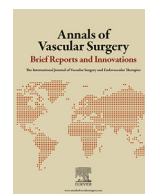




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Venous gangrene associated with COVID-19: Successful limb preservation strategies with optimal wound management [☆]



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ABSTRACT

During the COVID-19 pandemic, high rates of arterial and venous thromboembolic (VTE) events were noted in association with increased rates of major amputation. VTE appears to be a significant source of morbidity and mortality for this patient population and numerous methods have been described to achieve limb salvage. Nevertheless, best management remains unclear. We describe the case of a 60-year-old male with severe venous gangrene secondary to a non-occlusive mid-femoral and occlusive infrapopliteal deep venous thromboses associated with COVID-19 infection who ultimately underwent meticulous local wound care and transmetatarsal amputation, which allowed for maximal preservation of foot function and limb salvage.

Introduction

Venous thromboembolism (VTE) events such as deep venous thrombosis (DVT) and pulmonary embolism (PE) are well-documented occurrences associated with severe acute respiratory syndrome coronavirus-2 infection, otherwise known as COVID-19.^{1–6} Current evidence suggests that these events are associated with hypercoagulable and inflammatory states induced by viral infection and endothelial dysfunction.^{2,3} Current recommendations recommend VTE prophylaxis for inpatients with confirmed COVID-19 infection with severe infection, comorbidities, and immobilization.^{3,7} Close monitoring of this patient population for DVT/ PE should prompt immediate intervention and transition to therapeutic anticoagulation.⁷

Furthermore, pedal gangrene associated with VTE in the context of COVID-19 infection has been reported in some case reports.^{8–12} Currently, methods such as anticoagulation alone, mechanical thrombectomy, catheter-directed thrombolysis, prone positioning with venovenous extracorporeal membrane oxygenation, and amputation have been trialed with varying levels of success.^{8–12} In other similar reports, COVID-positive patients with concomitant VTE and arterial thromboembolism (ATE) ultimately required more proximal amputation in the acute setting.^{9,13,14} Here we present the case of a 60-year-old male who presented with significant venous gangrene of the left lower extremity secondary to COVID-19 infection. To the best of our knowledge, we report the first case in which the primary method of limb salvage was via a

combination of anticoagulation, meticulous local wound care allowing for ischemic demarcation, and transmetatarsal amputation (TMA).

Case report

The patient is a 60-year-old male with a past medical history of hypertension who presented to the emergency department at an outside hospital after being found down at home for approximately one to two weeks secondary to a fall (according to a family member). At the time his chief complaint was of left lower extremity rest pain. On physical exam, the patient was edematous to the mid-thigh on the left, compartments were soft, and there was intact foot dorsiflexion and plantar flexion with preserved sensorium in the left first web space. The foot appeared cyanotic and ischemic, particularly in toes one through five with purple discoloration in the forefoot through just above the ankle (Fig. 1).

As part of the initial workup, the patient underwent arterial duplex ultrasonography (US) which revealed no arterial stenosis or occlusion with accompanying triphasic waveforms in the bilateral lower extremities. Ankle-brachial indices and additional lower extremity imaging were not performed due to the normal arterial duplex findings. Lower extremity examination on the right was within normal limits. Lower extremity venous duplex US revealed a non-occlusive left mid-femoral DVT as well as occlusive thromboses of the left anterior tibial, peroneal, and posterior tibial veins (Fig. 2).

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Fig. 1. Appearance of the patient's left foot and lower extremity upon initial vascular surgery consultation. Cyanotic and ischemia is observed with purple discoloration in the forefoot through just above the ankle.



Fig. 2. Left-lower extremity duplex ultrasonography was performed on initial presentation which demonstrated a non-occlusive mid-femoral DVT.

Additionally, the patient was in respiratory failure, requiring high flow oxygen but ultimately avoided intubation. In the emergency department he received computed-tomography (CT) scan of the thorax that revealed extensive patchy bilateral airspace disease and multiple small, subsegmental PE and was found to be COVID-19 positive (Fig. 3). Secondary causes of DVT were not investigated in this patient. Initial clinical exam, history and laboratory findings were unsuggestive of occult malignancy or hematologic/ thrombophilic conditions. Admitting diagnoses were left lower extremity DVT, acute kidney injury (AKI), rhabdomyolysis, and bilateral subsegmental PEs with acute-on-chronic hypoxic respiratory failure secondary to COVID-19 pneumonia. In hospital, the patient required Remdesivir and Decadron treatment for respiratory failure.

