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ORIGINAL ARTICLE

Combined acute arterial and deep vein thrombosis following COVID-19 infection: A case report

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ABSTRACT

Patients with Coronavirus-2019 (COVID-19) commonly develop thrombosis complication. The hypercoagulable state cause arterial and venous thrombosis lead to high morbidity and mortality. The acute limb ischemia is the presentation of arterial thrombosis which occur during COVID-19 pandemic situation. The successful rate of revascularization was trend to lower than expected with high amputation rate and mortality for these patients. We report a case of a 58-year-old woman who developed acute thrombosis of popliteal artery and deep vein thrombosis after treatment of COVID-19 pneumonia. The patient had successful revascularization by endovascular mechanical thrombectomy with intraoperative thrombolysis and well recovered post operation.

Keywords: acute limb ischemia, deep vein thrombosis, thrombosis, COVID-19

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Introduction

Patients with Coronavirus-2019 (COVID-19) commonly develop pulmonary and cardiovascular complications.[1] There has been demonstrated that patients with COVID-19 infection are in hypercoagulable state, causing arterial and venous thrombosis.[1] Acute limb ischemia (ALI) is one of the emergency conditions in vascular disease caused by a sudden decrease in arterial limbs perfusion. The incidence of ALI has significantly increased during COVID-19 pandemic and successful revascularization was lower than expected with high amputation rate and mortality.[2,3] Furthermore, Venous thromboembolism (VTE) is a common complication from COVID-19 inpatients.[1] In this study, we present a case of combine acute limb ischemia and deep vein thrombosis after recovering from COVID-19 pneumonia. The patient provided written inform consent for the report of the details and imaged related to her case.

Case presentation

A 58-year-old woman presented with left lower limb pain for 11 days prior to presentation. The patient felt pain at plantar side of left foot and progress to left calf pain. She had recent history of COVID-19 pneumonia, confirmed on swab test and CT-chest treated with Favipiravir and Dexamethasone for 2 weeks (Figure 1) and discharged 2 weeks ago (COVID-19 RNA was still detectable on discharge swab). Her significant past medical history includes type II diabetes and hyperthyroid. The patients had body mass index 19.38 kg/m^2. On examination, left foot was mild swollen and cold on palpation. The plantar side was tender but without any weakness. The left femoral pulse was present, while popliteal artery, dorsalis pedis artery, and posterior tibial artery were absent on palpation and doppler signal. The respiratory system was unremarkable.

Laboratory tests showed high D-dimer, normal coagulation, and normal hypercoagulable state workup (Table 1). On admission day, The COVID-19 RNA was still detectable. The echocardiogram revealed normal finding.

Acute thrombosis at left popliteal artery (Rutherford's category 2a) was initially diagnosed, and Computed tomography angiogram (CTA) showed intraluminal thrombus involving proximal left popliteal artery to tibioperoneal trunk and incidental finding of circumferential luminal thrombus of left common femoral vein (Figure 2).

Systemic heparinization was initiated and emergency surgical revascularization of left lower limb was performed by endovascular technique. The operation was performed under local anesthesia with conscious sedation.

Initially, Antegrade approach of left common femoral artery was successed using introducer sheath 8Fr by ultrasound guidance. Angiogram demonstrated thrombus occlusion of proximal popliteal artery extended down to tibioperoneal trunk. There was no reconstitution to distal arteries. Hydrophilic guidewire 0.035" (TERUMO GLIDEWIRE®;NJ, USA) was easily passed the thrombus to peroneal artery due to fresh clot. Aspiration thrombectomy device (Penumbra Indigo system; CA, USA) 8 Fr was used for thrombectomy at popliteal artery and then 6Fr catheter for tibial arteries. Angiogram still showed residual thrombus at popliteal artery, subsequently recombinant tissue plasminogen activator (Actilyse Boehringer Ingelheim; Milan Italy) 2.5 mg was infused via catheter for 15 minutes then repeated thrombectomy with 8 Fr catheter for popliteal artery and 6 Fr catheter for tibial arteries, respectively. Completion angiogram showed no residual thrombus and established antegrade flow down to the foot.

