

Vascular complications in viral infections: Case series of cerebral Venous Thrombosis in COVID-19

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Vascular complications in viral infections: Case series of cerebral Venous Thrombosis in COVID-19

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ABSTRACT

A growing number of critically ill COVID patients have been reported to have thrombotic complications, like CVST (Cerebral Venous Sinus Thrombosis), which can manifest in a wide range of neurologic signs and symptoms. This case series focuses on 5 case reports of COVID 19 positive cases who later developed cerebral venous thrombosis, with an emphasis on their variable clinical presentation and outcome. MRI brain imaging identified the superior sagittal sinus as the most frequent site of cerebral venous sinus thrombosis (CVST) (100%), followed by the sigmoid sinus (80%), transverse sinus (60 %), straight sinus (20 %) & inferior jugular vein (20 %). For acute management, 60% of patients received unfractionated heparin, while 40% were treated with low molecular weight heparin. The observed mortality rate was 40%. A high index of suspicion (HIOS) is crucial for prompt diagnosis and effective treatment. The administration of anticoagulants and supportive measures in the medical management of CVST has yielded excellent clinical outcomes.

Keywords: COVID-19, MRI, cerebral venous thrombosis, superior sagittal sinus

INTRODUCTION

A virus called SARS-CoV-2, or coronavirus disease 19 (COVID-19), is the cause of SARS (Severe Acute Respiratory Syndrome). Due to the virus's binding to ACE2 receptors in lower respiratory tract pneumocytes, COVID-19 is mainly an infectious disease with respiratory symptoms [1].

A rising number of critically ill COVID patients have been reported to have thrombotic complications, like CVT [2]. Increased coagulation factor concentrations, acquired antiphospholipid antibodies, and decreased endogenous anticoagulant protein concentrations result in a state of hypercoagulability [3].

CVST refers to the total or partial blockage of the feeding cortical veins or the main sinuses. CVST can result in focal or generalized neurological deficits as well as secondary effects of vascular congestion⁴. Cerebral venous thrombosis (CVT) manifests with a diverse spectrum of symptoms, including headache, altered consciousness, abnormal behavior, seizures, speech difficulties, and motor paresis [4,5]. This report examines five cases of COVID-19 patients who exhibited variable clinical outcomes and presented with CVST.

MATERIALS AND METHODS

Our research involved a cohort of five patients spanning a research period from June 2021 to September 2022. These patients presented with various symptoms such as headache, stroke, and blurred vision, prompting comprehensive evaluation that included routine MRI (Magnetic Resonance Imaging) of the brain and MR (Magnetic Resonance) venography. The diagnosis of cerebral venous sinus thrombosis (CVST) was established based on both clinical assessment and radiological findings in individuals who tested positive for SARS-CoV-2 infection. Specifically, our study included patients who either simultaneously presented with COVID-19 and CVST or developed CVST within two weeks of initial COVID-19 symptoms. Excluded were cases where COVID-19 developed post-hospitalization for CVST following diagnosis. Diagnostic criteria for COVID-19 were based on SARS-CoV-2 detection in nasopharyngeal or oropharyngeal samples from clinically suspected individuals. Diagnosis of CVST required the presence of relevant neurological symptoms (such as focal deficits, intracranial hypertension, headache, and/or encephalopathy) confirmed through imaging modalities including CT (Computed Tomography), brain MRI, CT venography, and/or MR venography. Additionally, we assessed the interval between CVST onset and clinical suspicion of SARS-CoV-2 infection. For each case, comprehensive data encompassing clinical and radiological features of CVST were collected, including affected areas, treatment modalities, and outcomes. The investigation covered demographic details, prominent COVID-19

symptoms, confirmatory tests for SARS-CoV-2 infection, the interval between SARS-CoV-2 diagnosis and CVST onset, clinical and radiological characteristics of CVST, treatment strategies, outcomes of CVST and mortality rates.

CASE SERIES

The clinical profile of 5 individuals who had tested positive for SARS-CoV-2 / COVID 19 and developed cerebral venous thrombus is summarized.

Case 1: A male patient, fifty years old, complained of a headache and recently developed limb weakness. Upon MRI brain, he was diagnosed to have Dural venous thrombosis in the right sigmoid and transverse sinus, the posterior part of the straight sinus, proximal aspect of the left transverse sinus with corresponding flair hyperintensities and collaterals. Risk factors for venous thromboembolism were found to be negative. His COVID RT-PCR was positive and he had a CORADS score of 6. His D-DIMER was >500.

Case 2: A forty-year-old man reported having a headache and new onset seizure, upon MRI, was diagnosed to have non-visualization of superior sagittal sinus, right transverse sinus, and right sigmoid sinus with non-visualization of the right internal jugular vein. Risk factors for venous thromboembolism were found to be negative. His Covid RT-PCR was positive and he had a CORADS score of 6. His D-DIMER was >500.

Case 3: The patient, a 28-year-old woman, complained of a seizure that had just started. her MRI showed the presence of a thrombus in the anterior part of the superior sagittal sinus. Risk factors for venous thromboembolism were found to be negative. Her covid RT-PCR was negative and she had a CORADS score of 5. Her D-DIMER was <500.

