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Case Report

Cerebral venous sinus thrombosis as a complication of COVID-19 infection – A case report

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ABSTRACT

Introduction and importance: Severe acute respiratory distress syndrome coronavirus 2 is the causative agent of COVID-19 (Coronavirus 2019) infection. Although symptoms are usually associated with the respiratory system, its neurological involvement should not be underestimated. The most common cerebrovascular complication following the infection is ischemic stroke however, CVST (Cerebral Venous Sinus Thrombosis) has been reported.
Presentation of case: We report a unique case of a young patient who had a history of headache and abnormal body movement immediately after COVID-19 infection. His brain Computed tomography scan and Magnetic Resonance Imaging (MRI) showed typical images of CVST. He was admitted and treated with Low Molecular weight heparin.
Discussion: CVST is a rare form of stroke which may have devastating complications. The diagnosis is clinically challenging due to its non-specific presentation like headache and altered sensorium alone. Inflammatory process and hypoxic state after the virus infection may favor the hypercoagulable state in CVST. Our patient did not have any other predisposing factor for a hypercoagulable state other than the COVID-19 infection.MRI and venography and computed tomographic venography are the preferred modalities. The Patient is generally treated with anticoagulation therapy.
Conclusion: High index of suspicion of CVST is necessary when a patient presents with unexplained neurological manifestation following a recent COVID-19 infection to prevent from life-threatening complications. Furthermore, clinicians should not underestimate the multisystem involvement of COVID-19.

1. Introduction

Coronavirus disease 2019 (COVID -19) infection was first reported in Wuhan city, China on January 7, 2020 [1] and was declared to be a world pandemic on March 11, 2020 [2]. The causative agent of this disease is Severe acute respiratory distress syndrome coronavirus 2 (SARS- CoV-2) [2]. Although complications are generally related to the respiratory system, COVID-19 has a heterogeneous spectrum of multisystem involvement [3] with associated neurological involvement in 36%–65% of hospitalized patients [4]. The pathogenesis of neurological involvement due to COVID -19 infection is widespread, among which cerebrovascular events due to the hypercoagulable state have been increasingly reported [1,4].

The most common cerebrovascular complication following the infection is ischemic stroke [4], however, CVST (Cerebral Venous Sinus Thrombosis) (a rare form of stroke <1%) [4] has also been reported. The estimated incidence of CVST is 1.3–1.6/100,000/year [5]. CVST has a non-specific clinical presentation and diagnosis can be challenging [2]. Although death is uncommon in patients without COVID-19 (4%) [1], neurological deterioration in CVST is common (23%) [4] which can be fatal. Therefore, early diagnosis can prevent inappropriate management of COVID-19 and associated complications.

We experienced a case of CVST as a late complication of COVID-19 infection that was successfully treated with LMWH (Low Molecular Weight Heparin). This case report has been reported in line with the SCARE Criteria [6].

2. Case presentation

A 28- year-old man with a BMI (Body Mass Index) of 24.1 kg/m2 presented to Annapurna Neurological Institute and Allied Sciences,

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Abbreviation list

BMI	Body Mass Index
COVID -19	Coronavirus disease 2019
CRP	C- Reactive Protein
CT	Computed Tomography
CVST	Cerebral Venous Sinus Thrombosis
IJV	Internal Jugular Vein
LMWH	Low Molecular Weight Heparin
MRI	Magnetic resonance imaging
PCR	Polymerase Chain reaction
SARS- CoV-2	Severe acute respiratory distress syndrome coronavirus 2

