



THE JOURNAL OF INDONESIAN ORTHOPAEDIC & TRAUMATOLOGY

journal homepage: <http://journal.indonesia-orthopaedic.org>

Case Report

Acute Limb Ischemia Rutherford Classification III and COVID-19: A Case Report

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Article Info :

Article History :
Submission: April 27, 2022
Revision: March 5, 2023
Accepted: March 26, 2023

Keywords :
Covid-19
Acute limb ischemia
Arterial thrombosis
Amputation

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Abstract

Background: COVID-19 is caused by SARS-CoV-2 infections, which are responsible for the recent pandemic. COVID-19 infection increases thromboembolic events, including Acute Limb Ischemia (ALI) by causing elevated cytokine levels, systemic inflammation, hypercoagulation state, and hyperinflammation responses. This complication might cause loss of limbs.

Case description: We report a case of a 61-year-old male with COVID-19 who developed an ALI. He presented to the emergency department with acute left leg pain since a day before admission and shortness of breath three days before admission. His left foot was bluish-discolored, cold to the touch, and mottled in appearance. Chest x-ray showed bilateral inhomogeneous consolidation. Left lower limb X-ray revealed a gangrenous appearance. CT-Angiography suggested severe distal stenosis of the left femoral artery with complete occlusion of its distal aspect. COVID-19 was diagnosed based on RT-PCR testing. He received antibiotics and anticoagulation. Unfortunately, he underwent an amputation procedure.

Conclusion: A high index of suspicion should be maintained for ALI in COVID-19 patients, which is a vascular emergency. Some patients can achieve revascularization with observation or medical and/or surgical intervention, but other patients succumb to either amputation or death.

Introduction

COVID-19 is a pathological condition caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection. Since the first case was reported in Wuhan, the symptoms of the infection have not been specific and are frequently associated with pulmonary complications.¹

Various extrapulmonary manifestations of COVID-19 have been described and associated with acute thromboembolic phenomena, including systemic inflammation, endothelial injury, and platelet dysfunction at the cardiopulmonary, cerebrovascular, and peripheral venous and arterial levels. These manifestations affect at least 49% of patients and overshadow the patient's prognosis. Recent publications have reported a sudden increase in cases of arterial

thrombosis in patients with COVID-19, impacting the incidence of ALI and surgical emergencies.¹ Although most cases are asymptomatic, further primary prevention is urgently needed. Primary health care facilitators play an essential role in early diagnosing and managing patients who present with symptoms of ALI or who have risk factors for developing ALI, particularly in populations with a history of COVID-19. An adequate management strategy will improve the patient's quality of life. Herein, we report a case of a 61-year-old male with Rutherford Class III Acute Limb Ischemia associated with COVID-19.

Case Report

A 61-year-old male came to the Emergency Department in Karawang General Hospital with chief



Figure 1. Patient's condition on admission

complaints of pain in his left leg a day before admission. The pain was sudden, especially in the knee area. Along with the pain, he felt tingles, cold, and bluish discoloration in his leg. He also complained of shortness of breath, cough, and fever since three days ago. He had hypertension and congestive heart failure and underwent a stent angioplasty in 2017. History of diabetes mellitus and COVID-19 vaccination was denied.

From a general physical examination, the patient looks weak. From the primary survey, his airway, breathing, and circulation were within normal limits, and he is fully conscious (*compos mentis*). His blood pressure was 170/100 mmHg; the respiratory rate was 26 breaths/minute; pulse rate was 120 beats per minute; the temperature was 36.8°C, and oxygen saturation was 97% in the room air. From the secondary survey, his left foot was bluish-discolored, cold to the touch, and mottled in appearance. The left lower limb's dorsalis pedis artery and posterior tibial artery were absent on palpation, and capillary refill time could not be detected.

Laboratory examination revealed hemoglobin 13,7 g/dL, hematocrit 41,2%, erythrocyte 4700000 cells/mm³, total leukocyte count 14930 cells/mm³, platelets 507000 cells/mm³, urea 58.6 mg/dl, creatinine 1.58 6 mg/dl, NLR 5,205, ALC 2.245, and ESR 99 mm/h at the time of presentation. His random blood sugar was 150 mg/dL, CRP was reactive, and HIV was negative. The SARS-CoV-2 real-time PCR examination showed positive results. Chest x-ray showed inhomogeneous consolidation in bilateral pulmonary inferior zones, suspecting viral pneumonia. X-ray of his left foot and leg suggested a gangrenous appearance. CT-Angiography suggested severe distal stenosis of the left femoral artery with complete occlusion of its distal aspect.

According to the patient's history, physical examination, and additional tests, he was diagnosed with Acute Limb Ischemia Rutherford category III and COVID-19. In the ED, he was given intravenous fluid with NaCl 0.9%, Ceftriaxone, Heparin 3000 units bolus next 600 units per hour, Atorvastatin, Aspilet, Clopidogrel, Captopril, Paracetamol, Bicnat, Avigan, Azithromycin, Vitamin D, N-acetylcysteine. He was planned to be referred to a hospital with an isolation

operating room for COVID-19, but he refused therefore we managed the patient with debridement and left leg amputation.

