



Case Report

Concurrent intracranial infarct and intraventricular hemorrhage with spontaneous nontraumatic extradural hemorrhage in follow-up: An enigma of COVID-19-associated intracranial vasculopathy

Sanjeev Sreenivasan¹, Chinmay Arora², Sandeep Vaishya², Rana Patir²

¹Department of Neurosurgery (Trauma and Emergency), All India Institute of Medical Sciences, Raipur, Chhattisgarh, ²Department of Neurosurgery, Fortis Memorial Research Institute, Gurgaon, Haryana, India.

E-mail: *Sanjeev Sreenivasan - sanjeev_ariyan@yahoo.com; Chinmay Arora - chinmay17arora@gmail.com; Sandeep Vaishya - svaishya@hotmail.com; Rana Patir - ranapatir@hotmail.com



***Corresponding author:**

Sanjeev Sreenivasan,
Department of Neurosurgery
(Trauma and Emergency),
All India Institute of
Medical Sciences, Raipur,
Chhattisgarh, India.

sanjeev_ariyan@yahoo.com

Received : 01 February 2022

Accepted : 16 February 2022

Published : 11 March 2022

DOI

10.25259/SNI_132_2022

Quick Response Code:



ABSTRACT

Background: Several neurological manifestations have been described in the literature, in patients affected with COVID-19 infection. Some common forms include ischemic stroke, cardioembolic stroke, intraparenchymal hemorrhage, and multicompartamental hemorrhage. Concurrent brain infarct and intraventricular hemorrhage (IVH) have not been described in the literature previously.

Case Description: A 35-year hypertensive and COVID-19-positive patient developed sudden-onset spontaneous IVH with concurrent infarct in the left internal capsule. In spite of undergoing an initial CSF drainage procedure, he had persistent worsening sensorium and increasing midline shift on CT imaging, so he underwent a left-sided decompressive craniectomy. One month after discharge, he developed spontaneous extradural hemorrhage at the operative site. In view of impending cerebral herniation, emergency hematoma evacuation was done, which restored his neurological status.

Conclusion: This is the first reported detailed case of concurrent intracranial infarct and IVH in a patient affected with COVID-19 infection. We also report a rare phenomenon of nontraumatic noncoagulopathic extradural hemorrhage on the decompressive craniectomy site, in this patient 1 month after surgery.

Keywords: Brain infarct, COVID-19, Intraventricular hemorrhage, Spontaneous extradural hemorrhage

INTRODUCTION

Although multicompartamental intracranial hemorrhage has been reported in the past, simultaneous occurrence of intracranial infarct and intraventricular hemorrhage (IVH) has not been detailed in the literature. Spontaneous extradural hemorrhage has been reported in patients on treatment with anticoagulants/antiplatelets. Occurrence of this phenomenon in a hypertensive and COVID-19-positive patient, in the absence of such medication, presents an interesting challenge for surgical management.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2022 Published by Scientific Scholar on behalf of Surgical Neurology International

CASE DETAILS

A 35-year male patient presented with sudden-onset altered sensorium and right-sided hemiparesis for 6 h. There was no history of hypertension (HTN), diabetes mellitus (DM), coronary artery disease, and recurrent transient ischemic attacks.

He had been treated for pneumonia secondary to coronavirus-2019 (SARS-CoV-2) infection (COVID-19) 4 weeks ago, when he was admitted with cough and breathlessness. A positive reverse transcriptase polymerase chain reaction test for COVID-19 infection was noticed. Serum assays reported D-dimer level of 0.6 ug/ml (normal) and fibrinogen level of 4.2 g/L (normal range <7 g/L). Total leukocyte count, platelet count, troponin, prothrombin time, and creatinine phosphokinase were normal. Inflammatory markers, C-reactive protein and serum ferritin levels, were 4.6 mg/l and 316 ng/ml, respectively. High-resolution computed tomography (HRCT) of chest showed atypical findings – patchy ground-glass opacity in the left upper lobe and evidence of hilar lymphadenopathy. This was assigned a CORADS score of 3 (indeterminate, Coronavirus Disease-2019 Reporting and Data Systems). Other signs such as bilateral ground-glass opacities, consolidation, prominent vessels, or bronchial dilatation were absent. He was diagnosed with mild COVID-19 infection based on HRCT chest findings, D-dimer assay, and level of inflammatory markers. He received dexamethasone and remdesivir along with antibiotic azithromycin. He received medications (amlodipine and telmisartan) for new-onset HTN. Supportive care in the form of incentive spirometry, chest physiotherapy, and humidified oxygen supplementation was also given. His general condition improved within 5–6 days of admission, following which he was discharged.