Vascular surgery at our institution was consulted and given the acuity of his respiratory status, no acute vascular intervention was performed. Anticoagulation was initially managed with intravenous unfractionated heparin (IVH) drip transitioned to direct oral anticoagulation (DOAC) treatment with Eliquis. IVH was selected due to the presenting diagnosis of acute kidney injury secondary to rhabdomyolysis. On

admission, creatinine was 1.47 and the kidney injury resolved during the hospital stay prior to discharge. Given the resolution of the kidney injury before starting DOAC treatment and the lack of any preceding chronic renal disease, renal dosing adjustments to the Eliquis regimen were not indicated and he was started on 5 mg twice per day.

In lieu of surgical intervention, local wound care management and observation allowed demarcation to define level of ischemia while he completed anti-coagulation treatment. The patient's forefoot and left lower extremity gangrene initially was widespread however by mid-admission had demarcated to the transmetatarsal level of the left foot (Fig. 4a). In-hospital, local wound care was performed using Xeroflow, gauze and kerlix wrapping. Prior to discharge (on hospital day 25) the majority of venous gangrene demarcated at the level of the patient's toes (one through five), including both the dorsum and plantar aspects of the foot (Fig. 4b).

Following the duration of anticoagulation, the patient has been followed regularly in the outpatient clinic and with venous duplex US at three months. Findings of the repeat duplex US revealed a stable, non-occlusive, and chronic mid-femoral DVT, while the infra-popliteal DVTs

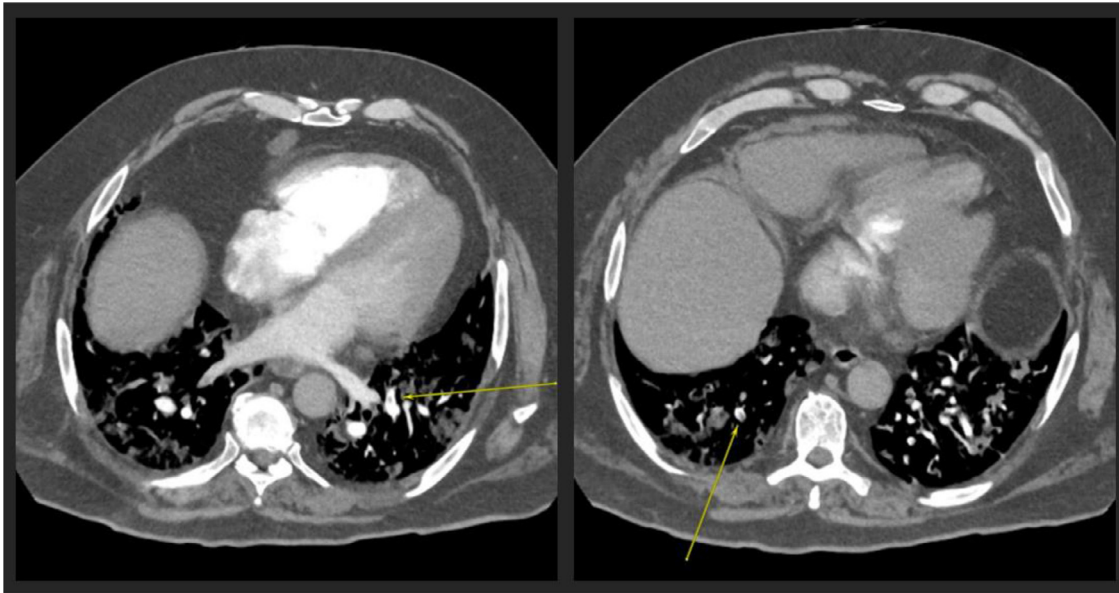


Fig. 3. CTA Thorax demonstrating extensive patchy bilateral airspace disease consistent with COVID-19 pneumonia as well as multiple small, subsegmental PEs (yellow arrows).



Fig. 4. Appearance of the patient's lower extremity wound at various stages of care reveals demarcation of ischemia and ultimate appearance after TMA. (a) Mid-admission the wound demarcated to the transmetatarsal level. (b) By hospital day 25 with careful wound care, there was vast improvement with disease primarily involving toes one through five. (c) Appearance at three months follow-up after transition to wound care with Aquacel Ag reveals the wound included the plantar aspect of the foot. (d) Immediate and one month (e) post-operative outcomes following TMA with excellent wound healing.

remained chronically stable and occlusive. Local wound care was continued and transitioned to Aquacel Ag. The wound ultimately demarcated to the majority of toe one, and the distal aspects of toes two through five with involvement of the plantar aspect of the foot (Fig. 4c). Pre-operatively, there was no clinical evidence of arterial disease. Given the extensive ischemic damage to the toes, a toe-brachial index (TBI) was not attainable, however repeated doppler examination demonstrated biphasic blood flow suggestive of good arterial supply. Thus, the patient was presumed to have sufficient arterial supply to heal the wound after surgical intervention. Due to the ischemia observed in the plantar

flap, we elected for left TMA with primary closure (Fig. 4d). On follow-up in clinic, the patient's TMA site has remained well-healed, and he is ambulating using his left foot without any difficulty (Fig. 4e).

