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Case report

Cerebral venous thrombosis in COVID-19-associated coagulopathy: A case report

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ABSTRACT

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first reported in Wuhan, China in December 2019, and is ongoing pandemic. While a majority of patients with SARS-CoV-2 infection shows asymptomatic or mild disease, hospitalized patients can develop critical condition, such as pneumonia, sepsis, and respiratory failure. Some cases deteriorate into sever systemic disease and multiorgan failure. Many patients of severe COVID-19 show hypercoagulable state and complicate with venous thromboembolism and atrial thrombosis. We herein reported a case of COVID-19 who developed cerebral venous thrombosis (CVT) co-incidence with pulmonary thromboembolism (PTE). A 56-year-old Japanese man was presented with fever and malaise and diagnosed with COVID-19. He was treated with ciclesonide and azithromycin, but his respiratory condition deteriorated. Thus, systemic corticosteroids and favipiravir were initiated and these treatments resulted in afebrile state, improving malaise and respiratory failure. However, he suddenly developed severe headache and vomiting with increased concentration of D-dimer. Brain CT and MRI showed typical images of CVT in the left transvers sinus and CT pulmonary angiography showed PE. Administration of unfractionated heparin followed by edoxaban treatment reduced the levels of D-dimer and improved his clinical presentation and thrombosis. Monitoring coagulopathy is important in COVID-19 patients and in case of venous thromboembolism, including cerebral venous system, appropriate anticoagulant therapy should be initiated.

1. Introduction

Coronavirus disease 2019 (COVID-19) is caused by Severe Acute Respiratory Crоronavirus-2 (SARS-CoV-2) infection. COVID-19 is associated with a high risk of thrombotic complication, such as venous thromboembolism (VTE) and cerebrovascular disease [1]. In addition to the cardiovascular risk factors, hypercoagulability may be the most important mechanisms of thrombosis [2]. Though it is rare, cerebral venous thrombosis (CVT) is a serious cerebrovascular event that shows variable clinical presentation highly likely due to the delay of the diagnosis [3]. We experienced a case of CVT and co-incidence of pulmonary thromboembolism (PTE) with COIVID-19 that was successfully treated with intravenous unfractionated heparin (UFH) followed by edoxaban.

2. Case presentation

A 56-year-old Japanese man, who had no remarkable medical history, visited our unit with fever and malaise. Chest computed tomography (CT) images demonstrated bilateral multiple lobe ground-glass opacities (GGO), but the SARS-CoV-2 reverse-tran scriptase-polymerase-chain-reaction assay (RT PCR) test was negative. Four days later after the first visit, his symptoms were deteriorated and admitted to our medical center. Body temperature was 38.8 °C with blood pressure 138/78 mmHg, heart rate 108/min, respiratory rate 20/min, and oxygen saturation of 98%. Laboratory findings revealed normal count of white blood cell (5000/μL) and a slight increase in CRP (0.77 mg/dL). The levels of D-dimer (1.1 μg/mL) and ferritin (435.5 ng/mL) were not elevated. Re-evaluation of chest-CT images were worse compared with the

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ones scanned at the first visit (Fig. 1), and the secondary test for SARS-CoV-2 RT PCR was positive. The treatment by inhaled ciclesonide (400 μg bid) and intravenous azithromycin (500 mg daily) began, but his symptoms deteriorated and the levels of serum ferritin increased (Fig. 3). Because bilateral GGO progressed and oxygen administration was required, we administered favipiravir (1800 mg bid on the 1st day followed by 800 mg bid) and intravenous methylprednisolone (80 mg daily) from day 5 (Fig. 3). As the levels of D-dimer were slightly elevated (2.7 μg/mL), he received subcutaneous injection of unfractionated heparin (10,000 unit/day). After initiating favipiravir and methylprednisolone, he got afebrile, improving malaise, and the oxygen was not required anymore. However, he suddenly suffered from severe headache and vomiting on day 12. D-dimer was steeply elevated to 10.3 μg/mL (Fig. 3). Non-contrast CT (NCCT) and magnetic resonance imaging (MRI) showed compatible with CVT from confluences of sinus to left transvers sinus (Fig. 2). A CT pulmonary angiography (CTPA) also showed the filling deficit within the inferior lobar arteries of bilateral lung compatible with PTE (Fig. 2). After treatment of dose adjusted intravenous UFH instead of