Examination findings

The patient was conscious, alert, and oriented to time, place, and person (Glasgow Coma Scale, [GCS] = E4V5M6) on presentation to the emergency department. Pulse rate was 90/min and blood pressure (BP) 126/80 mmHg. He had right-sided hemiparesis with power <3/5 (MRC grade) on neurological examination. Within an hour of admission, he developed persistent headache and vomiting. Noncontrast computerized tomography of head (NCCT) showed evidence of intraventricular hemorrhage (IVH) in bilateral lateral ventricles, third and fourth ventricles [Figures 1a and b]. Mild-to-moderate hydrocephalus was seen. His GCS score deteriorated to E3V2M5 and in view of falling neurological status, urgent cerebrospinal fluid (CSF) diversion procedure, that is, an external ventricular drainage (EVD), was performed [Figures 1a-d and 2].^[11] Intraoperatively, blood-tinged CSF was seen to egress out at high pressure (20 cm

water as verified by an arterial pressure transducer). This was connected to an external drainage system to allow the clearance of hemorrhagic CSF from the ventricular circulation [Figure 2]. After the procedure, his GCS improved to E4 V4 M6 level. He had persistent right-sided hemiparesis. Once he was clinically stable, contrast MR angiography of brain was done. This did not reveal any vascular anomaly like AVM or aneurysm [Figures 3a-d]. CSF routine examination showed plenty red blood cells, glucose – 91 mg/dl, protein – 195 mg/dl, and no leukocytes. On postoperative day (POD) 4, his GCS was E4 V4 M6 and there was an improvement in

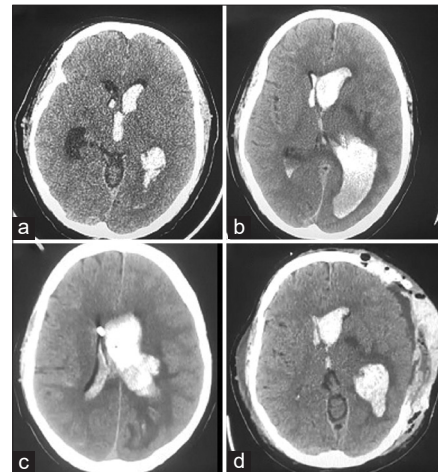


Figure 1: (a) NCCT head showing intraventricular hemorrhage, (b) NCCT head showing intraventricular hemorrhage with ventriculomegaly, (c) NCCT head showing EVD catheter tip inside right lateral ventricle, with reduced ventriculomegaly, and (d) NCCT head showing post decompressive craniectomy status – reduction in midline shift. NCCT: Noncontrast computerized tomography of head, EVD: External ventricular drainage.

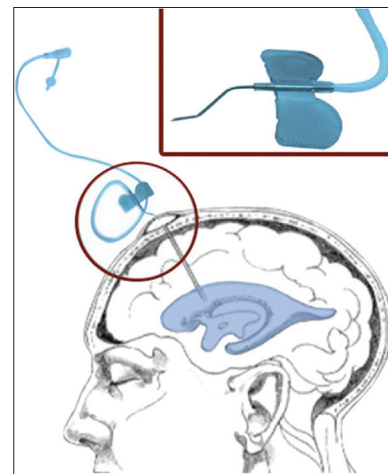


Figure 2: Method of external ventricular drainage used at our institute. Insertion of Ommaya catheter through Kocher's point and 22 gauge scalp vein bent and inserted into the Ommaya chamber to create a continuous CSF drainage flow system.

the right side power to 3/5. External ventricular drain was *in situ* through which CSF was drained intermittently to allow clearance of the hemorrhagic component. Decongestant medication (mannitol) was gradually tapered off over 3 days (POD 1 to POD 3). On POD 5, patient's GCS improved and he began following commands.

