

CASE REPORT

COVID-19 outbreak as a probable cause of increased risk of intracranial rebleeding in partially treated cerebral arteriovenous malformations

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Funding information

There is no funding institute or supporting company or organization

Abstract

Patients who are infected with COVID-19 and have cerebral arteriovenous malformations which are partially treated or untreated may be more liable to rupture or bleed than not infected patients.

KEYWORDS

cerebral AVM, COVID-19, intraventricular hemorrhage

1 | INTRODUCTION

The effect of recent outbreak of COVID-19 on the pathophysiology of vascular malformation is not well understood. In this article, we report two patients with partially embolized cerebral arteriovenous malformations (AVM) having intraventricular (IVH) at time of being infected with COVID-19. The first case was an eleven-year-old male patient presented to our emergency department 11 months ago having small AVM nidus at right frontoparietal lobe, treated with partial embolization. After 9 months, his condition was deteriorated as he was infected with COVID-19 and had intraventricular hemorrhage. After being COVID-19 free, a session of transarterial embolization was elected and the residual nidus was embolized. The second patient was 25-year-old female patient

with intraventricular and intracerebral hemorrhage (ICH) was discovered to have left basal ganglia AVM. A session of embolization was done for her, and partial embolization was done seven years ago and was referred to perform Gamma knife. In April 2020, she was admitted having left basal ganglia ICH and IVH and was infected with COVID-19. After being COVID-19 free, a session of transvenous embolization was elected and the residual nidus was embolized near completely. Cerebrovascular surgeons must be aware about the increased rate of complications as IVH and ICH that may occur to the patients with untreated or partially embolized cerebral AVM who are infected with COVID-19.

Respiratory symptoms are the most common problems encountered in patients infected with the novel coronavirus disease 2019 (COVID-19), however; some other

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systemic involvements have been reported.¹⁻³ The most common symptoms described as cough, fever, shortness of breath, myalgia, anosmia, malaise, headache, diarrhea, and confusion were observed.⁴ Neurological complications in COVID-19 are rare, and the literature about it are scarce, however; they do happen. Limited articles were published about intracranial hemorrhages related to COVID-19.⁵ Cerebral arteriovenous malformation (AVM) is a tangle of abnormal blood vessel having a feeding artery and a draining vein without an intervening cerebral tissue. The presence of an AVM sometimes leads to the permanent neurologic deficit or even death. Stand-alone curative embolization plays a role in treating specific types of cerebral AVM as it enables high occlusion rates and their respective short- and long-term safety profile.⁶ In a meta-analysis done by Subat et al, the total hemorrhage rates of cerebral AVM after embolization were 2.6% per procedure.⁷ The effect of recent outbreak of COVID-19 on the pathophysiology of vascular malformation is not well understood. In this article, we report two patients with partially embolized cerebral AVM having intraventricular (IVH) and intracerebral (ICH) hemorrhages at time of being infected with COVID-19.

2 | CLINICAL PRESENTATION

2.1 | Case 1

An 11-year-old male patient presented to our emergency department with headache nausea and vomiting 11 months ago. His Glasgow Coma Scale (GCS) was 15/15 with no neurological deficit. Brain CT revealed IVH. The past medical history was positive PDA (persistent ductus arteriosus) which was repaired but pulmonary hypertension exists. Catheter angiography showed small AVM nidus at right frontoparietal lobe that fed by right anterior cerebral artery (ACA) and was drained into right cortical venous system, Spetzler Martin grade (S-M grade) 2 (Figure 1A). A session of embolization was decided two weeks later through transarterial embolization with occlusion of 2 feeders from the third part of ACA (A3) with Onyx, and near-complete occlusion of nidus was performed (Figure 1B). After 9 months (in April 2020), he was admitted to our hospital with headache, vomiting, fever, and dry cough. The evaluation showed that he was infected with COVID-19 according to positive test real-time polymerase chain reaction (PCR) of nasopharyngeal

