Acute necrotizing encephalopathy and myocarditis in a young patient with COVID-19

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A 33-year-old woman, previously healthy was admitted with generalized status epilepticus. Four days before, she had developed generalized fatigue, fever, headache, and nasal congestion. On hospital arrival, she was comatose (Glasgow coma scale 5 [E1/V1/M3]), febrile (38.6°C), tachycardic (145/min) with a blood pressure of 100/60 mm Hg, and tachypneic (35/min) with hypoxemia (pulse oximetry 80%). She was emergently intubated and started on mechanical ventilation and received IV midazolam and valproic acid for seizure control. Chest x-ray showed mild edema. The initial blood test results showed elevated myocardial enzymes; high-sensitivity troponin-I, 2,210 pg/mL; probrain natriuretic peptide, 992 pg/mL; creatine phosphokinase, 1858 mcg/L; and creatine kinase-MB, 22.5 ng/mL. Blood count revealed a white blood cell count of 14,550/μL with absolute lymphopenia of 0.92/μL. C-reactive protein and erythrocyte sedimentation rate levels were high, whereas procalcitonin and lactic acid were normal. ECG showed sinus tachycardia and diffuse ST segment elevation. Bedside echocardiography showed diffuse myocardial dyskinesia with low left ventricular ejection fraction (29%) and small pericardial effusion. Head CT showed diffuse brain edema.

On day 2, brain MRI showed bilateral hemorrhagic thalamic (figure, A–C) and cerebellar lesions (figure, E–G). Noninvasive and invasive cerebral angiographies excluded venous or arterial occlusions and showed no signs of vasculitis. Lumbar puncture had an opening pressure of 22 cmH2O, and CSF showed a white cell count of 26 cells/μL (90% lymphocytes), protein of 541 mg/dL, no oligoclonal bands, and normal glucose; PCR tests results for herpes simplex types 1 and 2, varicella-zoster, cytomegalovirus, Epstein-Barr virus, West Nile virus, Coxsackie viruses, echovirus, and dengue were negative. Testing for the presence of SARS-CoV2 in the CSF was unable to be performed. Follow-up chest x-ray showed worsening bilateral alveolar and interstitial lung edema. Serum interleukin-6 (IL-6) was 378 pg/mL, whereas IL-6 in the CSF was not performed. High-dose IV methylprednisolone (1,000 mg/d) was started for presumptive diagnosis of acute necrotizing encephalitis (ANE).

On day 3, a nasopharyngeal swab specimen was tested for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Follow-up brain MRI with gadolinium showed rim enhancement of the bilateral thalamic and cerebellar lesions (figure, D and H); it also disclosed signs of acute pansinusitis (figure, H). Cardiac MRI showed diffuse myocardial signal hyperintensity in both ventricles and associated pericarditis. Blood tests for autoimmune diseases were negative; moreover, blood, urine, and sputum cultures revealed no organism growth.

On day 4, the patient remained comatose and hypoxemic. Blood tests revealed new thrombocytopenia and elevated liver enzymes. The patient then had sudden neurologic deterioration with anisocoria and extensor posturing. Emergent head CT demonstrated diffuse brain swelling with right thalamic and right cerebellar hemorrhages.
On day 5, she suffered a cardiopulmonary arrest, and resuscitation attempts were unsuccessful. One day later, the results of her nasopharyngeal swab confirmed the detection of SARS-CoV2 by PCR.

**Discussion**

Neurologic complications from SARS-Cov2 infection are insufficiently understood. ANE has been described in children and adults after various acute viral respiratory infections, most notably influenza A (H1N1). Concomitant extrapulmonary manifestations includes myocarditis and pericarditis. Our patient had confirmed SARS-Cov2 infection and presented with features consistent with fulminant ANE and myocarditis in addition to hypoxemic respiratory failure from ARDS. We know of only 1 previously reported case of ANE associated with SARS-Cov2 infection, and myocarditis has been documented. The frequency of these complications is unclear. Necropsy was not performed in our patient, but her neuro-radiologic findings were quite characteristic for the diagnosis of ANE. This diagnosis must be considered in patients with SARS-CoV-2 infection presenting with or developing altered consciousness.

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**Appendix**

**Authors**

| Name              | Location                  | Contribution                                      |
|-------------------|----------------------------|---------------------------------------------------|
| Ahmed Elkady, MSc | Mataria Teaching Hospital, Cairo, Egypt | Major role in the acquisition of data; coordinated imaging |
| Alejandro A. Rabinstein, MD | Mayo Clinic, Rochester, MN | Conceptualized case; drafted the manuscript for intellectual content |

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