Acute arterial thrombosis in SARS-CoV-2 infection

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, whose main expression is an acute respiratory syndrome, is also associated with concurrent multisystemic involvement, coagulation disorders and thrombotic complications, both in patients with prior diseases and those without. We present the case of a patient admitted to our hospital with no prior medical problems who had documented SARS-CoV-2 infection. During hospitalization, the patient developed acute left lower limb pain and absent pedal and posterior tibial pulses, with acute arterial ischemia due to thrombosis confirmed with imaging tests. Other causes of thrombosis such as atheromatosis, embolism and coagulation disorders, among others, were ruled out. He was anticoagulated with low-molecular-weight heparin and cilostazol throughout hospitalization and was discharged on warfarin and cilostazol. SARS-CoV-2-related acute arterial thrombosis should also be considered in our region. **(Acta Med Colomb 2022; 47. DOI: https://doi.org/10.36104/amc.2022.2372).**

Keywords: *arterial thrombosis, acute arterial ischemia, COVID-19, SARS-CoV-2, coronavirus*.

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Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) disease has become a global health emergency. Since its appearance, it has been described as having respiratory symptoms like cough, odynophagia, fever, fatigue and complications related to pneumonia (COVID-19) and acute respiratory distress syndrome. However, other organs have been shown to be affected with atypical clinical presentations caused by heart, kidney, neurological or other system involvement. In addition, it has been associated with a systemic procoagulant response, which is multifactorial (1).

The risk factors for developing severe symptoms are advanced age, male sex, and the presence of comorbidities. Clinical and pathological data show an association between SARS-CoV-2 infection and coagulopathies which may manifest as pulmonary embolism (PE) and venous, arterial and/or microvascular thromboses which are associated with severe viral injury of the pulmonary endothelium. Therefore, there is a relationship between elevated D-dimer levels (despite being a nonspecific acute phase reactant) and fibrin degradation products in all conditions with an activated coagulation system like thrombosis, infection or malignancy. The clinical spectrum of infection ranges from a lack of symptoms to fatal septic shock, and this transition from mild to severe is caused by cytokine storms and greater hypercoagulability. Thus, prophylactic anticoagulation has been recommended for all patients hospitalized for SARS-CoV-2 infection as soon as possible to prevent thrombotic events and organ damage (2, 3).

Case presentation

This was a 51-year-old male security guard with no diagnosed illnesses, and a history of light smoking. He consulted due to 15 days of asthenia, fatigue, fever, chills, dry cough, odynophagia and dyspnea.

On admission, the patient had signs of respiratory distress. Arterial gases showed a severe oxygenation disorder. The patient had leukocytosis with neutrophilia; lymphopenia (950 cells/μL); elevated D-dimer (753 ng/mL), C-reactive protein (40.5 mg/dL), ferritin (1,029 ng/mL), and lactic dehydrogenase levels (505 U/L); and a positive polymerase chain reaction for SARS-CoV-2. The patient was transferred to the intensive care unit where he remained for four days. Due to clinical improvement, he was transferred to the general ward.

On his third day on the general ward, the patient had an episode of sudden-onset pain in his left leg, associated with absent pedal and posterior tibial artery pulses, distal coolness and paresthesias in the first and second toes of the left foot. His mobility was not affected.

A Doppler ultrasound of the arterial vessels was obtained along with tomography angiography of the left lower extremity. These showed absent anterior tibial, posterior tibial and peroneal artery flow, with no collateral circulation (Figure 1), which confirmed the diagnosis of acute arterial ischemia (AAI) due to thrombosis. The patient was given anticoagulation therapy with low molecular weight heparin and cilostazol and was discharged three weeks later on warfarin and cilostazol.

Discussion

SARS-CoV-2 infection can predispose to arterial and venous thromboembolic disease due to excessive inflammation, hypoxia, immobility and disseminated intravascular coagulation (4). The data presented here confirm that these hemostasis abnormalities during and after acute infection explain the onset of acute extremity ischemia in young patients with no history of arterial disease, as seen in our middle-aged patient (40-59 years) with no known medical history on admission (5).

In addition, studies have shown that males are frequently affected, especially older patients, although it has also been reported in younger patients with no comorbidities. Furthermore, there are more and more tests such as elevated fibrinogen concentrations and acute phase reactants showing significant coagulation mechanism abnormalities compared with non-infected patients, which allows these laboratory tests to be classified as early predictors of severe forms of the disease, as was also documented in our case.

Acute limb ischemia in SARS-CoV-2 infection may occur in two situations, one during the inpatient course of severe SARS-CoV-2 infection, reporting a median of 19 days (11-23 days) from the onset of symptoms of the infection to the installation of ischemia, or they may be admitted to the emergency room with this vascular disease with mild or absent respiratory symptoms (6). Our patient met the first case, as he was admitted with a 15-day history of general and respiratory symptoms characteristic of the infection, and on day 22 presented signs of acute ischemia of the left lower limb.

