Rare complication of COVID-19 presenting as isolated headache

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SUMMARY
An 18-year-old man presented with persistent isolated headache 2 weeks after recovering from acute COVID-19 illness. Extensive cerebral venous sinus thrombosis (CVST) was detected on CT venogram despite him having no other thrombotic risk factors. CVST can complicate COVID-19. A high index of clinical suspicion is warranted as it can often have a subtle presentation with paucity of neurological symptoms.

BACKGROUND
Cerebral venous sinus thrombosis (CVST) accounts for 0.5% of strokes and has a wide spectrum of clinical presentation1; however, headache is the most common manifestation occurring up to 90%, and sometimes it can be the only symptom. The majority of cases have a predisposing thrombotic risk factor.1 2 COVID-19 is caused by SARS-CoV-2 and typically presents as acute febrile illness with respiratory involvement as the most common presentation.2 The complete clinical spectrum remains to unfold, but the association between thromboembolic events and COVID-19 is increasingly recognised. We report a case of a young man developing CVST as a sequela of COVID-19.

CASE PRESENTATION
A young man with no comorbidities developed acute COVID-19 illness in the beginning of June 2020 with fever, cough and myalgia. He had confirmed positive throat swab PCR test in the community. The acute illness settled within a week at home, precluding hospital admission. A week later, he presented to the medical assessment unit with worsening headache. His headache was deemed to be a residual symptom of his recovery from initial COVID-19 illness. He had a negative COVID-19 swab test during that admission and was discharged after a period of observation.

However, his headache persisted on discharge, and he re-presented to medical admissions with worsening headache for 2 weeks. His headache was global, severe in intensity and persistent with associated mild photophobia, but there was no fever, rash, visual symptoms, neck stiffness or any other neurological symptoms. He had no thrombotic risk factors and no family history of thromboembolism.

On examination, he was alert and afebrile with Glasgow Coma Scale of 15/15. His saturations were 100% on air, respiratory rate was 20/min, blood pressure was 130/70 mm Hg and heart rate was 90/min. There were no signs of meningeal irritation or any neurological deficit. Rest of the examination was within normal limits.

INVESTIGATIONS
Initial investigations showed normal cell counts with normal platelets. His coagulation profile, including prothrombin time, activated partial thromboplastin time and fibrinogen, was normal. C reactive protein was 30 mg/L.

An initial plain CT of the brain did not show any focal parenchymal abnormality but showed hyperdense internal cerebral veins, raising the possibility of venous sinus thrombosis (figure 1). A subsequent CT venogram showed filling defects throughout the sigmoid and transverse sinuses bilaterally, extending into straight and superior sagittal sinuses (figure 2). There was no intracerebral haemorrhage.

TREATMENT
His headache was managed with simple analgesia. Following discussion with the haematology and neurology teams, he was commenced on therapeutic dose of low-molecular-weight heparin and was monitored over 24 hours.

OUTCOME AND FOLLOW-UP
He was discharged with the plan of continuing therapeutic dose of enoxaparin for 3 months and follow-up with the neurology team. The patient was followed up via telephonic consultation after 2 weeks, and he reported significant improvement in his symptoms and almost complete resolution of headache.

DISCUSSION
While the clinical knowledge about COVID-19 is still evolving, there is growing evidence that COVID-19 predisposes to thromboembolic events and a hypercoagulable state.

A multicentre Dutch study comprising 184 patients with COVID-19 pneumonia reported up to 49% cumulative incidence of thrombotic complications despite all patients receiving at least prophylactic anticoagulation.1 An Italian study of 388 patients reported a 21% cumulative incidence of thrombotic events.4 However, the majority of studies showed a higher frequency of thrombotic events in patients with severe disease requiring intensive care unit (ICU) admissions compared with those on general wards.5 Severe disease and ICU admission seem to aggravate the pre-existing risk. Cytokine-driven inflammatory immune response with subsequent endothelial damage could explain the increased risk. Hypoxia is another factor driving pulmonary thrombosis in ventilated patients in ICU.
COVID-19 has a neurotropic potential, and complications including acute cerebrovascular events, encephalitis and Guillain-Barré syndrome have been reported. However, these are rare events, with CVST being an extremely rare complication of COVID-19. It has been previously reported, but those cases had severe disease with significant neurological deficit at presentation, contrary to our case. Cavalcanti et al reported three cases, all of whom have developed significant COVID-19 pneumonia and severe neurological deficit. All three died of COVID-19 complications. Hughes et al reported a case presenting with aphasia and hemiparesis with recent COVID-19 infection. He also had other comorbidities including diabetes and hypertension. Our reported case is unique as he recovered from the initial COVID-19 illness which was mild and did not even require hospital admission. Headache was the only persisting symptom leading to his admission after he recovered from initial respiratory illness. He did not have other risk factors for venous thromboembolism.

The extensive CVST in this case suggests that perhaps there are other unexplained factors that contribute to thrombosis in COVID-19, and it is likely that the infection itself is an independent risk factor. Further studies are required to explain the exact pathophysiology behind thromboembolic events in COVID-19.

CVST can be challenging to diagnose because headache rather than focal neurological deficit is the prominent feature. Headache can also be part of acute COVID-19 illness, which can further complicate the clinical picture. Given the thrombotic risk with COVID-19, a persistent worsening headache should be fully investigated especially in the presence of other thrombotic risk factors. This case highlights the need for continued vigilance to look out for this complication in COVID-19. A missed diagnosis of CVST could potentially result in fatal consequences including raised intracranial pressure and intracerebral haemorrhage. We suggest that it should be considered in the differential diagnosis in patients presenting with worsening headache after acute or recent COVID-19 infection.

**Learning points**

- Current evidence suggests a clear link between COVID-19 and thromboembolic events.
- Cerebral venous sinus thrombosis (CVST) can present with a wide range of clinical manifestations; however, headache can be the only presenting symptom.
- Clinicians should have a high index of suspicion for CVST in COVID-19, even in patients with mild illness.

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**REFERENCES**


**Figure 1** Plain CT of the head showing suspicious hyperdense area (arrow), raising the possibility of venous sinus thrombosis.

**Figure 2** CT venogram showing filling defects throughout straight and superior sagittal sinuses (arrows), confirming cerebral venous sinus thrombosis.