

REPORT

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Post-COVID-19 tibial and fibular arterial thrombosis: therapeutic approaches

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ABSTRACT

Introduction: Current evidence suggests that hypercoagulability may be a sequel to hyperinflammation, a key pathogenic mechanism that contributes to increased mortality in COVID-19. The objective of this study was to report a case of arterial occlusion of the tibial arteries 21 days after hospital discharge from COVID-19 and analyze the approach. **Report:** Female patient with 47 years old was admitted to the infirmary with COVID-19 for 21 days, without other comorbidities. The patient had no history of previous disease or family thrombotic events. During this period, she had prophylaxis with enoxaparin 40 mg 12/12. The D-dimer assessment was performed routinely, without evident changes. Five days after leaving the hospital had symptoms of pain in the left limb. In clinical evaluation, the femoral and popliteal pulses were palpable, but distally, there was no pulse or flow at the bedside Doppler. The embolization was successful, and a significant amount of thrombus was removed; the appearance of a posterior tibial pulse was noted at the end of the procedure. She remained under full heparinization for 72 hours for transition to oral anticoagulation and hospital discharge with significant clinical improvement, leaving only moderate pain when walking. In the first return patient, have discrete pain with walking, but all palpable and symmetrical pulses, and full anticoagulation is maintained. **Conclusion:** Acute arterial occlusion in COVID-19 has a new etiology, and we know little about its behavior. The therapeutic approach differs from the arteriosclerotic cause, mainly regarding the anticoagulation time, which has no definition in the literature.

Keywords: COVID-19; mesenteric ischemia; arterial occlusive diseases; tibial arteries.

INTRODUCTION

Current evidence points to a state of hypercoagulability, as a sequel to hyperinflammation, as an important pathogenic mechanism that contributes to increased mortality in COVID-19. This theory is supported by reports of high inflammatory and clotting markers, and a correlation between high levels of interleukin-6 (IL-6) and fibrinogen¹⁻³.

Meta-analysis study detected deep vein thrombosis in 20% of hospitalized patients, pulmonary embolism in 8% and arterial thrombosis in 5%, with patients admitted to intensive care units (ICU) in serious condition being significantly higher⁴.

An autopsy study shows that 81% of patients with COVID-19 with the main cause of death, had thrombotic phenomena in the lungs. The extrapulmonary thrombotic events observed in the study were ischemic stroke 4 (3.95%), acute myocardial infarction 3 (2.94%), and critical lower limb ischemia 1 (0.98%)⁴.

The underlying mechanisms proposed for these serious manifestations included immune dysregulation, including a state similar to antiphospholipid syndrome, complement activation, viral spread with direct systemic endothelial infection, viral RNAemia with immunothrombosis, activation of the hypoxemia-mediated coagulation pathway, and immobility⁵. The antiphospholipid syndrome is associated with arterial and venous thrombosis, but other causes of congenital thrombophilia, such as protein C deficiency, Protein S, antithrombin III, and others, should be considered^{6,7}.

Anticoagulation is one of the approaches associated with reducing mortality. However, the dosage and what is the best option are study objectives. One of them evaluating the intermediate dosage had 2.5% major bleeding events in the intermediate dose group with 1.07% fatal events and 4 (1.4%) major bleeding events in the prophylactic standard dose group with no mortality⁸.

Anticoagulants prevent the formation of thrombosis, have anti-inflammatory and antiviral properties, and can be particularly effective in the treatment of patients⁹ with COVID-19. However, the approach to be taken about anticoagulation is essential; however, we do not have studies defining the maintenance of this post-COVID-19 anticoagulation.

The objective of this study was to report a case of thrombosis of the tibial arteries 21 days after hospital discharge from COVID-19 and analyze the approach taken.

