

Acute Lower Limb Ischemia in a Patient with COVID-19 and Septic Shock Requiring Amputation

Adolfo Leyva-Alvizo, Cristina Villar-Canton, Alberto Riojas-Garza *

School of Medicine and Health Sciences, Tecnológico de Monterrey, Monterrey, México

Email address:

adolfoleyva@gmail.com (A. Leyva-Alvizo), ariojasg16@gmail.com (A. Riojas-Garza)

*Corresponding author

To cite this article:

Adolfo Leyva-Alvizo, Cristina Villar-Canton, Alberto Riojas-Garza. Acute Lower Limb Ischemia in a Patient with COVID-19 and Septic Shock Requiring Amputation. *World Journal of Medical Case Reports*. Vol. 3, No. 2, 2022, pp. 25-28. doi: 10.11648/j.wjmcr.20220302.13

Received: April 12, 2022; **Accepted:** April 26, 2022; **Published:** May 10, 2022

Abstract: Increased incidence of thromboembolic events in patients with severe COVID-19 infection has been documented. Acute limb ischemia as a complication in critically ill patients due to coagulopathy has been reported, worsening prognosis and increasing limb amputation rate. Delayed recognition could lead to irreversible ischemia and clinical deterioration requiring amputation. We present the case of a 54-year-old male with severe COVID-19 infection who developed clinical deterioration and acute lower limb ischemia at day 7 of hospitalization in the intensive care unit. Skin color changes suggested necrotic tissue and skin bullae. Arterial doppler ultrasound revealed a thrombus on the distal superficial femoral artery with absence of blood flow. Irreversible ischemia was diagnosed. The patient underwent an above the knee amputation, showing favorable clinical evolution during the next three days. Nonetheless, septic shock persisted, and 14 days later the patient presented cardiorespiratory arrest and passed away. Acute limb ischemia could present as a complication in critically ill patients treated in the intensive care unit, increasing amputation rate and worsening prognosis. In patients with critical management, physical examination and laboratory analyses are essential for clinical evolution concerning peripheral vascular disease. Efforts should be made to diagnose such complications on time with a more rigorous and protocolized limb perfusion examination.

Keywords: Limb Ischemia, Amputation, COVID-19, Septic Shock

1. Introduction

As COVID-19 worldwide continues to increase with more than 18.5 million cases reported to the World Health Organization, research concerning physiopathological, epidemiological and clinical aspects of SARS-CoV-2 infection increase as well [1].

Clinical characteristics range from mild and moderate symptoms such as fever, cough and sore throat, to severe and critical manifestations such as dyspnea, acute respiratory distress syndrome (ARDS), septic shock, and multiple organ failure [2]. An epidemiological study in China reported 80% of SARS-CoV-2 hospitalized patients as mild pneumonia, 13.8% as severe infection, and 4.7% as critical infection with a fatality rate of 50% in critically ill patients [3, 4]. Approximately 20% of hospitalized patients require admittance to the Intensive Care Unit (ICU) for critical management, where complications include ARDS, acute

cardiac injury, multiple organ failure and thromboembolic events [2, 5].

Increased incidence of symptomatic acute pulmonary embolism, deep vein thrombosis, ischemic stroke, myocardial infarction, and systemic arterial embolism in critically ill COVID-19 patients suggest SARS-CoV-2 implication [5, 6]. Vascular thromboembolism in ICU patients has been estimated in 31%, where 27% and 3.7% of cases account for venous and arterial thrombosis respectively [5]. Associations between COVID-19 patients and lower extremity thrombosis has been reported, with an increased incidence of limb amputation and death [7]. Delayed recognition of acute limb ischemia as a complication of severe COVID-19 infection could lead to irreversible ischemia and clinical deterioration, where limb amputation remains as the only surgical treatment [8].

Although physiopathological mechanisms concerning vascular disease are yet to be clarified, coagulation function differences have been found between COVID-19 patients and

controls [9]. It is estimated that 20-55% of patients hospitalized for COVID-19 have laboratory evidence of coagulopathy [6]. Decreased prothrombin time and antithrombin values, as well as increased D-Dimer, and fibrinogen values have been reported [9, 10]. Even more, such parameters have been found to be associated with poor clinical outcome [11].

