Late-post-COVID-19 cerebral venous sinus thrombosis and stroke: a case report
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Introduction
Coronavirus disease 2019 (COVID-19) disease increases risk of venous thromboembolisms (VTE), primarily deep vein thrombosis and pulmonary embolism. Only a few cases of cerebral venous sinus thrombosis (CVST) in association with a COVID-19 infection have been reported and are limited to acute COVID-19 disease. Hypercoagulable conditions persist in postacute COVID-19 disease, which carries an increased risk of VTE.

Case presentation
We report a case of CVST and stroke 56 days post-COVID-19 infection presenting with an atypical clinical picture.

Discussion
To the best of our knowledge, this is one of the first observations of CVST in the postacute phase of COVID-19 disease. Clinicians should be aware of this potential late complication and should consider appropriate diagnostic imaging techniques in patients with COVID-19-infection history.

Keywords: case reports, cerebral venous sinus thrombosis, coronavirus, coronavirus disease 2019

Coronavirus disease 2019 (COVID-19) disease is an established cause of venous thromboembolisms, mostly deep vein thrombosis (DVT) and pulmonary embolisms (PE).1,2 Cerebral venous sinus thrombosis (CVST) is far less frequent and reported mostly during active COVID-19 infection.3–7 We present a female patient with stroke due to CVST 56 days post-COVID-19 infection.

Case presentation
A 35-year-old woman with no relevant medical history developed sudden onset of confusion 8 weeks post-COVID-19 infection. She did not recognize her husband, could not use her mobile phone, and was disoriented in time and space. In the emergency department, global dysphasia and dyspraxia were observed, without other neurological features. A noncontrast computer tomography scan demonstrated a subcortical and cortical 2 × 2 cm hypodense area in the left temporal lobe (Fig. 1a). Computer tomography angiography of the central nervous system showed no pathology in the arterial system; the venous system had a filling defect in the left inferior anastomotic vein and the left transverse sinus (Fig. 1b and c). Based on patient symptoms, clinical examination, and imaging findings, stroke due to CVST was diagnosed and the patient was admitted to the intensive care unit. Subcutaneous dalteparin was initiated, along with other routine supportive measures. On admission, the complete blood count, routine biochemistry, lipids, and coagulation parameters including D-dimer were normal. Comprehensive hypercoagulability evaluation of antithrombin III, protein C, protein S, prothrombin gene mutation, Factor V Leiden gene mutation, lupus anticoagulants, anticardiolipin, and beta-2-glycoprotein-I antibodies was within normal range. The patient reported use of an etonogestrel/ethinyl estradiol contraceptive vaginal ring for 10 years without complications.

During the hospital stay, her neurological status gradually resolved to normal, with complete recovery by Day 5. Control computed tomography and magnetic resonance imaging scan of the central nervous system confirmed a cerebral infarct area in the left temporal lobe without extension from the initial area and no hemorrhagic transformation. We switched treatment from dalteparin to warfarin and discharged her on Day 7 without any subjective complaint or neurological deficit. At 1-month follow-up, her international normalized ratio (INR) was within therapeutic range, and she did not experience any neurological complications.

At 1-year follow-up, her neurological status was stable and normal. The CVST was concluded to have been triggered by the COVID-19 disease and warfarin treatment was terminated.

Discussion
COVID-19 disease is a serious condition with manifold thrombotic presentations in the acute phase,1–2 including CVST.3–9 Recently, the focus has shifted to the...
postacute phase and COVID-19 complications.10–12 Previously reported CVST cases occurred during the first 14 days from COVID-19 diagnosis.3–7 In most cases, patients presented with at least mild COVID-19 symptoms.3–7 Nonetheless, presentation can be very subtle as in a recent report of a male patient with CVST after an asymptomatic COVID-19 infection.8 The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse transcription-polymerase chain reaction (RT-PCR) was negative and the infection was confirmed with positive immunoglobulin G (IgG) antibodies.

To our knowledge, our case is the first report of postacute COVID-19-related CVST that started with nonspecific symptoms 8 weeks after a positive SARS-CoV-2 RT-PCR and mild COVID-19 disease. When thrombosis occurs,
especially in rare locations (CVST accounts for <1% of strokes), comprehensive evaluation of potential risk factors is needed.\(^\text{13}\) In our patient, all laboratory markers of increased coagulation risk were negative and only local hormonal contraception could be identified as a risk factor. Systemic effects are known to occur in this form of contraception and CVST cases have been described; however, these occurred early, usually within 2 years.\(^\text{14}\) Since our patient has been using this contraceptive method for approximately 10 years without any complications and based on her clinical course, we assume that local hormonal contraception made her more susceptible to venous thromboembolism (VTE) and that the COVID-19 infection finally triggered the CVST. From a clinical perspective, the presentation was atypical for CVST, and diagnosis was challenging.\(^\text{13}\) Also, the patient was admitted during the COVID-19 pandemic which per se presented severe resource challenges (personnel, equipment, time) towards non-COVID-19 patients.\(^\text{10}\)

Many biomarkers are known to be elevated during acute SARS-CoV-2 infection and several mechanisms seem to contribute to acute SARS-CoV-2 infection related systemic involvement, including enhanced coagulation.\(^\text{9,11,15}\) Our report, along with the literature,\(^\text{8,11}\) suggests that the hypercoagulable state of a COVID-19 infection may persist for a longer time relative to the initial infection. It is also in line with the recent global report about COVID-19 vaccination associated CVST, which in significant part (25/90 or 28% of cases) was not associated with vaccine-induced immune thrombotic thrombocytopenia which we also did not observe in our patient.\(^\text{16}\) Apparently, there are other mechanisms responsible for unusual VTE locations after COVID-19 vaccination or disease.

One of the first studies on the mechanisms of late vascular complications after a COVID-19 infection suggests an association between a SARS-CoV-2 infection and endothelial and vascular dysfunction, independently of disease severity.\(^\text{11}\) Hence, it is vital to immediately initiate anticoagulation therapy in patients with an appropriate indication and accompanying COVID-19 disease history. In our patient’s case, anticoagulation therapy was started without delay. According to the literature such a course of action has been associated with a more favorable clinical course in COVID-19 patients.\(^\text{12}\)

With this case, we highlight late COVID-19 associated complications presenting as VTE of uncommon location, in a form of CVST with atypical clinical presentation. Clinicians should be aware of unusual post-COVID-19 complications and consider appropriate clinical and imaging tools in patients without full-blown neurological clinical presentation.

**Conflicts of interest**

There are no conflicts of interest.

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