American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2022; 23: e938571
DOI: 10.12659/AJCR.938571

Received: 2022.10.07
Accepted: 2022.11.28
Available online: 2022.12.05
Published: 2022.12.30

Encephalopathy as the Only Manifestation in Simultaneous Arterial Infarct and Cerebral Venous Sinus Thrombosis in Recent COVID-19 Infection

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF Yi Rong Chiew
E Yongyao Kong

Department of Neurology, National Neuroscience Institute, Singapore, Singapore

Corresponding Author: Yi Rong Chiew, e-mail: chiew.yi.rong@singhealth.com.sg
Financial support: None declared
Conflict of interest: None declared

Patient: Male, 33-year-old
Final Diagnosis: Concurrent arterial infarct and cerebral venous thrombosis related to recent COVID-19 infection
Symptoms: Encephalopathy
Medication: —
Clinical Procedure: —
Specialty: Neurology

Objective: Unusual clinical course

Background: Emerging cases of SARS-CoV-2 infection associated with cerebral thromboembolism episodes manifesting as arterial strokes or cerebral venous thrombosis have been reported. However, the co-occurrence of arterial strokes and cerebral venous thrombosis is rare.

Case Report: We report the case of a previously healthy young patient with recent SARS-CoV-2 infection, who presented with encephalopathy. His computed tomography venography and magnetic resonance imaging of the brain showed thrombosis of the vein of Galen and straight sinus, and arterial infarcts in both hemispheres. His inflammatory markers, D-dimer levels, and coagulation profile were normal. He was started on anticoagulation and recovered well.

Conclusions: Concurrent arterial and venous thrombosis can happen rarely in patients with SARS-CoV-2 infection, including patients who have recently recovered from COVID-19. Cerebral thromboembolism associated with SARS-CoV-2 can present with a variety of subtle clinical manifestations, including encephalopathy without focal neurological deficits. Inflammatory markers, D-dimer levels, and coagulation profiles can be normal, especially in patients with mild infection or who have recovered from the infection. Therefore, it is important to be vigilant and recognize this clinical entity so that the diagnosis can be made and treatment can be started promptly. However, larger and prospective studies are needed to determine the clinical outcomes, therapeutic benefits, and complications of concurrent arterial stroke and cerebral venous thrombosis associated with SARS-CoV-2 infection.

Keywords: COVID-19 • Ischemic Stroke • Venous Thrombosis

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/938571

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Background

There have been increasing reports of hypercoagulability associated with SARS-CoV-2 infection leading to thromboembolism, such as arterial cerebrovascular infarcts or cerebral venous thrombosis [1-6]. However, the co-occurrence of arterial strokes and cerebral venous thrombosis is rare. To the best of our knowledge, only 3 cases of concurrent arterial infarct and cerebral venous thrombosis have been reported [1,5,6]. Moreover, as the COVID-19 pandemic continues and new variants emerge, it is important to remain vigilant for associated neurological complications, even in recently recovered COVID -19 patients and in patients with subtle, non-specific symptoms, such as encephalopathy without focal neurological deficits, as shown in our case.

Case Report

A previously healthy, 33-year-old man with a history of recovered SARS-CoV-2 infection 1 month prior to admission had an altered mental status for 1 day. His SARS-CoV-2 infection was mild, resulting only in upper respiratory tract symptoms. It was diagnosed by a self-administered antigen rapid test, and the patient did not require supplemental oxygen or hospitalization. He was brought to the hospital by his parents because