Our institution is a high specialty center in Monterrey. To date, more than 700 COVID-19 patients have been treated since the beginning of the pandemic. This institution is an important COVID-19 center in Mexico with a mortality rate estimated at 6.7%.

Here we present the case of a patient with COVID-19 severe pneumonia complicated with lower limb arterial thrombosis causing acute limb ischemia and septic shock requiring limb amputation.

2. Case Report

A 54-year-old male with a past medical history of hypertension, diabetes mellitus and obesity presented to the emergency department with fever, dry cough, fatigue, malaise and shortness of breath that progressed over a 10-day period. He denied tobacco or alcohol consumption. Vital signs at the emergency department included heart rate of 98 beats/min, blood pressure of 90/60 mmHg, oxygen saturation of 79% on room air and temperature of 37.2°C. Physical examination revealed bilateral crackles on both lung bases at auscultation with no other alteration. Laboratory analysis at admission is reported in table 1. The patient underwent a nasopharyngeal swab which confirmed COVID-19 infection diagnosis with a reverse transcriptase polymerase chain reaction (RT-PCR) assay. A chest x-ray showed bilateral ground-glass opacities and diffuse hazy infiltrates (figure 1).



Figure 1. Chest X-ray showing bilateral diffuse ground-glass opacities and hazy infiltrates.

Table 1. Laboratory analysis at admission.

	Value	UM	Normal range
Hemoglobin	12.8	g/dL	13.2-18
Hematocrit	38.5	%	38.4-52.4
White blood cells	10.4	$\times 10^3/\mu\text{l}$	4.5-11
Platelets	284	$\times 10^3/\mu\text{l}$	150-420
Glucose	103	mg/dL	60-100
Creatinine	0.8	mg/dL	0.7-1.3
Blood urea nitrogen	47	mg/dL	8.9-25.7
Albumin	2.9	g/dL	3.5-5.0
AST	80	U/L	5-34
ALT	35	U/L	0-55
Troponin	27.4	ng/mL	<0.03
D-dimer	707	ng/mL	<0.5
Partial thromboplastin time	28	Sec	25.4-36.9
LDH	635	U/L	140-271
CRP	31.7	mg/L	0.0-8.0
Ferritin	1533	ng/mL	15-300
Procalcitonin	0.32	ng/mL	<0.05
BNP	59.4	pg/mL	<100

AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, CRP: C- reactive protein, BNP: B type natriuretic peptide.

Due to the patient's ventilatory decompensation, endotracheal intubation was pursued, followed by admittance to the ICU for critical management. Thromboprophylaxis was prescribed with enoxaparin 80 mg.

During the next few days, clinical deterioration was noted with constant increase of white-blood cell count, ferritin, D-Dimer, procalcitonin and BNP values. Refractory metabolic acidosis was documented requiring renal replacement therapy with hemodialysis. Vasopressor support was needed to maintain a mean arterial pressure >60 mmHg. On day 7 physical examination revealed changes in skin color on the lower left extremity, suggestive of limb necrosis accompanied with skin bullae and gangrene extending to the upper third of the tibia (figure 2).



Figure 2. Ischemic tissue associated with skin bullae and necrotic ulcer in the left lower limb.

Arterial doppler ultrasound of the lower left limb showed an echogenic image compatible with thrombus, observed in the distal portion of the superficial femoral artery with extension to the popliteal artery and proximal portions of tibial arteries in which blood flow was absent (figure 3). The case was presented to the surgery department where limb amputation was suggested.

