A Rare Case With Arterial and Venous Thrombotic Complications After COVID-19

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Abstract

Background

Recently, it has been reported that there is an increase in the incidence of arterial and venous thrombotic complications associated with severe COVID-19 disease. Studies have revealed the definition of COVID-19-associated coagulopathy as the underlying cause of these complications. With the emergence of hypercoagulability, systemic anticoagulant therapy was required at variable doses and durations in COVID-19 patients.

Case Report:

We present the case of a 79-year-old female patient who developed ischemic stroke, deep vein thrombosis, and acute pulmonary embolism, respectively, despite the use of anticoagulants since hospitalization for severe COVID-19 disease.

Discussion

Owing to SARS-CoV2 infection may be accompanied by comorbidities such as hypoxia, immobilization, active cancer, and obesity, close patient monitoring should be performed during the period of active disease and recovery.

Conclusion

The most important message to be taken from this case is that even in patients using anticoagulants, there is still a higher risk of thrombotic complications.

Background

In late 2019, the coronavirus disease 19 (COVID-19) pandemic started in Wuhan, China's Hubei Province, and throughout the world for the whole of 2020. Several studies have demonstrated that arterial and venous thrombotic complications, such as stroke, acute pulmonary embolism (PE), deep vein thrombosis (DVT) and systemic arterial embolism, which are included in the context of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV2)-mediated hypercoagulability. Prophylactic or therapeutic systemic anticoagulants are used to prevent these complications in patients with SARS-CoV2 infection. Unfortunately, there are no specific suggestions about the timing or dosing of these drugs. COVID-19-associated coagulopathy (CAC) underlying pathophysiological processes can be summarized as excessive inflammation, hypoxia, immobilization, and diffuse intravascular coagulation (DIC).
In patients with severe COVID-19 symptoms; the frequency of clinical presentations associated with hypercoagulability was higher due to comorbid diseases, profound hypoxemia, and systemic hyperinflammation.\textsuperscript{3,4}

In this report, we present a patient who developed arterial thrombosis (ischemic stroke) in the acute period and venous thromboembolic processes (DVT and PE) in the mid and long term of the COVID-19 infection.

**Case Presentation**

A 79-year-old female patient with a history of hypertension applied to the emergency department with complaints of fatigue and dry cough for 4–5 days. The patient had normal vital signs and was in good general condition, cooperative, orientated and had a normal level of consciousness, and there was no significant finding except for the right basilar rales on lung auscultation. Basic laboratory findings demonstrated an elevated white blood cell count (11.3 k/uL) with neutrophilic predominance (79.1%) and lymphopenia (9.8%), with anemia (11.7 gm/dL), and preserved platelet count (204 k/uL). Pathological values in the metabolic panel were mild hyponatremia (132 mmol/L), elevated LDH (311 U/L), and hypoalbuminemia (3.3 g/dL). When inflammatory markers are scanned; it was noteworthy that the CRP (152 mg/L) and D-dimer (1.5 mcg/mL) levels were high despite the mildly elevated procalcitonin (0.06 ng/mL) and preserved ferritin (62 ng/mL). The SARS-CoV2 nasopharyngeal PCR test was positive and Computed tomography (CT) of the chest showed that peripherally located consolidation in the lateral basal segment of the right lung lower lobe (Fig. 1).

The patient was consulted by the departments of infection and chest diseases and was hospitalized. During the follow-up, the patient had low blood oxygen saturation and chest radiography showed patchy infiltrations on the right lung's middle and lower lobes (Fig. 1). She received five doses of hydroxychloroquine, ten days of azithromycin. Aspirin 100 mg once a day orally as antiplatelet therapy and enoxaparin 40 mg twice daily by subcutaneous (sc) injection as antithrombotic therapy was applied. Repeated SARS-CoV2 tests during her hospitalization were twice negative. Upon the developing clinical observations of dysarthria, left central facial paralysis, and left-sided weakness detected on the morning of the 11th day of hospitalization, cranial CT represented hypodense appearance compatible with acute infarction in the right middle cerebral artery (MCA) territory and the right basal ganglia.

Further, MR-DWI consisted of a well-defined area of low T1 signal / high T2 signal with diffusion restriction in the right MCA territory (Fig. 1). The patient who was diagnosed with ischemic stroke was transferred to the neurology service. No atrial fibrillation, cardiac thrombus focus, and carotid or vertebrobasilar artery stenosis were observed. After seven days of hospitalization in the neurology service, where her treatment was updated to clopidogrel 75mg orally once a day and enoxaparin 40mg sc twice a day, the patient was transferred to the physical medicine and rehabilitation (PM&R) inpatient clinic for neurological rehabilitation.
She has left-sided hemiplegia, a sequel of ischemic stroke. The patient's Brunnstrom stages were stage 2 for lower extremity, stage 1 for upper extremity, and stage 1 for hand. Although there were no clinical symptoms, no pathological condition was detected in the venous Doppler ultrasound (VDUS) examination performed for control. The patient was immobile for about 15 days when rehabilitation started under close monitoring. In the 50th session of her rehabilitation (in the 3rd month of hospitalization), the patient developed sudden onset of shortness of breath, tachypnea, and tachycardia. She had elevated D-dimer (5.4 mcg/mL) in the laboratory findings, and her lower extremity VDUS findings were consistent with thrombus in the left common femoral vein and superficial femoral vein lumen. CT pulmonary angiography (CTPA) showed a filling defect compatible with embolism in the lobar and segmental branches on the left (Fig. 1) and subsegmental branches on the right in the pulmonary artery. The pulmonologist quickly evaluated the patient, and the treatment was arranged as enoxaparin 60mg twice a day and clopidogrel 75mg once a day. By dint of the neurological rehabilitation program that continues after pulmonary recovery, which lasted a total of 90 sessions in PM&R inpatient clinic and was including intramuscular administration of 200 units botulinum toxin type A for spasticity in the left biceps, brachialis, pronator, gastrocnemius, and soleus muscles, the degree of ambulation of the patient has reached the level of the community.