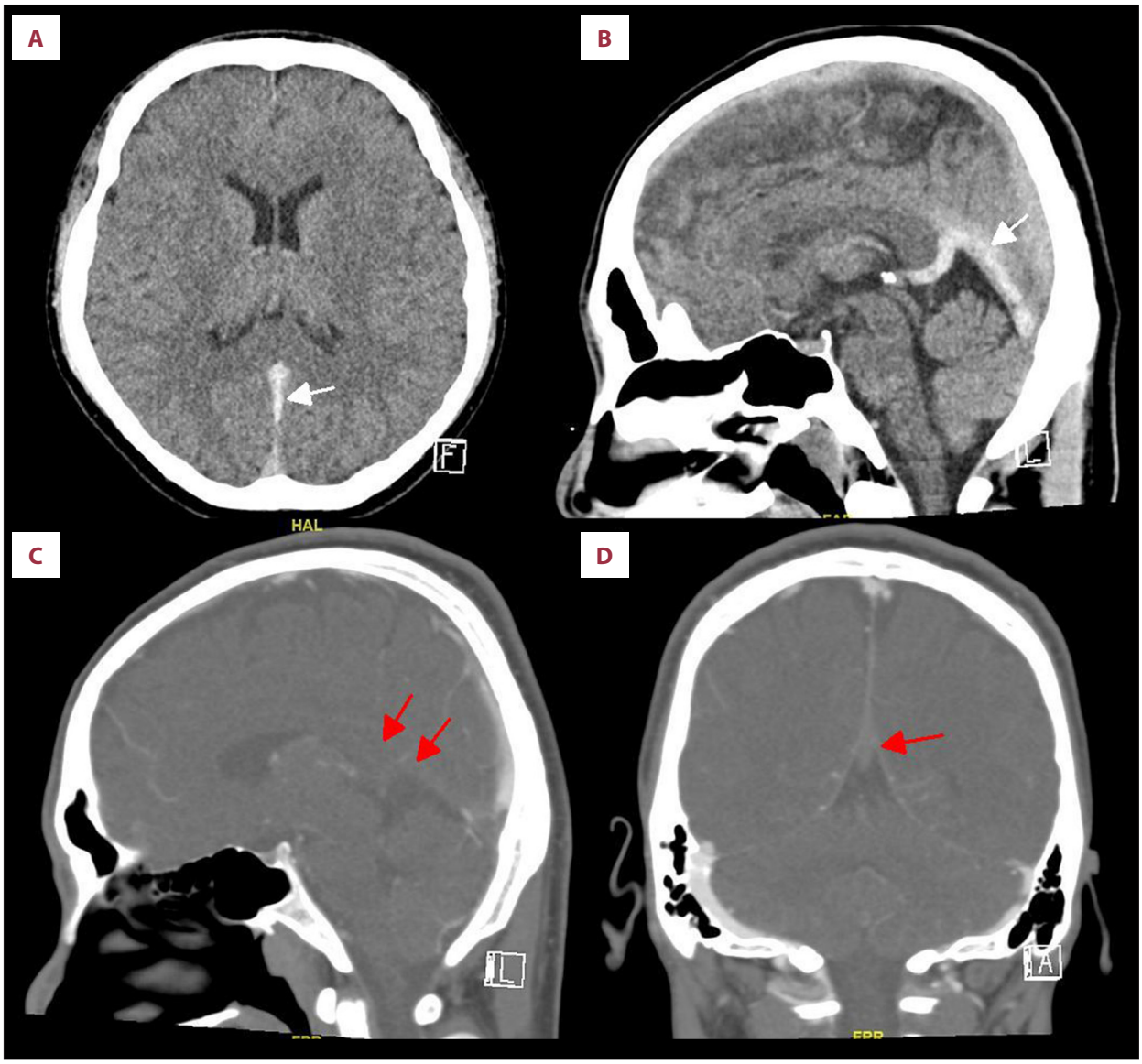

Figure 1. Axial (**A**) and sagittal (**B**) planes of the non-contrast-enhanced computed tomography (CT) brain show hyperdensity of the straight sinus, indicating venous sinus thrombosis (**white arrows**). Sagittal (**C**) and coronal (**D**) planes of CT venography show filling defects suggestive of thrombosis of the straight sinus and vein of Galen (**red arrows**).

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

he was "speaking confusedly". He had no seizure, weakness and numbness of limbs, visual disturbances, fever, headache, or dizziness. There was no recent history of long-distance travel, head trauma, recreational drug use, chronic steroid use, or hormone therapy. There were no skin rashes, recurrent ulcers, or joint pain. There was no history of malignancy or autoimmune or coagulation disorders.

On clinical examination, his Glasgow coma scale score was 14 (eye 4, verbal 4, motor 6). He was disorientated to time, place, and person. He could obey commands to verbal cues consistently and he could name objects and repeat words and sentences. There were otherwise no cranial nerve deficits, visual or sensory neglect, or cerebellar dysfunction. His hydration status was fair. His muscle strength was normal in his limbs. There were no extrapyramidal signs, ataxia, and sensory deficits on clinical examination. His Babinski reflexes were normal. His vital signs were stable on admission, he had no fever, and his blood pressure and heart rate were normal.

