



## Case Report

## Post COVID-19 cerebral venous sinus thrombosis; a case report

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## ABSTRACT

**Introduction:** Cerebral venous sinus thrombosis (CVST) in the setting of coronavirus disease 2019 (COVID-19) is an uncommon phenomenon with increasing incidence. This study aims to present a rare case of post COVID-19 CVST.

**Case report:** A 58-year-old female presented with headache, nausea, left sided weakness, and slurred speech. She recently recovered from COVID-19 who had severe presentations. On examination, mild left central facial palsy, high grade left sided hemiparesis (Grade 2/5), positive Babinski on left side, left side hypoesthesia, and inability to walk were observed. Laboratory and ultrasound findings were not significant, however magnetic resonance imaging (MRI) revealed CVST. The patient was prescribed Clexane 6000 IU twice daily, and after 14 days, it was changed to warfarin with an INR between 2 and 3. After 3 weeks of treatment, the patient was able to walk, and after 3 months her warfarin medication was discontinued.

**Discussion:** COVID-19 has been reported to be linked with CVST, however there is limited information about it. The exact figures regarding the affected groups and incidence rates are highly controversial. The diagnosis of CVST poses a challenge to physicians as their symptoms are highly unspecific, hence MRI is required for definitive diagnosis. Anticoagulant is commonly used in their treatment; however, the ideal anticoagulant of choice and the management duration are yet to be known.

**Conclusion:** Active or recently resolved COVID-19 can be considered as an independent risk factor for developing CVST and it rises the mortality rate of the disease.

## 1. Introduction

The coronavirus disease 2019 (COVID-19) is a contemporary global pandemic that is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the first ever case was reported in Wuhan city in China at the end of 2019 [1]. The World Health Organization (WHO) recognized and announced COVID-19 as a pandemic on March 11, 2020 [2]. Usually, those cases infected with SARS-CoV-2 lack symptoms or have only mild ones, such as; dry cough and fever, however diabetic, hypertensive, and elderly patients are the risk groups for developing a much more severe and life-threatening condition called acute respiratory distress syndrome (ARDS) [3]. Despite COVID-19 being primarily considered as a respiratory disease which is associated with pneumonia in severe cases, recent evidence suggests its association with a wide spectrum of systemic complications involving various parts of the body, such as; immune, nervous, gastrointestinal, and cardiovascular systems

[4]. In severe hospitalized cases, COVID-19 has been frequently associated with hematologic conditions, such as a high rate of venous thrombosis, and in addition, neurological manifestations have also been increasingly reported [5]. Cerebral venous sinus thrombosis (CVST) is an uncommon cause of stroke and a rare condition of the nervous system with an annual incidence of 2–5 cases/million [6]. Even though venous thromboembolism in association with COVID-19 has been well described in the literature, reports of CVST in the setting of active COVID-19 are still uncommon [7]. The occurrence of CVST after the resolution of COVID-19 is an even rarer incidence, with only a single case currently being present in the literature [8].

This study aims to present a rare case of post COVID-19 CVST. For writing of this paper SCARE 2020 guidelines have been considered [9].

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## 2. Case presentation

**Patient information:** A 58-year-old female presented to our neurological clinic; she was complaining from headache and nausea for the last 24 hours. On the day of her visit, she awakened with left sided weakness and slurred speech. She was a recently recovered from COVID-19 who had a relatively severe condition with dyspnea and hypoxia which required oxygen therapy. She was infected and diagnosed one month before her former complaints, and visited neurological clinic 4 days after full recovery. Past history was unremarkable.

**Clinical findings:** On examination, the patient was conscious, oriented, dysarthric, non-aphasic, she had no meningism, and her pupils were isocoric and bilaterally reactive to light. There were mild left central facial palsy, high grade left sided hemiparesis (Grade 2/5), positive Babinski on left side, left side hypoesthesia, and inability to walk.

**Diagnostic approach:** COVID-19 condition was previously confirmed via RNA PCR testing and she was associated with an elevated CRP level measuring 42.13 mg/L (normal range is less than 5mg/L). Routine laboratory tests were all normal, and laboratory screening for thrombophilia and vasculitis also showed to be normal, apart from borderline Anti-dsDNA antibody. Carotid doppler ultrasound (US) examination revealed normal findings. Echocardiography and electrocardiography of the patient were also normal. Magnetic resonance imaging (MRI) of the brain showed loss of normal signal intensity and flow with restricted diffusion of the left transvers sinus, sigmoid sinus, and part of the superior sagittal sinus, and some cerebral signal changes at the left side cerebral tissue were observed.

**Therapeutic intervention:** The patient was prescribed Clexane 6000 IU twice daily, and after 14 days, it was changed to warfarin with an INR target between 2 and 3. INR was controlled on regular bases.

**Follow-up and outcome:** The patient was able to walk and move independently after 3 weeks of treatment. After 3 months, warfarin was no longer required and it was discontinued. Neurological examination showed no focal neurological deficits.