**Discussion**

COVID-19 is associated with thrombotic complications in both arterial and venous systems and caused sudden deaths resulting from the complications in many previous studies. Initially, CAC was defined as DIC-like consumptive coagulopathy due to increased D-dimer levels, decreased platelet count, and fibrinogen level in a study investigating the causes and risk factors of mortality. However, in contrast to D-dimer progression, laboratory findings showing variability in platelet count, clotting times, and fibrinogen levels revealed marked differences between CAC and DIC and led to an alternative etiology coagulopathy associated with excessive inflammation. Later in another study, CAC was defined as a combination of low-grade DIC and localized pulmonary thrombotic microangiopathy. The major mechanisms in pathophysiology are direct endothelial cell damage, diffuse inflammation with immune system dysregulation, followed by cytokine storm, hypoxia-induced thrombosis, and increased levels of antiphospholipid antibodies.

In a retrospective observational study, acute ischemic stroke was specified in 5% of 221 patients. In a related case series of young patients with ischemic stroke secondary to COVID-19 disease in New York; CAC is the most important cause of strokes in this population. However, the transthoracic echo and DUS for the carotid and vertebrobasilar systems should be performed to determine the possible causes.

Demonstrating high D-dimer concentration and thrombotic microangiopathy in the pulmonary vessels by autopsies was suggested that pulmonary embolism may be a significant cause of acute respiratory failure in COVID-19 patients. A review examining thrombotic complications in COVID-19 patients; the overall incidence of VTE was determined to be 21.9%. Although the incidence of acute PE in patients
hospitalized for COVID-19 varies between studies, the highest rate was determined in patients with severe
disease who were treated in the intensive care unit. Looking at the literature; studies on the incidence of
DVT in COVID-19 patients are more limited. In a study, DVT was found in 46.1% of the COVID-19 patients
through DUS scanning of the lower extremities. The high heterogeneity observed between studies
causes inconsistencies in PE with or without DVT. Principally, close clinical and ultrasonographic follow-
up should be important in the early diagnosis of DVT, especially if there are additional risk factors such
as a history of stroke and immobilization during patients’ rehabilitation process with a history of severe
SARS-CoV2 infection.

The International Thrombosis and Hemostasis Association recommends a prophylactic dose of LMWH
for all hospitalized patients with SARS-CoV2. Prophylaxis with LMWH or direct oral anticoagulants until
45 days after discharge was accepted, although not unanimously, in patients with risk factors for VTE
and with a D-dimer height more than twice the upper value. Notwithstanding the initiation of
anticoagulation, sustained assessment for the progress of de novo thrombosis is recommended. In this
case, who was under anticoagulant treatment due to ischemic stroke associated with severe COVID-19
disease and was closely monitored in the neurological rehabilitation program, was rapidly treated after
the diagnosis of PE because of sudden dyspnea.

In a patient who had one of the complications mentioned before; the likelihood of relapse of the same
complication and other new thrombotic processes has increased. As in this case, the anticoagulant used
in prophylactic doses in a patient with a history of CAC-related ischemic stroke may be insufficient to
prevent new thrombotic complications. Perhaps it would be better to use higher doses of systemic
anticoagulant drugs used in such cases. It is also necessary to reveal how long the anticoagulant
treatment will last and what should be the combination options with other anticoagulant drugs in future
studies. We believe that all clinicians should be prepared for possible COVID-19 related thrombotic
complications, even with prophylactic anticoagulant dosing.

One of the limitations of this case was the inability to obtain antiphospholipid antibodies associated with
hypercoagulability in COVID-19 patients.

**Conclusion**

In summary, COVID-19 is an infectious disease that causes both arterial and venous micro-macrovascular
thrombotic circumstances leading to a hyperinflammatory and prothrombotic state. Accordingly, early
identification and close monitoring of the thrombotic complication of COVID-19 can be lifesaving. Please
note that clinical conditions caused by arterial and venous thrombotic complications associated with
COVID-19 may also occur even when they are under anticoagulant therapy, especially in the long-term
follow-up of these patients.

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Consent to Publication: Written informed consent was obtained from the participant's son included in the study.

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