Discussion

Coronavirus disease 2019 (COVID-19) is caused by the virus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which is very contagious and caused a pandemic recently. The primary manifestation involves the respiratory system. Up to July 13th, 2021, the Indonesian Government reported 2.615.529 confirmed cases, 68.219 deaths, and 2.139.601 recovered from COVID-19.^{2,3}



Figure 2. Chest X-Ray



Figure 3. CT-Angiography



Figure 4. Post-amputation condition

The exact pathogenesis is still debatable and has yet to be explored in detail. Nevertheless, SARS-CoV-2 mainly infects airway cells lining the alveoli and binds with receptors, specifically ACE-2 into the host cell. Glycoprotein within the spike envelope will bind with a cellular receptor in ACE2, duplicate its genetic material then synthesize proteins essential for generating new virions. Dysregulation of the immune system plays a role in tissue damage during infection. On the other hand, excessive immune response might cause tissue damage.⁴

This virus mainly attacks the respiratory system. Diagnosis is made based on clinical manifestation. Typical signs and symptoms of COVID-19 are acute respiratory problems, fever ($>38^{\circ}\text{C}$), cough, and breathing difficulty. Additionally, patients might have ageusia, anosmia, nausea, and vomiting. About half of the cases suffer from dyspnea within a week. The mean incubation time is 5-6 days, with the longest reaching 14 days. A severe form of COVID-19 might provoke sepsis, extreme pneumonia, ARDS, kidney failure, and even death. An X-ray examination might show ground-glass opacity and diffuse pneumonic infiltrate in both lung fields.^{5,6}

A recent study reported clinical characteristics and overall results of COVID-19 with its effects on the healthcare system. Two studies highlight coagulopathy and its association with a higher mortality rate. Tang et al. found abnormal coagulation profiles, marked with spiking D-dimer and fibrin degradation products, commonly found in deceased patients due to COVID-19 pneumonia. Han et al. showed that coagulation function was significantly disturbed compared to healthy individuals, and monitoring coagulation parameters potentially supported identifying severe

cases earlier. COVID-19 infection is associated with increased thromboembolic events, including ALI. Acute limb ischemia might develop even in young and healthy adults with anticoagulation prophylaxis. Before COVID-19, studies had found that the overall incidence of ALI had decreased significantly, and hypercoagulation was the unusual cause in a broad population with ALI.^{7,8}

Acute limb ischemia is a vascular emergency associated with a high risk of limb loss and death. Most cases result from in situ thrombosis in patients with pre-existing peripheral arterial disease or those undergoing vascular procedures, including stenting and bypass grafts. The other common source is cardioembolic.⁹

The causative mechanism for ALI is a systematic inflammatory process triggered by a massive activation of macrophages that generate a cytokine storm. COVID-19 causes elevated cytokine levels, including but not limited to tumor necrosis factor- α , IL-1 β , IL-6, procalcitonin, and interferon γ . The coupling of inflammation and coagulation has also been described in the literature, sharing common molecular pathways.¹⁰ The typical clinical presentation of ALI is encompassed by "the rule of P's": pain, pulselessness, pallor, poikilothermia (cool extremity), paresthesia, and finally, the onset of paralysis.⁹

The clinical classification for ALI, as proposed by Rutherford et al. and subsequently adopted by the Society of Vascular Surgery and the International Society of Cardiovascular Surgery, considers the clinical findings such as sensory and muscle weakness and the Doppler indices of the arterial and venous systems. This classification helps to determine urgency, prognosticate the success of limb salvage, and guide decision-making in terms of therapy (Table 1).¹⁰

Due to hypercoagulation, ALI management in COVID-19 might be more challenging than expected. The patient might benefit from *unfractionated heparin* (UFH) after prolonged surgery. Bellosta et al. described 20 patients (18 male) with ALI associated with COVID-19 for three months. Seventeen patients underwent surgical care with revascularisation, and only 12 succeeded (70,6%). The lower success rate than expected might be due to a hypercoagulative state. Previous studies have proven that the pathogenesis of arterial thrombotic disease in COVID-19 was different from classic arterial thrombosis.⁸

COVID-19 patients might present with acute non-atherosclerotic thrombosis. Several mechanisms have been suggested to explain those phenomena. Hyperinflammation response was expected to be responsible for both arterial and venous thromboembolic events in COVID-19 patients. Increased D-dimer, fibrinogen, coagulation factors, acquired antiphospholipid antibody, decreased protein C, protein S, antithrombin, and platelet and neutrophil

Category	Description	Clinical finding		Doppler signals		Prognosis
		Sensory Loss	Muscle weakness	Arterial	Venous	
I	Viable	None	None	Audible	Audible	Not immediately threatened, can attempt revascularization
II	Threatened					
IIa	Marginally threatened	Minimal (toes) or none	None	Often inaudible	Audible	Salvageable with prompt revascularization
IIb	Immediately threatened	More than toes, associated with rest pain	Mild or moderate	Usually inaudible	Audible	Salvageable with immediate revascularization
III	Irreversible	Profound, anesthetic	Profound, paralysis (rigor)	Inaudible	Inaudible	Major tissue loss or permanent nerve damage is inevitable, consider amputation

