Original Research Article

Acute advanced bilateral lower limb ischemia in patient infected with COVID-19

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Abstract

Coronavirus disease 2019 (COVID-19) has emerged as a pandemic across the world[4]. The extraordinary prothrombotic manifestations of Coronavirus Disease-2019 (COVID-19) caused by severe acute respiratory syndrome CoV (SARS-CoV-2) virus, presenting as venous and arterial thrombosis have been reported in the literature. The incidence of arterial thrombosis is reported to be 4% in critically ill COVID-19 patients. Arterial thrombosis in the setting of COVID-19 has been reported to occur in a multitude of organs leading to ischemic strokes, ST-segment elevation, myocardial infarction, aortic thrombus and acute limb ischemia[3]. We report the case of a 55-year-old female patient with COVID-19 Pneumonia, diagnosed with Acute Limb Ischemia. From clinical examination, which included physical examination and laboratory results as well as HRCT chest, a suspicion of Acute Limb Ischemia was found in a patient with COVID-19 pneumonia. The SARS-CoV-2 real time PCR examination showed positive results. In this patient, the diagnosis of acute advanced limb Ischemia, secondary to Covid-19 Pneumonia was established through a multidisciplinary approach covering the fields of pulmonology, radiology and surgery.

Keywords: Severe acute respiratory syndrome(SARS-CoV-2), Lower limb ischemia, COVID-19, Arterial Thrombosis, Immune thrombosis, Gangrene.

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INTRODUCTION

Severe acute respiratory syndrome (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), is an enveloped RNA β-coronavirus, which has resulted in a growing number of cases and mortality globally. The infection was first considered to cause solely respiratory dysfunction; however, various clinical presentations have shown that COVID-19 is a systemic disease, not restricted to the lungs. Between 20–55% of COVID-19 infected patients develop abnormal coagulation, including changes in prothrombin time(PT), activated partial thromboplastin time(aPTT) and increased D-dimer, which correlates with infection severity and is linked to higher mortality. COVID-19 coagulopathy patients are prone to venous and arterial thromboembolic events as opposed to haemorrhage.

CASE REPORT

A female patient aged 55years, presented to the emergency department with severe pain in both the lower limbs with blackish discoloration of skin below the level of both the knees. She was in a state of shock with the following recordings on clinical examination, Blood pressure-90/60mm of Hg, Pulse rate–150/min, low volume, Temperature–39°c, Respiratory rate-20 cycles/min with 86% peripheral O_2 saturation on room air. Patient is not a known hypertensive or diabetic and had no history of cardiovascular disorders. Her both

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lower limbs showed evidence of gangrene below knees with associated foul smelling. Patient was resuscitated and planned for emergency amputation as the patient's general condition was poor. Her recent past history revealed the symptoms of fever, myalgia and loss of taste(ageusia) about 3 weeks ago and found to have been tested positive for COVID–19 on RT PCR. The patient then opted for home isolation and no further treatment details were available. In consideration with the past history, present worsening condition of the patient and following abnormal laboratory investigations as in, raised D-Dimer value of 890 ng/ml(normal range<500 ng/ml), leukocytosis with leukocyte value of 16,380(normal value:4700–11,300) and raised CRP value of 4.23(< 0.3), emergency below knee guillotine amputation surgery of both lower limbs was resorted to. Patient was then referred to the radiology department for follow up. She initially underwent a Venous and Arterial Doppler USG which showed the following findings.

RIGHT LOWER LIMB: Long segment thrombosis of proximal superficial and deep femoral veins, with superior extension into right common femoral vein.

LEFT LOWER LIMB: Long segment thrombosis of popliteal vein, entire course of superficial and deep femoral veins, common femoral vein, external iliac vein and common iliac vein. Partial thrombus was also noted in proximal great saphenous vein (Figure-1d).

ARTERIAL DOPPLER IN BOTH LOWER LIMBS:

Diffuse extensive long segment atherosclerotic changes with calcifications and complete thrombus in the bilateral popliteal arteries, bilateral anterior and posterior tibial arteries upto the level of stump.

Diffuse subcutaneous and muscle planes edema was also noted more so in left lower limb.The patient then underwent CT pulmonary and peripheral angiogram which confirmed the above findings in addition there is complete occlusion of bilateral popliteal arteries, bilateral anterior and posterior tibial arteries upto the level of stump with few adjacent collaterals from thigh (Figure-3) and is negative for pulmonary artery thrombosis. The patient was started with anticoagulation therapy and follow up USG Doppler was repeated. There is progression of thrombus into inferior venacava(infra renal) (Figure-1a) (Figure-2a,b). The patient was then referred to higher care center as the patient was unresponsive to the ongoing treatment and the patient was unavailable for further follow up.

A B C D

Figure 1: Doppler ultrasonography of both lower limbs a) presence of partial thrombus in infrarenal inferior venacava. b) presence of complete thrombus in right common femoral vein. c) presence of complete thrombus in left common femoral vein. d) presence of partial thrombus in left proximal great saphenous vein.