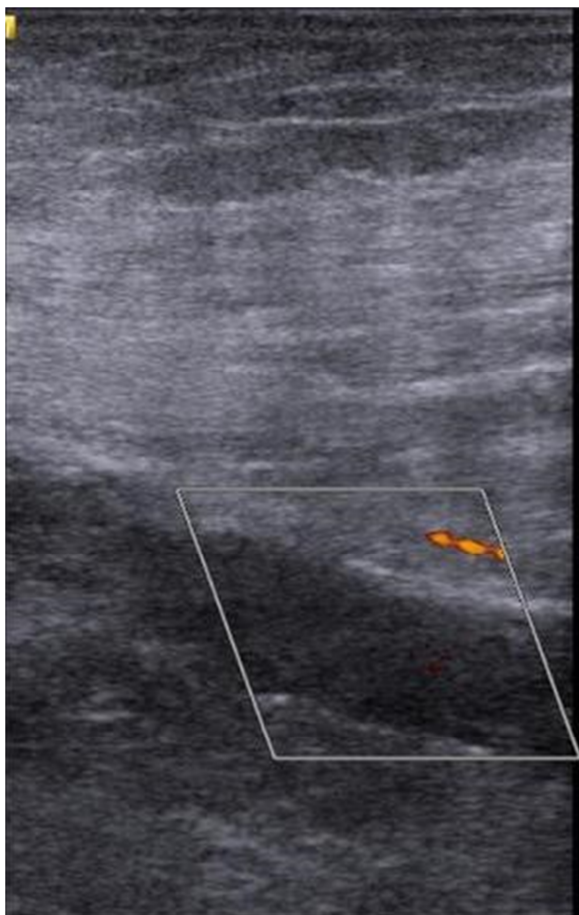


Figure 3. Arterial doppler ultrasound of lower left limb showing an echogenic mass compatible with thrombus causing complete obstruction of distal femoral artery.

Above the knee amputation of the left limb was done, after which inflammatory markers decreased with favorable clinical evolution over the next three days. Nonetheless, septic shock persisted and multiorgan failure progressed three days after surgery. Unfortunately, 14 days later the patient presented cardiorespiratory arrest and passed away.

Medication administered in the ICU included noradrenalin, enoxaparin, dexamethasone, lopinavir, ritonavir, ceftaroline, fosamilo, azithromycin, ribavirin, baricitinib, piperacillin, tazobactam, and linezolid.

3. Discussion

We present the case of a 54-year-old male with COVID-19 severe pneumonia complicated with lower limb arterial thrombosis. This is a pattern seen in patients with SARS-CoV-2 severe infection. Case reports and case series have

observed this phenomenon urging attention.

An observational cohort study during the COVID-19 pandemic reported an increased incidence rate of acute limb ischemia during the present year. Twenty patients positive to SARS-CoV-2 infection with acute limb ischemia were analyzed. Most patients were male with a median age of 75 years. Rutherford stage IIb was diagnosed in most patients, with a revascularization attempt in 17 of them, 12 of which were successful. Three patients did not receive a revascularization procedure due to critical conditions, two of them had Rutherford III stage. Mortality was estimated at 40% [12].

Acute limb ischemia in patients with severe COVID-19 infection has male predominance, with age ranging from 43 to 83 years [12]. Laboratory analyses show a D-dimer median value range of 1190 – 13600 ng/ml and partial prothrombin time of 27.8 – 80 sec [12, 13, 15, 17, 18]. Time from disease onset to thromboembolic event diagnosis varies from 0 to 14 days [14]. In hospitalized patients, diagnosis has been described at admission and 7 – 14 days after hospitalization [13, 15, 17, 18]. In this case, our patient had altered laboratory findings, with an increasing D-dimer value and increased partial thromboplastin time. Time from admission to thrombotic event diagnosis was 7 days, although physical examination revealed at least a 12-hour gap between thrombotic onset and diagnosis.

Scarce information regarding limb necrosis associated to COVID-19 septic shock has been published [17]. Limb amputation has been reported as treatment for irreversible limb ischemia [12, 14]. In our case, irreversible limb ischemia was found in a patient with severe COVID-19 infection, associated with septic shock and deleterious evolution. Limb necrosis could be contributing to a non-responsive septic shock by increasing cytokine production worsening clinical evolution [19]. Limb amputation in this case was a reasonable therapeutic pathway. A clinical improvement was noticed during the next three days after surgery. Nonetheless, multiorgan failure and septic shock persisted, leading to death 14 days after surgery.

Hospitalized patients treated outside ICU who develop arterial thrombosis, or with acute limb ischemia symptoms at admission, would expect to receive a prompt diagnosis with more favorable outcomes [12, 17]. On the other hand, critically ill patients with severe COVID-19 infection in ICU are generally managed with orotracheal intubation and sedation, avoiding symptom communication and recognition. In these cases, constant physical examination and laboratory analyses are crucial for patient follow up. Acute limb ischemia as a complication of severe COVID-19 infection in patients treated in the ICU could end more frequently in irreversible ischemia and limb amputation than patients outside the ICU or with limb ischemia symptoms at admission.

