Endovascular thrombectomy for critical lower limb ischaemia in a patient with COVID-19

Subhash Kumar,[1] Anup Kumar,[2] Ruchi Sinha ,[3] Mala Mahto[4]

[1]Department of Radiodiagnosis, All India Institute of Medical Sciences Patna, Patna, Bihar, India
[2]Department of Orthopaedics, All India Institute of Medical Sciences Patna, Patna, Bihar, India
[3]Department of Pathology & Lab Medicine, All India Institute of Medical Sciences Patna, Patna, Bihar, India
[4]Department of Biochemistry, All India Institute of Medical Sciences Patna, Patna, Bihar, India

Correspondence to
Dr Ruchi Sinha;
ruchidoctor@gmail.com

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SUMMARY

Hypercoagulable and proinflammatory states induced by the novel coronavirus (SARS-CoV-2) lead to thrombotic and embolic events. In this case report, the authors describe how they successfully managed acute critical limb ischaemia in a patient of COVID-19 illness with severe pulmonary disease and high thrombus burden in the infrapopliteal arteries.

BACKGROUND

SARS-CoV-2 induces the coronavirus disease, COVID-19, first reported in China and later becoming a pandemic. It produces a respiratory and systemic clinical syndrome with varying extent of pneumonia, lung damage, hypercoagulable state and multiorgan failure with death in severe cases.[1 2]

Acute lower limb ischaemia has been reported by various workers and can broadly be categorised into two groups. The first type is the 'COVID-19 toe' wherein distal acral 'chilblain-like' features are seen, and the second type is the large artery thrombosis, with resultant risk of gangrene, amputation and possible fatal outcomes.[3–5] Management of moderate and severe COVID-19 includes use of anticoagulants, including heparin (usually low molecular weight heparin), as per national guidelines.[6] Despite use of such medications, ischaemic events have still been reported.[7]

Surgical embolectomy, the standard of care, may not be feasible in some cases due to the severity of lung disease. Endovascular approaches are less morbid,[8] which may provide a better chance at treatment in such cases of severe lung disease.

CASE PRESENTATION

A 75-year-old man, a surgeon by profession, presented with dry cough, fever and loose stools for 7 days, progressively increasing respiratory distress for the past 3 days. He had no significant antecedent medical or surgical history. He was found to be SARS-CoV-2 positive on a real-time reverse transcription PCR test at admission. He had oxygen saturation (SpO_2) of 87%, heart rate of 102 beats/min and temperature of 101.8°F.

BASELINE INVESTIGATIONS

On admission, he had pre-renal azotaemia, which improved rapidly in the next 48 hours. Blood investigation results are summarised in table 1.

A CT examination of the chest showed extensive ground glass opacification of both lungs with some areas of consolidation, bronchiectasis, and thickened lobular and interlobular septae (figure 1). A two-dimensional echo examination and ECG were normal.

HOSPITAL STAY AND TREATMENT

The patient was started on inj. dexamethasone 6 mg per day, inj. enoxaprin 60 mg two times per day, tab. azithromycin 500 mg per day, tab. paracetamol 500 mg four times per day, 2.5 mg salbutamol nebulisation four times per day, non-invasive ventilation and prone positioning for 18 hours a day. He was given inj. remdesivir 200 mg intravenous on day 1 followed by 100 mg intravenous daily for 4 days. His condition did not improve, although the fever subsided on the third day of admission. As his SpO_2 dropped to 60% intermittently, non-invasive ventilation was performed. Two doses of inj. tocilizumab and convalescent plasma transfusion were also given as per notified institutional guidelines.

On the 14th day of admission, he started complaining of burning sensation of right great toe, and a day later, discolouration of the toes of the right lower limb was noticed with slight oedema (figure 1C). A bedside colour Doppler examination showed no evidence of deep venous thrombosis and normal colour filling of femoral, popliteal and infrapopliteal arteries. The toe discolouration was thought of as 'COVID-19 toes' and was managed conservatively. However, on the 18th day of admission, pain and paraesthesia increased; hence, a CT angiography (CTA) was performed which showed complete occlusion of the posterior tibial artery (PTA) and the peroneal artery (PA) from origin and occlusion of the anterior tibial artery (ATA) from mid leg. The CTA was a dual phase study and the second phase also did not show any collateral or delayed opacification of the occluded arteries (figure 1D and E).

After interdepartmental discussion, endovascular therapy was offered and the patient consented, considering his poor clinical status which precluded long anaesthesia duration required for surgical revascularisation.