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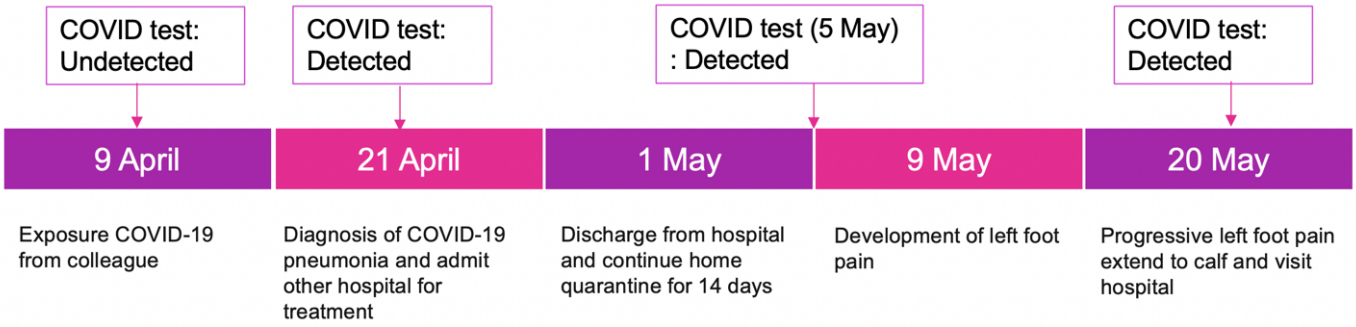

Figure 1: Timeline of this patient since first visit the hospital.

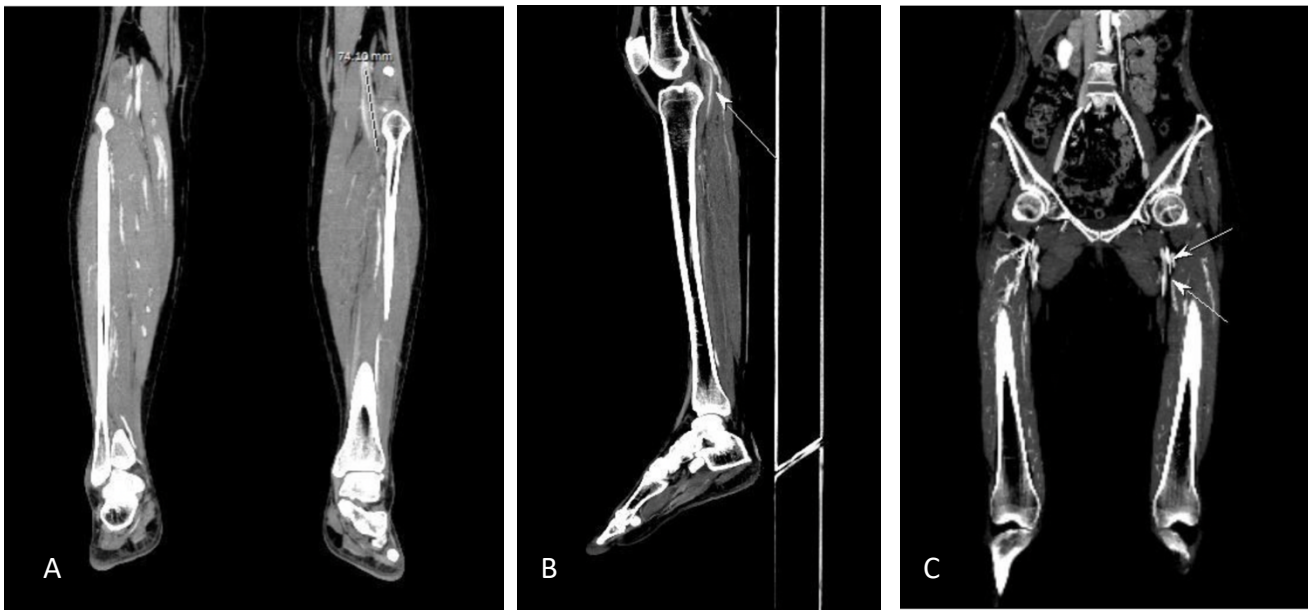

Figure 2: Computed tomography angiogram (CTA) shows thrombosis of left popliteal artery on coronal view (A), sagittal view (B) and thrombus in left common femoral vein (C).

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Table 1: Laboratory results on admission

	Result	Reference value
Complete blood count		
Hemoglobin	11.9	11-14.7 g/dl
Hematocrit	36.5	35.2-46.7 %
MCV	95.5	87.1-102.4 fl
MCH	31.2	26.8-32.4 pg
MCHC	32.6	19.6-32.5 g/dl
White blood cell	5,380	3,170- 8,400 /ul
Platelet count	332,000	167,000-390,000 /ul
Neutrophil	53.9	39.7-71.2 %
Lymphocyte	37.5	21.9-50.3%
Monocyte	5.4	4.2-9.6%
Eosinophil	2.6	0.6-4.9%
Chemistry		
BUN	6	6-20 mg/dl
Creatinine	0.63	0.51-0.95 mg/dl
eGFR	99.2	ml/min
Sodium	144	136-145 mmol/L
Potassium	3.6	3.5-5.1 mmol/L
Chloride	104	98-107 mmol/L
CO_2	30	22-29 mmol/L
Glucose	150	70-110 mg/dl
HbA1C	8.4	4.8-5.9 %

MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; CO_2, carbon dioxide; HbA1C, glycated hemoglobin; g, gram; dl, deciliter; fl, femtoliter; pg, picogram; ul, microliter; mg, milligram; min, minute; mmol, millimole

Table 1: Laboratory results on admission (cont.)