Kathmandu, Nepal in the Emergency Department. Seventeen days prior to the presentation to our hospital, the patient developed a fever up to 100° F for 6 days. The fever was acute in onset and intermittent type associated with cough and chest pain. He went to another hospital where investigations were sent. Chest radiography showed bilateral infiltrates. A nasopharyngeal swab COVID -19 PCR (Polymerase Chain reaction) test was done at that time which was positive. Further investigation showed an elevated levels of D-dimer, ferritin, C-reactive protein (Table 1). Other laboratory report at the time was normal. He was discharged from the hospital after 8 days with a negative COVID -19 PCR report. Immediately following his discharge he had a severe, generalized headache, throbbing type, associated with 2–3 episodes of vomiting. There was reported history of an episode of constant up rolling of the eye, lasting for 5 minutes. With these complaints, he came to our hospital. The patient did not have previous history of arterial or venous thrombosis and did not use any solid medications. He had never smoked and there were no known cases of vein thrombosis in first-degree relatives. His general physical examination revealed no abnormality. The patient exhibited intact neurological and systemic examination.

A repeat PCR test was done in our hospital at the time of admission which was negative. Blood investigation were sent which showed deranged CRP, Erythrocyte Sedimentation Rate, Lactate Dehydrogenase, Prothrombin time, partial thromboplastin time, Total leukocyte count. Thrombocheck profile showed normal ANF (ANA), *Anti*-dsDNA IgG, Protein C activity, Protein S activity, antithrombin activity, Antiphospholipid IgM antibody, Antiphospholipid IgG antibodies (Table 2). The serum homocysteine level was normal and Lupus anticoagulant was absent. Electroencephalography was done due to reported abnormal body movement which was normal.

A CT (Computed Tomography) head was done which showed hyperdensity over the right transverse venous sinus (Fig. 1). An MRI (Magnetic Resonance Imaging) of the head, cerebral Magnetic Resonance Angiography, and Magnetic Resonance Venography were done which showed findings suggestive of CVST (Fig. 2A, B, C and Fig. 3). The patient was treated with an injection low molecular weight heparin (LMWH) 60mg twice a day. A repeat CT head was done on the fourth day of hospital stay which was normal (Fig. 3). He was discharged on the fifth day of admission and he was commenced with dabigatran 150 mg and levetiracetam 500mg twice a day. During his follow-up visit after two weeks, his symptoms had significantly improved (Fig. 4).

Table 1
Summary of laboratory findings when the patient was positive for COVID-19.

Sample type (when the patient was positive for COVID-19)		
CRP	83.84	0–6
D-dimer	0.99 mg/L	0–0.05
S. Ferritin	405.1ng/ml	30–400 in male

CRP: C- reactive protein, S. Ferritin: Serum Ferritin. Abnormal values have been bold.

Table 2
Summary of laboratory findings when the patient was negative for COVID-19.

Sample type (done in our hospital after negative COVID-19)	At admission	Normal Range
ANF(ANA)	0.5 AU/mL	<40: negative, >40: Positive
Anti- dsDNA IgG	1.1 IU/ml	0.79–800
CRP	**60.2mg/L**	**0–6**
ESR	**30 mm in 1st hour**	**0–9 in male**
LDH	**637 u/L**	**225–450**
Lymphocytes	14%	25–45
Neutrophils	**79%**	**45–75**
TLC	**14300/cumm**	**4000–11000**
PT	**14 seconds**	**10–12**
PTT	**46.1 seconds**	**30.3–41.2**
Platelets	283000/cumm	150,000–400000

Abnormal values have been bold.
CRP: C- Reactive Protein; ESR: Erythrocyte Sedimentation Rate; LDH: Lactate Dehydrogenase; TLC: Total Leukocyte Count; PT: Prothrombin time; PTT: Partial thromboplastin time.

