

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Cerebral venous sinus thrombosis related to SARS-CoV-2 infection in a pediatric patient: A case report ☆,☆☆

Nguyen Duong Quoc Anh, MD^{a,1}, Tran Chi Cuong, MD, PhD^{b,1}, Le Minh Thang, MD^b,
 Nguyen Dao Nhat Huy, MD^b, Nguyen Thi To Tran, MD^c, Nguyen Luu Giang, MD^b,
 Ngo Minh Tuan, MD^b, Bui Thi Bich, MD^a, Vo Thanh Tung, MD^a, Nguyen Minh Duc, MD^{d,*}

^a Department of Radiology, Can Tho S.I.S General Hospital, Can Tho, Vietnam^b Digital Subtraction Angiography Unit, Can Tho S.I.S General Hospital, Can Tho, Vietnam^c Department of Surgery, Can Tho S.I.S General Hospital, Can Tho, Vietnam^d Department of Radiology, Pham Ngoc Thach University of Medicine, 2 Duong Quang Trung Ward 12 District 10, Ho Chi Minh City, Vietnam

ARTICLE INFO

Article history:

Received 28 March 2023

Revised 26 June 2023

Accepted 23 July 2023

Keywords:

COVID-19

SARS-CoV-2

Cerebral venous sinus thrombosis (CVST)

Pediatric thrombosis

Magnetic resonance venography (MRV)

ABSTRACT

Coronavirus disease 2019 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); it has recently been associated with several hematologic disorders. A 4-year-old boy who had SARS-CoV-2 10 months prior was admitted to the emergency department of our hospital with seizures. His SARS-CoV-2 IgG II level was 885.7 AU/mL. Neuroimaging with cranial computed tomography after admission showed abnormal images of the venous sinus, but this was not sufficient to diagnose cerebral venous sinus thrombosis. Therefore, magnetic resonance imaging and digital subtraction angiography were conducted, which confirmed the diagnosis. He was treated with thrombectomy and anticoagulation drugs, and the clinical outcomes were satisfactory. Because our patient had a medical history of SARS-CoV-2 and exhibited no other risk factors, we present this case as evidence of a potential association between cerebral venous sinus thrombosis and SARS-CoV-2.

© 2023 The Authors. Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; CVST, cerebral venous sinus thrombosis; CT, computed tomography; MRI, magnetic resonance imaging; MRV, magnetic resonance venography; ANA, antinuclear antibody; DSA, digital subtraction angiography; ACE2, angiotensin-converting enzyme 2; MIS-C, multisystem inflammatory syndrome in children; VTEs, venous thrombosis events.

☆ Acknowledgments: None to declare.

☆☆ Competing Interests: The authors declare that they have no competing interests.

* Corresponding author.

E-mail address: bsnguyenminhduduc@pnt.edu.vn (N.M. Duc).¹ These authors contributed equally to this article as co-first authors.<https://doi.org/10.1016/j.radcr.2023.07.060>

1930-0433/© 2023 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has posed a massive threat to global health. Recently, COVID-19 has been associated with several hematologic disorders. SARS-CoV-2 infection affects a pro-thrombotic state, but the long-term effects of COVID-19 on the prevalence of vascular diseases are not clear. According to several studies conducted during the COVID-19 pandemic, infectious SARS-CoV-2 in children is typically mild and nonfatal, but it can lead to serious diseases and long-term sequelae [1,2].

Cerebral venous sinus thrombosis (CVST) is an uncommon subtype of stroke; the prevalence of CVST was reported to be approximately 2.34 cases per 100,000 per year before the COVID-19 pandemic and approximately 4.5–20 cases per 100,000 during the pandemic [3–5]. CVST has many known genetic and acquired risk factors. CVST has a good prognosis with treatment, but it can be fatal if it is not treated or treated late. However, it is very difficult to diagnose CVST with only clinical examination because patients (especially pediatric patients) can present with a wide of nonspecific symptoms, such as headache, vomiting, and seizures [6–8].

