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True Aneurysm on Posterior Tibial Artery as Late Complication of SARS-CoV-2

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ABSTRACT: We describe the story of a 70-year-old Italian male that almost 4 months later respiratory infection by SARS-CoV-2 presented a rapid evolution of a true aneurism of the right posterior tibial artery (PTA).

INTRODUCTION
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a global pandemic. The development of an acquired thrombophilia with activation of the coagulation cascade in response to the inflammatory process has been described. SARS-CoV-2 appears to have an affinity for vascular endothelium due to angiotensin-converting enzyme 2 receptors that seem to be downregulated, which may drive the proinflammatory and/or prothrombotic and vascular consequences.

We describe the story of a 70-year-old Italian patient who presented 4 months after COVID-19 infection with a true aneurysm of the posterior tibial artery (PTA).

CASE PRESENTATION
A 70-year-old male was referred to the vascular outpatient clinic with history of a pulsatile lump behind his right ankle over the last 2 months. Apart from the presence of a lump, he denied any other complaints including any violent or repeated trauma. He also suffered from hypertension. He was not taking any antiplatelet or anticoagulation medications and denied any use of tobacco. He was hospitalized on April 2020, as the result of acute hypoxic respiratory failure due to community-acquired pneumonia, with positive results for SARS-CoV-2 infection in patient’s reverse transcription-polymerase chain reaction (RT-PCR) test from nasopharyngeal swab. Doppler at that time had not revealed superficial or deep venous thrombosis or other abnormalities. At physical examination a 3 × 4 cm size lump just behind the right medial malleolus was identified, which was non-tender and pulsatile. The patient confirmed a rapid increase of the dimensions during the last month. The peripheral pulses were easily palpable on either side. There was no evidence of aneurysm anywhere else in the body on clinical examination. He underwent Doppler ultrasound examination which confirmed 1.6 cm size pseudoaneurysm of PTA with presence of circumferential mural thrombus. The distal and proximal parts of PTA, anterior tibial artery and popliteal artery were normal.

He underwent an operation in the form of excision of aneurysm (Fig. 1) followed by end-to-end anastomosis of PTA (Fig. 1). Histology confirmed true aneurysm of PTA with mural thrombus attached to the intima of the vessel. The arterial wall did not show evidence of connective tissue disorders. Pathology specimen was examined using hematoxylin and eosin (H&E) stain. The specimens were assessed for inflammatory cells associated with endothelium and/or apoptotic bodies, mononuclear cells, small vessel congestion,
and lymphocytic endotheliitis, mainly T CD3+. The bacteriology examination did not reveal any organisms nor grown any organisms in the culture media. He recovered well postoperatively and was discharged on forth postoperative day. At follow up at one year, he did not develop any complications and color Doppler revealed patent PTA.

**DISCUSSION**

Aneurysms are more common in the proximal arteries such as femoral and popliteal arteries compared to distal small vessels. It is a rare pathology of the infra-popliteal region, where false aneurysms are more common and are usually associated with trauma.\(^1\) The true aneurysms of infrapopliteal region are extremely rare and most of them have been reported to be associated with trauma, collagen vascular pathology, fibromuscular dysplasia, inflammation, infection, and atherosclerosis.\(^2\) False aneurysms are more common in comparison to the true aneurysms even in infrapatellar blood vessels. The precise etiological factors are not identified, but trauma is suggested as possible causality.\(^3\)

Italy was the first western country to be stricken by the coronavirus pandemic. The most common COVID-19 symptoms of the disease at onset were fever, fatigue, dry cough, dyspnea, runny nose, or other upper respiratory tract symptoms. Ageusia and anosmia were also found to be characteristic symptoms, albeit with more rare presentation, while gastrointestinal symptoms, focal neurological deficits as a result of strokes arising from thrombosis and thromboembolism, account for a minority of cases. Cutaneous manifestations with an array of morphologies have also been documented.\(^3\)

The demonstration of endothelial cell injury across vascular beds of different organs gives light to unexplained symptoms and clinical courses described in early reports of the COVID-19 pandemic. In particular, histological analysis revealed that the presence of the virus within endothelial cells was associated with clusters of inflammatory cells. This finding suggests that SARS-CoV-2 infection initiates endothelial inflammation throughout the entire human organism, as well as apoptosis, something that explains the systemic macro and microcirculatory involvement in different vascular beds and their clinical sequelae in patients with COVID-19.\(^4\) Moreover, evidence of viral endothelial injury helps to explain why patients with pre-existing cardiovascular disease are particularly associated with adverse outcomes in COVID-19.

Since the initial reports, an increase in circulating D-dimer levels has been reported. The addition of systemic proinflammatory cytokines release as a consequence of endothelial inflammation, as well as the expression of the ACE2 receptors for SARS-CoV-2, might contribute to the clinical presentation associated with COVID-19. Further studies are needed to clarify the role of inflammation in the pathogenesis of COVID-19-related complications.
CoV-2 on the membrane of the vascular muscle and endothelial cells, may help to explain why COVID-19 patients are also susceptible to arterial thrombosis, even in young non-arteriosclerotic individuals. Vascular biomarkers confirm that COVID-19, a disease initially thought to be exclusively an interstitial pneumonia with varying degrees of severity, can also be considered a vascular disease. In case reports published of PTA aneurysms, false and true, etiology suggested was trauma, infections or unknown. Degenerative changes lesions secondary to mycotic infection, polyarteritis nodosa are also described as responsible for true aneurysm. In our patient, we could not find any etiological factor, such as trauma, atherosclerosis or connective disorders. The only recent inflammatory event in our patient was the SARS-CoV-2 infection.

We are living an historical era due to the ongoing global pandemic, and we are all inclined to correlate situations without a certain causality to SARS-CoV-2. This patient is one of those cases in which we find no other etiological correlation with the recent onset of the PTA pseudoaneurysm. On the other hand, however, the presence of lymphocytic infiltrate in the wall of the PTA, already highlighted as a histological finding in certain cases of vascular damage in SARS-CoV-2, and not reported in other cases of pseudoaneurysms in literature, can confirm our doubt. Additionally, the negative bacteriology is important in determining this diagnosis, since mycotic aneurysms, which is on the differential, tend to be positive for bacteria in most cases.

The management options vary from conservative approach to surgical excision followed by reconstitution of PTA. Due to very limited number of published cases, a standard treatment has not been defined. Although ligation of posterior tibial artery may be performed, especially in emergency settings, surgical excision with posterior tibial artery reconstitution either by primary repair or by interposition vein graft is the preferred treatment. Endovascular embolization and percutaneous occlusion of aneurysm with various modalities are more commonly used in pseudo-aneurysms and are associated with risk of limb ischemia.

In this case, patient underwent surgical excision followed by end-to-end anastomosis. The anterior tibial and pedis arteries were intact and one might question the need for operation in this report, however we believe that those aneurysms should be treated irrespective of symptomatology due to the risk of embolization, thrombosis, and rupture leading to potential ischemia and amputation.

The vascular community should be aware of this new complication in critically ill patients with COVID-19. The finding in this patient is likely an infectious angitis due to COVID 19, and surgery showed to be a valuable treatment option.

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