	Result	Reference value
Coagulation test		
Prothrombin time	11.5	9.3-12.3
INR	1.02	
aPTT	22.8	20.9-30.1
aPTT ratio	0.92	
Fibrinogen	385.4	165-400
D-dimer	5,724	<500
CPK	26	<170 U/L
LDH	193	240-480 U/L
Hypercoagulable state workup		
Anticardiolipin IgM	< 2	< 12 U/mL
Anticardiolipin IgG	< 2	< 12 U/mL
Beta 2 Glycoprotein IgG	< 2	< 20 U/mL
Beta 2 Glycoprotein IgM	< 2	< 20 U/mL
Protein C	74.7	70-140 %
Protein S	50.9	54.7-123.7 %
Lupus anticoagulant aPTT	53.90	44.2-75.1 sec
Lupus anticoagulant dRVVT	50.90	29.8-47.3 sec
Antithrombin activity	75.5	83- 128 %

INR, international normalized ratio; aPTT, activated partial thromboplastin time; CPK, reatine phosphokinase; LDH, lactate dehydrogenase; Ig, immunoglobulin; dRVVT, diluted russell viper venom time; U, unit; mL, milliliter; sec, second

After operation, the patient denied any foot pain or calf pain. Physical examination found palpable popliteal pulse, anterior tibial artery and posterior tibial artery. Systemic heparinization was continued postoperatively, with no complication. Patient was discharge after 6 days of hospitalization with Rivaroxaban. Treatment of COVID-19 infection after diagnosis of ALI, we did not restart antiviral or steroid due to suspected inactive disease in opinion of infectious specialist because of finishing COVID-19 treatment for 1 month and COVID-19 RNA test showed high CT value (>35). At postoperative day 2, we repeated COVID-19 RNA test and found undetectable.

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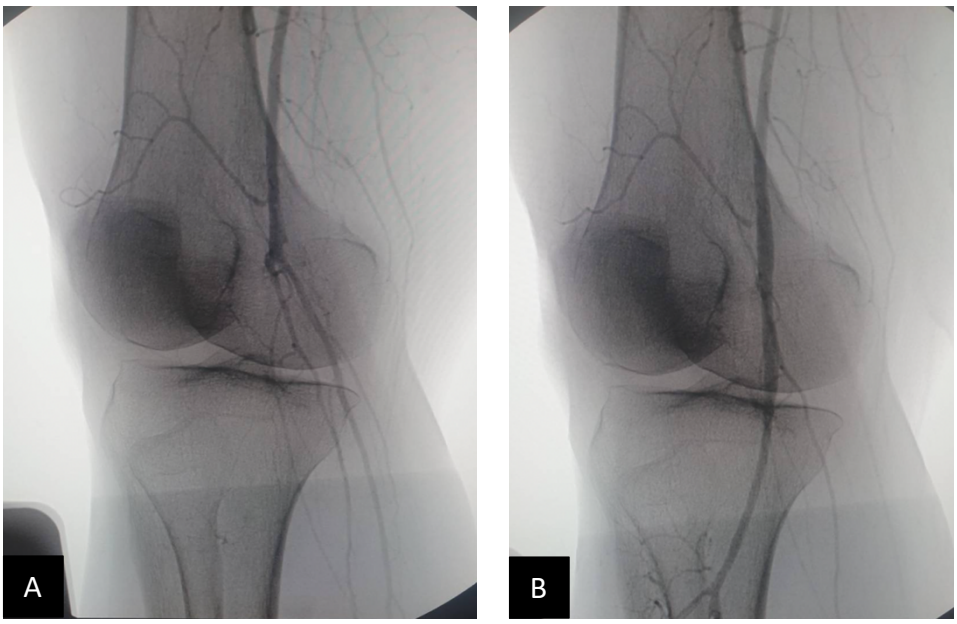

Figure 3: Intraoperative angiogram shows occlusion of proximal popliteal artery before (A) and after revascularization (contrast flows to tibial artery, (B))

Discussion

COVID-19 is a novel disease with a very broad spectrum involving different organ systems that mainly caused by hypercoagulable state. The pathophysiology of COVID-19 induces thrombosis is complex. COVID-19 is a single-stranded RNA virus that acts on vascular endothelium via angiotensin-converting enzyme-2 receptor and induce intense immune response known as the cytokine storm, the cytokine storm precipitate systemic inflammatory response syndrome (SIRS) causing systemic macrothrombosis and microthrombosis[1]. Elevation of D-dimer levels commonly related to thrombotic complication.[4] In this case, the patient had an elevated D-dimer. However, there is no evidence available on how long inflammation and thrombotic derangement would last after recovery from COVID-19 symptoms.