4. Conclusion

Evidence suggests an association between severe COVID-

19 infection and thromboembolic events. Acute limb ischemia could present as a complication in critically ill patients treated in the ICU, increasing amputation rate and worsening prognosis. Particularly in patients with critical management in ICU, physical examination and laboratory analyses are essential for clinical evolution concerning peripheral vascular disease. We developed based on this case, and other similar cases not requiring amputation, a protocol in which nurses in the ICU included revision of capillary refill in toes every 24 hours, in COVID patients receiving vasopressor medications. We believe this measure will prevent further limb loss. As a final recommendation, efforts should be made to diagnose such complications on time with a more rigorous and protocolized limb perfusion examination, especially in patients in critical conditions.

Conflicts of Interest

The authors declare that they have no competing interests.

Ethical Responsibilities

This work has been approved by the appropriate ethics committee. All persons gave their informed consent prior to their inclusion in the study.

References

- [1] Tedros Adhanom Ghebreyesus. No Title. WHO Director-General's opening remarks at the media briefing on COVID-19 - 6 August 2020. 2020.
- [2] Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Med Infect Dis.* 2020; 34: 101623.
- [3] The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2020 Feb; 41 (2): 145–51.
- [4] Wang Y, Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. *J Med Virol.* 2020 Jun; 92 (6): 568–76.
- [5] Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res.* 2020 Jul; 191: 145–7.
- [6] Lee SG, Fralick M, Sholzberg M. Coagulopathy associated with COVID-19. *C Can Med Assoc J = J l'Association medicale Can.* 2020 May; 192 (21): E583.
- [7] Goldman IA, Ye K, Scheinfeld MH. Lower extremity arterial thrombosis associated with COVID-19 is characterized by greater thrombus burden and increased rate of amputation and death. *Radiology.* 2020 Jul; 202348.
- [8] Mascia D, Kahlberg A, Melloni A, Rinaldi E, Melissano G, Chiesa R. Single center vascular Hub experience after 7 weeks of COVID-19 pandemic in Lombardy (Italy). *Ann Vasc Surg.* 2020 Aug.
- [9] Han H, Yang L, Liu R, Liu F, Wu K-L, Li J, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. *Clin Chem Lab Med.* 2020 Jun; 58 (7): 1116–20.
- [10] Xiong M, Liang X, Wei Y-D. Changes in blood coagulation in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. Vol. 189, *British journal of haematology.* 2020. p. 1050–2.
- [11] Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost.* 2020 Apr; 18 (4): 844–7.
- [12] 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.
- [13] Galanis N, Stavraka C, Agathangelidis F, Petsatodis E, Giankoulof C, Givissis P. Coagulopathy in COVID-19 infection: a case of acute upper limb ischemia. Vol. 2020, *Journal of surgical case reports.* 2020. p. rjaa204.
- [14] Kashi M, Jacquin A, Dakhil B, Zaimi R, Mahé E, Tella E, et al. Severe arterial thrombosis associated with COVID-19 infection. Vol. 192, *Thrombosis research.* 2020. p. 75–7.
- [15] Kaur P, Posimreddy S, Singh B, Qaqa F, Habib HA, Maroules M, et al. COVID-19 Presenting as Acute Limb Ischaemia. *Eur J case reports Intern Med.* 2020; 7 (6): 1724.
- [16] Kaur P, Qaqa F, Ramahi A, Shamoony Y, Singhal M, Shamoony F, et al. Acute upper limb ischemia in a patient with COVID-19. *Hematology/oncology and stem cell therapy.* 2020.
- [17] Schultz K, Wolf JM. Digital Ischemia in COVID-19 Patients: Case Report. *J Hand Surg Am.* 2020 Jun; 45 (6): 518–22.
- [18] Vacirca A, Faggioli G, Pini R, Teutonico P, Pilato A, Gargiulo M. Unheralded Lower limb threatening ischemia in a COVID-19 patient. *Int J Infect Dis IJID Off Publ Int Soc Infect Dis.* 2020 Jul; 96: 590–2.
- [19] Simon F, Oberhuber A, Floros N, Busch A, Wagenhäuser MU, Schelzig H, et al. Acute Limb Ischemia-Much More Than Just a Lack of Oxygen. *Int J Mol Sci.* 2018 Jan; 19 (2).