On POD 6, GCS became E2 V3 M5 and right-side hemiparesis worsened. A magnetic resonance imaging brain with angiography was done which was suggestive of an acute infarct in the left internal capsule [Figures 4a-d] and no angiographic abnormalities or no focal flow limiting stenosis. A midline shift of 10 mm was seen. Injection mannitol was administered as 300 mg intravenous bolus. The patient also had spike of fever (101 F) for which blood and urine cultures were sent, and antibiotic was upgraded from cefuroxime to meropenem. Six hours after initiation of decongestant therapy, GCS worsened to E2 V1 M5. The patient was taken to operative room (OR) for surgery under general anesthesia and a left-sided frontotemporoparietal decompressive craniectomy with lax duraplasty and with the placement of bone flap in bone bank was done. The right-sided external ventricular set was completely changed to a new ventricular catheter and drainage system. Gram staining of CSF did not reveal any microorganism or cells. Postoperatively, the patient was shifted to intensive care unit and mechanical ventilation was continued. Postoperative NCCT head showed a

craniectomy defect with IVH with reduced ventriculomegaly compared to the previous NCCT head.

On POD 1 after second surgery, his GCS was E2VtM5. Since GCS was lower than preoperative level, mannitol was restarted and periodic CSF drainage was continued from the EVD system. On POD 2, as his GCS improved to E3 VT M6 (occasionally following commands), he was removed of mechanical ventilation. Antibiotic coverage was escalated in view of fever and haziness in the lower zone of the left lung (suggestive of aspiration pneumonia). External CSF drainage system was removed on POD 3, as regular clear CSF flow was noticed and measured pressures were in the range of 10–12 cm H₂O. GCS improved to E4 V1 M6 (following command). The left-sided pneumonia gradually improved with antibiotics, chest physiotherapy, nebulized bronchodilators (salbutamol), and mucolytics (N-acetylcysteine). On POD 7, repeat NCCT head showed operative changes with a resolving IVH. Over next few days of hospital stay, there was an improvement in the right upper limb finger movements and flexion movements at the elbow joint.

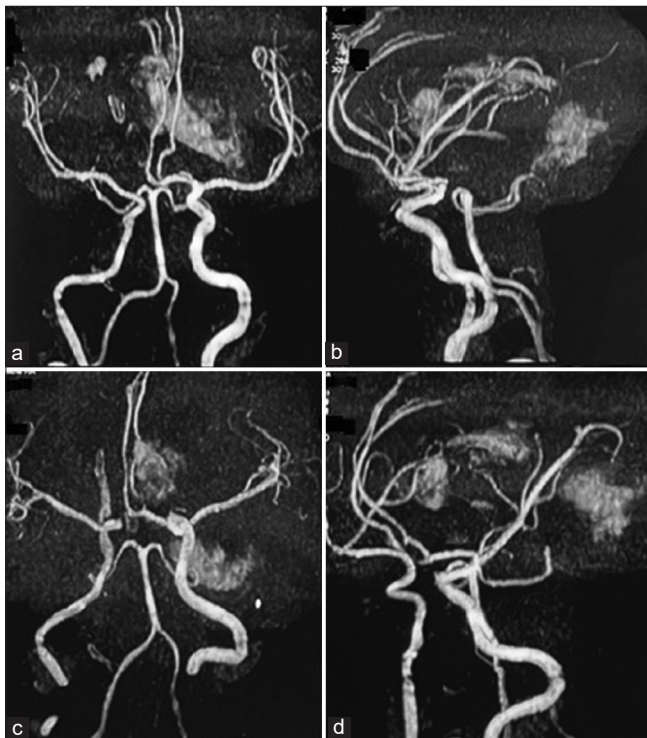


Figure 3: (a and c) MR angiography anteroposterior views showing grossly normal findings – no AVM or aneurysm. (b and d) MR angiography oblique and lateral views showing normal findings.

