CNS Lymphocytic Vasculitis in a Young Woman With COVID-19 Infection

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Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with several neurologic manifestations including the development of cerebral lesions resembling CNS vasculitis in elderly patients with severe coronavirus disease 2019 (COVID-19). Here, we report additional evidence for COVID-19–related CNS vasculitis, confirmed by biopsy, in a young healthy patient with otherwise mild COVID-19 infection.

Case Report

A 26-year-old woman experienced 4 days of anosmia, dysgeusia, malaise, and fatigue 6 days after an airplane flight in mid-March 2020. Approximately 2–3 weeks later, she noticed difficulty keeping “flip-flops” on her left foot slowly progressing to dragging of her left foot in July 2020. Neurologic examination revealed left pyramidal tract dysfunction with left-sided weakness (4+/5 Medical Research Council Scale of left elbow flexion, hip flexion, knee flexion, and foot dorsiflexion) and hyperreflexia (3+ in biceps, brachioradialis, triceps, patellar, and Achilles reflexes with unsustained foot clonus and pathologic reflexes). The rest of her examination was normal, and she denied headache or any change in mental status or cognition.

Her initial brain MRI demonstrated multiple, irregular, peripherally enhancing lesions clustered within the right frontoparietal white matter. These lesions also had peripheral diffusion restriction and surrounding T2/fluid-attenuated inversion recovery hyperintensity suggestive of edema and internal susceptibility likely reflective of blood products (Figure, A, B, F, G). Cervical spine MRI was normal. CSF analysis showed a cell count of 1/mm³, protein level of 29 mg/dL, and glucose of 59 mg/dL. SARS-CoV-2 PCR testing was not available during the episode of presumed COVID-19 symptoms in March 2020 and was nonreactive in August 2020 during her initial hospitalization. SARS-CoV-2 antinucleocapsid antibody testing was significant for 2 positive test results (Roche assay) in September 2020, although she had negative results in simultaneously obtained additional serologic assays (Diazyme, Abbott; Figure, K). No SARS-CoV-2 PCR was performed in the CSF.

Evaluation in a COVID-19 infectious disease clinic resulted in confirmation of a prior COVID-19 infection by clinical criteria. Otherwise, extensive laboratory workup of the patient’s serum and CSF for other infectious, neoplastic, or autoimmune causes was negative.

Stereotactic biopsy of one of the right frontoparietal lesions demonstrated findings consistent with lymphocytic vasculitis, including infiltration of vessel walls by lymphocytes (predominantly CD3⁺ [mixture of CD4⁺ and CD8⁺] T cells with a sparse admixture of CD20⁺ B cells) with endothelial hypertrophy. In addition, edematous and gliotic white matter changes with extensive lymphoplasmacytic perivascular inflammation were noted, along with parenchymal necrosis and abundant dystrophic calcification. No viral inclusions were seen (Figure, L–V).

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The patient was treated with IV methylprednisolone 1,000 mg daily for 3 days, followed by an oral prednisone taper over 6 months starting at 60 mg daily. After 2 months, mycophenolate mofetil was added and uptitrated over 3 weeks to 1,000 mg twice daily with a 4-month overlap with the ongoing prednisone taper. The patient showed continued clinical improvement of her left-sided hemiparesis with minimal residual left lower extremity weakness on most recent examination. Follow-up brain MRIs at 1, 3, and 6 months after initiation of corticosteroids showed continuing decrease in the size and intensity of the lesions.
Discussion

We report a case of biopsy-confirmed CNS vasculitis that shortly followed a COVID-19 infection. To our knowledge, this is the fifth reported case of COVID-19–related CNS vasculitis and the first to be confirmed by biopsy or to occur in a young patient with otherwise mild COVID-19 infection. As the patient’s slowly progressive neurologic deficit began 2–3 weeks after her COVID-19 infection, this temporal correlation suggests a causal relationship, although there remains diagnostic uncertainty as PCR testing was not performed during her acute infection.

Notably, all 4 previous cases demonstrating CNS vasculitis were diagnosed based solely on imaging findings with no biopsy confirmation. All 4 were older (aged 64–69 years), experienced a more severe COVID-19 infection requiring intensive care unit level care, and developed earlier severe manifestation of neurologic symptoms compared with our case.1-4

A possible underlying mechanism is an endotheliitis caused by direct SARS-CoV-2 infection of endothelial cells through binding to the angiotensin-converting enzyme 2 receptor, which has been shown in renal, gastrointestinal, pulmonal, and cerebral vasculature.5,6 Alternatively, a proinflammatory state may have unmasked a primary CNS vasculitis. Interesting differences between this case and typical primary CNS vasculitis include the lack of headache or alteration in mental status/cognition, although a variety of phenotypes can be seen in this condition. Regardless of the mechanism, our case demonstrates that young patients with mild COVID-19 infection are still at risk for neurologic complications. Further studies of long-term outcomes in similar cases are needed to optimize the choice and duration of immunosuppression.

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