

## A CASE REPORT OF ACUTE LIMB ISCHEMIA (ALI) – SEQUALAE TO COVID-19 INFECTION

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### ABSTRACT

**INTRODUCTION:** Acute limb ischemia (ALI) is characterised by rapid decrease in blood flow due to sudden occlusion of peripheral arteries. The symptoms of ALI are abrupt presenting with pain, numbness, coldness of the limb, paraesthesia, and irreversible purpura with the exacerbation of ischemia. If ALI is not treated promptly and effectively, the prognosis would be bad.

**CASE REPORT:** Herein, we report a case of acute limb ischemia in a COVID-19 positive patient. A 61-year-old gentleman presented with pain in his right lower limb for 10 days. Patient tested positive for COVID-19 infection 15 days prior to onset of symptoms. Examination revealed cold extremities and absent peripheral pulses on right lower limb. Doppler showed absent colour flow in the distal third of Posterior Tibial Artery (PTA) and Dorsalis Pedis Artery (DPA) on the right side, suggestive of complete occlusion. Computed Tomography of lower limb angiography revealed partial contrast filling defect of Deep Femoral Artery (DFA) suggestive of thrombosis, complete contrast non opacification in DPA and distal PTA suggestive of complete occlusion on the right side. Patient was managed conservatively and discharged.

**CONCLUSION:** The objective of this study is to present a case of patient infected with the novel coronavirus (COVID-19) who presented with acute limb ischemia (ALI) and had been treated successfully. Severely infected COVID-19 patients with abnormal coagulation profile should undergo prophylactic doppler examination of the lower limb in order to reduce the amputation rates and salvage limbs.

**KEYWORDS :** Covid-19, Coronavirus, Acute Limb Ischemia, Arterial Thrombosis

### INTRODUCTION:

In the present situation, Coronavirus disease 2019 (COVID-19) has been declared a worldwide pandemic and is giving rise to a myriad of coagulation abnormalities along with the constitutional and respiratory tract symptoms. The most common coagulation abnormalities noted so far include thrombotic events in major venous vessels, with various derangements in inflammatory markers especially D-dimers and fibrinogen. Here we report, an interesting clinical scenario of arterial thrombus formation in a COVID-19 patient, resulting in acute limb ischemia of right lower limb.

### CASE REPORT:

A 61-year-old gentleman was referred to the out-patient department, with history of pain in the right lower limb for the past 10 days. Patient had complaints of breathlessness 15 days prior to present symptoms, and tested positive for COVID-19. He was admitted at his native place for the same. Five days later, patient developed pain in the right lower limb which was acute onset, progressive, continuous, cramping type of pain with no radiation and no aggravating or relieving factors. Patient received intravenous heparin and meropenem in the previous hospital and was referred to our institute for further evaluation. Patient is a known diabetic for the past 10 years, on oral hypoglycaemic agents (OHA). No surgical history in the past. No similar complaints in his past as well as in the family members.

On clinical examination, right lower limb was cold and dusky

(Figure 1). Femoral and popliteal pulses were palpable, ATA, PTA and DPA pulses were not palpable whereas peripheral pulses are palpable on the left lower limb. Laboratory investigations revealed raised C-Reactive protein (CRP) and rest of the parameters were within normal limits. Chest radiograph showed subtle air space opacification in the peripheral part of the right lower zone. Right lower limb arterial and venous doppler revealed distal third of PTA and DPA with absent colour flow suggestive of complete occlusion and atherosclerotic changes in the visualised arteries in the form of intimal thickening and wall calcification. CT lower limb angiography showed atherosclerotic changes in the abdominal aorta in the form of calcifications and mural plaques. Right lower LIMB Shows Partial Linear contrast filling defect measuring approximately 1.3 cm causing 30 to 40% occlusion in the DFA, suggestive of thrombosis. Complete contrast non opacification is seen in the DPA, and dorsal most PTA, suggestive of occlusion. Echocardiography revealed a normal study with normal ejection fraction.



Figure 1 Depicts The Right Lower Limb With Ischemic Changes

Patient was managed conservatively with Oral Aspirin, Clopidogrel, Atorvastatin, Pentoxifylline, xanthinol nicotinate, Cilostazol and intravenous heparin. Blood sugar levels were maintained within normal ranges with insulin administration and then switched back to OHAs. Patient was discharged after two weeks. On follow up patient was asymptomatic and leading a normal life.