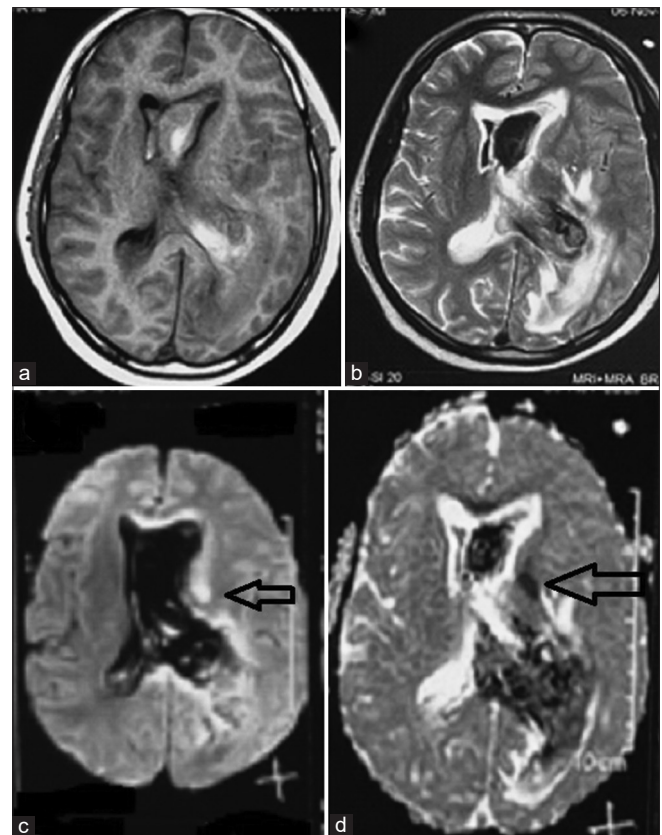


Figure 4: (a) T1-weighted MR image showing intraventricular hemorrhage, (b) T2-weighted MR image showing intraventricular hemorrhage, (c) diffusion-weighted image showing infarct in the left internal capsule, and (d) apparent diffusion coefficient image showing infarct in the left internal capsule (horizontal black arrow).

At the time of discharge, his vitals were stable and GCS was E4V3M6. Pupils were 2 mm bilaterally. He had right-sided weakness –3/5 (MRC grade) in elbow and fingers of upper limb, and 1/5 (MRC grade) in the lower limb. He was discharged with advice to continue antihypertensives and antiepileptics. In view of intracranial hemorrhage, antiplatelets and injectable antithrombotic measures were avoided.

POD 36 (Follow-up)

He was brought to ED in an unconscious state. His relatives reported a history of headache and one episode of the right-sided focal seizure followed by unconsciousness, while he was at home. Home recorded BP was 200/100 mmHg, at the onset of headache. On examination, his GCS was E1V1 M2 with extensor posturing. Anisocoria was present with a dilated left-sided pupil. NCCT head showed a large extradural hematoma [Figures 5a and b] over previous decompressive craniectomy site with mass effect and a midline shift of 2.7 cm. In view of an impending uncal herniation, the patient underwent emergency reexploration of scalp flap and hematoma evacuation in the emergency room. Then, he was rapidly intubated, ventilated, and shifted to the OR for surgical site hemostasis. No obvious arterial bleeder could be identified during surgical exploration. Scalp flap closure was done over a subgaleal Romovac drain. After the procedure, his GCS improved to E2Vt M5. NCCT head showed extradural air collection, no residual hematoma, or midline shift [Figures 5c and d]. Drain was removed on POD 1. Blood culture showed growth of *Acinetobacter* and antibiotics were upgraded according to the culture and sensitivity pattern. Chest and limb physiotherapy were done regularly. Gradually, his GCS improved to E3V1M6 and mechanical ventilation was discontinued. In view of recurrent bleeding episodes, injectable antithrombotics were avoided and mechanical compression was continued for the lower limb DVT prophylaxis.

