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INTRODUCTION

The novel Sars-CoV-19 pandemic has affected the globe, changing every dimension of society. Since the beginning of 2020 national healthcare systems have faced an unprecedented emergency. In the last 12 months, an enormous number of studies have been published regarding COVID-19 infection, highlighting the systemic impact that this virus can have on infected patients.[1]

The incidence of coagulopathy disorders in COVID-19 patients have gained substantial interest. Hypercoagulable state in patients with COVID-19 has been demonstrated by several studies,[2] highlighting the negative impact that thromboembolic events could have on mortality rates.

In addition to an increased incidence of vein thromboembolism,[3] a higher number of Acute Limb Ischemia (ALI) have been also observed.[4,5]

In Italy, the number of patients with severe COVID-19 infection has been one of the highest globally. Luckily, the vast majority of patients are followed at home with no need for hospitalization and intensive care observation. These patients have different needs with different follow-up protocols.

In this perspective, with this paper, we want to report a series of 3 patients who have recovered from a nonhospitalized nonsevere COVID-19 infection with subacute limb ischemia that occurred during quarantine and were diagnosed and treated with a significant time-delay (Table 1).

All subjects gave informed consent and the ethical committee of the hospital was informed of the no-experimental of the study and it.

CASE 1

A 78-year-old male patient with a previous medical history of idiopathic myelofibrosis JAK-2-correlated and no reported thromboembolic events, presented to our emergency department with right leg pain, foot cyanosis, and poikilothermia.
**Table 1.** Presentation features of the three patients admitted

|                       | Duration of COVID-19 Positivity | Use of LMWH during COVID-19 infection | Onset of ALI symptoms respect to negativization day | Admittance day after COVID-19 negativization | Rutherford grading at admittance | Other embolic sources |
|-----------------------|---------------------------------|---------------------------------------|-----------------------------------------------|--------------------------------------------|----------------------------------|----------------------|
| Case #1               | 27 days                         | No                                    | -5                                            | 9 days                                     | II b                             | No                   |
| Case #2               | 30 days                         | No                                    | -7                                            | 14 days                                    | II b                             | No                   |
| Case #3               | 23 days                         | No                                    | -4                                            | 10 days                                    | II b                             | No                   |

**Fig. 1.** A) Appearance of the right lower limb at admission. B) Appearance of the right lower limb after in-hospital re-occlusion and before the amputation.

A Rutherford IIb ALI grade was defined (Fig. 1A). Duplex vascular ultrasound (DUS) revealed complete occlusion of superficial femoral (SFA) and popliteal (PA) arteries. The patient referred that leg pain started two weeks earlier, when he was forced to COVID-19 quarantine. Vital signs were stable, and the blood sample revealed only a mild leukocytosis. Antiphospholipid antibodies and lupus anticoagulant were tested but resulted negative. The patient was moved to the operating room (OR) and hybrid revascularization was performed. Fogarty's embolectomy led to the remotion of a large amount of organized blood clots. Vacuum-assisted thrombectomy (Indigo CAT 8 and CAT 6, Penumbra Inc, Alameda, CA, USA)\[6\] was also performed with the restoration of direct perfusion to the foot assured by patent posterior and anterior tibial arteries (Fig. 2). A continuous infusion of unfractionated heparin was started after the procedure. The following day, DUS examination revealed a re-occlusion of the entire limb arterial tree. The patient was moved again to the OR and a catheter for intraarterial fibrinolysis was positioned in the anterior tibial artery. Administration of recombinant-Tissue-Plasminogen-Activator was performed for 36 hours. Completion angiography and a further thromboaspiration procedure resulted in the patency of SFA, popliteal and Anterior Tibial Artery (ATA), although perfusion of foot microcirculation remained very poor. On the 13th postoperative day after first intervention, an above-the-knee amputation was performed due to a newly complete occlusion and progression of distal gangrene and worsening of general clinical status (Fig. 1B).

The hospitalization continued uneventfully, and the patient was discharged home in stable condition on the 21st postoperative day.