## DISCUSSION:

Acute limb ischaemia is defined as the sudden diminution in limb perfusion that jeopardises the viability of the limb. Complete or even partial occlusion of the arterial supply to a limb can lead to rapid ischemia and poor functional outcomes. Aetiology can be classified into 3 categories:

1. Embolization (most common), whereby a thrombus from a proximal source travels distally to occlude the artery. The source of thrombus may be a result of AF, post MI, mural thrombus, abdominal aortic aneurysm or prosthetic heart valves.
2. Thrombosis in situ, where an atheroma plaque in the artery ruptures and a thrombus forms on the plaque's cap
3. Trauma (less common)

Classically, the signs and symptoms of acute limb ischaemia can be described using the 6 Ps (the first three here being the most common initial features): Pain, Pallor, Pulselessness, Paraesthesia, Poikilo-thermia, Paralysis. (Deitcher et al., 2001) COVID-19 was declared as a pandemic by the World Health Organization on March 11, 2020. (WHO Director-General's Remarks at the Media Briefing on 2019-nCoV on 11 February 2020, n.d.) While many patients develop mild-to-moderate symptoms (fever, fatigue, myalgia, headache, diarrhoea, dry cough, and dyspnoea), several patients have been described to have severe systemic disease, resulting in countless coagulation abnormalities. The suggested mechanism through which SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) causes the systemic disease is through angiotensin-converting enzyme 2 (ACE-2) receptors. The SARS-CoV-2 proteins infect human cells through ACE-2 receptors, which are expressed in various degrees in alveolar epithelial cells, large and small arterial endothelial cells, small intestinal epithelial cells, immune tissues, and various other types of cells. (Han et al., 2020; Yang et al., 2020) SARS-CoV-2 directly attacks vascular endothelial cells and activates the coagulation cascade after causing endothelial injury. This pathologic insult is suggested to result in excessive cytokine release which leads to activation of widespread coagulation factors while inhibiting fibrinolysis causing extensive thrombosis similar to disseminated intravascular coagulation. IL-6 is a key factor in SARS-CoV-2 induced inflammatory storm. While IL-6 can stimulate the liver to synthesize fibrinogen and thrombopoietin, it also upregulates the expression of vascular endothelial growth factor to disrupt the stability of vascular barrier and stimulate monocytes to express more tissue factors, thereby activating the extrinsic pathway of coagulation. (Lu et al., 2020)

These coagulation abnormalities are indicators for higher mortality predisposing the patients to a variety of ischemic and thrombotic events. Various elevated markers including D-dimers, partial thromboplastin time (PTT), prothrombin time (PT), fibrinogen, fibrin degradation products (FDP), and IL-6 have been described to determine the progression of sepsis-induced prothrombotic disease secondary to SARS-CoV-2. In a series of 1099 patients with COVID-19 from China, elevated D-dimer (>0.5 mg/L) was found in 260 (46%) of 560 patients. (Wu & McGoogan, 2020) The coagulation changes associated with COVID-19 suggest the presence of a hypercoagulable state that might increase the risk of thromboembolic complications. Immobilisation and vascular damage are other factors that can increase the risk of thrombosis. Patients with COVID-19 have anecdotally been reported to have had

pulmonary embolism, suggesting that there could be a disproportionately high incidence of venous thromboembolism and possibly arterial thrombosis in patients with COVID-19. In critically ill patients, the incidence of thromboembolic complications ranges from 5% to 15%. (Xiong et al., 2020)

Tang et al. (Tang et al., 2020) in their study of 499 patients with COVID-19, out of which 99 patients received low molecular weight heparin (LMWH) therapy, reported that anticoagulant therapy mainly with LMWH appears to be associated with better outcomes in severe COVID-19 patients. The role of anticoagulants in preventing thrombotic complications and improving the overall prognosis in COVID-19 has not been clearly established. In view of the hypercoagulable state of patients with severe COVID-19, and the potential increased risk of thrombosis, it is suggested that all patients with COVID-19 that are admitted to a hospital should receive this prophylactic treatment in the absence of medical contraindications. If LMWH is not available, unfractionated heparin could be used, although this requires more frequent injections; an alternative is fondaparinux, but whether this drug has the postulated anti-inflammatory benefits of heparin is unclear. The role of higher-dose thromboprophylaxis in patients with severe COVID-19 is being tested in several multicentre, randomised, controlled trials. Prolonged systemic heparin might be warranted for both limb salvage and improved survival.

## CONCLUSION:

COVID-19 infection might increase the incidence of acute limb ischemia and show poor surgical results owing to the associated hyper-coagulability. The subject of COVID-19 induced coagulation abnormalities leading to thrombotic complications requires further large-scale studies thoroughly at the molecular level. We conclude that prophylactic doppler ultrasound examination of lower limbs is necessary in severely infected COVID-19 patients, especially elderly with comorbidities and those with abnormal coagulation profile, also it will help to establish the diagnosis of thrombotic complications associated with it and will prevent millions of amputations across the globe.

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