At 6-month follow-up visit, his GCS was E4V1 (Aphasic) M6 with the right hemiparesis (3/5 MRC grade at shoulder, elbow, and wrist joints). MR brain did not reveal any new infarcts [Figures 6a and b].

At 11-month follow-up visit, the patient was E4V1 M6 with residual paresis in the right side (3/5 MRC grade in the upper and lower limbs). MR brain showed a resolving infarct without any new hemorrhagic changes [Figures 6c and d]. He underwent cranioplasty with autologous bone to cover the calvarial defect (Figures 7a and b: Preoperative and postoperative NCCT head).

DISCUSSION

Several case reports and series have demonstrated the wide nature of COVID-19 infection-related intracranial

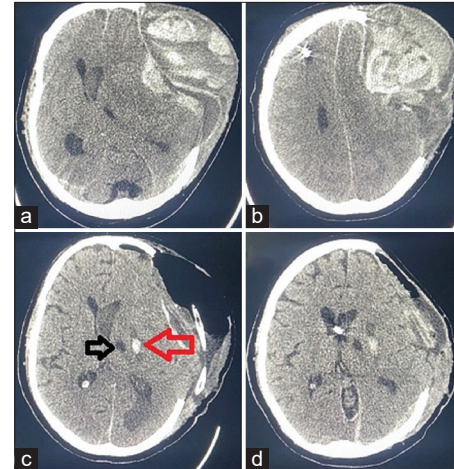


Figure 5: (a and b) NCCT head at POD 36 showing large extradural hematoma at the site of decompressive craniectomy, (c) postoperative NCCT head showing air in the extradural space after evacuation of hematoma, horizontal black arrow showing gliotic region of old infarct, and horizontal red arrow showing new area of putaminal hemorrhage, and (d) sequential cut image of postoperative NCCT head showing reduced midline shift after hematoma evacuation and old ventricular catheter tip in the right lateral ventricle. NCCT: Noncontrast computerized tomography of head, POD: Postoperative day.

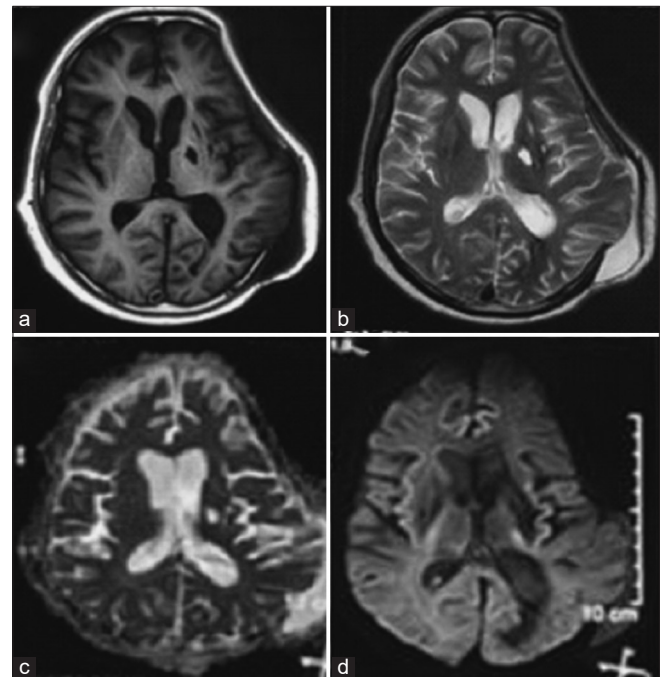


Figure 6: (a) Follow-up MRI at 6 months – T1 image – no new infarcts or midline shift, (b) follow-up MRI at 6 months T2-weighted image, (c) follow-up MRI at 11 months – diffusion-weighted image, and (d) follow-up MRI at 11 months – apparent diffusion coefficient image.