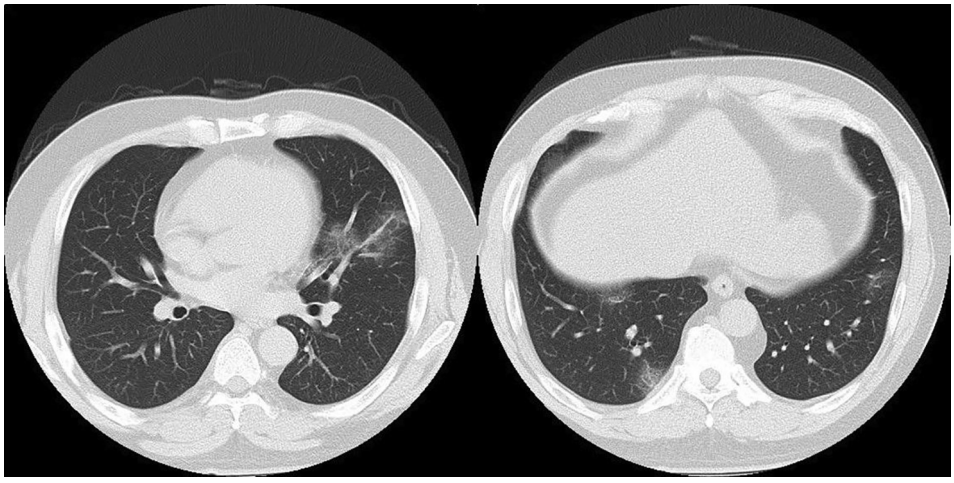

Fig. 1. Chest computed tomography images at the second visit to our unit demonstrated bilateral multiple lobe ground-glass opacities, which were worse compared with the ones scanned at the first visit.

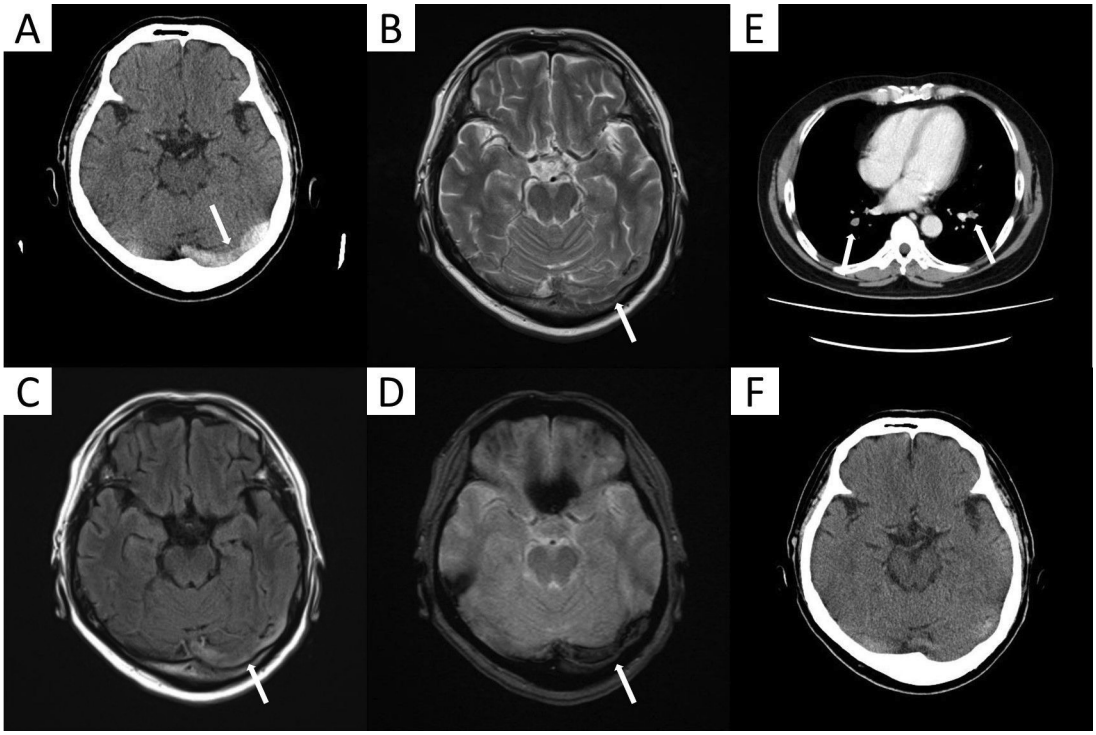

Fig. 2. Non-contrast computed tomography (NCCT) on day 12 demonstrated hyperdensity area of left transverse sinus as the cord sign (arrowed) (A). T2-weighted magnetic resonance imaging (MRI) demonstrated isointensity area (arrowed) (B) and T2 FLAIR-weighted MRI demonstrated abnormal hyperintensity area (arrowed) (C) in left transverse sinus as absence of flow void. T2*-weighted MRI demonstrated hypointensity area in left transverse sinus (arrowed) (D). These findings suggested cerebral venous thrombosis. A CT pulmonary angiography showed the filling deficit within the inferior lobar arteries of bilateral lung (arrowed) (E). Re-evaluation of NCCT on day 26 demonstrated disappearance of hyperdensity area of left transverse sinus (F).