The endovascular treatment was done on a Philips Allura Clarity digital subtraction angiography (DSA) machine under local anaesthesia. Ten millilitres of 1% plain lidocaine was used first, and further 10 mL was given after 1.5 hours of the procedure. A long sheath was inserted into the right common femoral artery under ultrasound guidance and thrombectomy was done using Navien (Medtronic; Irvine, California, USA) 6Fr aspiration catheter (figure 1F–K). Multiple passes were made to recanalize the ATA and PTA. Most of the clots were fragmented and of dark colour with few hard,

Table 1 Summary of blood investigations

Laboratory tests	At admission	Day 3	Day 5	Day 14	Day 35
Haemoglobin (130–170 g/L)	100.0	100.0	98.0	95.0	92.0
White blood cell count (4–10 x10^3/µL)	9.2	15.96	20.00	14.64	12.90
Neutrophils (40%–80%)	70.3	86.2	92.1	85	68.2
Lymphocytes (20%–40%)	24.2	12.5	5.0	11.6	24.0
Platelet count (150–450 x 10^9/L)	98	254	222	136	256
Alanine Aminotransferase/Serum glutamic pyruvic transaminase (13–40 U/L)	73.7	70.6	65.2	19.7	27.6
Aspartate Aminotransferase/Serum glutamic oxaloacetic transaminase (<37 U/L)	109.2	84.3	86.9	27.0	22.6
Serum urea (13–43 mg/dL)	49.6	27.5	34.8	26.2	28.3
Serum creatinine (0.7–1.3 mg/dL)	1.41	0.84	0.90	0.53	0.64
Uric acid (3.5–7.2 mg/dL)	8.30	4.13	3.83	3.72	4.26
C reactive protein (mg/L)	60	247.65	79.60	3.12	<2.8
Serum ferritin (22–322 ng/mL)	1574.6	1530.3	1631.9	400	270.7
D-dimer (<0.2 µg/mL)	1.74	12.25	>20	17	2.33
Fibrinogen (100–400 mg/dL)	98	126	538	165	–
Lactate dehydrogenase (230–460 U/L)	–	1353.7	1753.96	1673.33	614.88
Activated partial thromboplastin time (s)	30.12	31.16	32.17	35.16	28.8
Prothrombin time (11-13.5 sec)/international normalised ratio (0.8–1)	10.9/0.94	12.1/1.04	12.17/1.05	13.78/1.18	13.5/1.16

white coloured 'rubbery' plaques also noticed in the retrieved material (figure 1L). The distal segments of the arteries required angioplasty with 3.0 and 2.0 mm sized balloons (BD Ultraverse peripheral balloon, Abbott NC Trek coronary balloon). The PTA was recanalized in its entire length with the distalmost segment still having some clot remnants, and the ATA was recanalized until just above the ankle. The dorsalis pedis artery (DPA), plantar arch and digital arteries did not opacify well even though late and slow filling of the medial and lateral plantar arteries was visible. Angioplasty of the DPA and plantar arch was done with long 2.0 mm sized balloons but the vessels collapsed immediately after balloon removal. Then injection urokinase was infused in the terminal ATA, PTA, DPA, lateral plantar artery and the plantar arch using a Terumo Progreat 2.7F microcatheter. A total of 500 000 units of drug was given as 10 000 unit bolus over 10 min at each of these sites. However, persistent contrast filling of DPA and plantar arch could not be achieved. The digital arteries remained unopacified. The patient had immediate on-table relief of pain and paraesthesia. The long sheath was replaced with a short sheath, stitched in place, attached to a heparinised pressure flush line (2 units of heparin per millilitre of saline) and the patient was transferred to the dedicated COVID-19 intensive care unit for further management. The entire procedure lasted for approximately 3 hours.

Microscopy of the retrieved fragments showed fibrinous material, haemorrhage and mixed inflammatory cells along with focal fibrous tissue (figure 1M). Histopathological features were in favour of an organised thrombus.

Inj. enoxaprin 60 mg two times per day was continued and oral aspirin 325 mg daily, clopidogrel 150 mg daily and atorvastatin 40 mg daily were added to the treatment. A colour Doppler was done daily and showed normal values in the ATA and PTA with no flow in DPA and monophasic flow in metatarsal and digital arteries. From the third postoperative day, DPA and metatarsals also had biphasic flow.

OUTCOME AND FOLLOW-UP

Patient's pain and paraesthesia improved; however, the discolouration progressively extended to involve the midfoot and forefoot (figure 1N). Medical management was continued, with progressive improvement in general health, and he was discharged on day 40 of admission with SpO_2 94% on room air. A chest CT done at 6 weeks and later at 6 months showed significant improvement, and the patient was able to walk and perform all daily activities independently (figure 1O and P). A two-stage Lisfranc amputation of the right foot was done at 2 months to treat the gangrene of the foot.

