Intracerebral Hemorrhage and Reversible Cerebral Vasoconstriction Syndrome in a Patient With COVID-19

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Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) is a condition characterized by reversible multifocal narrowing of cerebral arteries [1]. Patients commonly present with sudden onset severe headache. The condition may result in focal neurologic deficits secondary to ischemic or hemorrhagic stroke or subarachnoid hemorrhage (SAH) [1,2]. The pathophysiology of this condition is not fully understood but is associated with vasoconstricting drugs and the postpartum period. The postpartum state is the most important contributor accounting for 50%-60% of cases. Other identified triggers include vasoactive drugs such as sympathomimetics, migraine abortive medications, interferon, NSAIDs, alcohol, blood transfusions, erythropoietin, intravenous immunoglobulin, migraine and trauma [3].

COVID-19 is a pandemic disease caused by infection with SARS-CoV-2. Common complications include acute hypoxic respiratory failure, progressing to acute respiratory distress syndrome (ARDS) in a significant minority of patients. Neurologic symptoms are varied; many are related to hypercoagulability associated with the viral infection [4]. In this case report, we present a rare case of intracerebral hemorrhage (ICH) and SAH secondary to RCVS in a patient with SARS-CoV-2 infection.

Case Description

An 18-year-old African American male with a past medical history of asthma presented to the emergency department with a thunderclap headache, nausea, and vomiting for the past two days. The blood pressure at admission was 149/79 mmHg, and there were no focal deficits on neurological examination. Blood tests were grossly unremarkable. Initial CT head without contrast showed no acute intracranial abnormality (Figure 1A). CT angiogram of the head showed multifocal areas of stenosis, predominantly involving M2/M3 segments of bilateral middle cerebral arteries (MCA), and P2/P3 segments of bilateral posterior cerebral arteries (PCA), as well as A2 segment of the right anterior cerebral artery (ACA), (Figures 2A-2C). Four hours after the initial presentation, the patient became unresponsive with a Glasgow coma score (GCS) of 3. STAT repeat CT head without contrast revealed a 6.4 x 4.4 x 4 cm (66 cc) hemorrhage in the right frontal lobe with 7 mm of leftward midline shift, mass effect on the right lateral ventricle, and SAH in the right frontal and temporal lobes (Figure 1B). The ICH score was 3 with 72% mortality. The patient was transferred to ICU and intubated. Emergent right decompressive craniectomy was performed. Subsequent MRI brain with and without contrast (Figure 3) ruled out any clear etiology that would explain the patient intracranial and SAH.

Vasculitis evaluation including antinuclear antibody (ANA), C-reactive protein (CRP), sedimentation (SED) rate, anti-neutrophil cytoplasmic antibody (ANCA) and serum neurosyphilis antibody was negative. Urinary drug screen (UDS) revealed the presence of THC. Conventional cerebral angiogram revealed mild to moderate diffuse focal intracranial stenosis concerning RCVS (Figure 4A). 80-mg of IV verapamil every 8 hours was initiated to treat the RCVS. The patient was successfully extubated on day 11 of hospitalization. Repeat cerebral angiogram on hospital day 13 showed almost near-complete resolution of the previously seen diffuse focal stenosis (Figure 4B) supporting the diagnosis of RCVS. Verapamil was slowly weaned off the following days. The patient was later transferred to an inpatient physical rehabilitation facility for two weeks of treatment and eventually made a full functional recovery over the course of the following three months.

Patient Imaging

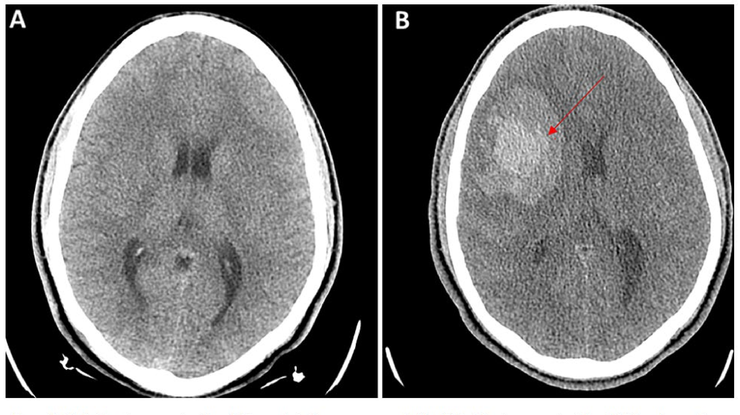

Figure 1: (A) Axial cut, non-contrast head CT on admission was unremarkable. (B) Axial cut, non-contrast head CT four hours after admission demonstrated 6.4 x 4.4 x 4 cm right fronto-parietal intracranial hemorrhage with mass effect and 7 mm right to left midline shift. Subarachnoid hemorrhage in the right frontal and temporal lobes.