Neuroimaging is critical for the diagnosis of CVST. Computed tomography (CT) scans and magnetic resonance imaging (MRI) are routinely indicated to detect these brain parenchyma injuries. Nonenhancement CT imaging is not sensitive for detecting thrombosis in the cerebral sinus venous system and only identifies 25%–56% of cases [9–11]. MRI pulse sequences (both enhanced and nonenhanced techniques) are very effective for CVST diagnosis and have variable strengths. In addition, digital subtraction angiography (DSA) is essential to confirm a diagnosis of an occluded venous sinus. Furthermore, patients with CVST could be treated by DSA with modern techniques, such as the thrombectomy method or venous stents.

Case presentation

A 4-year-old boy was admitted to the emergency department with seizures. He had experienced headaches and vomiting during the 7 days before admission without treatment. His symptoms became more severe and progressed to seizures. On admission, his vital signs were as follows: blood pressure, 110/72 mm Hg; heart rate, 88; respiratory rate, 16; and normal body temperature. He had SARS-CoV-2 10 months before admission.

On admission, labs, including biochemical tests and complete blood count, were obtained and were within normal range. Further evaluation with noncontrast head CT was then performed, demonstrating bilateral hypodense thalamic lesions and hyperdensity in the right transverse sinus, straight sinus, vein of Galen, and inferior sagittal sinus (Fig. 1). Then, he was then scanned by a Siemens MAGNETOM Spectra 3

Tesla MRI scanner with a noncontrast technique to visualize the vascular brain parenchyma, and the parameters were assessed by syngo.via software version 4.1.

The result of MRI sequences showed increased signal intensity in the bilateral thalami with fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging (DWI), and apparent diffusion coefficient (ADC) (Fig. 2). Occlusion of the right transverse sinus, straight sinus, vein of Galen, and inferior sagittal sinus due to the thrombosis was apparent on susceptibility-weighted imaging (SWI) and MRV images (Fig. 3).

DSA confirmed these predicted sinus occlusions in the MRI (Fig. 4). Based on the results of CT, MRI, and DSA, the diagnosis of CVST was confirmed for the patient. The patient's treatment was continued with mechanical thrombectomy with angioplasty; 5F and 8F sheaths (Terumo) were used to access the superficial femoral artery and the femoral vein, respectively. The right internal carotid artery was accessed with a diagnostic 5F vertebral catheter (Merit Medical) and a 0.035" wire (Terumo) to generate a roadmap of the cerebral sinus. A coaxial system consisting of a Neuron Max 6F 088 Long Sheath (Penumbra) catheter with a Vertebral 5F (Merit Medical) diagnostic catheter and a 0.035-inch wire (Terumo) was used to access the internal jugular vein. Then, a SOFIA Plus aspiration catheter 6F (Microvention) with a Headway 21 microcatheter (Microvention) and a Traxcess 0.014 microwire (Microvention) were passed through the straight sinus occlusion into the internal cerebral vein and the inferior sagittal sinus, respectively. Although the Solumbra technique was applied with CatchV35 stent (Balt) twice, the cerebral sinuses remained occluded. A JADE 4.0 × 40 mm balloon (OrbusNeich) was dilated at the occlusive sites. Angiography revealed that the recanalization was ultimately successful in the straight sinus and the right transverse sinus (Fig. 4).

After mechanical thrombectomy, the patient (who weighed approximately 20 kg), was treated with a half dose of enoxaparin 4000 anti-Xa IU/0.4 mL twice a day for 10 days, after which rivaroxaban 15 mg was administered once a day; this treatment was maintained for 6 months. On the seventh day after the thrombectomy, the biochemical tests, which were used for finding risk factors or causes of CVST, were indicated for our patient. The level of SARS-CoV-2 IgG II was 885.7 AU/mL (Reference range: Negative <50.0 AU/mL; Positive ≥ 50.0 AU/mL). However, the hypercoagulation ability workup, including protein C, protein S, antithrombin III, antithrombin/antithrombin III, anti-ANA, antiphospholipid IgG, antiphospholipid IgM, Factor VII G10976A, Factor XIII F13A1, Factor V Leiden, Factor V Leiden mutation, prothrombin gene mutation (G20210A), Factor V R2 A4070G, MTHFR A1298C, was unremarkable.