He continues to improve and has normal daily activities as of now with healed and healthy flaps (figure 1Q).

DISCUSSION

Ischaemic events are seen in a large proportion of COVID-19 cases, affecting most body organs and systems, with reports of deep venous thrombosis, pulmonary thrombosis and embolism, stroke, cardiac events, limb ischaemia and mesenteric ischaemia.[7 9–13]

Acute lower limb ischaemia (ALLI) has been reported in up to 0.54% of COVID-19 cases,[7] and in some reports, COVID-19 cases have constituted up to 16.3% of all ALLI cases.[14] Medical comorbidities, including hypertension, diabetes, cardiovascular and respiratory diseases, renal diseases and obesity have been

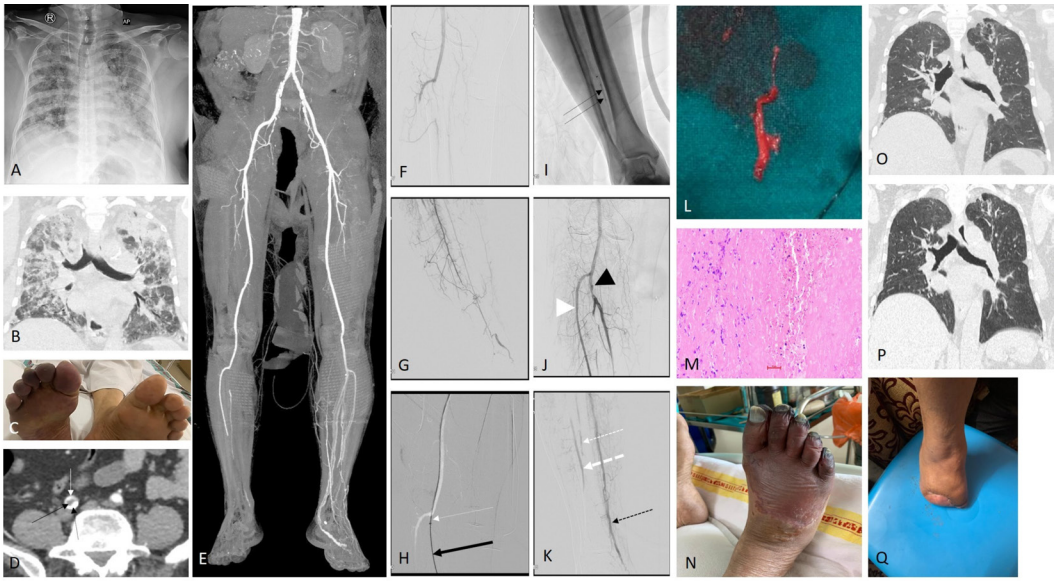

Figure 1 (A) Initial frontal chest radiograph after admission showing extensive opacification of both lungs, a central line is inserted in the right internal jugular vein. (B) High-resolution CT (HRCT) scan of chest, coronal reformatted view, at admission, showing extensive ground glass opacification of nearly entire lung volume on either sides with some areas of consolidation, ectasia of airways and thickening of the interlobular and intralobular septae. (C) Clinical photograph at initial reporting, showing discolouration of the toes of right foot. (D) Axial image of CT angiography (CTA) showing calcified plaque in the right common iliac artery (dashed black arrow) with hypodense thrombus in the lumen (solid black arrow), minimal lumen opacification is seen anteriorly (solid white arrow). (E) CTA of the lower limbs, maximum intensity projection image showing non-visualisation of the posterior tibial and distal half of the anterior tibial artery and partial opacification of the peroneal artery, possibly via collaterals. (F) Digital subtraction angiography (DSA) image showing occlusion of the tibioperoneal trunk (TPT) from origin, ATA occlusion has progressed further higher up, some filling of peroneal artery via collaterals. (G) DSA image at leg level showing the filling of the mid part of the peroneal artery with occlusion distally, a long thin collateral is coming down and opacifying a small length of the posterior tibial artery around the ankle level. (H) Aspiration catheter lodged in the TPT (dashed white arrow), with a guidewire passed through it; (solid black arrow) multiple passes of the catheter was done in all the three vessels. (I) Angioplasty balloon in the distal ATA (dashed black arrows); angioplasty of all the three arteries was done at various levels. (J) Final DSA image at knee showing opening of the TPT (black arrowhead) and the ATA (white arrowhead). (K) DSA image at leg level showing patent PTA in entire length (dashed black arrow), peroneal (thick dashed white arrow) and ATA (thin dashed white arrow) are seen upto distal leg. (L) A sample of the retrieved material, appearing bright white. (M) Histopathology section showing thrombus composed of fibrinous material, haemorrhage and inflammatory cells (H&E stain, ×400 magnification). (N) Progressively increasing discolouration and gangrene to involve midfoot. (O) Coronal reformatted view of HRCT chest scan at 6 weeks of onset, showing significant resolution of the extensive ground glass opacification and consolidation, with some areas of hyperlucency; a diffuse background 'haze' persists. (P) Coronal reformatted view of HRCT chest scan at 6 months of onset, showing near normal lung with some areas of opacities, possibly representing fibrosis, in the left upper zone. (Q) Current status of foot, post amputation and with completely healed suture line.

