analgesics and was associated with increased proinflammatory parameters (leukocytes 10.3 × 10^9/L, CRP 284.7 mg/L, IL-6 802.3 pg/mL, d-dimer 4.2). Patient had negative antigen and PCR tests for SARS-CoV-2 virus at the beginning of current symptoms. Headache was followed by progressive cognitive deterioration and mental state alterations. Due to the possible development of post-acute COVID-19 syndrome, corticosteroid therapy was immediately introduced (initially methylprednisolone 80 mg intravenously, per day). Extensive diagnostic procedures were performed. Vitamin B12, thyroid status, tumor markers, electrophoresis, and immunofixation of serum and urine were all negative. Lumbar puncture showed 5 lymphocytes with normal proteinorrhagia and glycorrhagia. Isoelectric focusing of cerebrospinal fluid (CSF) and serum was also negative and sediment of CSF showed no malignant cells. Antineuronal and paraneoplastic antibodies were in reference range. Microbiological analysis of serum and CSF (bacteriological examination, HIV, HBsAg, anti HCV, HSV-1, TPHA, Borelia Burgdorferi) were all negative. Serum analysis revealed positive ANCA (IIF) of an atypical pattern at titre 1/320, with normal MPO-ANCA and PR3-ANCA (ELISA). Standard EEG showed normal activity. Brain MRI performed 13 days after lumbar puncture showed supratentorial microischemic lesions, periventricular leukoencephalopathy, hygroma, and postcontrast enhancement of meninges and temporal arteries, which can be in correlation with cerebral vasculitis (Fig. 1). DWI sequence did not show any active lesions, but the MRI was performed 8 weeks after the disease onset due to technical reasons. MRI angiography presented annular stenosis of the P2 segment of the right cerebral posterior artery and distal part of the basilar artery. CT cerebral venography was normal. A whole-body ^18F-FDG-PET/CT revealed inflammation of the thoracic and abdominal aortic wall, and iliac and femoral arteries, leading us to a possible diagnosis of large vessel vasculitis (LVV) (Fig. 2).

According to the diagnosis, high doses of methylprednisolone were prescribed (1000 mg iv/daily during 5 consecutive days, in two cycles, followed by Prednisone 30 mg/ daily). Three cycles of therapeutic plasma exchange were
performed every 3 weeks. Having in mind that the patient suffers from post-acute COVID-19 syndrome manifested as cerebral and systemic vasculitis, and 49-fold increased values of IL-6, the IL-6 inhibitor (tocilizumab) was initiated in June 2021, in doses of 8 mg/kg monthly. Intensive immunosuppressive therapy led to complete recovery, 2 months after its initiation. Follow-up ANCA was done 3 months after the immunosuppressive therapy initiation and the result was negative.

Neurological complications relative to COVID-19 infection have been already recognized at the very beginning of the pandemic. Taquet and colleagues performed a retrospective cohort study and followed up 236,379 patients with COVID-19 infection for 6 months and concluded that incidence of neurological or psychiatric comorbidities was estimated to 33–62% [4]. Also, authors from France performed their investigation and showed that 16% of patients with COVID-19 developed possible cerebral vasculitis with focal neurological deficit, 12–40 days after the first manifestations of the infection [3]. Our patient experienced first neurological symptoms 6 weeks after COVID-19 onset.

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has the ability to bind to angiotensin-converting enzyme 2 (ACE2) receptor, which is widely expressed on endothelial cells in the neurons, but also in heart, lung, skin, kidney, and other organs leading to systemic and cerebral vasculitis and multiorgan dysfunction [5]. On brain MRI, he had supratentorial microischemic lesions, periventricular leukoencephalopathy, hygroma, and postcontrast enhancement of meninges and temporal arteries, which can be related to cerebral vasculitis, associated with LVV as a manifestation of post-acute COVID-19 syndrome. Our diagnosis has been supported with a positive therapeutic response to immunosuppressive therapy and tocilizumab.

To conclude, post-acute COVID-19 syndrome can be presented as a cerebral and systemic vasculitis which is able to lead to progressive brain damage, multiorgan dysfunction, and indirect morbidity related to this infection. Accurate and timely established diagnosis is necessary for rapid initiation of immunosuppressive therapy.

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Declarations

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