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Case of COVID-19 presenting as cerebral venous thrombosis: a deviation from the established timeline

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Abstract:
COVID 19 infection is known to cause vascular thrombosis in all the systemic vasculature. Ischemic stroke and cerebral venous thrombosis have been reported in the medical literature. Existing medical database does tell us that these events take occur in a predictive manner with the incidence of venous thrombosis, pulmonary embolism and cerebral venous thrombosis being higher in critically ill patients that are already admitted in the intensive care unit and also occur after a lag period from the date of infection. However, this novel virus is relentlessin surprising us. We report a COVID 19 case where seizure, as a clinical manifestation of cerebral venous thrombosis was the first and the only presenting complain. Though nasopharyngeal swab test was negative, computed tomography of chest showed features of COVID pneumonitis and the inflammatory markers were raised. Unlike the previous reported cases where antithrombotic prophylais were initiated based on abnormal coagulation profile and in critically ill patients, to prevent vascular thrombosis, we had no option to prevent such an event and rather had to treat it as this patient presented to us with cerebral venous thrombosis from the first day itself. The treating team should be aware of the possibility of such a deviation from the clinical profile and timeline that is already established in medical literature so that it can be handled safely and timely.

Key words: *CVT in COVID 19, CVT at presentation, venous thrombosis in COVID-19, sinus thrombosis, transverse sinus thrombosis*

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I. Background:

Although corona virus disease-19 (COVID 19) is primarily a pulmonary ailment, involvement of multiple organ systems have called for efforts from multidisciplinary teams to strategize a management plan.[1] Inflammatory response, leading to activation of the coagulation cascade and endothelial dysfunction do increase the risk of vascular thrombosis in such patients. [2] While fatal acute arterial ischemia in various systemic vessels have been reported, we have also seen a progressive increase in the number of cases with acute ischemic stroke. [3,4] Similarly, venous thrombosis in the form of deep vein thrombosis, pulmonary embolismand cerebral venous thrombosis (CVT) have a higher prevalence in COVID 19 cases, especially in the critically ill patients that are admitted in intensive care unit. [5]However, cerebral venous thrombosis in covid cases is a relatively rare entity and its occurrence at the time of first presentation to hospital is even rarer. [6,7,8]

For the first time we report a case of a young individual, with no known comorbidities who was brought to the emergency department with seizures being the only presenting complain. On evaluation she was found to have CVT with SARS-CoV-2 infection on computed tomography of chest, though the nasopharyngeal swab test was negative. What makes this case worth reporting is the fact that at the time of detection of CVT she was neither critically ill nor there was any time lag from the day of infection.

Case presentation:

A 36 year housewife presented to our outpatient department with chief complain of single episode of generalized tonic clonic seizure. Antiepileptic was prescribed and necessary imagings were planned. Next morning she again presented to the emergency department with multiple episodes of seizures. Neurologically she was conscious, oriented and had NIHSS score of zero.SW sequence in MRI brain showed blooming in the region of right transverse and sigmoid sinus, suggesting cerebral venous sinus thrombosis with parenchymal hemorrhage in temporo-occipital region. CT venography showed non-opacification of straight sinus, right transverse and sigmoid sinus, again confirming cerebral venous sinus thrombosis (Figure-1). She was immediately started on low molecular weight heparin. As a routine screening protocol in this pandemic, her nasopharyngeal swab for Covid RTPCR was done before admission, which turned out to be negative.

Hematologic work up did not show Factor V mutation and protein S activity was normal. She was also negative for anticardiolipin antibodies and lupus anticoagulants. The D-dimer level was raised (356 ng/ml). We could not find any known risk factors for cerebral venous thrombosis from a detailed history and examination.

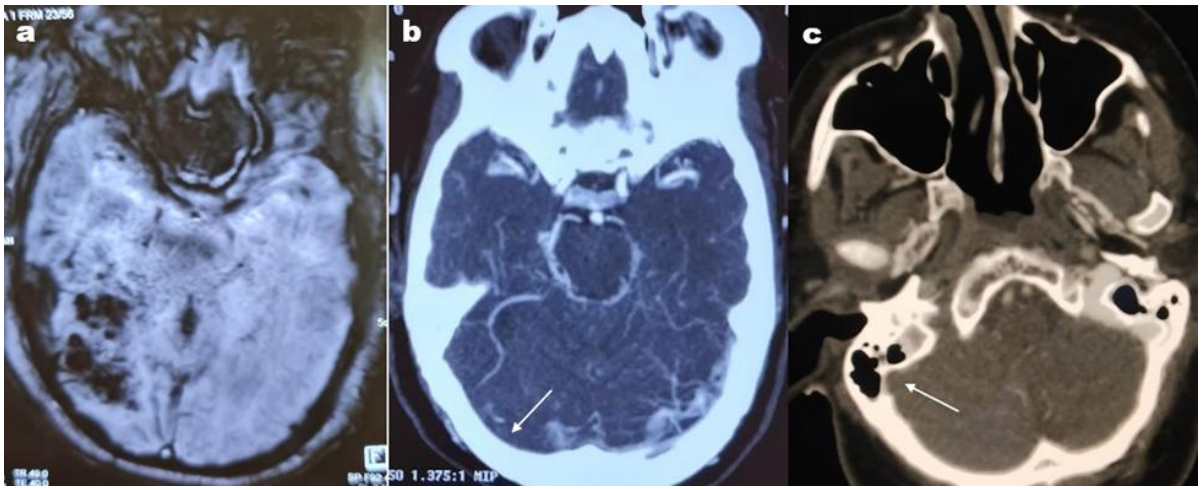

Figure-1: Magnetic resonance imaging showing intraparenchymal hemorrhage in the right temporo-parietal region[a]. CT angiography showing filling defect in [b]right transverse sinus(arrow) and right sigmoid sinus(arrow)[c].