On the 10th day after the thrombectomy, an MRV was performed, demonstrating the recanalization of the cerebral sinus system (Fig. 5). D-dimer (blood) was indicated for our patient after 10 days of using anticoagulation drugs. Quantitative D-dimer (blood) revealed a level of 1.52 ug/mL (Reference range: < 1 ug/mL). Our patient continued the anticoagulation method with good clinical outcomes.

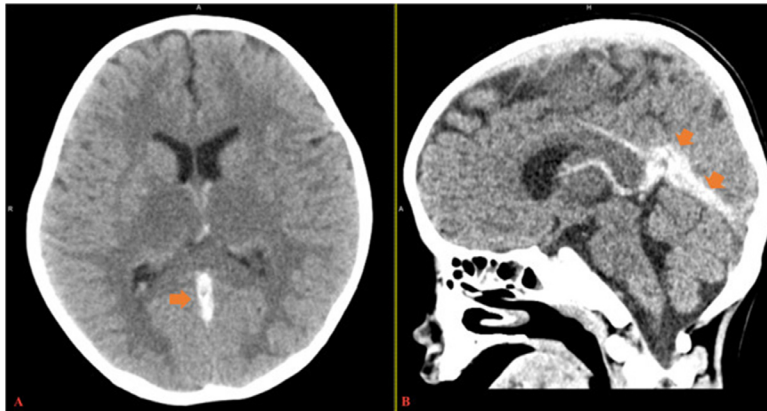


Fig. 1 – Computed tomography images. (A) Shows an axial cross-section of the thalamus showing bilateral hypodense thalamic lesions. (B) shows the hyperdense cerebral venous sinus system (orange arrow).

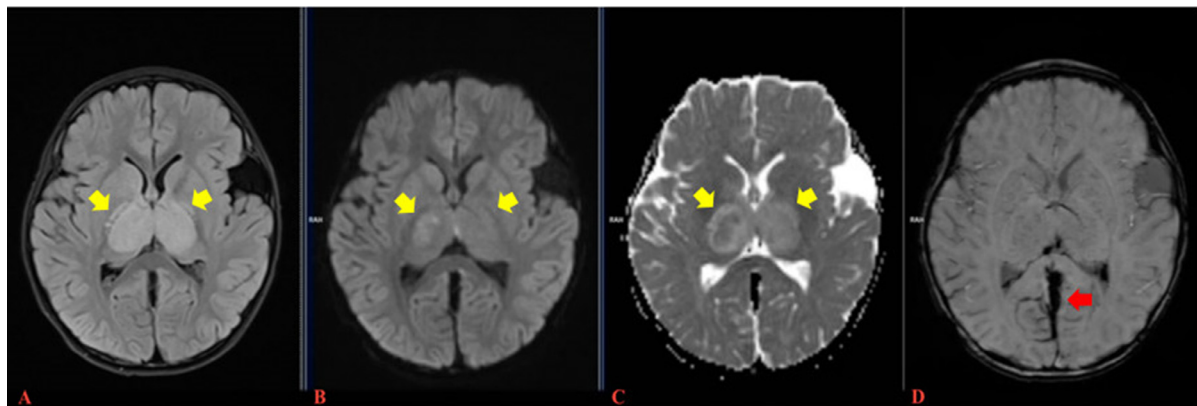


Fig. 2 – Parenchymal lesions on MRI brain. (A), (B), (C) illustrates bilateral hyperintense thalamic lesions (yellow arrows) with axial fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging (DWI), and apparent diffusion coefficient (ADC), respectively, which gives a suspicion for parenchyma edema. (D) shows hypointensity of the straight sinus with susceptibility-weighted imaging (SWI) (red arrow), which gives a suspicion for thrombosis in the sinus.