## 3. Discussion

COVID-19 has been frequently reported to be linked with hypercoagulability, especially in severe and hospitalized patients. This has led to a high prevalence of venous thromboembolism which is more commonly observed in the lung vasculature [10]. Meanwhile, hypercoagulability may also affect the brain vasculature in a small percentage of COVID-19 cases (2%), leading to neurological manifestations [11]. CVST is an uncommon cerebrovascular disease and a rare cause of stroke [12]. While CVST in the setting of active COVID-19 has been recently reported in a few case reports and series, CVST post COVID-19 with no active infection has only been described once in the literature [8].

There are many risk factors for CVST, including genetic susceptibility, hormonal contraceptive drugs, malignancy, and infections [10]. The condition has also been linked to a wide range of viral infections, and according to the recent reports, COVID-19 can be considered as an independent risk factor for CVST as 75% of CVST in COVID-19 cases were not associated with other identifiable risk factors [7,13]. The exact figure regarding the incidence of CVST in COVID-19 cases is yet to be available [14]. However, studies with different results have been published. In a recent study by Hinduja and colleagues, an incidence of less than 0.0001% was reported [15]. On the other hand, a meta-analysis by Baldini and associates reported an incidence rate of 0.08% [16]. Meanwhile, Abdalkader et al. observed an incidence of only 0.02% [13]. Despite the controversies, all studies agree that the incidence of CVST is much higher in COVID-19 individuals than in the general population [13,15,16].

The pathogenesis of CVST in COVID-19 is yet to be understood. However, multiple mechanisms have been proposed including damage to the endothelial cells caused by the virus, cytokine storm due to

extreme immune response, excess production of thrombin, and inhibition of fibrinolysis which can in turn activate a thrombotic cascade leading to hypercoagulation [7]. In addition, the presence of hypoxia among COVID-19 cases have reportedly been associated with increased blood viscosity, hence making thrombosis more likely [13]. The current case also presented with hypoxia during her past infection.

CVST is considered as a disease that mainly affects the young population with much higher female predominance [7]. However, the affected age and gender groups of CVST in the setting of COVID-19 hold some controversy. In a case series by Abdalkader and colleagues, most of the reported cases were elderly female patients [13]. On the contrary, there are other studies reporting that most of these cases are of middle-aged patients with a lower female-to-male ratio [17]. The patient in the current report was a 58-year-old female.

The clinical manifestations of CVST include seizures, decreased consciousness, headache, focal neurological deficits, weakness of extremities, and disorientation, which may be missed during diagnosis in COVID-19 cases as they can also be associated with neurological manifestations [14]. The current case was oriented and conscious, but she was presented with headache, nausea, and slurred speech. The severity of COVID-19 cases has been reported not to be directly correlated to the development of CVST, as even in the absence of pulmonary COVID-19 symptoms CVST has developed in multiple cases [12].

The diagnosis of CVST poses a challenge to physicians as their symptoms are highly unspecific, hence further investigations are required for definitive diagnosis [13]. Even though US can be used in the diagnosis of other thrombotic conditions with a sensitivity of 77.8–90%, it is mostly not suitable for the diagnosis of CVST and a more sensitive imaging techniques are required for these cases, such as MRI or magnetic resonance venography imaging modalities [13,14]. Amongst cases of CVST, the superior sagittal sinus is the most regularly observed location for the occurrence of the condition [17]. Moreover, CVST of multiple sites have been increasingly reported, with a predominance of the transverse sinus [13]. In this case, multiple similar sites were also involved.

In general, anticoagulation therapy is the standard management approach for thrombosis, and heparin and warfarin have been used as first line treatments for CVST cases [7]. Meanwhile, the ideal anticoagulant of choice and the management duration is yet to be known for CVST in COVID-19 cases [18]. These cases can be associated with good outcomes if they are diagnosed and treated on early onset of the disease [14]. However, various figures have been put forward regarding the mortality rates associated with CVST in COVID-19 patients. Hinduja et al. and Abdalkader et al. reported mortality rates of 11.9% and 12.5%, respectively [13,15]. In contrast, Ostovan and associates reported a much higher mortality rate of 35% [12]. Whichever the case, the mortality rates associated with CVST in COVID-19 cases are much higher than that of non-COVID-19 cases [13]. The current case associated with good outcome.

In conclusion, active or recently resolved COVID-19 can be considered as an independent risk factor for developing CVST and it rises the mortality rate of the disease. It is highly under-reported due to their non-specific presentations; hence physicians should be aware of their presence in cases with current or previous SARS-CoV-2 infection in order to provide early treatment.

### Conflict of interest

None to be declared.

### Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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**Ethical approval**

Approval is not necessary for case report in our locality.

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**Author contribution**

Shwan A. Ahmad, Hemin S. Mohamad: neurologist and physician diagnosing the case, following up the patient, and final approval of the manuscript. Fahmi H. Kakamad, Bestoon Kh. Salih, Shwan H. Muhamad, Berwn A. Abdulla<sup>2</sup>, Abdulwahid M. Salih: literature review, writing the manuscript, final approval of the manuscript.

**Consent**

Consent has been taken from the patient and the family of the patient.

**Registration of research studies**

According to the previous recommendation, registration is not required for case report.

**Guarantor**

Fahmi Hussein Kakamad is the Guarantor of submission.

**Declaration of competing interest**

There is no conflict to be declared.

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