Over the next 24 hours, she developed low grade fever with shortness of breath. Due to drop in her oxygen saturation levels she had to be keptonoxygen nasal prongs. Computed tomography of chest (Figure-2) showed confluent areas of ground glass opacities in both the lungs, suggestive of COVID pneumonitis(CORADS V). Detailed history did reveal her contact with a positive SARS-CoV-2 positive patient three days back. Patient was immediately put on the covid management protocol and the inflammatory markers were sent, which were found to be increased.A repeat nasopharyngeal swab test, done onfifth day of admission was again negative. During her twenty five days of hospital stay she had to be put on mechanical ventilatory support in view of covid pneumonia and had to undergo tracheostomy for prolonged ventilation. At the time of discharge, she was conscious, oriented and was prescribed oral anticoagulants, with necessary advice on neurologic and hematologic monitoring.

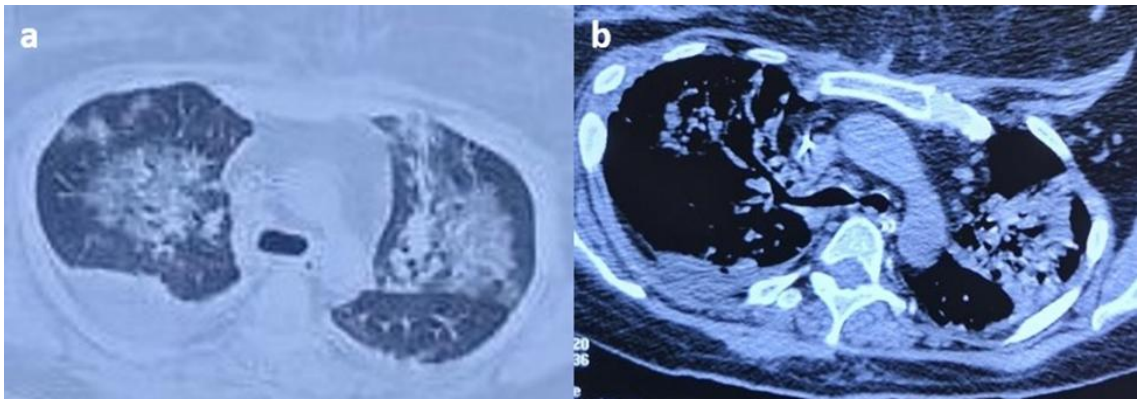

Figure-2: CT chest on the day of admission showing ground glass opacities in bilateral lung fields, suggesting COVID pneumonitis[a]. CECT chest done twenty-five days later showing slight resolution of consolidation in right lung field[b].

II. Discussion:

Angiotensin converting enzyme-2 receptor is the primary docking site for the covid virus inorder to gain entry into the cell. These receptors are expressed not only in the lungs, but also in central nervous system and endothelial lining of all the vessels, which increases the risk of thrombotic complications in such patients.[9] Though cerebro-venous thrombosis in covid cases lags behind in the incidence rate compared to other thrombotic complications, the number of case reports are ever increasing. [10] A review of medical literature showsthe risk of thrombotic complications to be higher for patients that are admitted in the intensive

care unit compared to those that are not critically ill and there is a lag time of 7-14 days from the date of infection todevelopment of thrombotic complication. [11,12,13] This case presented to our outpatient department with seizure being the first and only complaint. A day later she again presented to the emergency room with multiple episodes of generalized seizures. This deviation from the established time line of thrombotic event in covid patients deprived us from the chance of prescribing any kind of antithrombotic prophylaxis to the patient, which we routinely used to do based on the D-dimer values.

In this case the two consecutive nasopharyngeal swab test for SARS CoV-2(at admission and five days after hospitalization) was negative. Given the low sensitivity of the tests, if we assume a test to be 70% sensitive and a population has 50% chance of pretest positivity, the probability of false negativity is as high as 23%.[14]Hence, until we improve the sensitivity of the available tests and standardize the diagnostic criteria, we should always take into consideration the clinical complications, no matter how rare they might be, as a hint towards the diagnosis of COVID infection, inspite of a negative test result.Persistent headache, seizures, altered sensorium shouldalertthe emergency team to keepcerebral venous thrombosis as a differential diagnosis. And, in the absence of any known risk factors of hypercoagulability, the clinician should employ a high degree of suspicion for COVIDassociated coagulopathy, despite a negative swab test.[15]

III. Conclusion:

Although medical literature has a handful of reported cases on CVT in COVID 19 cases, almost all are seen in critically ill cases requiring ICU admission and develop as a complication to COVID 19 infection in due course of time. However, we have shown that COVID 19 can present with CVT (with seizure as its clinical manifestation) as the first and only presenting sign. The treating doctor in the emergency room and the neurosurgeon should be aware of this deviation from the established clinical profile, timelineof COVID associated coagulopathy, the false negativity of the nasopharyngeal swab test for COVID 19and must be prepared enough to handle such cases in accordance with the COVID protocol, without increasing the risk of cross infection.

Abbreviations:

COVID	corona virus disease
CVT	cerebral venous disease
SARS-CoV-19	severe acquired respiratory syndrome corona virus 19
CT	computed tomography
NIHSS	national Institute of health stoke scale
SW	Susceptibility weighted
MRI	magnetic resonance imaging
RTPCR	reverse transcription polymerase chain reaction
CORADS	covid-19 reporting and data system
ICU	intensive care unit

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