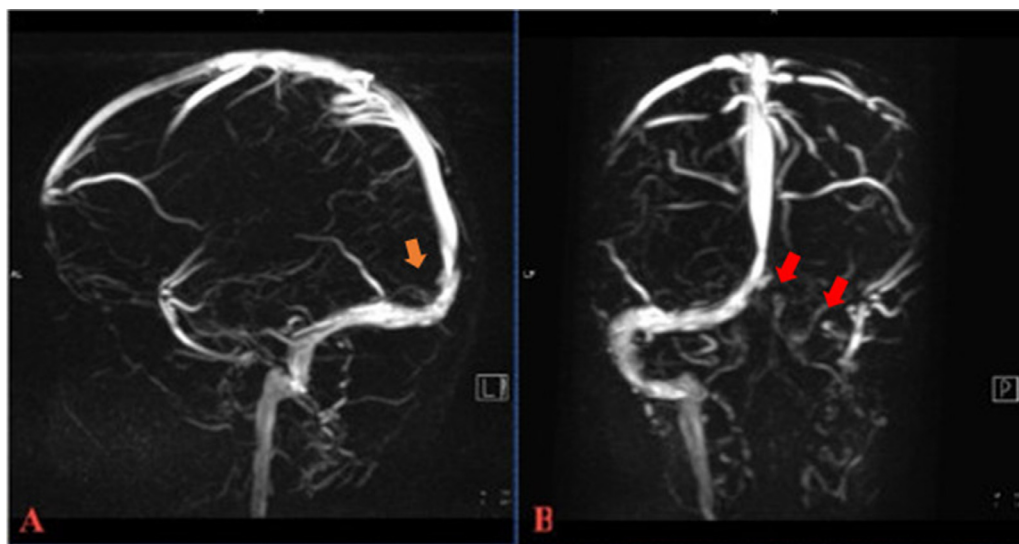


Fig. 3 – Imaging of cerebral venous sinus system on MR Venography before treatment. (A), (B) Shows the occlusion of the straight sinus (orange arrow) and right transverse sinus (red arrows) on MRV images before treatment.

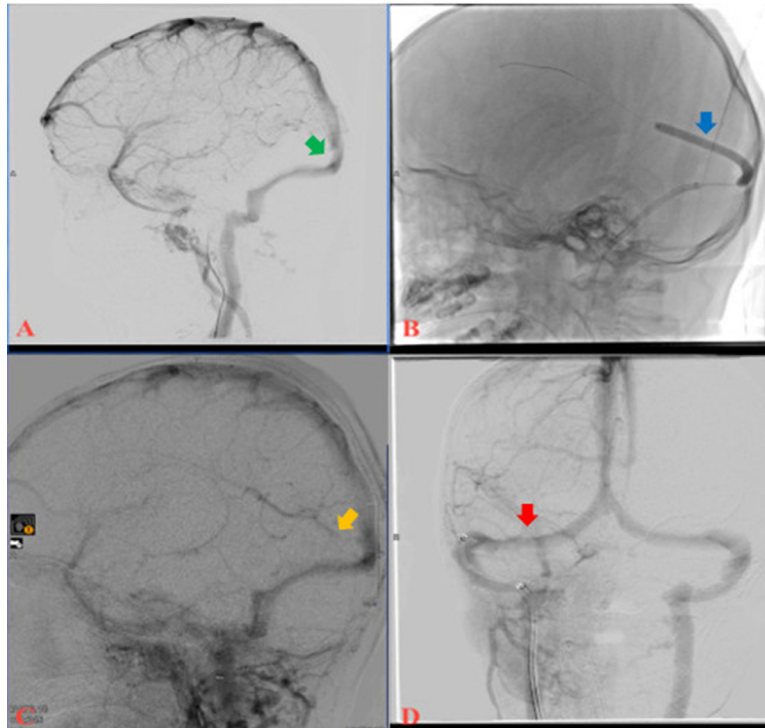


Fig. 4 – Imaging of cerebral venous sinus system on DSA before and after treatment. (A) Shows Occlusion of the straight sinus (green arrow) on digital subtraction angiography (DSA) before treatment. (B) Shows angioplasty from the right transverse sinus to the straight sinus (blue arrow). (C), (D) Show the recanalization of the cerebral sinuses system after thrombectomy including the right transverse sinus, a vein of Galen, straight sinus, and inferior sagittal sinus.

