Pedal gangrene in a patient with COVID-19 treated with prone positioning and extracorporeal membrane oxygenation

Amanda Siegel, DPM,[a] Ammar Al Rubaiay, DPM,[a] Andrew Adelsheimer, MD, MBA,[b] John Haight, DPM,[a] Scott Gawlik, DPM,[a] *and* Alisha Oropallo, MD,[b,c] *Lake Success and Hempstead, NY*

ABSTRACT

Many patients hospitalized with coronavirus disease 2019 are treated with venovenous extracorporeal membrane oxygenation and prone positioning to optimize oxygenation. However, this combination can result in lower extremity tissue necrosis, especially without adequate offloading. We report the case of a 31-year-old man who required mechanical ventilation and venovenous extracorporeal membrane oxygenation secondary to complications from coronavirus disease 2019, and subsequently developed pedal dry gangrene. The patient was discharged and healed without requiring an amputation. Our institution has since revised the prone positioning protocol to address offloading the lower extremities and feet. (J Vasc Surg Cases and Innovative Techniques 2021;7:357-60.)

Keywords: COVID-19; ECMO; Hypercoagulable; Necrosis; Offload; Prone position

Although most patients with coronavirus disease 2019 (COVID-19) experience mild symptoms, some progress to develop severe acute respiratory distress syndrome, requiring mechanical ventilation and prolonged stays in the intensive care unit.[1] Those with hypoxemia refractory to mechanical ventilation and prone positioning might be considered for venovenous extracorporeal membrane oxygenation (VV-ECMO), which provides temporary pulmonary support via gas exchange.[2,3] The combination of prone positioning, VV-ECMO, and vasopressors can result in lower extremity tissue necrosis, especially without adequate offloading. In this report, we present the case of a 31-year-old man who required mechanical ventilation and VV-ECMO secondary to complications from COVID-19, and subsequently developed pedal dry gangrene. The patient provided verbal consent to the publication of the case details and clinical images.

CASE REPORT

A 31-year-old man presented to the emergency department with a 5-day history of fevers and a 2-day history of dry cough. Past medical history included hypertension and obesity. On presentation, he was found to be febrile, hypoxic, and tachycardic. Physical examination revealed bilateral pulmonary crackles and a computed tomography scan of the chest showed peripheral bilateral diffuse ground glass opacities. He was admitted to the general medicine floor and started on empiric ceftriaxone and azithromycin. A nasal swab was positive for COVID-19, and therapy with chloroquine, thiamine, vitamin C, and anakinra was started. He continued to have persistent fevers (maximum temperature 104.5°F), and developed acute hypoxemia, for which he was intubated and transferred to the intensive care unit. The patient was hypotensive, requiring vasopressor support. For deep venous thrombosis prophylaxis, he was placed on continuous heparin infusion, with goal activated partial thromboplastin time of 50 to 70 seconds, as per hospital COVID-19 treatment guidelines.

Despite high ventilator settings, medical therapy, and prone positioning for an average of 15-hour intervals over 6 days, he remained with severe acute respiratory distress syndrome and respiratory acidosis, so he was placed on extracorporeal carbon dioxide removal. He was subsequently transitioned to VV-ECMO for refractory hypoxemia and was started on methylprednisone. The ECMO cannulas were placed in the right internal jugular vein and the right femoral vein. Once ECMO was initiated, anticoagulation therapy was transitioned to argatroban continuous infusion, as per hospital protocol. Dosing was therapeutic with a goal activated partial thromboplastin time of 50 to 90 seconds. The patient's intensive care unit course was complicated by new-onset atrial fibrillation, with emergent successful cardioversion. He was treated with amiodarone. ECMO was successfully decannulated on day 24, and the patient was extubated on day 34.

From the Department of Podiatry,[a] and Department of Surgery,[b] Comprehensive Wound Care Healing and Hyperbarics, Northwell Health, Lake Success; and the Department of Vascular Surgery, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead.[c]

Author conflict of interest: none.

Correspondence: Alisha Oropallo, MD, Northwell Health's Comprehensive Wound Healing & Hyperbaric Center, 1999 Marcus Ave, Ste M6, Lake Success, NY 11042 (e-mail: aoropallo@northwell.edu).

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2468-4287

https://doi.org/10.1016/j.jvscit.2021.02.013

Fig 1. Partial thickness gangrene in bilateral feet on hospital day 35. All necrotic areas were dry and stable in appearance with no associated fluctuance or crepitus, no malodor, no surrounding edema or erythema, and no signs of infection.

Podiatry was consulted on day 35 for concern of new-onset pedal gangrene. Vascular examination revealed palpable femoral, popliteal, dorsalis, pedis and posterior tibial artery pulses bilaterally. Epicritic sensation was intact to the toes bilaterally. There was partial thickness dry gangrene on the plantar aspect of the right hallux, plantar distal aspect of the right second digit, plantar distal aspect of the left fifth digit, and the plantar aspect of metatarsal heads 3 to 5 of the left foot. The left plantar forefoot skin was slightly dusky and mottled in appearance (Fig 1). No signs of infection were present. It was noted that the patient's feet were firmly pressed against the footboard of the hospital bed and not properly offloaded. Z-flow boots for offloading of the feet were placed on at this time, and local wound care with betadine paint every other day was started. The plan was to await demarcation of the gangrene to determine if the skin would become viable or ultimately require an amputation.