manifestations. The neurological sequelae include encephalitis, anosmia, stroke, and encephalopathy. Stroke represents one of

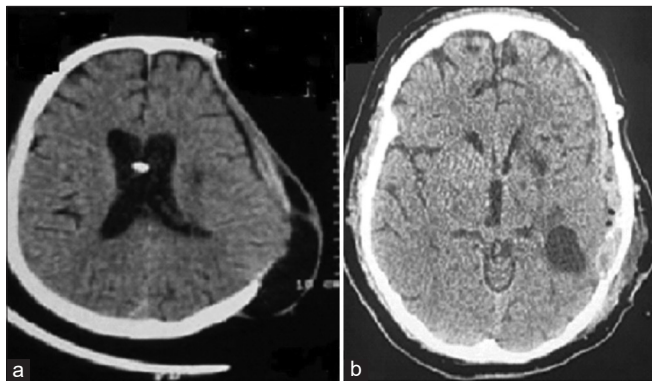


Figure 7: (a) Preoperative NCCT head (before cranioplasty) and (b) postoperative NCCT head after cranioplasty. NCCT: Noncontrast computerized tomography of head.

the most devastating complications.^[8] Multicompartmental hemorrhage has been previously reported in seven patients of a case series by Altschul *et al.* and a single case report by Sharifi-Razavi *et al.*^[2,10] At the onset of this pandemic, a case series reported nine out of 86 patients had simultaneous infarction and hemorrhage. However, details regarding individual clinical presentations and outcome were unavailable.^[4] We believe that our case is the first detailed description of SARS-CoV-2 affected patient with concurrent brain hemorrhage and ischemic infarct.

Time interval between diagnosis of COVID-19 and occurrence of stroke

Our patient suffered a stroke 4 weeks after the diagnosis of mild COVID-19-associated pneumonia. Available literature shows a duration of 2–25 days separating the two events.^[3]

Use of anticoagulation

It is believed to contribute to the development of hemorrhagic stroke in patients admitted in intensive care. Anticoagulation with low-molecular-weight heparin (LMWH) became a choice of the treatment for COVID-19-infected patients with elevated D-dimer assays. Our patient did not receive LMWH or antiplatelets (aspirin or clopidogrel). Hence, both episodes of hemorrhage were considered noncoagulopathic in nature.

Role of HTN in COVID-19 encephalopathy

Vicenzi *et al.* demonstrated rise in systolic BP in COVID-19-infected patients with poor pulmonary function reserve. This was seen even in the absence of prior history of HTN.^[15] Almost 80% in a consecutive case series of ICH in COVID-19-infected patients had vascular risk factors such as HTN or DM. Approximately 70% had severe COVID-19 pneumonia and five required mechanical ventilation. Inflammatory markers and D-dimer were elevated in all patients with

confirmed COVID-19 infection.^[3] Evidence also suggests that systolic BP variability also affects morbidity in patients with ICH.

Pathophysiology of neurological manifestations

Ischemic stroke has been attributed to COVID-19-related vasculitis, cardiomyopathy, and hypercoagulability.^[8] Lobar ischemic stroke involving temporal, parieto-occipital, cerebellar, and basal ganglia has been reported extensively. Our patient presented with a small infarct in the genu of internal capsule. There was no associated mass effect with this lesion. This later on evolved naturally into an area of gliosis, as seen on subsequent NCCT scans. There was no evidence of hemorrhagic transformation within the lesion.