A meta-analysis analyzed on 1,083 COVID-19 patients showed that the prevalence of thrombosis was 22% and increase to 43% after admit to intensive care unit (ICU).[4] Patients with thrombosis were at high risk to death.[5] Klok et al analyzed 184 patients with COVID-19 in ICU,and found that the incidence of thrombosis was 31%: 27% were VTE and 3.7% were ALI.[5]

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Venous thromboembolism is common, especially in patient with severe COVID-19. Several autopsy studies showed significant incidence of deep vein thrombosis (DVT) 58%, pulmonary embolism 19-42% and microthrombi formation in alveolar capillaries 45%.[6,7] Other series reported higher VTE rate of 20-43% with prophylaxis dose of anticoagulant, but the rate is as high as 65-69% in studies that perform routine surveillance with bilateral leg ultrasound.[5,8,9] Multiple guidelines were published for screening, prevention and treatment of VTE in hospitalized patients with COVID-19.

Acute limb ischemia (ALI) is less commonly than venous thrombosis in patients with COVID-19. ALI in COVID-19 can occur in two situations, firstly during the severe COVID-19 infection,[10] Zhan et al reported a median of 19 days (11-23 days) from the appearance of symptoms of infection to presentation of ischemia.[11] Secondly, they can be admitted to emergency room for this vascular condition with mild or no respiratory symptoms.[12-13] There were reports on patients suffered from ALI after complete treatment of COVID-19 with a negative nasopharyhgeal swab. ALI were also found after respiratory symptoms 15-45 days and after negative nasopharyngeal swab for 3-6 day.[14,15] Bozzani et al analyzed on 9 patients who developed ALI related to COVID-19 infection,[16] three patients developed ALI 41 to 149 days after infection. Silingardi et al suggest preoperative workup by thoracoabdominal CT scan in embolic complication because they found two cases of asymptomatic aortic floating thrombus detected incidentally.[17] Furthermore, there are several reports on ALI that occurred while on therapeutic dose of anticoagulant or in patient with heparin resistance.[18,19]

The largest retrospective study on 30 patients with ALI and COVID-19 infection demonstrated that mean age was 60+/- 15 years old,[3] and ALI was more common in males; 76.6%, more than half of patients had severe respiratory symptom. The Rutherford severity staging was predominantly IIA (75.9%) and IIB (17.2%). The anatomical location of thrombosis was 73.3% on lower limbs and 26.6% on upper limbs, with popliteal artery (10.7%) and brachial artery (8.7%) being the most affected. Embolectomy was the main operation approximately 75.9% and high amputation rate 30%, mortality rate was 23.3%.

Other studies showed that the location of ALI was predominantly in lower extremity and more severity of Rutherford's category. [2,20-22] Amputation rate were 6-25% depend on severity of COVID-19 infection. Seventy-seven percent of patients with amputation were moderate to severe infection. Most of the revascularization technique were conventional embolectomy.[2, 20-22]

Pharmacological thrombolysis was applied in few reports,[2,20] other treatment described were angioplasty with or without a stent or bypass.[20] A case report of ALI in COVID-19 infection was successful treated by mechanical thrombectomy with catheter directed thrombolysis.[15]

Mortality rate in ALI patients with COVID-19 infection were between 23-40% and most of patients had age>80 years old and predominantly in men.[20-22] Thromboembolic complication rate and mortality rate correlate with severity of infection.[20]

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This patient presented with gradual onset of limb pain for 11 days before hospital admission. ALI developed at 21 days after the diagnosis of COVID-19 pneumonia. Incidental finding of DVT in the same leg was found on CTA. This patient had combined arterial and venous thrombosis that likely a sequalae from COVID-19 infection. She had successful revascularization by endovascular mechanical thrombectomy with intraoperative thrombolysis and well recovered after operation without postoperative complication. There was no strong recommendation on how long anticoagulant should be continued in patients with ALI. She will continue rivaroxaban for at least 3 months as primary treatment and consider continued anticoagulant after 3 months by D-dimer level and duplex ultrasound. If normal D-dimer level and no residual clot from duplex ultrasound, we will consider discontinuing anticoagulant. Limitation of this study was incompletely workup cause of acute limb ischemia, especially CTA whole aorta. There was the important investigation because of increasing evidence of aortic floating thrombus in patient with ALI in COVID-19 infection.[17] Moreover, we did not completely pulmonary embolism workup by CTA pulmonary artery despite of requirement for DVT workup.

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