Throughout the hospital course, increased necrosis was noted to the left plantar forefoot (Fig 2). Based on the stable nature and partial-thickness depth of the gangrene, the prognosis for healing and prevention of limb and toe loss was favorable. The patient was discharged to acute rehabilitation after a 55-day duration of stay. The plan was to continue wearing offloading boots, wound care with betadine paint every other day, and regular follow-up with podiatry to monitor demarcation. Unfortunately, the patient was lost to follow-up. The patient was called for follow-up, and family revealed that he had moved to the Dominican Republic and that his foot wounds healed without requiring amputation.

DISCUSSION

The cause of pedal gangrene in this patient was likely multifactorial, including the use of ECMO and vasopressors, prone positioning without proper offloading, and the hypercoagulable nature of COVID-19. Here, we delve further into the role of prone positioning and ECMO in the development of pedal tissue necrosis and discuss the other contributing factors.

Prone positioning can optimize oxygenation in patients with worsening hypoxemia.[4] However, necrosis can develop at pressure points without proper offloading. Intubated patients typically remain prone for 12 to 16 hours per day, increasing the probability of developing pressure wounds.[4] Risk factors for the development of prone-related pressure injuries include high body mass index, male sex, and age greater than 60 years, two of which pertain to this patient.[5,6] Although the dorsal feet and toes are main pressure points in the prone position, no studies have detailed lower extremity wounds secondary to prolonged prone positioning.

Patients who remain hypoxic despite prone positioning may require ECMO support. The use of ECMO throughout the pandemic has steadily increased with promising results.[7,8] However, patient selection is stringent and is reserved for those younger than 65 years, with a body mass index of less than 40, who are not immunocompromised,

Fig 2. Partial thickness gangrene in bilateral feet on hospital day 45. Increased necrosis of the left plantar forefoot gangrene, which was dry and stable in appearance.

and who have been on mechanical ventilation for fewer than 10 days.[7,9] Therefore, this patient was an ideal candidate. Limb ischemia can result from ECMO owing to vessel damage during cannulation, preexisting atherosclerotic disease, and prolonged vasopressor use.[10] Prior case series on pedal complications after ECMO show gangrene occurring more readily in younger patients, possibly secondary to smaller caliber vessels and fewer collaterals.[10-12] Patients are typically on ECMO for 1 to 3 weeks, and the risk of ischemia increases with prolonged duration (13 days in this patient).[3,13]

Coagulopathy and limb ischemia in the setting of COVID-19 is widely recognized.[14-16] Studies have reported on the hypercoagulable effects of COVID-19 resulting in the development of acute limb ischemia and digital gangrene despite anticoagulation.[15-17] Low-intensity heparin infusion is recommended in critically ill patients with COVID-19 and has been associated with survival benefit.[16,18,19] This finding is reflected in our hospital's anticoagulation protocol.

Vasopressors are associated with the development of digital gangrene, because they create peripheral vasoconstriction to perfuse organs during hemodynamic instability.[20] This patient was on vasopressors (epinephrine injection, phenylephrine, and norepinephrine infusions) for 30 days. Vasopressor-induced digital necrosis is a known side effect reported in the literature, often reported as being bilateral and symmetrical in the toes.[21-23] Atrial fibrillation has also been associated with toe necrosis owing to showering of microemboli, although less likely in this patient owing to the short duration of arrhythmia.[24]

The lack of adequate offloading perhaps played the largest role in the development of pedal gangrene in this patient. Constant pressure to an area creates capillary occlusion, ultimately leading to tissue ischemia owing to inadequate oxygenation.[25] Therefore, proper offloading in the bed is of great importance. Heel offloading boots have been found to decrease heel contact forces and can alleviate pressure from the footboard.[25] Placing a pillow underneath the shins or positioning the feet off the end of the bed can alleviate pressure on the dorsal feet and toes when the patient is prone. Pressure redistribution support surfaces and prophylactic silicone dressings over bony prominences as well as frequent repositioning can also prevent these injuries.[4] At our institution, the podiatry, vascular, and wound care teams have since revised the prone positioning protocol to address offloading of the lower extremities and feet.

CONCLUSIONS

We have presented this case to highlight the importance of proper offloading to decrease pressure necrosis injuries from occurring in patients with COVID-19. In patients who are prone positioned and on ECMO and vasopressor support, the risk of developing these wounds is only exacerbated. Efforts to decrease lower extremity pressure wounds are paramount in decreasing the rates of partial and total limb loss.

REFERENCES

1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-13.