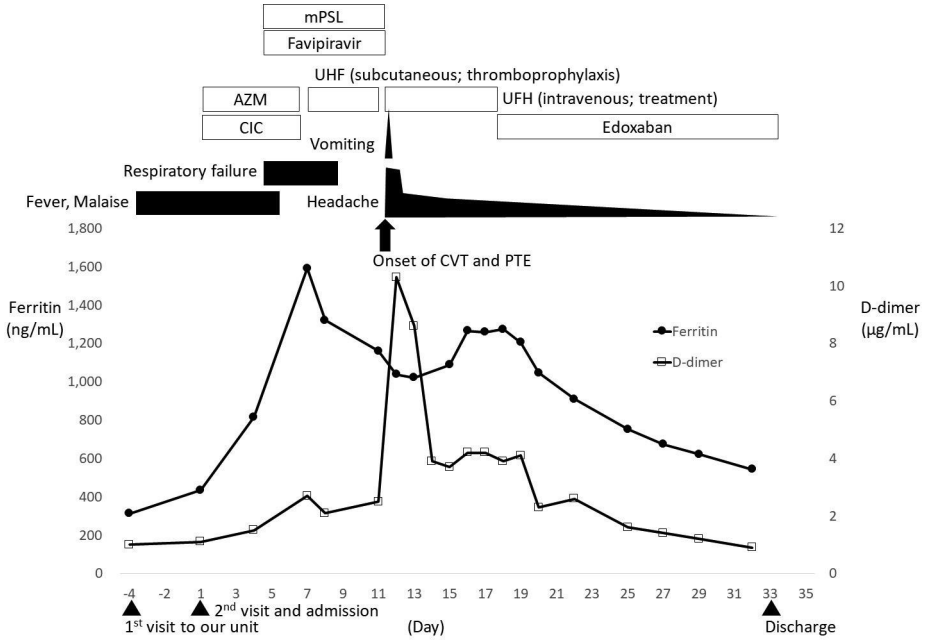

Fig. 3. Clinical course of the present case. AZM: azithromycin, CIC: ciclesonide, CVT: cerebral venous thrombosis, mPSL: methylprednisolone, PTE: pulmonary thromboembolism, UHF; unfractionated heparin.

subcutaneous injection, the levels of D-dimer decreased followed by improvement of headache and vomiting. UFH was switched to edoxaban (60 mg/day) on day 18 (Fig. 3), and re-evaluation of NCCT demonstrated significant improvement of sinus thrombus (Fig. 2), and he was discharged on day 33. The treatment with edoxaban had continued and he remained free from symptom for 14 days after discharge.

3. Discussion

COVID-19 has been reported to increase the risk of thrombotic complications and the incidence of VTE and ischemic stroke are approximately 20% and 3%, respectively [1]. The incidence of PTE based on the CTPA was 30% irrespective of presence of clinical suspicion for PTE [4]. However, the incidence of CVT in COVID-19 remains unknown while one retrospective study demonstrated 1/221 (0.5%) had CVT [5]. Headache is the most common clinical symptom of CVT [3] and the prevalence of headache was 13% in COVID-19 patients in Wuhan [6]. Further study will be needed to explore how many patients will have CNS involvement complaining headache in COVID-19. We administered initial parenteral anticoagulation followed by DOAC, and this treatment succeeded in resolution of clinical symptoms and sinus thrombosis. It has been suggested by current guideline in COVID-19 patients with proximal DVT and PTE [7] and will be applicable for the treatment of CVT. Our patient showed a gradual increase of plasma ferritin and D-dimer preceded the CVT onset. As these coagulation and inflammatory biomarker are associated with thrombotic complication in COVID-19 [8], we should pay a special attention to these biomarkers and the risk of systemic thrombosis in acutely ill hospitalized patients with COVID-19.

4. Conclusion

COVID-19 is highly risky for development of venous thromboembolism, including cerebral venous system. Physicians should consider the possibility of CVT if patients show neurological symptoms and an increase of biomarkers in case of COVID-19.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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