Recently published studies, mostly in Asia, Europe and the United States, have usually described more venous than arterial involvement since the beginning of the pandemic. In the short and isolated reports, the most commonly involved arteries were in the lower limbs, predominantly the popliteal, anterior and posterior tibial, superficial femoral, iliac and distal aorta (6).

The Rutherford classification is most frequently used to classify limb acute arterial ischemia (AAI). This classification divides AAI into class I or viable limb; class II, IIa if there is a marginal threat, or IIb if there is an imminent threat to the limb; and III when the damage is irreversible (7). Our patient had class IIa AAI, due to an acute arterial thrombosis documented on tomography angiography of the left lower limb.

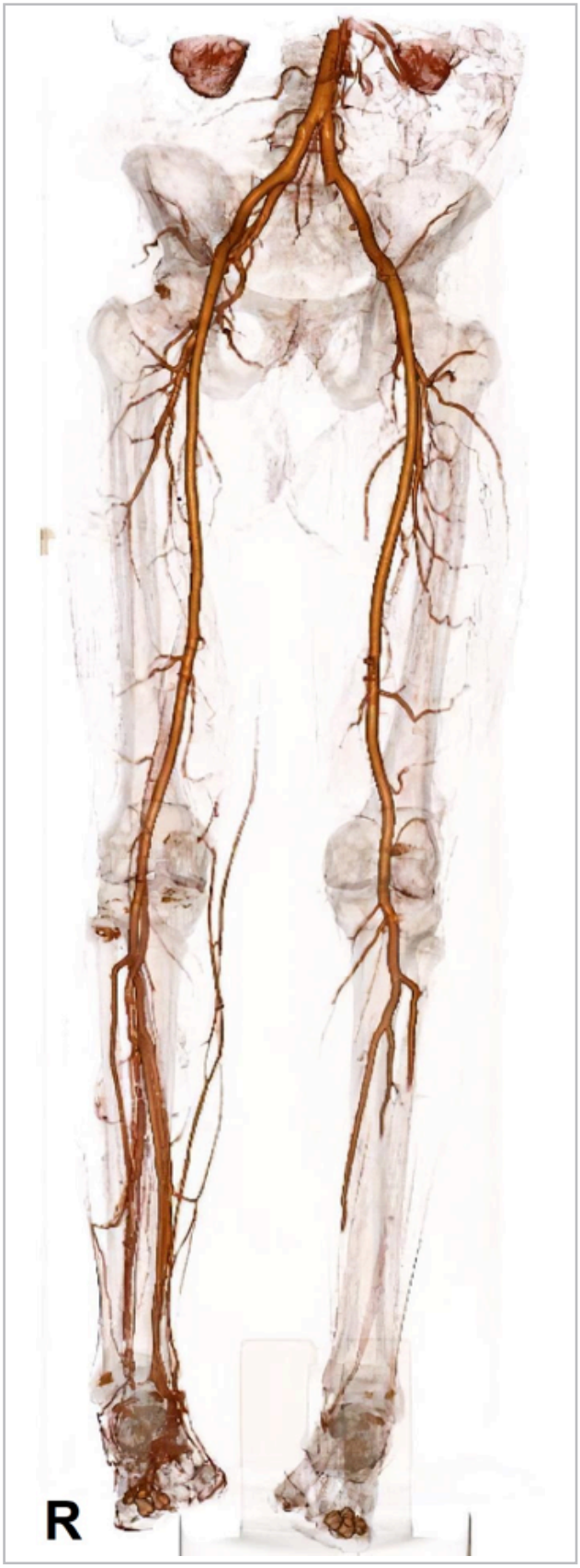

Figure 1. *Tomography angiography reconstruction of the lower limbs. Absent flow in the middle third of the anterior and posterior tibial and peroneal arteries in the left leg.*

When evaluating arterial thrombosis, atherosclerosis and cardioembolism should be studied first (8). Our patient was not overweight, had only engaged in light smoking and did not have hypertension. A tomography angiography of the aorta and great vessels was performed, along with a transthoracic echocardiogram and Holter arrhythmia monitoring, which ruled out atheromatous plaques, thrombi in the heart chambers and cardiac arrhythmias, respectively. The patient was diagnosed with type 2 diabetes mellitus, with 5.9% glycosylated hemoglobin. However, acute arterial thrombosis has only been reported in diabetic patients with acute decompensation, a condition which our patient did not have (9, 10). Other causes of thrombosis, like hormone therapy, medications, Buerger's disease, autoimmunity and anatomic variations were also ruled out (8). In addition, thrombophilic states were ruled out with negative anticardiolipin antibodies, anti-β-2-glycoprotein antibodies and lupus anticoagulant. There were no JAK2 gene mutations. This was ultimately considered to be a SARS-CoV-2-related episode of acute arterial thrombosis. Many case reports of patients with SARS-CoV-2 infection and arterial thrombosis have been published (11, 12). This manifestation may also occur in patients in our region.

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