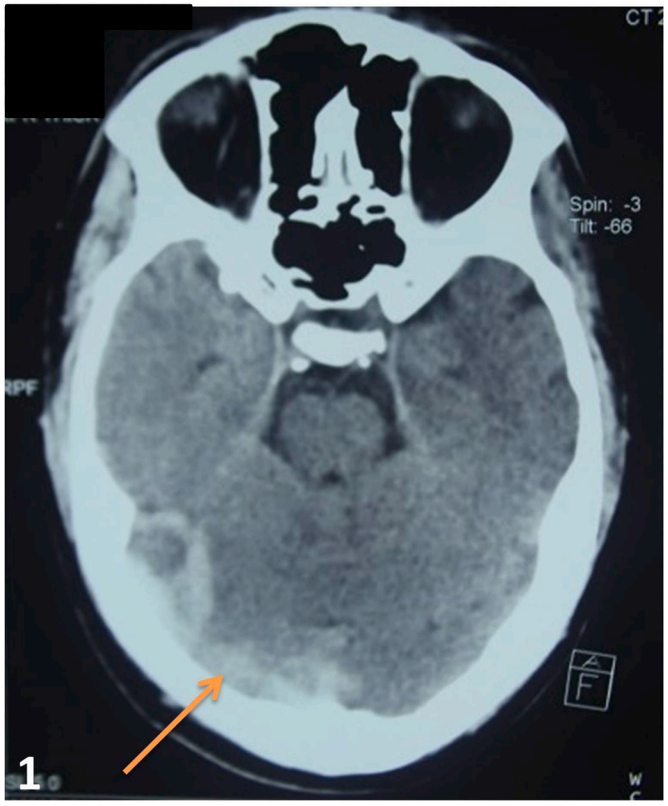

Fig. 1. Axial non-enhanced Computed Tomography Scan done at the time of admission shows hyperdense right transverse sinus suggestive of sinus thrombosis.

3. Discussion

The most common reported symptoms of COVID -19 include fever, cough, fatigue, shortness of breath [2]. Common complications of COVID-19 include sepsis followed by respiratory failure, ARDS (Acute Respiratory Distress Syndrome), heart failure, septic shock [7]. Although it mostly affects the respiratory system, neuro-invasive disease, para-infectious complications as well as the risk of stroke and

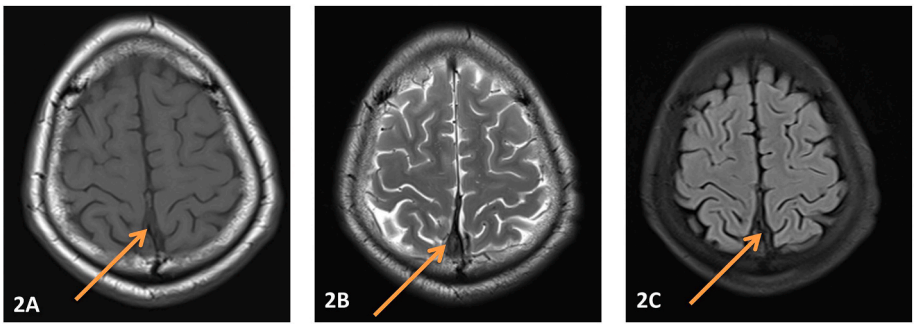

Fig. 2. Axial magnetic resonance imaging of brain. A.) Abnormal isointense signal change in T1 weighted image due to thrombosis of superior sagittal sinus. B.) T2 hypointense signal change due to thrombosis of superior sagittal sinus. C.) FLAIR image shows isointense signal change in the superior sagittal sinus.