2. Pavlushkov E, Berman M, Valchanov K. Cannulation techniques for extracorporeal life support. Ann Transl Med 2017;5:70.
3. Pillai AK, Bhatti Z, Bosserman AJ, Mathew MC, Vaidehi K, Kalva SP. Management of vascular complications of extra-corporeal membrane oxygenation. Cardiovasc Diagn Ther 2018;8:372-7.
4. Team V, Team L, Jones A, Teede H, Weller CD. Pressure Injury Prevention in COVID-19 Pateints with Acute Respiratory Distress Syndrome. Front Med 2021.
5. Girard R, Baboi L, Ayzac L, Richard JC; Guérin C; Proseva trial group. The impact of patient positioning on pressure ulcers in patients with severe ARDS: results from a multicentre randomised controlled trial on prone positioning. Intensive Care Med 2014;40:397-403.
6. Le MQ, Rosales R, Shapiro LT, Huang LY. The down side of prone positioning: the case of a COVID-19 survivor. Am J Phys Med Rehabil 2020;99:870-2.
7. ELSO. Extracorporeal life support organization (ELSO) COVID-19 interim guidelines. Available at: https://www.elso.org/Portals/0/Files/pdf/ELSO%20covid%20guidelines%20final.pdf 2020;(April):1–30. Accessed March 15, 2021.
8. Barbaro RP, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, et al. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. Lancet 2020;396:1071-8.
9. Shekar K, Badulak J, Peek G, Boeken U, Dalton HJ, Arora L, et al. Extracorporeal Life Support Organization Coronavirus Disease 2019 Interim Guidelines: a consensus document from an international group of interdisciplinary extracorporeal membrane oxygenation providers. ASAIO J 2020;66:707-21.
10. Bonicolini E, Martucci G, Simons J, Raffa GM, Spina C, Lo Coco V, et al. Limb ischemia in peripheral veno-arterial extracorporeal membrane oxygenation: a narrative review of incidence, prevention, monitoring, and treatment. Crit Care 2019;23:266.
11. Sandgren T, Sonesson B, Ahlgren R, Länne T. The diameter of the common femoral artery in healthy human: influence of sex, age, and body size. J Vasc Surg 1999;29:503-10.
12. Martin HV, Lazzarini PA, Kinnear EM, Munck L, Fraser J. Dying feet in ICU: why might extracorporeal membrane oxygenation machines cause necrotic feet? J Foot Ankle Res 2013;6(Suppl 1):O26.
13. Marasco SF, Lukas G, McDonald M, McMilan J, Ihle B. Review of ECMO (extra corporeal membrane oxygenation) support in critically ill adult patients. Heart Lung Circ 2008;17(Suppl 4):S41-7.
14. Zhang Y, Xiao M, Zhang S, Xia P, Cao W, Jiang W, et al. Coagulopathy and antiphospholipid antibodies in patients with Covid-19. N Engl J Med 2020;382:e38.
15. Thompson O, Pierce D, Whang D, O'Malley M, Geise B, Malhotra U. Acute limb ischemia as sole initial manifestation of SARS-CoV-2 infection. J Vas Surg Cases Innov Tech 2020;6:511-3.
16. Bellosta R, Luzzani L, Natalini G, Pegorer MA, Attisani L, Cossu LG, et al. Acute limb ischemia in patients with COVID-19 pneumonia. J Vasc Surg 2020;72:1864-72.
17. Wang JS, Pasieka HB, Petronic-Rosic V, Sharif-Askary B, Evans KK. Digital gangrene as a sign of catastrophic coronavirus disease 2019-related microangiopathy. Plast Reconstr Surg Glob Open 2020;8:e3025.
18. Barnes GD, Burnett A, Allen A, Blumenstein M, Clark NP, Cuker A, et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. J Thromb Thrombolysis 2020;50:72-81.
19. Hippensteel JA, LaRiviere WB, Colbert JF, Langouet-Astrie CJ, Schmidt EP. Heparin as a therapy for COVID-19: current evidence and future possibilities. Am J Physiol Lung Cell Mol Physiol 2020;319:L211-7.
20. VanValkinburgh D, Kerndt CC, Hashmi MF. Inotropes and vasopressors. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020.
21. Ruffin N, Vasa CV, Breakstone S, Axman W. Symmetrical peripheral gangrene of bilateral feet and unilateral hand after administration of vasopressors during septic shock. BMJ Case Rep 2018;2018. bcr2017223602.
22. Daroca-Perez R, Carrascosa MF. Digital necrosis: a potential risk of high-dose norepinephrine. Ther Adv Drug Safety 2017;8:259-61.
23. Shin JY, Roh SG, Lee NH, Yang KM. Ischemic necrosis of upper lip, and all fingers and toes after norepinephrine use. J Craniofac Surg 2016;27:453-4.
24. Pradhan S, Gresa K, Nolke JR, Trappe H. Blue toe syndrome caused by emboli from anomalous left atrial septal pouch thrombus: a case report. Thrombosis J 2020;18:13.
25. Griffin CC, Dean T, Cayce JM, Modrcin MA. Pressure ulcer prevention: effectiveness of heel off-loading methodologies. Open J Nurs 2015;5:909-16.

Submitted Sep 14, 2020; accepted Feb 23, 2021.