Case 4: A 37-year-old male came with complaints of headache and new onset cerebrovascular accident and was diagnosed to have superior sagittal sinus and right transverse and sigmoid sinus thrombus, following a positive COVID RT-PCR repost. Risk factors for venous thromboembolism were found to be negative. He had a CORADS score of 6 with D-DIMER values >500.

Case 5: A 47-year-old female patient with limb weakness and a headache presented with RT-PCR negativity. Risk factors for venous thromboembolism were found to be negative.

Her diagnosis included sigmoid sinus thrombus with CORADS 5 and D-DIMER <500, as well as superior sagittal sinus with left transverse pressure.

RESULTS

The median age of the patients was 41 years, ranging from 28 to 50 years. All five patients had confirmed SARS-CoV-2 infection concurrent with confirmed CVST. The majority of patients were over 40 years old (80%) and male (80%). The primary presenting complaint was headache in 60% of cases, while 40% presented with new-onset seizure or acute limb weakness (acute CVA). The mortality rate was 40%. On MRI, CVST predominantly involved the superior sagittal sinus (100%), followed by the sigmoid sinus (80%), transverse sinus (60%), straight sinus (20%), and inferior jugular vein (20%). The median period from onset of COVID-19 symptoms and onset of CVT symptoms and CVT diagnosis was 8 days. For acute treatment, 60% of patients received unfractionated heparin, while 40% received low molecular weight heparin. In the long term, 40% received unfractionated heparin and 60% received low molecular weight heparin.

Table 1- Clinical Summary

Case no.	Age and sex	COVID RTPCR	Interval between COVID 19 symptom onset and CVT onset	CORADS score	D-DIMER	Cerebral Venous Thrombus location on MRI

1	50Y/M	+	7 days	CORADS 6	>500	Dural venous thrombosis in right sigmoid and transverse sinus, posterior aspect of straight sinus, superior sagittal sinus, proximal aspect of the left transverse sinus, with corresponding flair hyperintensities and collaterals
2	45Y/M	+	8 days	CORADS 6	>500	Absence of visualization of the right internal jugular vein along with the right transverse, sigmoid, as well as superior sagittal sinuses
3	28Y/F	-	10 days	CORADS 4	<500	Anterior aspect of superior sagittal sinus thrombus
4	37Y/M	+	6 days	CORADS 6	<500	Sigmoid sinus and superior sagittal sinus thrombus
5	47Y/F	-	8 days	CORADS 5	>500	Sigmoid and left transverse sinus thrombus in the superior sagittal sinus

DISCUSSION

The SARS-CoV-2 infection carries a significant risk of causing endothelial dysfunction, a hyperinflammatory state, platelet activation, and vascular stasis, or the activation of the Virchow's triad, which can result in venous and arterial thrombosis anywhere in the body [6–8].

The literature reports on several neurological complications related to SARS-COV-2 infection, including Guillain-Barré syndrome, encephalitis, meningitis, CNS vasculitis, myelitis, acute disseminated encephalomyelitis, other acute neuropathies allied with SARS-CoV-2 infection, and stroke [9]. The most common cerebrovascular complication to be reported was an ischemic stroke [10].

CVT also called cerebral sinovenous thrombosis or dural sinus thrombosis—constitutes approximately 0.5% of all stroke syndromes [11]. The symptoms of CVST include focal neurological defects, paralysis, seizures, and headaches. The presentation may also involve altered mental status, coma, mastoid pain, gaze palsy, visual impairment, etc. The levels of procoagulant biomarkers, such as d-dimer, activated partial thromboplastin time (aPTT), & fibrinogen, were frequently found to be excessive in COVID-19 patients, and routine computations of these biomarkers had been advised [12,13].

When an acute stroke occurs, MRI and CT scans provide crucial information to guide acute therapeutic interventions, confirm diagnosis, and inform long-term treatment

decisions. These imaging modalities detect vascular occlusion and identify infarcted regions. MRI and CT scans also assist in assessing the volume of the stroke. In a large series using MRI, 63% of individuals showed involvement of the superior sagittal sinus, the most frequently affected cerebral venous structure [14].

Unfractionated heparin (UFH) and low-molecular-weight heparins are the primary pharmacological treatments for CVT. In cases where neurological impairment worsens despite adequate anticoagulation, and in specialized settings, endovascular thrombolysis or mechanical thrombectomy are considered as treatment options [6,7].

Early identification is crucial as prompt anticoagulation and/or endovascular management can enhance outcomes by reducing complications such as raised intracranial pressure, bleeding rates, and cerebral edema. Further investigation is necessary to determine whether the association is coincidental or causal. Given the current circumstances, SARS-CoV-2 infection should remain highly suspected in the absence of other identifiable risk factors.

CONCLUSION

In conclusion, this case series underscores the significant association between COVID-19 infection and cerebral venous thrombosis (CVT). Our findings highlight the diverse clinical presentations and radiological characteristics observed in COVID-19 patients presenting with CVT. Early recognition and management are crucial, with anticoagulation playing a central role in treatment strategies. Despite challenges in determining causal links, our study emphasizes the importance of considering SARS-CoV-2 infection as a potential risk factor for CVT, especially in the absence of other identifiable causes. Further research is warranted to elucidate the pathophysiological mechanisms and optimize therapeutic approaches in these complex cases.

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