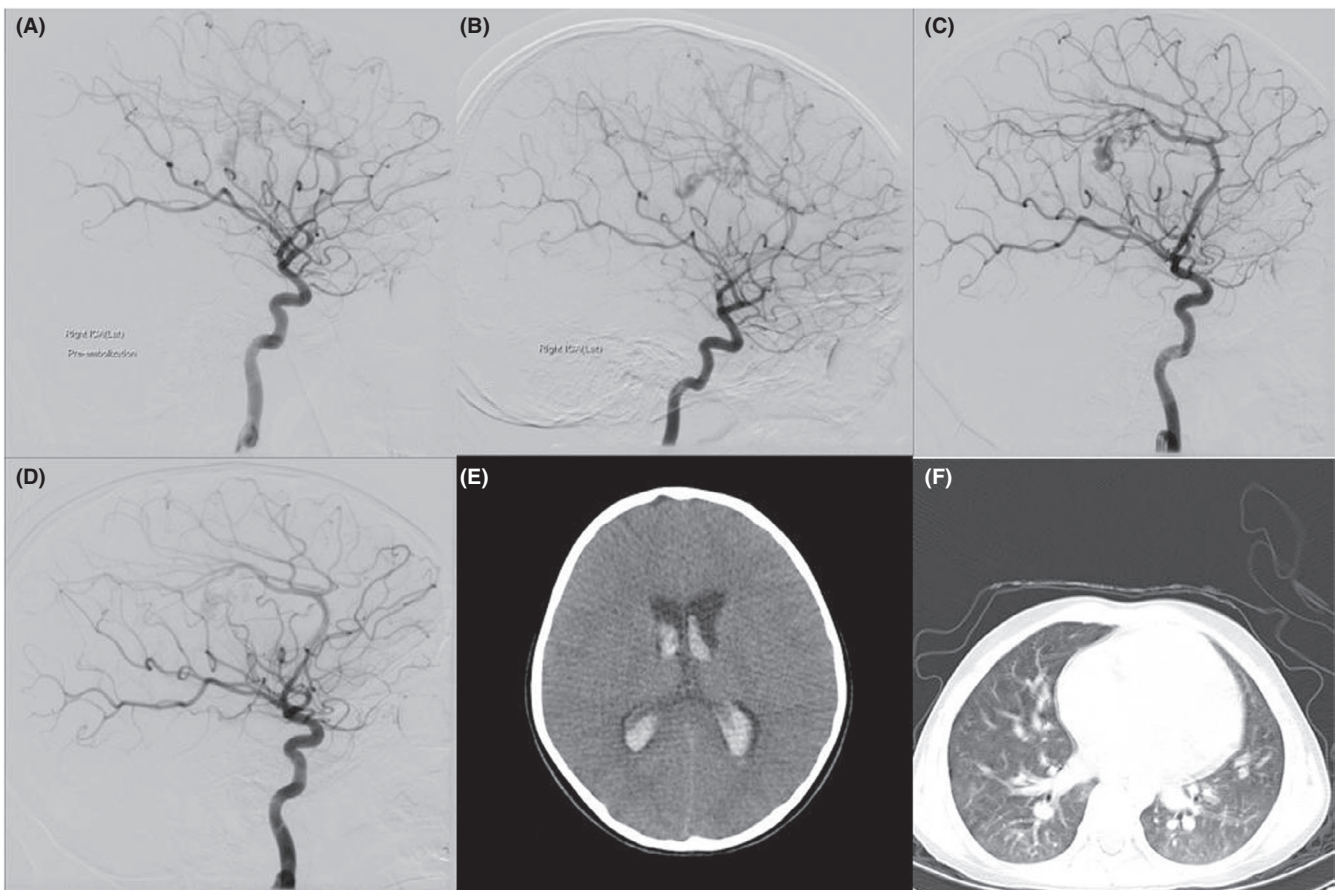


FIGURE 1 (A) Catheter angiography done showing right frontal AVM nidus. (B) Control angiography following partial arterial embolization. (C) Diagnostic angiography done when the patient was infected with COVID-19 showing the recanalized AVM nidus. (D) Control angiography after near-total arterial embolization. (E) Brain CT scan with IVH. (F) A ground glass appearance in chest CT scan

sample and peripheral ground glass appearance in chest CT scan (Figure 1F), he had thrombocytopenia and brain CT scan revealed IVH (Figure 1E). A diagnostic angiography was done and showed residual nidus of the right frontoparietal AVM (Figure 1C). He was transferred to the isolation ward for receiving care and treatment. After being COVID-19 free, a session of transarterial embolization was elected through right femoral artery and AVM nidus was completely embolized with 2 vials of Onyx (Medtronic Neurovascular Inc.) as shown in control DSA (Figure 1D). The patient was discharged home at post-intervention day 5 without neurological deficit.