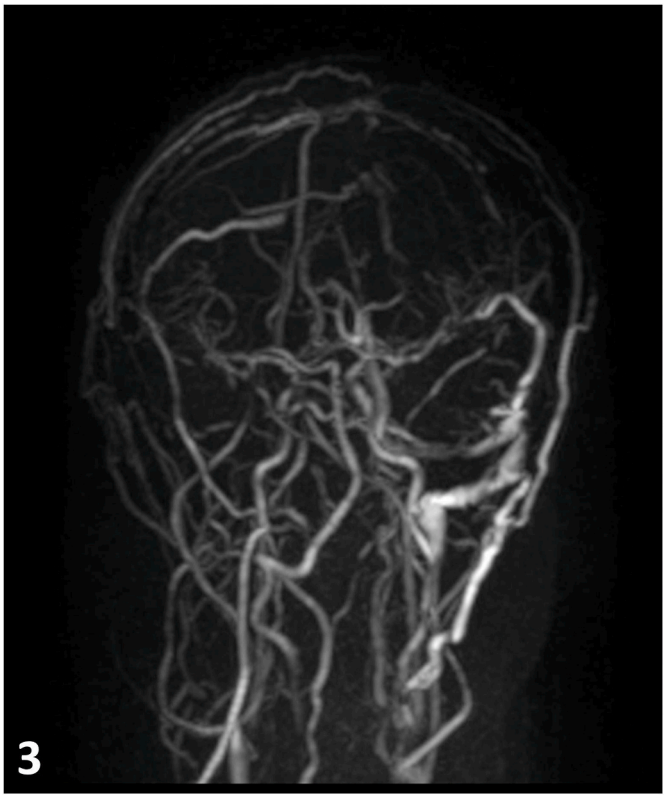

Fig. 3. Coronal Magnetic resonance venogram shows the dural sinuses and dural venous system which shows no signal flow in both the transverse venous sinuses, right sigmoid venous sinus, and superior sagittal sinus. There is reduced caliber of the left sigmoid sinus and left IJV (Internal Jugular Vein) with no signal flow in the right IJV.

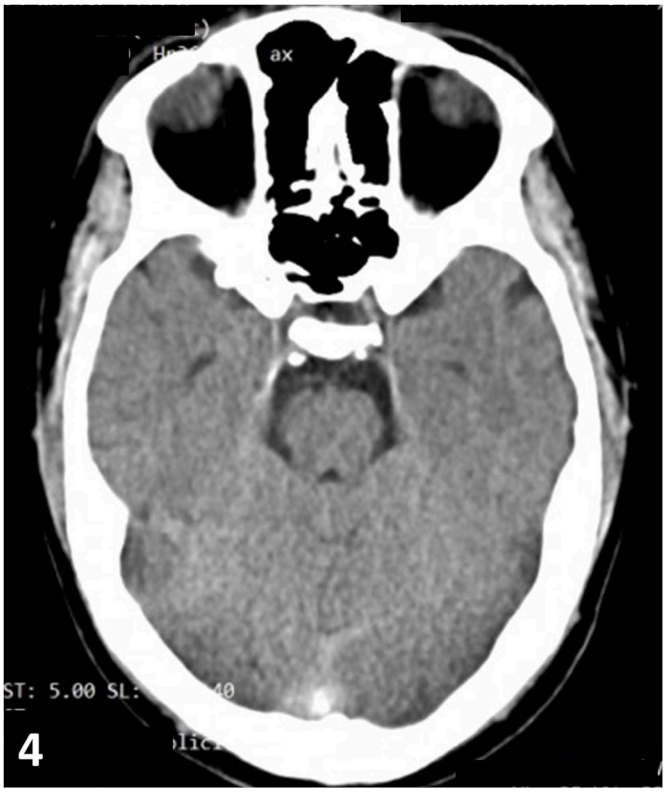

Fig. 4. Axial non- enhanced Computed Tomography Scan done at the time of discharge shows normal study of the brain.

hypercoagulopathy related complications have also been reported [2,8].

Neurological complications following COVID -19 infection are classified into three main categories according to the mechanism [2]. The first mechanism encompasses of effects of pulmonary disease associated with systemic diseases such as systemic inflammatory response syndrome, sepsis, and multi-organ failure [2]. Encephalopathy and stroke are triggered by this mechanism. The pathogenesis of conditions such as encephalitis due to COVID-19 is due to the second mechanism that results from direct intrusion of the central nervous system by the virus [2]. The last mechanism includes the immune response following the infection (e.g. Guillain-Barre Syndrome and its variants).

It is reported that 2% of patients with confirmed COVID-19 infection have involvement of brain vasculature due to the hypercoagulable state [3]. Hypercoagulability in COVID-19 causes thromboembolic effects in arterial and venous beds [2] causing complications such as pulmonary embolism, deep vein thrombosis, CVST [7].

