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Atypical Deep Cerebral Vein Thrombosis with Hemorrhagic Venous Infarction in a Patient Positive for COVID-19

L. Chougar, B. Mathon, N. Weiss, V. Degos, and N. Shor



ABSTRACT

SUMMARY: There is growing evidence that Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) has a neurotropic and neuroinvasive potential. In particular, neurologic complications associated with the infection by SARS-CoV-2 include strokes that may result from a dysregulated inflammatory response to the infection. We report an atypical deep cerebral vein thrombosis complicated with hemorrhagic venous infarction in a patient positive for SARS-CoV-2 with no risk factors for thrombosis.

ABBREVIATIONS: COVID-19 = coronavirus disease 2019; SARS-CoV-2 = Severe Acute Respiratory Syndrome coronavirus 2; RT-PCR = Reverse Transcriptase-Polymerase Chain Reaction; CSF = cerebrospinal fluid

Since the coronavirus disease 2019 (COVID-19) outbreak in December 2019 in China, an increasing number of patients infected with the Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) have been presenting with neurologic symptoms either simultaneously with the flulike syndrome or during the course of a SARS-CoV-2-associated pneumonia. Neurologic manifestations range from mild to severe, including impaired consciousness, acute cerebrovascular disease, and seizures.¹ A presumptive case of COVID-19-associated acute necrotizing hemorrhagic encephalopathy has been recently reported.² Most commonly, an increased risk of cerebrovascular complications has been associated with the COVID-19.³⁻⁵ Herein, we report an extensive deep cerebral vein thrombosis with hemorrhagic venous infarction in a patient positive for SARS-CoV-2 with no known risk factor for thrombosis.

CASE DESCRIPTION

A 72-year-old man with no relevant medical history presented with sudden left hemiparesis, altered mental status, and refractory

status epilepticus. Retrospectively, the patient's family reported mild respiratory symptoms a few days earlier.

The nasopharyngeal swab was positive for SARS-CoV-2 using the reverse transcriptase polymerase chain reaction (RT-PCR) and negative for influenza A and B viruses and adenoviruses. Cerebrospinal fluid (CSF) analysis showed an increased red blood cell count (500/mm³) due to traumatic lumbar puncture, and apleocytosis (30 white blood cells/mm³). The results of the RT-PCR including the SARS-CoV-2, herpes simplex viruses 1 and 2, varicella zoster virus, cytomegalovirus, and Epstein-Barr virus as well as the bacterial culture, were negative in the CSF.

Noncontrast CT revealed a right deep hemispheric hypodensity with some hyperdense areas, involving the thalamus, basal ganglia, internal capsule and splenium of the corpus callosum, and the deep white matter. A subtle hypodensity within the left thalamus could also be seen. These abnormalities caused a moderate mass effect on the midline structures. Among the scattered areas of parenchymal hemorrhage, spontaneous hyperdensity was detected within the internal cerebral veins and the vein of Galen. A CT venogram showed no opacification of these veins, confirming the diagnosis of acute deep cerebral vein thrombosis complicated by hemorrhagic venous infarction (Fig 1).

MR imaging performed ten hours later showed marked progression of the vasogenic edema, extending to the right cerebral peduncle and the pons, and increased hemorrhagic changes involving the lateral ventricles. Contrast-enhanced images evidenced a lack of enhancement within the deep brain regions, corresponding to necrotic areas associated with the venous infarction. Associated involvement of the basal veins of Rosenthal and thalamostriate veins was suspected on susceptibility-weighting images.

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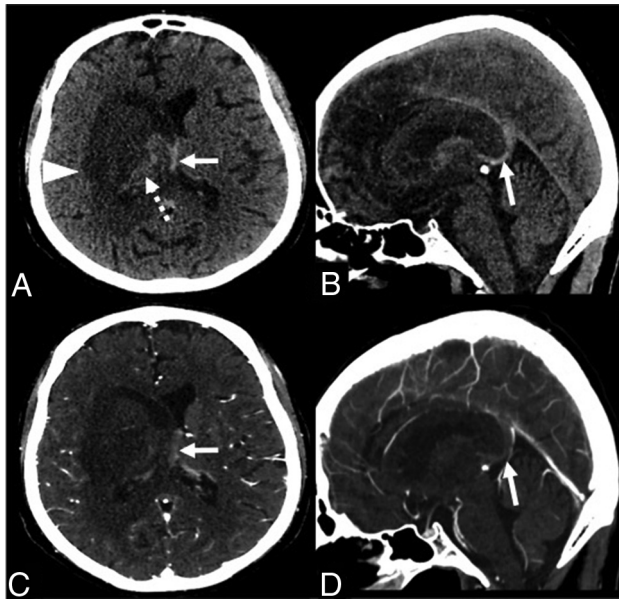


FIG 1. Axial (A and C) and parasagittal (B and D) CT images without (upper row) and with contrast injection (lower row) show a right deep hypodensity involving the gray and white matter (A, arrowhead), with areas of hemorrhage (A, dashed arrow). The internal cerebral veins are shifted to the left and appear spontaneously hyperdense (A and B, arrows), without noticeable opacification (C and D, arrows).

