Cerebral deep venous thrombosis and COVID-19: case report

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Herein, the authors present the case of a 54-year-old male diagnosed with coronavirus disease 2019 (COVID-19) during a screening test. The patient was asked to self-isolate at home and report with any exacerbations of symptoms. He presented later with pneumonia complicated by encephalopathy at days 14 and 15 from initial diagnosis, respectively. MRI of the brain showed bithalamic and gangliocapsular FLAIR signal abnormality with mild right-sided thalamic and periventricular diffusion restriction. A CT venogram was obtained given the distribution of edema and demonstrated deep venous thrombosis involving the bilateral internal cerebral veins and the vein of Galen. CSF workup was negative for encephalitis, as the COVID-19 polymerase chain reaction (PCR) test and bacterial cultures were negative. A complete hypercoagulable workup was negative, and the venous thrombosis was attributed to a hypercoagulable state induced by COVID-19. The mental decline was attributed to bithalamic and gangliocapsular venous infarction secondary to deep venous thrombosis. Unfortunately, the patient's condition continued to decline, and care was withdrawn.

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KEYWORDS COVID-19; SARS-CoV-2; central nervous system; cerebrovascular disease; hypercoagulable state; deep venous thrombosis; vascular disorders; infection

ON March 11, 2020, the World Health Organization declared that coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a pandemic.¹ The virus has a high reproduction number (2.0–2.5) allowing it to infect a large number of the world population.² The primary organ affected is the respiratory system; however, neurological manifestations have been reported.³ Herein, we describe a case of COVID-19 infection with pulmonary manifestations and encephalopathy due to cerebral venous infarction secondary to deep venous thrombosis.

Case Report

History and Examination

A 54-year-old male, with a medical history notable only for hypertension, tested positive for COVID-19 at another institution during a screening examination conducted due

to close contact with a COVID-19–positive individual on April 5, 2020. SARS-CoV-2 infection was confirmed by reverse transcriptase polymerase chain reaction (RT-PCR) assay. The patient was asked to self-quarantine; however, 9 days after testing positive, he presented with shortness of breath and cough. The patient was diagnosed with pneumonia and started on oxygen, ceftriaxone, and azithromycin. The patient's mental status declined (day 15 after the initial diagnosis), for which he required mechanical ventilation. CT imaging of the brain showed bithalamic and gangliocapsular hypodensity with mass effect and approximately 6 mm of rightward midline shift, as well as prominence of the bilateral temporal horns. Subsequent MRI of the brain showed bithalamic and gangliocapsular FLAIR signal abnormality with mild right-sided thalamic and periventricular diffusion restriction. The temporal horns were prominent with evidence of transependymal flow. He was transferred to our institution for further management.

ABBREVIATIONS COVID-19 = coronavirus disease 2019; CSF = cerebrospinal fluid; EVD = external ventricular drain; ICP = intracranial pressure; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

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FIG. 1. **A:** Axial FLAIR MRI showing hyperintense signal in the bilateral thalami (white arrows) and basal ganglia region (worse on the patient's right). Note the transependymal flow at the right frontal horn (blue arrow). **B:** Coronal CT scan showing the EVD in the right frontal horn (thick arrow). Note the dilated right temporal horn (small arrow) indicating hydrocephalus. Figure is available in color online only.

Upon admission to Thomas Jefferson University Hospital, the patient was obtunded, opening his eyes and grimacing only to deep noxious stimulation, localizing his bilateral upper extremities weakly, and withdrawing his bilateral lower extremities (Glasgow Coma Scale [GCS] E2V2M5). His pupils were equal and reactive, and protective brainstem reflexes were intact. Auscultation of his lungs revealed coarse breath sounds bilaterally, consistent with his known COVID-19 pulmonary pathology. Given

his poor mental status and concern for obstructive hydrocephalus, a right external ventricular drain (EVD) was placed for cerebrospinal fluid (CSF) diversion, intracranial pressure (ICP) monitoring, and CSF studies. The CSF opening pressure was 30 cm H₂O (Fig. 1). A CT venogram, obtained given the distribution of edema, demonstrated deep venous thrombosis involving the bilateral internal cerebral veins and the vein of Galen (Fig. 2), as well as progressive deep cerebral edema. Pertinent laboratory findings on admission to the intensive care unit are summarized in Table 1. Notable findings included elevated levels of D-dimer, erythrocyte sedimentation rate, lactate dehydrogenase, and serum ferritin. A complete hypercoagulable workup did not identify the provocative cause for the venous thrombosis, and the venous thrombosis was attributed to a hypercoagulable state induced by COVID-19 (antithrombin III, antiphospholipid antibodies, etc.). Also, CSF studies showed a markedly increased protein content and white blood cell count, initially suggesting the possibility of COVID-19 encephalitis. However, SARS-CoV-2 RNA was not detected in the CSF, and bacterial cultures remained negative.