CVST is caused by the occlusion of dural venous sinuses and/or cerebral veins due to venous thrombosis [4]. The risk factors include surgery, trauma, pregnancy, puerperium, antiphospholipid syndrome, cancer, inherited thrombophilia, exogenous hormones [9]. It is postulated that enhanced venous thrombosis in COVID -19 patients is due to hypoxia [2]. The hypoxic state results in increased blood viscosity and activation of coagulation and fibrinolysis due to the activation of hypoxia-related genes [1]. Moreover, infection of endothelial cells, induction of local inflammation [2], activation of cytokine cascade [4] resulting in vasculitic process in cerebral walls can be the contributing factors. The episodes of seizure in our patient may be explained by the breakage of blood-brain barrier due to the infection and the resultant release of pro-inflammatory cytokines causing cortical irritation [3]. The elevation of prothrombin time, d-dimer, and thrombocytopenia without hypofibrinogenemia is due to the viral infection mediated

stimulation of coagulation cascade [2].

In our reported case, the patient had no other associated risk factors of the hypercoagulable state apart from the COVID -19 infection. The symptoms of CVST appeared days after the initial diagnosis of COVID-19 suggesting that a prothrombotic state can persist after acute infection. The post-acute phase hypercoagulable state is common in COVID-19 infection resulting in variability in symptoms onset [4]. Moreover, it has been known that venous thromboembolic events such as CVST mostly occur in the first 30 days following hospital discharge or negative PCR report [4]. Therefore, a continuation of thromboprophylaxis up to 45 days following discharge for high-risk patients is suggested [4]. Although the SARS-CoV-2 test was negative at the presentation, we suspect COVID-19 was the main provoking factor for CVST in our patient.

The diagnosis of CVST is based on clinical and radiological criteria [2]. The symptoms of CVST are non-specific and may range from headache (90%) [5], visual complaints, or nausea to focal deficits or seizure (40%) [4,5]. MRI and venography and CT venography are the imaging modalities of choice [2]. The first-line therapy of CVST is the use of a therapeutic dose of low molecular weight heparin (LMWH) [2,4] according to European guidelines. Unfractionated heparin is recommended in patients with renal failure or with the possibility of rapid reversal of anticoagulation effect [5]. Anticoagulation with Vitamin K antagonist is prescribed till 3–12 months after CVST [5]. In case of recurrence or severe thrombophilia, indefinite use of anticoagulation therapy is recommended [5]. Aggressive hydration in addition to anticoagulation is also recommended however it is not tolerated by patients with acute respiratory distress syndrome or refractory hypoxemia [4].

Patients with severe COVID-19 infections are more prone to develop neurological complications [2]. Furthermore, early identification of this critical condition and treatment may decrease the progression such as cerebral edema, increased intracranial pressure, hemorrhage [1], focal or generalized post CVST seizures, papilledema, dural arteriovenous fistula [9].

4. Conclusion

As the neurological manifestation of COVID 19 may present as non-specific neurological symptoms, CVST should be kept in consideration. In addition, we tend to emphasize more on the respiratory symptoms while treating COVID-19 patients and therefore, the prevalence of neurological sequel might be underestimated leading to delay in diagnosis and treatment. From this case report, we aim to aware the clinicians that cases of CVST presenting with neurological manifestation without clear predisposing factors may be associated with COVID-19 infection in the recent pandemic situation.

Ethical approval

The case study was cleared by the institutional review committee of Annapurna Neurological Institute and Allied Sciences.

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Author contribution

Suyasha Rajbhandari: Writing, Original draft, Conceptualization, review and editing, Saujanya Rajbhandari: Writing; Review, editing, Avinash Chandra: Established the diagnosis and treated the patient, Pritam Gurung: Review and supervision, Pravesh Rajbhandari: Review and supervision, Basant Pant: Supervision.

Trail registry number

None.

Guarantor

Dr. Basant Pant.

Consent for publication

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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Declaration of competing interest

None of the authors have potential conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103326.

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