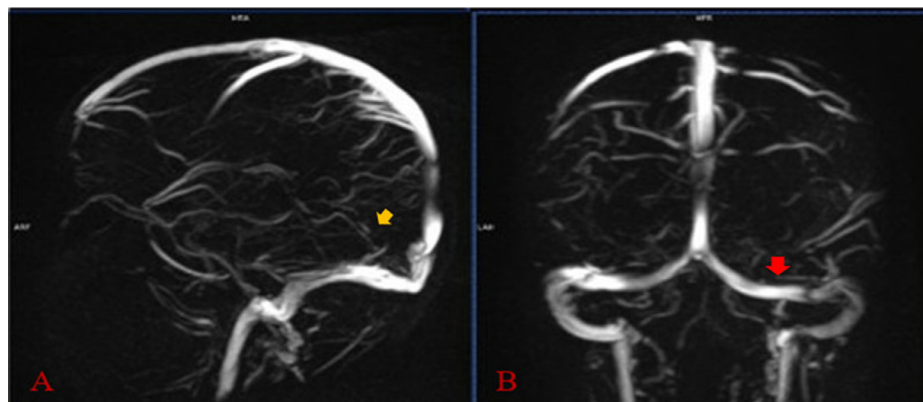


Fig. 5 – Imaging of cerebral venous sinus system on MR Venography on the 10th day after treatment. (A), (B) show the cerebral venous sinuses system on the 10th day after thrombectomy; straight sinus (yellow arrow) and right transverse sinus (red arrow).

Discussion

Patients with COVID-19 may have coagulation disorders that can lead to thrombosis [12]. SARS-CoV-2 has been suggested to lead to hypercoagulation conditions via many mechanisms. The pathogenesis of CVST in COVID-19 is yet to be

understood. However, multiple mechanisms have been suggested including injury to the endothelial cells caused by the connection between virus and angiotensin-converting enzyme 2 receptors, cytokine storm due to extreme immune response, excess production of thrombin, and inhibition of fibrinolysis which can lead to hypercoagulation [13–15]. Although vein thrombosis events have been described in pa-

tients with COVID-19, research has rarely reported CVST associated with COVID-19 [16–19]. The proportion of ischemic stroke in cases of SARS-CoV-2 infection (0.82%) and deep vein thrombosis in multisystem inflammatory syndrome in children (MIS-C) (4.3%) is lower than that in adults (1.2% and 21%, respectively) [18]. The prevalence of COVID-19 in children and adolescents is approximately 2.4% of all reported cases [17].

The true incidence of CVST in COVID-19 patients remains unknown. However, different results from studies have been published. Abdalkader et al. [20] observed an incidence of only 0.02%. Meanwhile, the percentage of CVST in COVID-19 was 0.08% in a meta-analysis by Baldini and associates [14]. CVST is difficult to diagnose with clinical symptoms alone because patients (especially pediatric patients) can present with a range of nonspecific manifestations, such as headache, vomiting, and seizures. Knight et al., estimating hazard ratios (HRs) separate time periods after diagnosis of COVID-19. The excess rate of venous thrombosis events (VTEs) in the first weeks after COVID-19 diagnosis decreased less than that of arterial ones, and it doubled by the 49th week. The adjusted hazard ratio for the first VTE after COVID-19 diagnosis decreased from 33.2 in week 1–1.8 in week 27–49. The proportion of high-risk arterial thromboses and VTEs 49 weeks after COVID-19 diagnosis are 0.5% and 0.25%, respectively [19].

Neuroimaging is a fundamental component in the diagnosis of CVST. Venous occlusion has more variable effects on the brain parenchyma than arterial occlusion, so imaging findings by CT and MRI are also different. In occluded sinuses, the progression of brain injuries can develop secondary to vasogenic edema, cytotoxic edema, or intracranial hemorrhage. Nonenhanced CT is the first-line imaging study for neurological emergencies, which is the ability to diagnose hemorrhage, bony fractures, brain edema, and herniation in short scanning times, but it's not enough information for determination diagnosis of CVST. MRI especially is more advantageous in diagnosing vascular diseases with these specific sequences. With nonenhanced MRI, the characteristic finding for CVST is edema of the bilateral thalamus, which is reported in approximately 86% of patients. Edema is easily observable by FLAIR and diffusion-weighted MRI pulse sequences. Nonenhanced venography techniques, including two-dimensional (2D) time-of-flight and three-dimensional (3D) phase-contrast MR venography, showed the loss of signal intensity in cerebral sinus system. However, contrast-enhanced techniques for both CT and MRI are essential to confirm filling defects. DSA is an essential diagnostic tool to identify occluded venous sinuses. Moreover, patients with CVST could be treated by DSA with modern techniques, such as the thrombectomy method or venous stents.