2.2 | Case 2

A 25-year-old female patient who was admitted to the emergency department seven years ago was suffering from right-sided weakness and aphasia. Her power for upper extremity was 4/5 and for lower extremity 3/5. Brain CT scan revealed left basal ganglia ICH and IVH. A diagnostic angiography showed left basal ganglia AVM nidus fed from left medial lenticulostriate arteries and deep perforators of left ACA and was drained into

deep venous system (Vein of Galen) with (S-M) grade 3 (Figure 2A). A session of transarterial embolization was arranged through right femoral artery, and partial embolization of the AVM nidus was performed using one vial of Onyx (Medtronic Neurovascular Inc.) (Figure 2B). The patient was referred to Gamma Knife center as an option to treat the remaining part of AVM nidus, after that, the patient did not visit for follow-up angiography.

In April 2020, the patient was admitted to the hospital with loss of consciousness, GCS 8/15, right hemiplegia, seizure, and fever. The patient was infected with COVID-19 (according to the positive real-time PCR of nasopharyngeal swab and peripheral ground glass appearance at chest CT scan) (Figure 2F). Unfortunately, the history revealed that the patient did not perform the session of Gamma knife Brain CT scan showed left basal ganglia ICH and IVH (Figure 2E). She was transferred to COVID-19 intensive care unit (ICU). The patient cured after two weeks, and a diagnostic angiography was done revealing residual nidus of left basal ganglia AVM fed mainly from left medial lenticulostriate arteries (Figure 2C). As the embolization of feeders was risky, a session of transvenous embolization was performed through right femoral vein using 3 vials of Onyx (Medtronic Neurovascular Inc.),

