

# Acute Extremity Gangrene in COVID-19 Patients

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As elective plastic surgery takes the backseat during the COVID-19 pandemic, we have noticed a pattern in the slew of referrals from the “COVID” ward of the hospital. Among the 2284 COVID-19 positive cases treated, we were asked to manage four cases of acute dry gangrene of extremities. A summary of all the patients is presented in ▶Table 1.

Some authors have provided early evidence of complement-mediated microvascular injury and coagulopathy in severe COVID-19 disease.<sup>1</sup> Wang reported two critically ill patients with COVID-19-related retiform purpura, progressing to digital gangrene, who demonstrated microthrombi in the blood vessels on biopsy, elevated D-dimer levels, antithrombin III deficiency, and positive anticardiolipin IgG/IgM antibodies.<sup>2</sup> A larger study from Italy concluded that the incidence of acute limb ischemia increased during

the pandemic, and revascularization was lower than usual due to the procoagulant state.<sup>3</sup>

The common etiological factor proposed is a state of hypercoagulability, which is induced by micro- and macroangiopathy, caused by either a direct complement-mediated effect of the virus or an antibody-mediated immunological response. The delayed immunological response seems to be a logical reason for 3 of 4 patients in our series, since patients 1, 2, and 4 developed gangrene only late in the course of the disease. However, in patient 3, acute gangrene was the presenting symptom in the absence of any other typical symptoms of COVID-19 infection which, might be due to direct effect of the virus on the vasculature.

Differential diagnosis for acute ischaemia in critically ill patients include vasopressor-induced extremity gangrene, myocardial infarction (MI) with thrombi in left ventricle, hypothermia, atherosclerotic thrombi, shock, disseminated intravascular coagulation (DIC), and thrombolytic therapy. In most cases, the causation is multifactorial.

Middelorp reported COVID-19 patients who received routine prophylactic doses of low-molecular weight heparin (LMWH) had significantly higher venous thromboembolism



**Fig. 1** Preoperative (a) and postoperative (b) pictures of patient 1.



**Fig. 2** Preoperative (a) and postoperative (b) pictures of patient 3.

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**Table 1** Summary of all patients in the case series

	Patient 1	Patient 2	Patient 3	Patient 4
<b>Age</b>	56	58	80	60
<b>Sex</b>	Male	Female	Male	Male
<b>Pattern of gangrene</b>	Left thumb up to IP joint	Left 4th toe up to IP joint	Left 1st and 4th toe up to MTP joint. Left 5th toe up to IP joint	Left foot great toe and all toes of right foot—up to IP joint
<b>Onset of gangrene (week of admission)</b>	6th week	3rd week	At presentation	3rd week
<b>Management of gangrene</b>	Revision amputation of left thumb at the head of proximal phalanx under local anesthesia (►Fig. 2)	Conservative	Forefoot amputation under spinal anesthesia (►Fig. 1)	Conservative
<b>Comorbidities</b>	Diabetes	Bronchial asthma	Diabetes, concentric left ventricular hypertrophy	Hypertension, bronchial asthma
<b>Doppler</b>	Not done	Arterial: bilateral CFA, SFA, PA, ATA, PTA, and DPA are patent and show normal flow and spectral waveforms Venous: bilateral DVT (dilated, noncompressible CFV, SFV with echogenic contents within suggestive of DVT, dilated PV with no flow within.	Not done	Arterial: right—triphasic flow in CFA and SFA. biphasic flow in PA, ATA, PTA. monophasic flow in DPA. Atherosclerotic changes in PA and below Left—triphasic flow CFA and SFA. Biphasic flow in PA. Monophasic flow in ATA, PTA and DPA Venous: normal
<b>Angioplasty</b>	Not done	Not done	Left SFA complete occlusion at origin and multilevel stenosis 40–50%	Not done
<b>d-dimer</b>	Not tested in current admission	Elevated	Not tested	Elevated
<b>Vasopressor support</b>	No	Yes	No	Yes
<b>Duration of hospital stay (cumulative)</b>	47 days	39 days	2 days	20 days
<b>Duration of ICU stay</b>	21 days	15 days	–	16 days
<b>Severity of COVID-19<sup>a</sup></b>	Severe (ARDS)	Severe (septic shock)	Mild	Severe (septic shock)
<b>COVID-19-related complications</b>	Pneumonia, critical care-induced neuromyopathy, grade III sacral pressure sore	Pneumonia, bilateral lower limb DVT, HIT, type 1 respiratory failure, hyperhomocysteinemia	–	Pneumonia
<b>Outcome</b>	Recovery	Recovery	Recovery	Death

Abbreviations: ARDS, acute respiratory distress syndrome; ATA, anterior tibial artery; CFA/CFV, common femoral artery/vein; DPA, dorsalis pedis artery; DVT, deep vein thrombosis; HIT, heparin-induced thrombocytopenia; IP, interphalangeal; MTP, metatarsophalangeal; PA/PV, popliteal artery/vein; PTA, posterior tibial artery; SFA/SFV, superficial femoral artery/vein.

<sup>a</sup> Based on Government of India guidelines—<https://www.mohfw.gov.in/pdf/ClinicalManagementProtocolforCOVID19.pdf>.

rate when compared with non-COVID acutely ill patients.<sup>4</sup> This suggests that prophylactic dose of LMWH may not be enough, and initiation of an appropriate dose of anticoagulant might be necessary.<sup>5</sup> Initiation of therapeutic dose of LMWH in admitted COVID-19 patients (with moderate-to-severe pneumonia or d-dimer greater than 500 ng/mL) is our current practice. We have neither seen any adverse effect of this protocol, like bleeding in our patients, nor has this been reported in literature. Those with limb ischemia and no contraindication for heparin use were treated with unfractionated heparin (UFH). We now await what difference this protocol makes in subsequent waves of the pandemic.

#### **Conflict of Interest**

None.

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