Table 1. Rutherford clinical classification.¹⁰

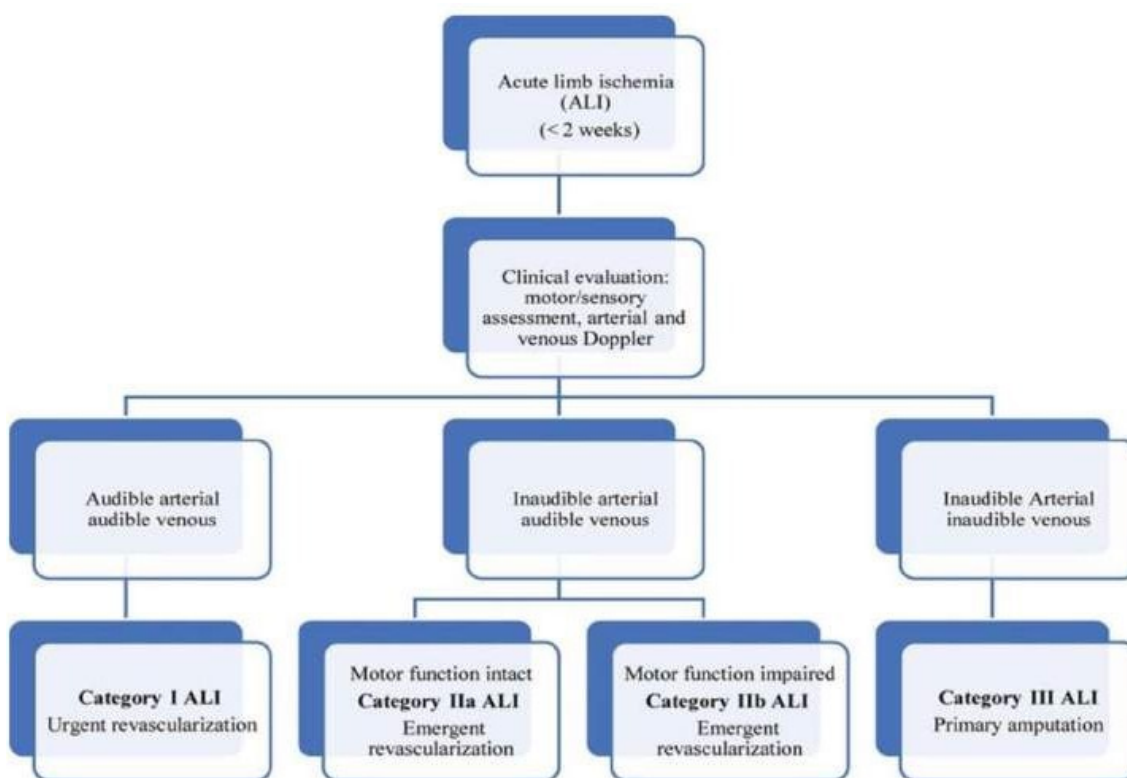


Table 5. Diagnosis and management of acute limb ischemia.⁹

hyperactivation had been observed. There was also speculation that direct viral infection from endothelial cells through ACE-2 might be the cause of arterial thrombosis in COVID-19.⁸

Rutherford's class, duration of ischemia, comorbidities, and therapy-related risks and outcomes. Fig. 5 outlines the initial assessment and recommended

revascularization strategies endorsed by professional societies.⁹ The main goals of CLI (Critical Limb Ischemia) treatments are to preserve limbs. Revascularization is the fundamental strategy to preserve extremities; however, in several patients, this measure did not improve both function and mobility of the limbs. When revascularization is considered,

arterial imaging helps identify the target and mode of revascularization. Due to the limitation of distal artery imaging non-invasively, the invasive angiography view regarding the management selection should be considered before amputation. Revascularization might not be suitable for all patients; therefore, requiring major amputation, including for patients with severe arterial, is commonly done to provide a better disease, infection, or tissue loss that is impossible to be preserved. Major amputation is a definitive therapy for those cases. Application of a grading system might help identify those with a high risk of undergoing major amputation.¹¹

Conclusion

COVID-19 is an exceptionally infectious disease that yielded a pandemic recently. COVID-19 infection is associated with an increased incidence of thromboembolic events, related to the increased mortality rate. Acute limb ischemia is the most severe peripheral arterial disease associated with an increased risk of limb loss. The primary purpose of therapy was to preserve the functionality of the affected body parts. Although revascularization had known to provide a good outcome; unfortunately, not all patients could be managed with revascularization; therefore had to undergo major amputation. Major amputation is a crucial treatment choice for managing the third category of ALI classification by Rutherford. A rational and wise approach is needed to choose between revascularization and amputation for high-risk patients.

Conflict of interest

The author has no conflict of interest related to this article.

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