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COVID-19 Case Report

Aortic thrombosis after DVT and PE in a young COVID-19 patient

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Abstract: A rare case of aortic thrombosis in a young COVID-19 positive patient is presented in this case report. Arterial thrombosis developed despite the administration of anticoagulants for treating DVT and PE. The patient underwent axillobifemoral bypass surgery. Limited surgical surveillance, administered steroids and critical health status resulted in wound site infection and consequent graft removal. Aortic endarterectomy and autovenous-patch plasty were performed after the patient's condition improved. Etiopathogenesis of arterial events in the setting of COVID-19 is not entirely understood. It has been suggested that SARS-CoV-2 infection strongly affects vascular endothelial glycocalyx (VEGLX), causes systemic inflammation - reactive microvascular endotheliosis (SIRME), and consequently results in arterial thrombosis.

Coronavirus disease 2019 (COVID-19) can result in various complications outside the respiratory tract including renal failure, neurological symptoms, septic shock, myocardial injury as well as coagulopathies. Prothrombotic condition in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected patients can lead mostly to venous thromboembolism (VTE), deep vein thrombosis (DVT), and less frequently to arterial thrombotic events.[1–3] Even though arterial thrombosis in COVID-19 patients is less common than venous thrombotic events, recently published studies imply that the rate of arterial thrombosis in such a clinical setting is growing.[1] Therefore, it is critically important to understand the pathological mechanisms of excessive arterial blood clotting which can lead to acute limb ischemia, myocardial infarction, and stroke.[4] Once the pathogenesis is fully understood, it will be easier to prevent and manage arterial thrombosis. It is important to increase awareness to succeed with early diagnosis by differentiating vasospasm, hypoxia, and acidosis caused by COVID-19 from those caused by arterial thrombotic events. A case of a young patient with thrombosis of the infrarenal aorta and bilateral occlusion of iliac arteries in the setting of COVID-19 is presented. Moreover, the patient has developed pulmonary embolism (PE) despite being on prophylactic dose of anticoagulants.

CASE REPORT

On December 15, 2020, a 51-year-old man was presented to an emergency department with chest pain and hypertensive crisis (arterial blood pressure, 220/110 mmHg) which was corrected with peroral drugs (ACE inhibitors). The patient's vital signs during admission were as follows: heart rate, 81 beats/min; temperature, 36,9°C; oxygen saturation, 95% with supplemental oxygen flow of 3 liters/min. The patient underwent a chest computed tomography angiography (CTA) scan with no signs of PE. However, the CTA scan showed bilateral pneumonia and subsequently, patient was tested positive for COVID-19. According to the latest local protocol, amoxicillin with clavulanic acid

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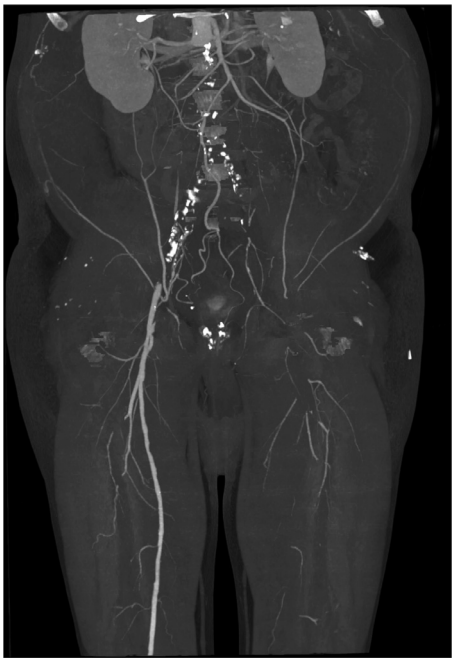

Fig. 1. CTA reconstruction. Aortoiliac occlusion.