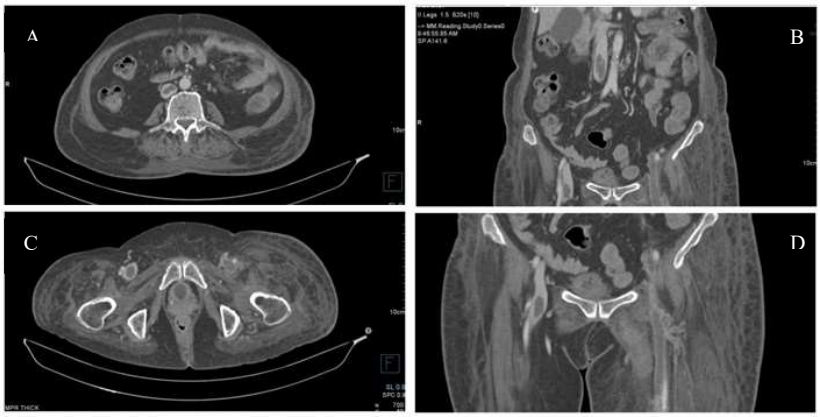

Figure 2: CT peripheral angiogram in both lower limbs(a) and (b) axial and coronal images showing hypodense thrombus at the level of inferior vena cava (infrarenal). (c) axial image showing hypodense thrombus in bilateral common femoral veins. (d) coronal image shows hypodense thrombus in bilateral common femoral veins and left superficial femoral vein.

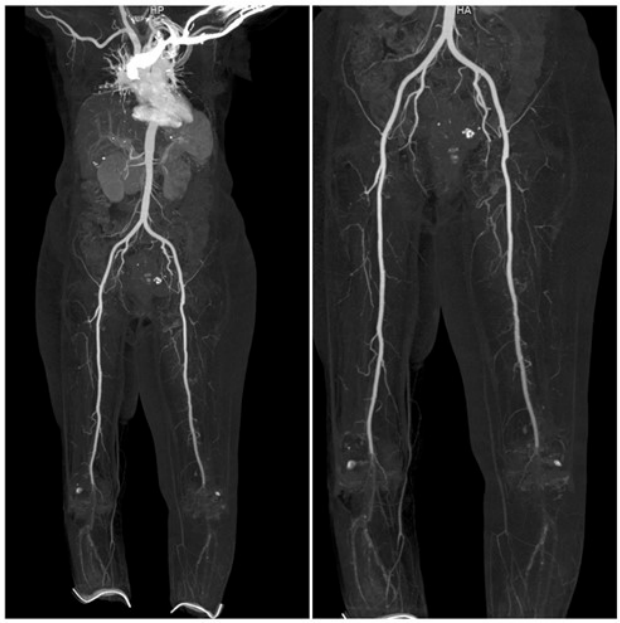

Figure 3: CT peripheral angiogram in both lower limbs showing complete occlusion of bilateral popliteal arteries, bilateral anterior and posterior tibial arteries upto the level of stump with few adjacent collaterals from thigh.

PATHOGENESIS

The pathophysiology behind this hypercoagulable state is multifactorial.

1. COVID-19 directly attacks vascular endothelial cells causing endothelial damage and activating the coagulation cascade which leads to vessel thrombosis in peripheral arteries and the aorta and causes major vascular events such as acute arterial ischemia[1].
2. The association of COVID-19 with increased levels of pro-inflammatory cytokines (IL-2, IL-6, IL-7, G-CSF, TNF, IP-10, MCP1, MIP1-α, etc.) in patients with a severe disease, which leads to cytokine release syndrome (CRS)[2,5].
3. The immobility and hypoxia of critically ill patients[2].

DISCUSSION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2(SARS CoV-2)[6] and has been declared a global pandemic by the World health organization.

1. It is a positive-sense, single-stranded, enveloped RNA virus with a helical capsid[2].
2. Coronavirus disease 2019 (COVID-19) is a multi-systemic infection that mainly affects the respiratory, hematologic, cardiovascular, neurological, immunologic and renal system[6].
3. COVID-19 causes a wide range of clinical symptoms, including bilateral pneumonia, acute respiratory distress syndrome(ARDS), endothelial dysfunction, hypercoagulability and multiorgan failure[5].
4. COVID-19 hematologic and cardiovascular involvement induces thromboembolic symptoms in various organs, most notably venous thromboembolism(VTE); peripheral arterial involvement is uncommon.
5. The majority of SARS-CoV-2 patients diagnosed with limb ischemia had increased inflammatory markers and were mostly elderly. Furthermore, angiotensin-converting enzyme 2, the SARS-CoV-2 receptor, is expressed on the membrane of vascular muscle and endothelial cells[7] and infection of these cells can cause an inflammatory response in the blood vessel walls, predisposing to the development of clot.
6. Acute limb ischemia(ALI) is a vascular emergency known as a dramatic drop in arterial perfusion of a limb that poses a challenge to the limb's viability.
7. The most frequent causes involve embolism from cardiac chambers and is most often combined with atrial fibrillation or acute myocardial infarction, embolism from arterial aneurysms, thrombosis of native limb arteries or artery grafts, iatrogenic thromboembolism after vascular procedures, aortic dissection and traumatic vascular injury.
8. COVID-19 patients present with acute lower extremity ischemia due to arteriosclerosis obliterans and venous thrombosis at the same time have a worse prognosis and a higher mortality rate. The prevalence of ALI correlated with COVID-19 patients that need hospitalisation varies from 3% to 15%.

CONCLUSION

COVID -19 patients with mild symptoms may also suffer from prothrombotic state resulting in acute arterial occlusions and arterial thrombosis should be suspected in these patients despite the absence of predisposing factors. Full dose anticoagulation with low molecular weight heparin is considered as a first line of management. Any delay in the diagnosis/treatment may lead to increase in morbidity, which may conclude with amputation, as in the above presented case.

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