Multiple pathogenic mechanisms have been described for hemorrhagic stroke in patients with underlying COVID-19 infection. SARS-CoV-2 has the ability to bind overexpressed endothelial protein angiotensin-converting enzyme 2 (ACE-2) and invade cerebral vasculature. This endotheliitis secondary to the presence of viral inclusion particles is a precursor for rupture of small caliber vessels.^[7,16]

The above mechanism also reduces serum ACE-2 levels and this unopposed action of angiotensin II, vasopressin, and aldosterone contributes to vasoconstriction and vascular inflammation.^[14] This finally precipitates development of ICH.

Another contributing factor to the development of ICH is the cytokine storm resulting from systemic inflammatory syndrome. This cytokine storm has a bimodal mechanism of action. First, the cytokines interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha activate matrix metalloproteinases which degrade the elastin and collagen constituents of the extracellular matrix.^[13] This reduces the vascular wall integrity, increasing the risk of rupture and subsequent hemorrhage. Second, they also activate the coagulation cascade causing thrombotic microangiopathy of vasa vasorum, which, in turn, causes arterial wall hypoxia.^[6,12]

Hemorrhage involving multiple cranial compartments was reported in 14 cases (9.5%). Single compartments were involved in the rest, with intraparenchymal hemorrhage (IPH) being the most common variety (62.6%), followed by subarachnoid hemorrhage (SAH) (15.0%), subdural hemorrhage (SDH) (11.6%), and IVH (1.4%). In patients with IPH, the most common location of the hemorrhage was the cerebral lobes (93.5%). Other sites included basal ganglia (5.4%) and the cerebellum (1.1%).^[3]

Role of inflammatory markers

Ageno *et al.* demonstrated that D-dimer levels were significantly higher in cardioembolic strokes compared to lacunar strokes.^[1,9]

Simultaneous occurrence of multiple neurological findings

Multicompartmental hemorrhage has been reported in seven patients out of a large series of COVID-19-infected patients with varied neurological findings.^[2] This included SDH, SAH, IPH, and IVH. Sharif-Razavi *et al.*^[10] reported one case of supratentorial and infratentorial hemorrhage. Another study by Katz *et al.*^[4] included nine patients with simultaneous hemorrhage and infarction, in the group with ischemic neurological manifestations. However, more detailed description of these patients could throw light on the possible pathogenesis. We report this rare case with concurrent brain infarct and IVH in a single patient. We believe that this represents a unique aspect of COVID-19-associated vasculopathy, as certain intraventricular vessels were prone to rupture while internal capsular vessels developed microthrombotic complications in the same time period.

Our patient developed spontaneous noncoagulopathic nontraumatic extradural hemorrhage at the site of decompressive craniectomy, 1 month after surgery. On surgical reexploration for the evacuation of hematoma, no active arterial cause could be identified. This presents a new picture of postoperative extradural vascular involvement in a neurosurgical patient, previously infected with SARS-CoV-2. Spontaneous extradural hemorrhage in a patient with sickle cell disease has been described in the literature.^[5] Our patient did not have any coagulopathic condition and he did not receive any anticoagulants/antiplatelets as part of treatment of mild COVID-19 pneumonia. In spite of multiple episodes of brain hemorrhages and infarct, the patient was able to recover and underwent cranioplasty at 11-month follow-up period. These multiple findings cannot be completely explained by the present theories of COVID-19-associated neurological vascular manifestations.

We believe that the good outcome in this patient can be attributed to the following: Timely intervention in the form of external CSF diversion procedure, good intensive care monitoring, early identification of postoperative complication, that is, spontaneous EDH and rapid decompression in the emergency room, good neurorehabilitation practices, prevention of secondary infection, and complications such as deep vein thrombosis and most importantly the good home care and nutrition by family members.