REPORT

Report a case of a female patient with 47 years old and was admitted to the infirmary due to COVID-19 for 21 days, requiring in use of a catheter and an oxygen mask, and was discharged without other comorbidities from the hospital. The patient had no history of previous disease or family history of thrombotic events. During this period, he underwent prophylaxis with enoxaparin 40 mg 12/12. The D-dimer evaluation was performed routinely, but without evident changes, and was discharged from the hospital in stable condition. After five days had symptoms of pain in the left limb appeared, but only after three days was evaluated in the hospital, with femoral and popliteal pulses palpable, but distally, there was no pulse or flow at the bedside Doppler. Without signs of necrosis, extended capillary filling time, without muscle stiffness, and with coldness in a contralateral relationship. The ankle-brachial index was 0.6 before surgery and after the procedure, 1 in the posterior tibial at hospital discharge, and 1 on return in both tibials. Made hypothesis of arterial thrombosis was made, and an arteriography was performed, which showed abrupt obstruction in the anterior tibial, posterior tibial, and fibular arteries, with no findings suggestive of chronic arterial disease, according to Figure 1 (1A and 1B). An embolectomy via infrapopliteal incision and a significant number of thrombi removed, the appearance of a posterior tibial pulse after the end of the procedure, and improved capillary filling time. She remained under full heparinization

and limb heating for 72 hours, transitioned to oral anticoagulation, and was hospitalized with significant clinical improvement, leaving only moderate pain when walking. First outpatient return patient denies pain in the left lower limb, all palpable and symmetrical pulses, and full anticoagulation is maintained, being programmed for 3 to 6 months, but no antiplatelet agent was associated. This study received approval from the institutional review board of the São Jose do Rio Preto School of Medicine #4.802.349.

DISCUSSION

The present study reports acute arterial occlusion of the tibial arteries in a post-COVID-19 patient who was successfully submitted to embolectomy but kept it in the calf while walking. There are several reports in the literature of arterial thrombosis associated with COVID-19, but the conduct can raise a series of doubts, and it is important to ask about them. It is an arterial thrombosis where, in other causes of thrombosis, the conduct would generally be a bypass or endovascular treatment.

In the case of arterial thrombosis, the lesion is on the vessel wall, whereas in arterial embolism, the vessel is theoretically normal, and embolectomy is the main approach. In cases of chronic embolism, post-revascularization thrombosis is common. However, in COVID-19 thrombosis, the main lesion is on the vessel wall, therefore subject to a major failure in the procedure.

In the present study, embolectomy opened the posterior tibial artery, but not the anterior tibial artery. This fact can be explained by a failure in the surgical procedure in which Fogarty cannot pass through this artery, or by immediate rethrombosis. In the postoperative period, there was no pulse in this artery; the patient was kept anticoagulated, and on return, all the pulses were present, and the ankle-arm index was 1.

Another detail to be analyzed, in this case, is that the patient has improved pain after revascularization, but not completely. Pain occurred when walking, and this fact suggests that there may have been an injury in the arterial microcirculation or even in the venous microcirculation or in small veins, causing pain during ambulation. An important aspect to be analyzed in the first return of the patient is the return of the distal pulses; however, the patient did not have the total improvement of pain in the calf, reinforcing the hypothesis of a thrombosis of the gastrocnemius veins that were not previously diagnosed.

The management of arterial thrombotic events associated with antiplatelet therapy with aspirin is the best approach. However, in post-COVID-19, oral anticoagulation seems to be the best option. Currently, a new option, rivaroxaban 5 mg/day, has been an option in the case of arterial disease. Therefore, arterial thrombosis in COVID-19 brings changes in conduct about arteriosclerosis¹⁰. The anticoagulation time suggested in arterial thrombosis is another factor to be questioned because there is no study in the literature; however, suggested to be from two to three months.

More than 9,000 patients were treated at the institution, more than 5,000 of whom were in intensive care units (ICU), reaching 200 patients/day, and approximately 70 to 80% underwent orotracheal intubation. More than 600 patients with deep vein thrombosis were detected, but were underdiagnosed due to a lack of routine screening. In one of the evaluations where all patients in a single intensive care unit were evaluated, it was diagnosed that 80% of them had deep vein thrombosis. Regarding arterial thrombosis in COVID-19 disease in the service, approximately 50 patients were diagnosed; however, there was an association of the AstraZeneca and Pfizer vaccines with thrombosis of the aortic arch and aorta¹¹. These data are consistent with data in the literature, where the venous thrombotic event was the most prevalent.

Conclusion

Arterial thrombosis in COVID-19 has a new etiology, and we know little about its behavior. The therapeutic approach differs from the arteriosclerotic cause, mainly regarding the anticoagulation time, which has no definition in the literature.

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Figure 1: Arteriography: (A) popliteal normal; (B) abrupt obstruction in the anterior tibial, posterior tibial, and fibular arteries.

