Autoimmune Encephalitis After SARS-CoV-2 Infection
Case Frequency, Findings, and Outcomes

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Study Question
What are the frequency and characteristics of autoimmune encephalitis (AE) in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection?

What Is Known and What This Paper Adds
Diverse neurologic disorders have been reported during the coronavirus disease 2019 (COVID-19) pandemic, but the frequency of AE associated with SARS-CoV-2 infection is unknown. The COVID-19 pandemic provides an opportunity to study postinfectious AE. This study found that AE was rare in patients with COVID-19 and that none of the affected patients had neural immunoglobulin G biomarkers or virus particles in the CSF.

Methods
This retrospective single-institution cohort study consisted of (1) a laboratory cohort of 556 patients who had been tested for AE-pertinent neural autoantibodies between November 1, 2019, and December 31, 2020, and who had residual sera that could be tested for the presence of total antibodies against the SARS-CoV-2 spike glycoprotein using the Roche Diagnostics Elecsys Anti-SARS-CoV-2 S electrochemiluminescence immunoassay and (2) an encephalopathy cohort of 31 patients with SARS-CoV-2 infection and encephalopathy encountered during inpatient and outpatient neurologic consultation at the Mayo Clinic in Rochester, Minnesota, and in whom diagnostic criteria were applied to ascertain the presence of AE and assign a level of diagnostic certainty.

Results and Study Limitations
Of 10,384 patients with any COVID-19 illness cared for at Mayo Clinic during 2020, AE was rarely encountered (just 5 patients met AE criteria: definite [n = 1], probable [n = 1], or possible [n = 3]). Among the 556 patients in the laboratory cohort who were tested for SARS-CoV-2 antibody, 18 (3.2%) tested positive (Figure). Clinical records of 16 patients with research consent available were reviewed. Two had AE; both were seen in consultation by the neurology service and their characteristics are included in the description of the encephalopathy cohort. The other 14 patients had a variety of clinical syndromes including postacute sequelae of SARS-CoV-2 infection, also known as PASC (n = 3), toxic-metabolic encephalopathy in the setting of severe COVID-19 pneumonia (n = 2), or diverse non–COVID-19–relatable neurologic diagnoses (n = 9). Of the 31 patients in the encephalopathy cohort, 5 met criteria for AE (16%), and the remainder were diagnosed with toxic-metabolic encephalopathy. Median symptom onset age of the 5 patients with AE was 61 years (range, 46–63) and 3 were women. All lived within the regional referral area of Mayo Clinic (Minnesota, n = 3; Iowa, n = 2) but none in the immediate vicinity (Olmsted County).

Data supportive of AE diagnosis included subacute encephalopathy (n = 5), abnormal EEG (n = 4), encephalitic-appearing MRI (n = 3), and inflammatory CSF (n = 2). All 3 patients with possible AE had spontaneous resolution. Two patients were treated with immune therapy: 1 had definite limbic encephalitis and improved and 1 had probable AE and died. Limitations of this study include underdetection of COVID-19–related AE cases due to false negativity of SARS-CoV-2 spike antibody among patients tested early in the disease course or nonreferral of mild, self-resolving AE.

Registration, Study Funding, and Competing Interests
This study did not receive targeted funding. Dr A. McKeon reports patents pending for antibodies pertinent to the diagnosis of AE (PDE10A, Septins-5 and -7, MAP1B, GFAP, KLCHL11). Go to Neurology.org/N for full disclosures.
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