CONCLUSION

Through this rare case scenario, we present the story of a patient with a history of COVID-19 pneumonia who developed concurrent intracranial infarct and IVH. The occurrence of spontaneous nontraumatic noncoagulopathic extradural hemorrhage at the site of decompressive

craniectomy presents an intriguing twist in his tale. These findings cannot be completely explained by existing theories of COVID-19 cerebral vasculopathy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Publication of this article was made possible by the James I. and Carolyn R. Ausman Educational Foundation.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Ageno W, Finazzi S, Steidl L, Biotti MG, Mera V, Melzi d'Eril G, *et al.* Plasma measurement of D-dimer levels for the early diagnosis of ischemic stroke subtypes. *Arch Intern Med* 2002;162:2589.
2. Altschul DJ, Unda SR, De La Garza Ramos R, Zampolin R, Benton J, Holland R, *et al.* Hemorrhagic presentations of COVID-19: Risk factors for mortality. *Clin Neurol Neurosurg* 2020;198:106112.
3. Cheruiyot I, Sehmi P, Ominde B, Bundi P, Mislani M, Ngure B, *et al.* Intracranial hemorrhage in coronavirus disease 2019 (COVID-19) patients. *Neurol Sci* 2021;42:25-33.
4. Katz JM, Libman RB, Wang JJ, Sanelli P, Filippi CG, Gribko M, *et al.* Cerebrovascular complications of COVID-19. *Stroke* 2020;51:e227-31.
5. Kotey SN, Dike NO, Nani E, Nyame K. Spontaneous epidural and corpus callosum hemorrhage in sickle cell disease an unusual presentation in a Ghanaian patient. *Cureus* 2020;12:e12292.
6. Martin JF, Booth RF, Moncada S. Arterial wall hypoxia following thrombosis of the vasa vasorum is an initial lesion in atherosclerosis. *Eur J Clin Invest* 1991;21:355-9.
7. Moriguchi T, Harii N, Goto J, Harada D, Sugawara H, Takamino J, *et al.* A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *Int J Infect Dis* 2020;94:55-8.
8. Owolabi LF, Raafat A, Enwere OO, Mustapha AF, Adamu B, AlGhamdi M. Hemorrhagic infarctive stroke in COVID-19 patients: Report of two cases and review of the literature. *J Community Hosp Intern Med Perspect* 2021;11:322-6.
9. Reddy ST, Garg T, Shah C, Nascimento FA, Imran R, Kan P, *et al.* Cerebrovascular disease in patients with COVID-19: A review of the literature and case series. *Case Rep Neurol* 2020;12:199-209.
10. Sharifi-Razavi A, Karimi N, Rouhani N. COVID-19 and intracerebral haemorrhage: Causative or coincidental? *New Microbes New Infect* 2020;35:100669.

11. Singh H, Patir R, Vaishya S, Miglani R, Kaur A. External ventricular drain related complications-whether continuous CSF drainage via ommaya reservoir is the answer? *Neurol India* 2020;68:458.
12. Spence JD, De Freitas GR, Pettigrew LC, Ay H, Liebeskind DS, Kase CS, *et al.* Mechanisms of stroke in COVID-19. *Cerebrovasc Dis* 2020;49:451-8.
13. Sprague AH, Khalil RA. Inflammatory cytokines in vascular dysfunction and vascular disease. *Biochem Pharmacol* 2009;78:539-52.
14. Verdecchia P, Cavallini C, Spanevello A, Angeli F. The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. *Eur J Intern Med* 2020;76:14-20.
15. Vicenzi M, Di Cosola R, Ruscica M, Ratti A, Rota I, Rota F, *et al.* The liaison between respiratory failure and high blood pressure: Evidence from COVID-19 patients. *Eur Respir J* 2020;56:2001157.
16. Zhou L, Zhang M, Wang J, Gao J. Sars-Cov-2: Underestimated damage to nervous system. *Travel Med Infect Dis* 2020;36:101642.

How to cite this article: Sreenivasan S, Arora C, Vaishya S, Patir R. Concurrent intracranial infarct and intraventricular hemorrhage with spontaneous nontraumatic extradural hemorrhage in follow-up: An enigma of COVID-19-associated intracranial vasculopathy. *Surg Neurol Int* 2022;13:90.