Our patient was admitted to the hospital with neurological manifestations. Neuroimaging with cranial CT showed some abnormal images of the venous sinus, but this is not sufficient to diagnose CVST. MRI imaging, especially MRV imaging, and DSA confirmed the diagnosis of CVST. The patient was treated with mechanical thrombectomy and anticoagulation therapy with good clinical outcomes. Because our patient had a medical history of SARS-CoV-2 and showed no evidence of other

risk factors, we present this case as evidence of a potential association between CVST and SARS-CoV-2.

Conclusion

COVID-19 causes a hypercoagulable state and the long-term effects of COVID-19 on the prevalence of vascular diseases are not clear. Certainly, if there are worrisome neurologic symptoms in these patients after the COVID-19 diagnosis, advanced imaging should be obtained to rule out thrombotic complications. CVST has a good prognosis when it is treated promptly. Pediatric patients with neurological manifestations should be indicated hypercoagulation factor test and scanned with MRI techniques to provide the exact diagnosis. With the abnormal imaging of the cerebral sinus on MRI, the patient should be evaluated by DSA to achieve the best treatment effects.

Patient consent

Informed consent for patient information to be published in this article was obtained.

Author's contributions

Nguyen Duong Quoc Anh and Tran Chi Cuong contributed equally to this article as co-first authors. Nguyen Duong Quoc Anh and Le Minh Thang: Case file retrieval and case summary preparation. Le Minh Thang and Nguyen Minh Duc: preparation of manuscript and editing. All authors read and approved the final manuscript.

Availability of data and materials

Data and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Our institution does not require ethical approval for reporting individual cases or case series. Written informed consent was obtained from the legal guardian(s) of patient(s) for their anonymized information to be published in this article.

Consent for publication

Not applicable.