was administered as well as dexamethasone, low-molecular-weight heparin in prophylactic dosage, and oxygen. The patient started complaining of worsening pain and weakness in the left lower limb on consecutive days. On December 17, because of high D-dimers (22145 ng/mL), venous duplex ultrasound was performed and no venous pathology was found. Leg pain was getting worse and the left femoral artery pulse could not be palpated. Due to deteriorating health status, a chest and lower extremities CTA was carried out on December 23. It showed bilateral viral pneumonia with partial resorption, as well as PE in the right middle lobes of lateral and medial segments. Due to occurred PE low-molecular-weight heparin dose was increased from prophylactic to therapeutic. CTA also revealed thrombosis of infrarenal aorta, bilateral common iliac arteries, and left external iliac artery. The proximal sections of left internal iliac and mesenteric inferior arteries were occluded as well (Fig. 1). Surgical revascularization was postponed because of the patient's severe condition and borderline saturation level which was only about 80% with maximum oxygen flow due to COVID-19 and PE. At that point in time limb ischemia was not critical and according to the local hospital's protocol of COVID-19 patient management, intubation must be avoided as long as it is possible. The patient's leg ischemia deteriorated the following days and the surgery was considered again. On December 28, the patient was stable enough to place the extra-anatomic axillo-bifemoral bypass. Endovascular treatment was rejected because of the unknown etiology of arterial thrombosis in the setting of COVID-19. Axillo-bifemoral bypass was chosen instead of aortobifemoral to carry out a less invasive procedure. However, on the 3rd post-operative day wound healing appeared to be compromised. Vascular graft infection was confirmed by ultrasound scan on the 5th postoperative day. Several risk factors might have contributed to the graft infection: ongoing pneumonia, prolonged preoperative hospitalization, administration of corticosteroid, obesity, limited access treatment in the COVID-19 unit. As soon as the patient was fully recovered from COVID-19, he was transferred to the Vascular Surgery unit. On January 8, the infected axillo-bifemoral shunt was removed. Additionally, an open endarterectomy of infrarenal aorta, right common iliac, and left external iliac arteries as well as remote endarterectomy in the left common iliac artery were performed. The left great saphenous vein was used for autovenous-patch plasty of the right common iliac, left external iliac, and bilateral common femoral arteries. The blood flow was restored to the patient's legs successfully: left popliteal pulse, as well as pulse in the left foot, were present. There were no complications during postoperative period, hence the patient was discharged from the hospital on the 25 of January.

DISCUSSION

Lately, a growing number of studies and case reports on coagulopathies associated with COVID-19 infection can be found. Despite the increasing number of thrombotic events in COVID-19 patients, the pathogenesis of hypercoagulability in this particular clinical setting is still poorly known.[5] Therefore, many theories have emerged to explain this problem. It has been suggested that all three components of Virchow's triad can be affected by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[6] Changes of prothrombotic factors, such as factor VIII, fibrinogen, neutrophil extracellular traps can be observed in patients critically ill with COVID-19 and they are reported to promote a hypercoagulable state.[7] Numerous experts have postulated that endothelial dysfunction plays a central role in the pathogenesis of clot formation in severely ill COVID-19 patients.[8–11] Some studies have reported that the alternative complement pathway is activated by SARS-CoV-2 spike protein,

which eventually results in the elevation of markers of complement activation and endothelial injury.[12] Moreover, endothelial dysfunction can be exacerbated by viral or bacterial inflammation because under such circumstances tissue factor (TF) production is elevated, as well as granulocytes, monocytes, and several cytokines including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNFα).[13] According to Minako Yamaoka-Tojo, the underlying cause of endothelial dysfunction during COVID-19 infection is the damage of vascular endothelial glycocalyx (VEGLX). It is a gel-like layer covering the inside of blood vessels and functioning as a barrier for vascular endothelial cells as well as controlling intracellular signals.[11,14] It has been well documented that hypertension, diabetes, heart failure, ischemic heart disease, kidney diseases, atherosclerosis, stroke, sepsis, multiple organ failure as well as obesity, smoking, and old age can lead to impaired VEGLX. On the other hand, VEGLX can also be strongly affected by SARS-CoV-2, which invades vascular endothelium and causes systemic inflammatory changes in endothelial cells as well as induces the release of inflammatory cytokines and leakage of plasma components resulting in VEGLX destruction and shedding. These pathological processes can be defined by systemic inflammation reactive microvascular endotheliosis (SIRME). It has been suggested that SARS-CoV-2 can better penetrate the endothelial cells with already impaired VEGLX on account of underlying diseases. Therefore, lethal conditions, for instance, acute respiratory distress syndrome (ARDS) or disseminated intravascular coagulation (DIC) have a higher incidence rate among COVID-19 patients that have at least one previously diagnosed chronic disease. As the fragmented VEGLX level in patient blood correlates with COVID-2019 severity, it is believed to be beneficial as a prognostic indicator.[10] However, in this clinical case, the amount of VEGLX was not tested. Risk management and treatment of thrombotic complications due to COVID-19 are challenging owing to the lack of high evidence data. According to the International Society on Thrombosis and Haemostasis, all hospitalized SARS-CoV-2 infected patients should get prophylactic anticoagulation therapy,[15] particularly those with risk factors such as smoking, physical inactivity, hypertension, diabetes, obesity, cardiovascular diseases, male gender, and older age.[16] However, it is being more commonly reported in existing literature as well as in our clinical experience that despite administration of thromboprophylaxis thrombotic events may still occur.[4,17,18] Extensive clinical trials are needed to clarify the best ways of preventing and managing thrombotic complications during COVID-19.

CONCLUSIONS

Arterial thrombosis in the clinical setting of COVID-19 appears less commonly than venous thrombotic events. However, it is crucially important to maintain a high index of suspicion on arterial manifestations. It can be challenging to diagnose it early because vasospasm, hypoxia as well as acidosis can be understood as symptoms of COVID-19, while they can appear due to arterial thrombosis. Also, delayed diagnosis can lead to severe complications and result in increased mortality and morbidity rate. Overall, COVID-19 has given various insights on mechanisms of arterial thrombosis which could potentially be used in clinical practice outside the field of COVID-19.

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