Treatment and Posttreatment Course

The patient was started on hydroxychloroquine for COVID-19 treatment. A heparin infusion was initiated given the cerebral deep venous thrombosis, and a 3% hypertonic saline infusion was administered given concerns over increasing mass effect due to cerebral edema. Serial CT scans revealed a punctate focus of hemorrhage in the right basal ganglia that remained stable. The patient had an episode of ICP crisis with a dilated right pupil that was responsive to 23.4% hypertonic saline administration. His right frontal ventricular drain was not draining CSF at this point. A subsequent CT scan showed the ventricle collapsed around the catheter tip, a dilated left ventricle, and progressive deep cerebral edema. The heparin infusion was temporarily held and a left-sided ventricular drain

FIG. 2. Sagittal CT venogram showing filling defects in the internal cerebral vein (top arrow) and vein of Galen (bottom arrow) consistent with thrombosis.

TABLE 1. Demographic and clinical characteristics and laboratory findings

Factor	Description
Demographic characteristics	
Age (yrs)	54
Sex	M
Initial findings	
Medical history	Hypertension
Symptoms at disease onset	Shortness of breath, cough
Imaging features	Lt lower lobe pneumonia
Treatment before admission to ICU	O ₂ , ceftriaxone, & azithromycin
No. of days from disease onset to thrombotic events	15
Findings on admission to ICU	
No. of days since disease onset	15
Disease severity	Severe
Laboratory findings	
WBC (B/L)	7.8
Differential count (B/L)	
Total neutrophils	6.42
Total lymphocytes	1.09
Total monocytes	0.17
Platelet count (B/L)	372
Hemoglobin (g/dl)	14.4
Albumin (g/dl)	3.7
ALT (IU/L)	67
AST (IU/L)	44
LDH (IU/L)	382
Creatinine (mg/dl)	1.06
Creatine kinase (IU/L)	190
EGFR (ml/min/1.73 m ²)	>60
hs-cTnT (ng/L)	14
Prothrombin time (sec)	11.8
aPTT (sec)	25
Fibrinogen (mg/dl)	429
Antithrombin III (%)	99
D-dimer (ng/ml)	3151
Serum ferritin (ng/ml)	508
Procalcitonin (ng/ml)	0.2
High-sensitivity CRP (mg/dl)	0.60
ESR (mm/hr)	47
CSF studies	
RBC count (cell/μl)	401
WBC (cell/μl)	10
Glucose (mg/dl)	38
Protein (mg/dl)	1104

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TABLE 1. Demographic and clinical characteristics and laboratory findings

Factor	Description
Findings on admission to ICU (continued)	
Imaging features	Encephalitis w/ midline shift; venous infarct involving bithalamic & basal ganglia; deep venous thrombosis involving straight sinus, vein of Galen, bilat internal cerebral veins, & rt basal vein of Rosenthal

ALT = alanine aminotransferase; aPTT = activated partial thromboplastin time; AST = aspartate aminotransferase; B/L = billion per liter; CRP = C-reactive protein; EGFR = estimated glomerular filtration rate; ESR = erythrocyte sedimentation rate; hs-cTnT = high-sensitivity cardiac troponin T; LDH = lactate dehydrogenase; RBC = red blood cell; WBC = white blood cell.
Bold values indicate higher than normal range.

was placed. These measures allowed for transient control of ICP, but unfortunately he developed progressive bilateral deep venous infarctions involving critical structures and sustained elevated ICPs, and care was withdrawn on the 9th day of the hospital stay.

Discussion

Neurological manifestations caused by COVID-19 range from mild to severe symptoms. Several published reports have noted severe headache, anosmia, encephalopathy, encephalitis, meningitis, and acute cerebrovascular disease such as ischemic and hemorrhagic stroke.^{3–5} The coronavirus family has previously shown the ability to directly infect the central nervous system, and this may be the cause of some such presentations. Additionally, some severe presentations are thought to be at least partly attributable to an unusually intense inflammatory response, which has been widely reported in pulmonary tissue.³ Such a response may predispose to a hypercoagulable state, putting patients at risk for stroke due to either arterial occlusion or venous congestion. There are numerous reports documenting an increased risk of thromboembolic events in COVID-19–positive patients.^{6,7} Cerebral infarcts secondary to antiphospholipid antibodies in COVID-19 patients have also been reported.⁷ It is paramount to keep a high index of suspicion of venous thrombosis when faced with an encephalitis picture in the setting of COVID-19. The management is completely different, in which anticoagulation may improve outcomes.

Conclusions

SARS-CoV-2 may induce a hypercoagulable state causing cerebral venous thrombosis. The radiological features may share similarities with several differential diagnoses, including encephalitis. It is paramount to perform a complete workup because the management is completely

different, and this affects the patient's outcome. It is crucial to account for such manifestations when managing patients with COVID-19.

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Disclosures

Dr. Jabbour is a consultant for Medtronic and MicroVention. Drs. Tjoumakaris and Gooch are consultants for Stryker.

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