His full blood count, C-reactive protein level, and renal, thyroid, and liver function tests were normal. Given the acute altered mental status, a brain computed tomography scan (CT) was performed. The non-contrast enhanced CT brain scan showed hyperdensity of the straight sinus, suggestive of venous sinus thrombosis. CT venography showed filling defects, suggestive of thrombosis of the straight sinus and vein of Galen (**Figure 1**). A magnetic resonance imaging (MRI) scan of the brain was performed, which showed bilateral subcortical arterial infarcts in the middle cerebral artery territories, involving bilateral centrum semiovale, corona radiata, white matter of the bifrontal and parietal lobes, and bilateral peritrigonal areas (**Figure 2**). There was neither venous infarction nor venous hemorrhage. There were no intracranial arterial steno-occlusions. Ultrasound of the bilateral carotid arteries was normal, and there was no deep venous thrombosis on ultrasound of the bilateral lower extremities.

The following tests were within the normal range: D-dimer level, coagulation profile, antinuclear antibody, anti-double-stranded DNA, erythrocyte sedimentation rate, lupus anticoagulant, anti-cardiolipin IgG and IgM antibodies, anti-beta-2 glycoprotein antibodies, anti-thrombin III, factor V Leiden gene test, homocysteine level, and protein C/protein S level. His HIV and syphilis tests were negative. His renal function test, thyroid function test, serum vitamin B12 level, and urine drug screen were unremarkable. His CT scan of the neck, thorax, abdomen, and pelvis showed no evidence of malignancy or infection. Holter monitoring and transthoracic echocardiogram, performed to exclude a cardioembolic cause for the arterial infarcts, were normal. He was also reviewed by an otorhinolaryngologist, who performed a nasoendoscopy and an otoscopy, which did not show evidence of infection.

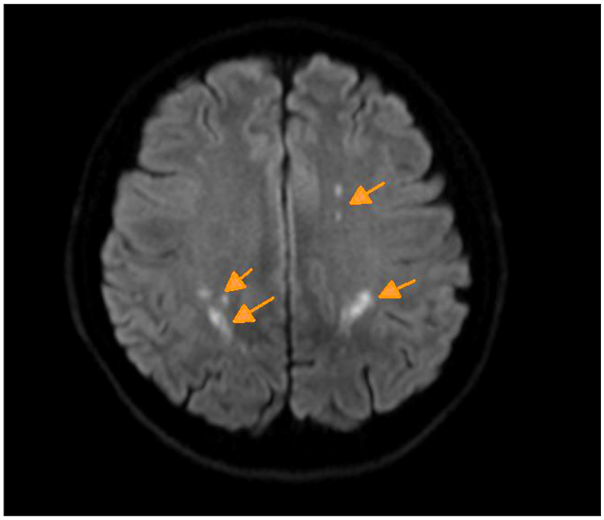

Figure 2. Axial plane of magnetic resonance imaging of the brain showing restricted diffusion in the bilateral centrum semiovale, corona radiata, white matter of the bifrontal and parietal lobes, and bilateral peritrigonal areas, suggestive of acute infarcts (**orange arrows**).

Nucleocapsid antibodies were performed to assess his SARS-CoV-2 infection status. His anti-N and anti-S antibodies were reactive, suggesting recent recovered SARS-CoV-2 infection. His cycle threshold was 36.5 (reference value: >25), indicating a low SARS-CoV-2 viral load.

A diagnosis of concurrent arterial infarction and deep cerebral venous thrombosis secondary to recent SARS-CoV-2 infection was made. He was given subcutaneous low-molecular-weight heparin within the first 2 h of his admission, when the CT venogram showed evidence of cerebral venous thrombosis. His encephalopathy resolved on the second day of admission, without new neurological deficits. After 7 days, he was switched to oral dabigatran and discharged, with follow-up scheduled in the outpatient clinic.