Patient Imaging

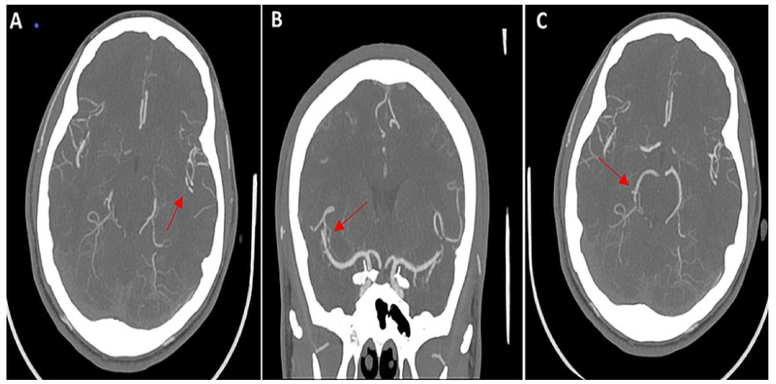

Figure 2: (A) Axial cut, CT angiogram of the head demonstrating focal areas of stenosis involving the left inferior M2 middle cerebral artery (MCA). (B) Coronal cut, CT angiogram of the head demonstrating focal areas of stenosis involving the right superior M2 MCA. (C) Axial cut, CT angiogram of the head demonstrating focal areas of stenosis involving the right P2 posterior cerebral artery.

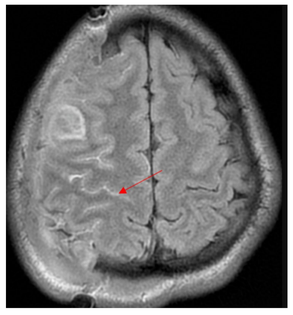

Figure 3: MRI brain with and without contrast post decompression, fluid-attenuated inversion recovery (FLAIR) sequence demonstrating subarachnoid hemorrhage in the right frontal and parietal lobe.

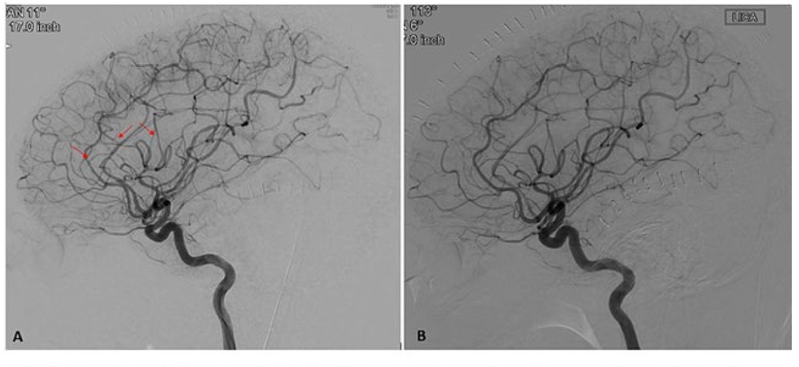

Figure 4: (A) Left internal carotid artery angiogram (lateral view) demonstrating mild to moderate diffuse focal stenoses involving the left MCA and bilateral ACAs. (B) Left internal carotid artery angiogram (lateral view) demonstrating near-complete resolution of previously seen diffuse focal stenoses.

Discussion

RCVS is a medical condition in which there is multifocal arterial constriction and dilation in the cerebral vasculature [1]. Complications of RCVS include ICH, SAH, posterior reversible encephalopathy syndrome (PRES) and ischemic infarction. Brain hemorrhage in RCVS tends to occur within the first three days. Infarction tends to occur with cases of severe proximal vasoconstriction. The pathogenesis of RCVS remains uncertain but autonomic dysregulation, oxidative stress and genetic predisposition have been postulated [2]. RCVS is generally not associated with a viral infection. The etiology of RCVS in COVID-19 is under investigation. Direct local effect of SARS-CoV-2 on ACE2 receptors leading to endothelial cell dysfunction and vasoconstriction with the concomitant local inflammatory release of vasoactive substances causing vasodilation and loss of cerebral autoregulation in the brain could result in RCVS.

To our knowledge, we report the first case of large ICH and SAH secondary to RCVS in the setting of COVID-19 infection. Our case is unique in that initial CTA and traditional cerebral angiography showed diffuse cerebral vasoconstriction, which resolved on subsequent angiography, and after treatment with verapamil. This case adds to the growing evidence of a possible association between RCVS and SARS-CoV-2 infection. RCVS is generally associated with SAH, but this case also features a large ICH. In addition, our patient did not have increased systemic inflammatory response or prothrombotic serum markers. SARS-CoV-2-related microangiopathic damage secondary to either direct viral damage or a local immune response leading to dynamic vessel wall changes could explain cerebrovascular events such as RCVS. Our patient suffered non-aneurysmal SAH and a rare complication of parenchymal hemorrhage in the frontal lobe. This patient's RCVS2 score is 9 (5 points for single thunderclap headache, 3 points for vasoconstrictive trigger identified, 1 point for SAH present on imaging), with a score of >5 having high specificity and sensitivity (99% and 90% respectively) for diagnosing RCVS [13].

Conclusion

ICH secondary to RCVS is a potential neurological sequelae of SARS-CoV-2 infection. We present one of the first case reports of a large ICH and SAH secondary to RCVS in a patient with COVID-19 infection. As our understanding of this infection and its clinical manifestations continue to grow, it is important to recognize the unusual and atypical extra-pulmonary manifestations of COVID-19.

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