implicated to induce a higher rate of events. However, ischaemic events in previously healthy patients, similar to our case, have also been reported.[10] The COVID-19-associated ALLI cases have typically been managed surgically using arterial cutdown and thrombectomy/embolectomy.[14]

The onset was insidious in the present case and initially thought to be 'COVID-19 toes', which presumably occurs due to the involvement of the smaller vessels, is managed medically and resolves spontaneously.[4 15] In our case, there was a diseased atherosclerotic ipsilateral iliac artery segment, and we hypothesised that the clinical features were at least in part due to a distal embolism after plaque rupture from this site. The recovery of the rubbery white fragments supports this hypothesis. Subsequently, the thrombotic occlusion progressed due to possible hypercoagulable state associated with COVID-19. However, COVID-19-related ALLI can also be seen in patients without pre-existing atherosclerosis.[16] The smaller vessels could not be opacified well in spite of smooth passage of wire, balloon, microcatheter and thrombolysis, and presented a strange phenomenon wherein they kept collapsing. This, we hypothesise, was due to poor demand from the already devascularised distal foot. It also has been referred to as 'desert foot'.[14] For this reason, the discolouration not only persisted but also progressed into a dry form of gangrene with eventual amputation of the dead parts of the midfoot and entire forefoot. It is noteworthy that the follow-up colour Doppler examinations had shown good flow in the foot arteries, indicating subsequent spontaneous total recanalisation possibly aided by the antiplatelets and enoxaparin.

The extensive pneumonia resulting in poor respiratory condition had precluded surgery in this case to an extent, and the patient had opted for endovascular option after discussion with the treating team.

It is noteworthy that COVID-19-associated arterial thrombosis has higher clot burden, amputation and death,[17] and is technically challenging to achieve full recanalisation.[14] In fact, in some series of surgical thrombectomy, residual and recurrent thrombus formation has been reported.[14] Further, there is apparent heparin resistance in patients with COVID-19-associated thromboembolism.[18]

Considering these factors, endovascular therapy appears a suitable alternative for limb revascularisation. Endovascular techniques have provided very high success rates (up to 95.5%) and equal amputation rates (9.1%) as compared with surgical techniques.[19] This, especially if the disease is old, as in our case

where 8 days had elapsed and the chance of the thrombus to organise had increased significantly. Further, it cannot be over-emphasised that in the setting of atherosclerotic disease, such as in our patient, arterial thrombosis very frequently requires angioplasty for adequate vessel recanalisation. This requirement, in fact, necessitates endovascular therapy as opposed to surgical thrombectomy.

Our case had ipsilateral iliac artery stenosis, and the patient has been explained to follow up with CTA and the requirement of angioplasty with stenting in case of persistent stenosis.

Patient's perspective

Following a difficult ICU course with COVID-19, I started experiencing a burning sensation around the great toe of the right foot. CT angiography for the lower limb revealed a thrombus in the lower limb arteries. Me being a General Surgeon and Orthopaedician, could see the implications of this occlusion.

The vascular intervention lasted for about three hours, and I was much relieved of the pain on the table itself.

Two months later, amputation was done through the right mid-foot and now I can walk on my native hind foot. I am thankful to the whole team of doctors, nurses, physiotherapist, and healthcare workers for taking a good care of me.

Learning points

- Endovascular minimally invasive interventional therapy (mechanical thrombectomy) for COVID-19-associated critical acute lower limb ischaemia is a feasible and safe option with good clinical outcome in select patients.
- Poor respiratory parameters and coagulation profile should not be considered as deterrents for endovascular revascularisation.
- Endovascular thrombectomy may be considered in arterial occlusions with high thrombus load and atherosclerotic arterial tree.

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ORCID iD

Ruchi Sinha http://orcid.org/0000-0003-0618-6320

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