**CASE 2**

An 82-year-old-male patients with a past medical history of hypertension, and diabetes mellitus presented to our noninvasive vascular examination
lab with a rapid onset and progression of trophic lesions located at the I, II toes of the left foot. The patient had fully recovered from a nonsevere COVID-19 infection 2 weeks before. DUS revealed a partially occluded popliteal artery with hypoechoic material within. Anterior and posterior tibial arteries were partially perfused from collateral vessels. The diagnosis was an acute on chronic limb ischemia, in a phase of partial recanalization (Rutherford class IIb). The patient was admitted to our department, and the day after an endovascular recanalization was performed. The popliteal artery was completely reopened with direct flow to the anterior and peroneal tibial arteries. The procedure was completed with the deployment of a GORE Viabahn (W. L. Gore & Associates, Flagstaff, AZ) endograft 5 × 100 mm in the popliteal artery in order to maintain the good patency of the artery. At the same time, a minor amputation was performed. The patient was discharged on the 5th postoperative day uneventfully.

**CASE 3**

An 84-year-old male with a medical history of hypertension, dyslipidemia and coronary artery disease was admitted to our emergency department with right lower limb pain, mild foot cyanosis and rapid progression of foot trophic lesions. The patient had fully recovered from a nonsevere COVID-19 infection 10 days before. He referred the initial onset of an unclear leg symptomatology (mild paresthesia) 2 weeks before. DUS revealed a complete occlusion from the distal SFA with some feeble flow only at level of the anterior tibial artery (Rutherford class II b). The patient was moved to the OR for an endovascular recanalization. Vacuum-assisted thrombectomy (Indigo Penumbra CAT XTORQ and separator) was performed to remove the partially organized thrombosis from the SFA, PA and ATA. Technical success was reached with full removal of the clots and recanalization of a chronically occluded peroneal artery. The patient underwent a minor amputation 4 days later and discharged on the 10th postoperative day.

**DISCUSSION**

Thromboembolic complications in patients with mild and severe COVID-19 infections may represent a challenging event. An increasing number of publications are focused on the deep vein thrombosis and pulmonary embolism occurrence in these patients. Arterial complications are less common reported, but their impact on hospitalized and non-hospitalized patients could be devastating.

Increased level of D-dimer, decreased prothrombin time and increased activated partial thromboplastin time are some of the most common coagulative alterations found.[7]

The management of ALI remains troubling, with a high risk of severe morbidity, high rates of deaths and limb loss.[8] The correct and prompt diagnosis and treatment are essential to reach technical and clinical success. COVID-19 has determined a complete rearrangement of the healthcare system and homecare.[9,10] Nonsevere COVID-19 patients are mostly treated at home with scheduled medical
examination trying to reduce the already high pressure on tertiary hospitals.

COVID-19 pandemic, consecutive social limitations and self-isolation have contributed to a critical evolution and worsening of chronic[11,12] and acute disease with consecutive impact of their management.

In our paper, we presented three cases of subacute limb ischemia that occurred during the final part of patients’ domiciliary quarantine. The occurrence of ALI in COVID-19 patients is not a novelty, and its diagnosis and treatment can be challenging even in hospitalized patients.[13–15] All patients arrived at our attention after a significant delay that may jeopardize the success of the revascularization. It is well-known how clinical success and limb salvage are time-dependent variables, and how delayed diagnosis and treatment are related to less favorable rates of amputation and mortality.[8]

COVID-19 patients have to be considered at high risk of thromboembolic complications and physicians should be aware of their occurrence also in nonhospitalized patients.

CONCLUSION

We presented a series of three cases of misdiagnosed acute limb ischemia that occurred during the home quarantine of patients affected by non-severe COVID-19 infection. The delayed time of diagnosis and management have determined a reduction of clinical and technical success of the revascularization procedures leading to significant clinical consequences, with a potential impact on the patients’ quality of life (minor and major amputations). From this perspective, we want to address that also in non-hospitalized COVID-19 patients, vascular assessment should be scheduled and routine performed to avoid eventual life- and limb-threatening manifestation consequences.

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