Discussion

Since the start of the pandemic, there have been numerous case reports and clinical studies documenting the impact of COVID-19 infection on the cardiovascular system such as ATE and VTE, limb ischemia, myocarditis, and stroke/ transient ischemic attack. Moreover, a study by

Schuijvens et al. reports on the observed increased incidence of amputations both related to COVID-19 infection and other primary vascular disease, such as peripheral arterial disease.¹⁵

Recent literature suggests that COVID-19-associated vascular pathology is largely due to a hypercoagulable-induced state along with systemic inflammation.^{2,3,6} Namely, it has been proposed that this is due to processes involving inflammatory cytokines and endothelial cell dysfunction/ viral infection of the endothelium ultimately leading to inflammatory thrombosis and coagulopathy.^{2,3,6} A systematic review and meta-analysis by Knutsor and Laukkanen concluded that hospitalized patients with COVID-19 (especially for “severe” disease) have a high incidence of thromboembolic events and complications.⁶ Moreover, the authors suggest that VTE occurs at a higher incidence than arterial thromboembolism.⁶

In accordance with published guidelines published, the patient was treated for VTE with anticoagulation according to the following: For acutely ill patients hospitalized with COVID-19 and associated proximal DVT or PE, initial treatment is parenteral anticoagulation with low-molecular weight heparin (LMWH) or IVH.^{7,16,17} When transitioned to outpatient care, these guidelines recommend using DOACs for such patients.^{7,16,17} Furthermore, pedal gangrene secondary to COVID-19 infection has been described in numerous case reports and appears to be related to VTE. Management with VTE prophylaxis versus therapeutic anticoagulation, local wound care, and consideration of amputation based on severity of illness and functional status are all methods that have been utilized.⁸⁻¹²

The abovementioned literature allows us to observe a few trends. First and foremost, VTE associated with COVID-19 is an uncharted territory with currently evolving literature. Second, standard management techniques are not sufficient. For instance, at our institution we noted that during the peak of the pandemic, COVID-positive patients presented with arterial lower extremity events and VTE at not only higher rates than expected, but also were often resistant to standard measures. These measures have included not only anti-coagulation, but also mechanical thrombectomy and catheter-directed thrombolysis.

Finally, it is critical to discuss the methodology in caring for this patient’s ischemic wound. In this case, our method of medical management and anticoagulation first combined with meticulous wound care and a “watch and wait” approach allowed for limb salvage and a good functional outcome. This abides by the principle that foot length preservation preserves foot function.¹⁸⁻²⁰ In a similar case report by Chun et al., we learn of a patient who presented with phlegmasia cerulea dolens despite being on chronic warfarin therapy who ultimately underwent mechanical thrombectomy and below-knee amputation (BKA).⁹ It should be noted that the authors nicely point out that their strategy of mechanical thrombectomy first followed by BKA allowed for preservation of limb length in this patient who may have otherwise required an above-knee amputation (AKA).⁹ Additionally, other reports have documented cases in which both ATE and VTE have occurred simultaneously, necessitating more proximal amputation.^{13,14} Future studies may consider investigating the severity of lower extremity ischemia and level of amputation with ATE versus VTE or both in combination.

In our case we see that observation and meticulous local wound care allowed for ischemic demarcation to the transmetatarsal level, primarily involving the digits necessitating TMA only. Thus, our unique approach to wound care and limb salvage for lower extremity venous gangrene secondary to COVID-19 VTE allowed for the avoidance of more proximal lower extremity amputation (e.g., BKA/ AKA). Our patient has experienced excellent wound healing with return to ambulation and daily activities of living.

Conclusion

This case adds to the literature involving proper management of VTE and venous gangrene in COVID-19 patients. Our unique approach, utilizing a combination of adherence to anticoagulation guidelines, metic-

ulous wound care, and limb salvage techniques allowed for preserved ambulatory function in a patient who may otherwise have undergone more proximal amputation in the acute setting.

Consent

The patient provided verbal consent to the publication of the case details and clinical images.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.av surg.2022.100095.

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