Discussion

In a study by Koh et al on the prevalence of various neurological manifestations associated with SARS-CoV-2 infection, acute ischemic stroke was the most commonly reported manifestation, while the occurrence of cerebral venous thrombosis was rare. Of the 47 572 patients prospectively studied in the study, no case of concurrent arterial stroke and cerebral venous thrombosis was reported [7]. Our case is the first reported case of concurrent arterial stroke and cerebral venous thrombosis associated with SARS-CoV-2 infection in Singapore and, as far as we know, the fourth reported case worldwide.

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

According to Koh et al, most patients with acute ischemic stroke reported in the study were asymptomatic for SARS-CoV-2 infection, and stroke was the first manifestation. Also, in cerebral venous thrombosis, all patients reported in the study had mild COVID-19 disease [7]. This result differs from previous publications reporting thromboembolism in severe COVID-19 disease [8,9]. According to previous reported cases of concurrent arterial and cerebral venous thrombosis [1,5,6], the cases reported by Malentacchi et al and Roushdy et al had significant COVID-19 symptoms requiring ICU admission [1] and oxygen supplementation [6]. Our case differs from these reports, as our patient had already recovered from his recent SARS-CoV-2 infection. This finding is interesting as it broadens the spectrum of clinical manifestations of COVID-19-related thromboembolism further, by illustrating the possibility of thromboembolic episodes in patients who are thought to have recovered from recent SARS-CoV-2 infections.

The clinical presentation of cerebral venous sinus thrombosis varies widely depending on the site of thrombosis and the sinuses involved. Deep cerebral venous sinus thrombosis, such as the vein of Galen and straight sinus thromboses, are often difficult to diagnose acutely, given the variable clinical symptoms with possible absence of focal neurological deficits [10]. In the other 3 cases of simultaneous arterial and venous thrombosis in SARS-CoV-2 infections reported by Malentacchi et al, Bermudez et al, and Roushdy et al [1,5,6], all patients showed significant neurological deficits including coma [1], pyramidal signs such as positive Babinski sign [1], weakness [5], ataxia [5], and seizures [6]. These findings differ from our patient, who had only encephalopathy without other significant neurological symptoms and focal deficits. Our case has highlighted the rare possibility of COVID-19 patients with cerebral thromboembolism presenting with subtle symptoms and clinical features such as encephalopathy, without obvious focal neurological deficits. Therefore, it may be appropriate to remain vigilant and perform continuous clinical surveillance for possible neurological complications in patients with SARS-CoV-2 infections, including recovered SARS-CoV-2 infections.

There are many different postulated mechanisms of thromboembolism associated with SARS-CoV-2 infections. Excessive inflammation and COVID-19-associated coagulopathy manifested by persistent fever, elevated inflammatory markers, increased serum D-dimers, thrombocytopenia, and an impaired coagulation profile was proposed by Gu SX et al [11]. This finding is similar to an observation by Kananeh et al, who suggested hypercoagulability due to a cytokine surge as a possible mechanism in the 4 patients reported [12]. All patients reported by Kananeh et al had moderate to critical COVID-19 symptoms, requiring ICU admission, and significantly elevated D-dimer levels. This is also consistent with the reports of Malentacchi et al and Roushdy et al, who reported impaired coagulation profiles and elevated D-dimer levels in their patients with moderate to critical SARS-CoV-2 infections and concurrent arterial and cerebral venous thromboses [1,6]. However, our patient had no fever, and his inflammatory markers, platelet count, D-dimer level, and coagulation profile were within the normal range. This demonstrates the possibility of a normal D-dimer level and coagulation profile in patients with mild symptoms or who have recovered from COVID-19. This also shows the importance of recognizing this clinical entity even when there is no evidence of hypercoagulability or coagulopathy, such as a high D-dimer level or an impaired coagulation profile, especially in patients with mild COVID-19 or who have recovered from it.