REFERENCES

- [1] Jiang L, Tang K, Levin M, Irfan O, Morris SK, Wilson K, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *Lancet Infect Dis* 2020;20(11):e276–88 Erratum in: *Lancet Infect Dis*. 2022 Oct;22(10):e279. PMID:32818434PMCID: PMC7431129. doi:[10.1016/S1473-3099\(20\)30651-4](https://doi.org/10.1016/S1473-3099(20)30651-4).
- [2] Rothan HA, Byrareddy SN. The potential threat of multisystem inflammatory syndrome in children during the COVID-19 pandemic. *Pediatr Allergy Immunol* 2021;32(1):17–22. doi:[10.1111/pai.13361](https://doi.org/10.1111/pai.13361).
- [3] Ashrani AA, Crusan DJ, Petterson T, Bailey K, Heit JA. Age- and sex-specific incidence of cerebral venous sinus thrombosis associated with Ad26.COV2.S COVID-19 vaccination. *JAMA Intern Med* 2022;182(1):80–3. doi:[10.1001/jamainternmed.2021.6352](https://doi.org/10.1001/jamainternmed.2021.6352).
- [4] Palaodimou L, Stefanou MI, Katsanos AH, Aguiar de Sousa D, Coutinho JM, Lagiou P, et al. Cerebral venous sinus thrombosis and thrombotic events after vector-based COVID-19 vaccines: a systematic review and meta-analysis. *Neurology* 2021;97(21):e2136–47. doi:[10.1212/WNL.00000000000012896](https://doi.org/10.1212/WNL.00000000000012896).
- [5] Siegler JE, Cardona P, Arenillas JF, Talavera B, Guillen AN, Chavarría-Miranda A, et al. Cerebrovascular events and outcomes in hospitalized patients with COVID-19: the SVIN COVID-19 multinational registry. *Int J Stroke* 2021;16(4):437–47. doi:[10.1177/1747493020959216](https://doi.org/10.1177/1747493020959216).
- [6] Chan KH, Slim J, Shaaban HS. Pulmonary embolism and increased levels of D-Dimer in patients with coronavirus disease. *Emerg Infect Dis* 2020;26(10):2522–33. doi:[10.3201/eid2610.202127](https://doi.org/10.3201/eid2610.202127).
- [7] Klein DE, Libman R, Kirsch C, Arora R. Cerebral venous thrombosis: a typical presentation of COVID-19 in the young. *J Stroke Cerebrovasc Dis* 2020;29(8):104989. doi:[10.1016/j.jstrokecerebrovasdis.2020.104989](https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104989).
- [8] Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art review. *J Am Coll Cardiol* 2020;75(23):2950–73. doi:[10.1016/j.jacc.2020.04.031](https://doi.org/10.1016/j.jacc.2020.04.031).
- [9] Sadigh G, Mullins ME, Saindane AM. Diagnostic performance of MRI sequences for evaluation of dural venous sinus thrombosis. *AJR Am J Roentgenol* 2016;206(6):1298–306. doi:[10.2214/AJR.15.15719](https://doi.org/10.2214/AJR.15.15719).
- [10] Bhaskar S, Sinha A, Banach M, Mittoo S, Weissert R, Kass JS, et al. Cytokine Storm in COVID-19-immunopathological mechanisms, clinical considerations, and therapeutic approaches: the REPROGRAM consortium position paper. *Front Immunol* 2020;11:1648. doi:[10.3389/fimmu.2020.01648](https://doi.org/10.3389/fimmu.2020.01648).
- [11] Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol* 2020;17(5):259–60. doi:[10.1038/s41569-020-0360-5](https://doi.org/10.1038/s41569-020-0360-5).
- [12] Virapongse C, Cazenave C, Quisling R, Sarwar M, Hunter S. The empty delta sign: frequency and significance in 76 cases of dural sinus thrombosis. *Radiology* 1987;162(3):779–85.
- [13] Abdulgayoom M, Abdelmahmoud E, Elfaki A, Halabiya MA. Cerebral venous sinus thrombosis as an unexpected complication of COVID-19 pneumonia. *Cureus* 2021;13(7):1–5. doi:[10.7759/cureus.16498](https://doi.org/10.7759/cureus.16498).
- [14] Baldini T, Asioli GM, Romoli M, et al. Cerebral venous thrombosis and severe acute respiratory syndrome coronavirus-2 infection: a systematic review and meta-analysis. *Eur J Neurol* 2021;1(1):1–13. doi:[10.1111/ene.14727](https://doi.org/10.1111/ene.14727).
- [15] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020;323(13):1239–42. doi:[10.1001/jama.2020.2648](https://doi.org/10.1001/jama.2020.2648).
- [16] Ortega-Paz L, Capodanno D, Montalescot G, Angiolillo DJ. Coronavirus Disease 2019-associated thrombosis and coagulopathy: review of the pathophysiological characteristics and implications for antithrombotic management. *J Am Heart Assoc* 2021;10(3):e019650. doi:[10.1161/JAHA.120.019650](https://doi.org/10.1161/JAHA.120.019650).
- [17] She J, Liu L, Liu W. COVID-19 epidemic: disease characteristics in children. *J Med Virol* 2020;92(7):747–54. doi:[10.1002/jmv.25807](https://doi.org/10.1002/jmv.25807).
- [18] Zaffanello M, Piacentini G, Nosetti L, Ganzarolli S, Franchini M. Thrombotic risk in children with COVID-19 infection: a systematic review of the literature. *Thromb Res* 2021;205:92–8. doi:[10.1016/j.thromres.2021.07.011](https://doi.org/10.1016/j.thromres.2021.07.011).
- [19] Knight R, Walker V, Ip S, Cooper JA, Bolton T, Keene S, et al. Association of COVID-19 with major arterial and venous thrombotic diseases: a population-wide cohort study of 48 million adults in England and Wales. *Circulation* 2022;146(12):892–906. doi:[10.1161/CIRCULATIONAHA.122.060785](https://doi.org/10.1161/CIRCULATIONAHA.122.060785).
- [20] Abdalkader M, Shaikh SP, Siegler JE, Cervantes-Arslanian AM, Tiu C, Radu RA, et al. Cerebral venous sinus thrombosis in COVID-19 patients: a multicenter study and review of literature. *J Stroke Cerebrovasc Dis* 2021;30(6):1–9. doi:[10.1016/j.jstrokecerebrovasdis.2021.105733](https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105733).