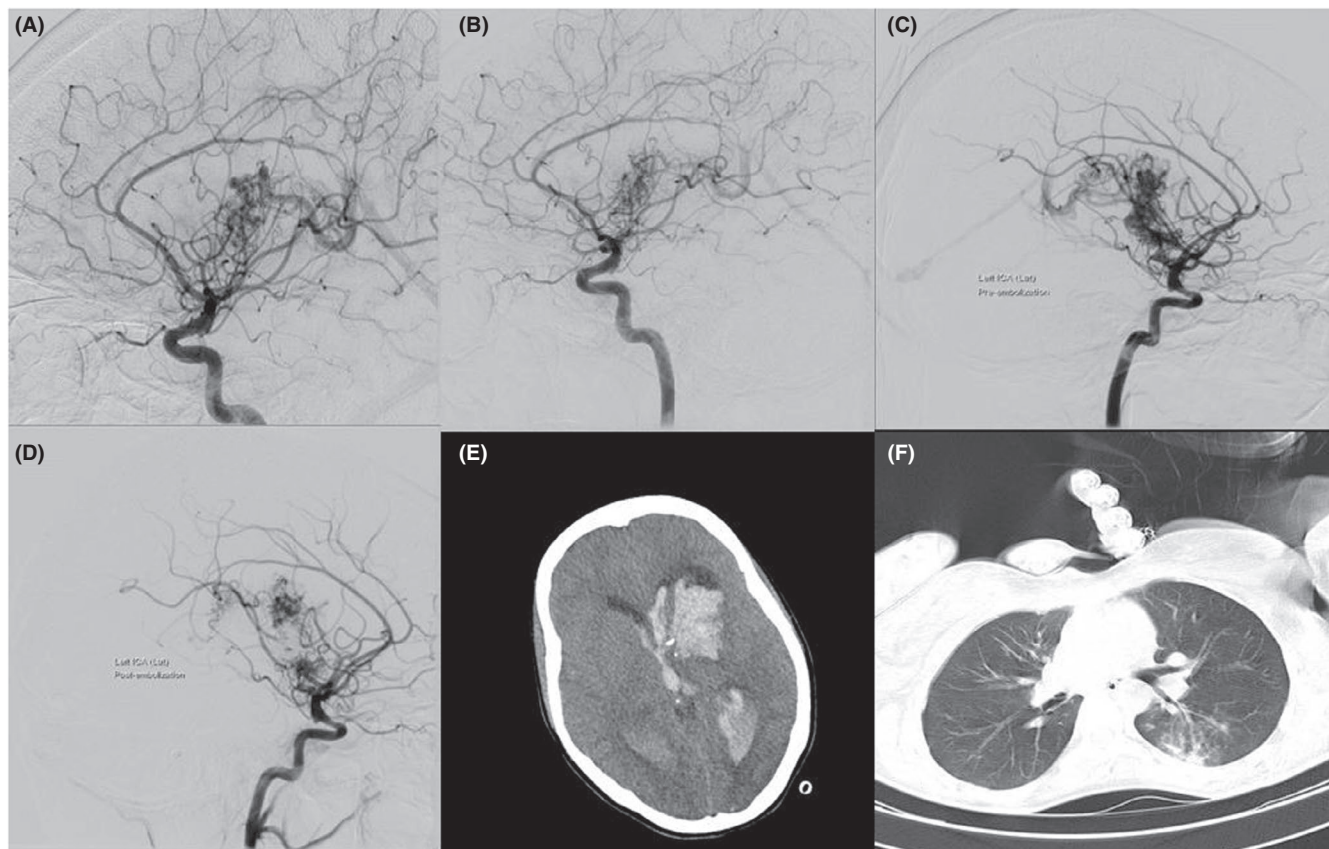


FIGURE 2 (A) The first diagnostic catheter angiography after intracranial hemorrhage. (B) Control angiography after partial arterial embolization. (C) Diagnostic angiography done after cure from COVID-19 infection. (D) Control angiography after partial transvenous embolization. (E) Brain CT scan shows IVH, left basal ganglia ICH. (F) Chest CT scan with ground glass appearance

control digital subtraction angiography (DSA) showed near-complete occlusion of the nidus (Figure 2D). On day 7 post-intervention, she was discharged home with improvement in the clinical status apart from right hemiparesis.

3 | DISCUSSION

According to the well-known facts and as it was published in the meta-analysis, the hemorrhagic complication of cerebral AVM embolization is not frequent and comprises about 2.6% per procedure.⁷ In this report, we have two patients with partial cerebral AVM embolization, they developed intraventricular and intracerebral hemorrhages at the time of being infected with COVID-19. In order to think about the relationship between COVID-19 and intracranial bleeding, especially we need to discuss the pathology. For the location, the proximity of these lesions to the ventricular system may be the cause as the hemorrhage leaked into the ventricles breaking the ependymal surface and it may happen with any hemorrhagic lesion located in the paraventricular region. In the second patient, ICH occurred as a result of rupture of the left basal ganglia AVM nidus. Regarding the effect of the viral infection, we will try to discuss two main pathologic processes: The first is the ability of the virus to use angiotensin-converting enzyme (ACE) II to enter cells.⁴ Angiotensin II is a vasoconstrictor, and its receptors are expressed in cerebrovascular endothelial cells and in the circumventricular organs.⁸ This expression has a hormonal regulatory function, water and sodium intake control, vascular autoregulation, and cerebral blood flow.⁹ According to that, we think reasonably in the injury occurred by the virus to the blood vessel as a result of the error in the function of enzyme receptors accompanied probably by temporary elevation in blood pressure, leading to vessel rupture and bleeding.

A second theory we may follow: It is well-known that the viral infections including COVID-19 induce cytokine storm (hypercytokinemia), which may lead to elevated systemic inflammation with high levels of interleukins IL-6, IL-1 β , and TNF, thus; causing breakdown of collagen and increasing the permeability of blood-brain barrier, with resultant vascular injury.¹⁰ As the natural history of any cerebral AVM involves a hemorrhagic complication since it is formed from a tangle of abnormal vessels with unstable wall;¹¹ in addition to the devastating pathologic processes caused by the novel COVID-19 to the vessel wall (instability of the already unstable vessel wall), we can put the light on the relationship between COVID-19 and bleeding from the embolized cerebral AVM.

3.1 | Conclusion

The literature discussing the effect of the virus on the cerebrovascular malformation are scarce; however, cerebrovascular surgeons must be aware about the increased rate of complications as IVH and ICH that may occur to the patients with untreated or partially embolized cerebral AVM who are infected with COVID-19.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

GL and FR conceived and designed the study. MG involved in overall supervision of the paper. All authors read and approved the final manuscript.

CONSENT

The patient's consent has been signed and collected in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: Ghorbani M, Lafta G, Rahbarian F. COVID-19 outbreak as a probable cause of increased risk of intracranial rebleeding in partially treated cerebral arteriovenous malformations. *Clin Case Rep.* 2021;9:e04893. <https://doi.org/10.1002/ccr3.4893>