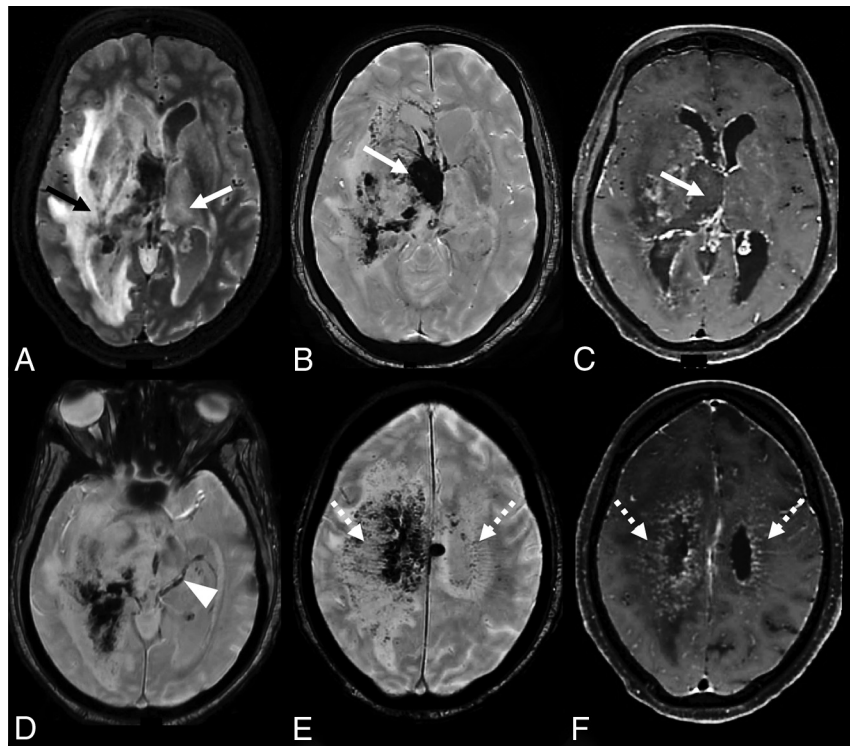


FIG 2. Axial FLAIR (A), SWI (B, D, and E), and postcontrast T1-weighted MR images (C and F). There is an extensive asymmetrical vasogenic edema including the deep gray and white matters (A, arrows), with hemorrhage (B, arrow) and necrotic areas (C, arrow), corresponding to a hemorrhagic venous infarction. The basal veins of Rosenthal also appear involved on SWI (D, arrowhead). The medullary veins are dilated (E, dashed arrows), with associated curvilinear gadolinium enhancement (F, dashed arrows).

The medullary veins were dilated, due to venous engorgement. Curvilinear gadolinium enhancement along the medullary veins was visible within the FLAIR hyperintensities in the centrum semi-ovale, corresponding to the opacification of the small-vessel lumen and/or enhancement of its perivascular spaces (Fig 2).

Tests for thrombophilia were negative. The patient was transferred to an intensive care unit where an endotracheal intubation was performed and curative anticoagulation and antiepileptic therapy were initiated. Four days after the admission, the patient evolved toward brain death.

DISCUSSION

It is increasingly recognized that COVID-19 is associated with a prothrombotic state. It has been established that patients with COVID-19 hospitalized in intensive care units are at higher risk of venous and arterial thrombotic events despite prophylactic or curative anticoagulation.^{3,4} More recently, a higher incidence of arterial stroke has provided evidence of central nervous system involvement associated with the COVID-19.³⁻⁵

Respiratory viruses including coronaviruses are known for their neurotropic and neuroinvasive potential, damaging the central nervous system through an immune-mediated mechanism in susceptible subjects and/or direct damage to nerve cells following viral invasion.⁶ Studies conducted on lung fibroblasts and umbilical vein endothelial cells, which are a classic *in vitro* model for brain endothelial cells, have demonstrated that respiratory viruses are able to

induce epithelial damage as well as platelet and endothelial cell dysfunction.⁷ More specifically, the angiotensin-converting enzyme 2 is a cellular receptor for the Severe Acute Respiratory Syndrome coronavirus and the new coronavirus (SARS-CoV-2), expressed by respiratory and cardiac endothelial cells.⁸ This receptor can also be found on the surface of brain endothelial cells and could be induced in neurons, reinforcing the hypothesis of potential brain damage caused by the infection.⁹ On the other hand, it has been suggested that the systemic inflammatory response syndrome seen in critically ill patients with COVID-19 may participate in the pathogenesis of vascular thrombosis through a dysregulated cytokine storm, without direct viral invasion or immune mediation. That massive inflammatory cascade may lead to reversible or irreversible end-organ dysfunction, including endothelial alterations and microthrombosis.³⁻⁵

This case of deep cerebral vein thrombosis with hemorrhagic venous infarction in a patient positive for COVID-19 showed some uncommon imaging features, including asymmetric deep brain involvement, the presence of large necrotic

areas within the venous infarction, and the extent of the intraventricular hemorrhage. Furthermore, there was striking and atypical curvilinear enhancement along the medullary veins in association with white matter signal abnormalities. This peculiar feature has been described in vasculopathies such as posterior reversible encephalopathy syndrome and Susac syndrome and in disorders with angiocentric infiltrates, especially neurolymphomatosis,¹⁰ and immune reconstitution inflammatory syndrome in patients infected with HIV.^{10,11} These findings raise the hypothesis of a potential vascular and/or perivascular involvement associated with the deep vein thrombosis.

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