Regarding antithrombotic therapy for COVID-19-related hypercoagulability, a recent study by Sahai et al showed no therapeutic benefit of antiplatelet agents in preventing thrombosis and death in COVID-19 [13]. The mainstay of therapy for cerebral venous thrombosis in patients with COVID-19 is therapeutic anticoagulation with adequate hydration [14]. The treatment of cerebral venous thrombosis associated with SARS-CoV-2 infection is no different from that of cerebral venous thrombosis without this infection, namely the initiation of parenteral anticoagulation (unfractionated heparin or low molecular weight heparin), followed by oral anticoagulation conversion [15]. In the 3 previous reports of concurrent arterial and venous thrombosis in SARS-CoV-2 infection [1,5,6], anticoagulation was started in all patients, but the outcomes were variable, with 2 of the patients dying [1,6], while 1 recovered well [5]. Unfortunately, given the rare co-occurrence of arterial infarct and cerebral venous thrombosis in SARS-CoV-2 infection, it remains difficult to draw a firm conclusion regarding the optimal treatment, its potential therapeutic complications, and clinical outcomes. Therefore, future large and prospective studies are needed to clarify this issue.

Conclusions

In conclusion, concurrent arterial and venous thrombosis can rarely happen in patients with SARS-CoV-2 infections, including patients who have recently recovered from COVID-19. Cerebral thromboembolism associated with COVID-19 can present with a variety of clinical manifestations, including subtle symptoms such as encephalopathy, without focal neurological deficits. Inflammatory markers, D-dimer levels, and coagulation profiles can be normal, especially in patients with mild infection or in patients who have recovered from the infection. Therefore, it is important to be vigilant and recognize this clinical entity so that the diagnosis can be made and treatment can be started promptly. Larger and prospective studies are needed to determine the clinical outcomes, therapeutic benefits, and complications of concurrent arterial stroke and cerebral venous thrombosis associated with SARS-CoV-2 infection.

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Malentacchi M, Gned D, Angelino V, et al. Concomitant brain arterial and venous thrombosis in a COVID-19 patient. Eur J Neurol. 2020;27(9):e38-e39
2. Zicarelli CAM, Martins JV, Doni WV, et al. Cerebral venous thrombosis and COVID-19: Literature review. J Neurol Stroke. 2021;11:57-68
3. Dakay K, Cooper J, Bloomfield J, et al. Cerebral venous sinus thrombosis in COVID-19 Infection: A case series and review of the literature. J Stroke Cerebrovasc Dis. 2021;30(1):105434
4. Fara MG, Stein LK, Skliut M, et al. Macrothrombosis and stroke in patients with mild Covid-19 infection. J Thromb Haemost. 2020;18(8):2031-33
5. Bermúdez S, Forero PA, Salej V, et al. Simultaneous arterial and venous brain infarctions in a patient with COVID-19: Case report. SN Compr Clin Med. 2021;3(12):2622-25
6. Roushdy T, Sharaf NK. Venous and arterial cerebral thrombosis: A COVID-19 dual pathology and single possible etiology – a case report. Egypt J Neurol Psychiatr Neurosurg. 2022;58(1):8
7. Koh JS, De Silva DA, Quek AML, et al. Neurology of COVID-19 in Singapore. J Neurol Sci. 2020;418:117118 [Erratum in: J Neurol Sci. 2021;424:117406]
8. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-69 [Erratum in: JAMA. 2021;325(11):1113]
9. Guan WJ, Ni ZY, Hu Y, et al. China Medical Treatment Expert Group for COVID-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-20
10. van den Bergh WM, van der Schaaf I, van Gijn J. The spectrum of presentations of venous infarction caused by deep cerebral vein thrombosis. Neurology. 2005;65(2):192-96
11. Gu SX, Tyagi T, Jain K, et al. Thrombocytopathy and endotheliopathy: Crucial contributors to COVID-19 thromboinflammation. Nat Rev Cardiol. 2021;18(3):194-209
12. Kananeh MF, Thomas T, Sharma K, et al. Arterial and venous strokes in the setting of COVID-19. J Clin Neurosci. 2020;79:60-66
13. Sahai A, Bhandari R, Godwin M, et al. Effect of aspirin on short-term outcomes in hospitalized patients with COVID-19. Vasc Med. 2021;26(6):626-32
14. Abdalkader M, Shaikh SP, Siegler JE, et al. Cerebral venous sinus thrombosis in COVID-19 patients: A multicenter study and review of literature. J Stroke Cerebrovasc Dis. 2021;30(6):105733
15. Ghosh R, Roy D, Mandal A, et al. Cerebral venous thrombosis in COVID-19. Diabetes Metab Syndr. 2021;15(3):1039-45

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]