**SARS-Cov2 and limb Ischemia**

Mnif K¹*, Rekik K¹, Chaabouni H¹, Fendri H², Smaoui F¹, Boughariou I¹, Maaloul I², Feki W², Marrakchi C¹, Mnif Z², Koubaa M¹ and Jemaa MB¹

¹Infectious Diseases Department, Hedi Chaker University Hospital, Tunisia
²Radiology Department Hedi Chaker University Hospital, Tunisia

*Corresponding author:
Khoulou Mnif,
Infectious diseases Department, Hedi Chaker University Hospital, Tunisia,
E-mail: Khoulou.mnif@hotmail.fr

Received: 16 Mar 2022
Accepted: 04 Apr 2022
Published: 09 Apr 2022
J Short Name: ACMCR

Copyright:
©2022 Mnif K. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially.

Citation:

Keywords:
COVID-19; Oxygen saturation; Hyperleukocytosis

1. **Abstract**

Patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection mainly present severe pneumonia associated with complications related to cytokine storm syndrome. So, it was associated with thrombotic incidents like acute limb ischemia and pulmonary embolism.

We report 3 cases of COVID-19 infection complicated by arterial thrombosis in the form of acute limb ischemia.

2. **Introduction**

At the end of 2019, a novel coronavirus disease 2019 (COVID-19) caused by the severe respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a worldwide epidemic.

Patients with COVID-19 usually present with respiratory symptoms like cough, fever, and shortness of breath. We found also a very high incidence of thromboembolic complications in patients hospitalized with COVID-19 pneumonia.

We report 3 cases of COVID-19 infection complicated by acute limb ischemia.

3. **Case Presentation 1**

A-71-year-old man with a medical history of diabetes mellitus and dyslipidemia presented to the emergency department with shortness of breath. One week previously, he had started to develop fever, asthenia, and anorexia. COVID 19 rapid test was positive. Clinical examination showed a Glasgow scale of 15/15, heart rate 74/min, oxygen saturation 86% on room air, and temperature 37.1°C. Electrocardiography showed the left anterior fascicular block. On initial laboratory evaluation, we found: lymphopenia (820 cells/mm³), hyperglycemia (18 mmol/l), hepatic cytolysis (1.5x N), and high C-Reactive-Protein (254 ng/ml). According to SFR, CT Scan showed SARS-CoV2 pneumonia with parenchymal involvement estimated at 25%-50%. The patient had received oxygen (10 liter/min), dexamethasone 12 mg a day, and low molecular weight heparin (LMWH) 0.4 mg a day. He had also received cefotaxime 3 g for the day. After one week, his breathing was improved but he had acute pain in his left limb. The distal third of the limb was cold and mottled. He had a sensory-motor deficit of his limb. The left pedal pulse was absent. He was treated with unfractionated heparin drip (UFH) 210 mg for day and vasodilator drug. But the limb ischemia was extended. The patient had a mid-leg amputation. Two days after, he had a cardiac arrest and died.

4. **Case Presentation 2**

A-73-year-old man with a medical history of diabetes mellitus and hypertension presented to the emergency department with complaints of shortness of breath. One week previously he had started to have fever and cough. Vital signs on presentation were: Glasgow scale 15/15, heart rate 92/min, blood pressure 140/70 mmHg, oxygen saturation 84 % on room air, and 95% on supplemental oxygen (12 liter/min). The COVID 19 rapid test was positive. The electrocardiography was normal. On initial laboratory evaluation, we found: hyperleukocytosis at 15900/mm³, lymphopenia at 660/mm³, anemia at 11.1 g/dl, elevated C-reactive protein at 91 mg/l, and hepatic cytolysis (3x reference). The patient had received LMWH 0.7 mg twice a day, dexamethasone 12 mg a day, cefotaxime 3 g a day, and furosemide 20 mg twice a day. After 7 days, he mentioned lower limb pain. On examination, his right foot was cold to the touch and cyanosis in appearance. His leg was...
mottled and cold. His right popliteal artery and pedal pulse were not palpable. Computed tomography angiography showed complete occlusion of the right superficial femoral artery extended to the popliteal artery (figure 1).

He was started on a therapeutic heparin infusion. He underwent an emergency right lower artery embolectomy Fogarty catheter. But his foot was cyanosis and his pedal pulse was not palpable. So, the patient had a mid-leg amputation. Two days after, the amputation stump was necrotic.

He had a mid-thigh amputation then transferred to intensive care for respiratory distress and he died a few days later.

Figure 1: CT angiography of aorta and iliofemoral arteries: Complete occlusion of the right superficial femoral artery extended to the popliteal artery

5. Case Presentation 3

An A-58-year-old man without medical history presented to the emergency department complaining of fever, asthenia, and shortness of breath.

Vital signs on presentation were: Glasgow scale, 15/15; temperature, 37°C; heart rate, 99 beats/min; blood pressure, 122/64 mmHg; oxygen saturation, 80% on room air and 96% on supplemental oxygen (16 liter/min of oxygen). His nasopharyngeal swap was positive for COVID-19 infection. The electrocardiography was normal. On initial laboratory evaluation, we found: hyperleukocytosis, 10700/mm$^3$; lymphopenia, 510/mm$^3$; elevated D-dimer 635 ng/mL and elevated C-reactive protein, 195 ng/mL.

The patient has been treated with dexamethasone 12 mg for a day, LMWH 0,4mg twice for a day, cefotaxime 3 g for a day. He had received insulin for newly diagnosed diabetes. Two days after, he had painful lower extremities. On examination, his bilateral extremities were mottled and cold. His femoral, posterior tibial, and pedal pulses were not palpable. Computed tomography angiography of the aorta and iliofemoral arteries showed complete occlusion of the abdominal aorta with extension to both common iliac arteries, complete occlusion of the right popliteal artery, the left anterior tibial artery (figure 2). It showed a splenic infarction. The patient had received UFH. But he had a distress respiratory and a cardiac arrest and died.

Figure 2: CT angiography of the aorta and iliofemoral arteries showed:
- Complete occlusion of the abdominal aorta extension to both common iliac arteries
- Complete occlusion of the right popliteal artery, the left anterior tibial artery
6. Discussion

COVID-19 significantly impacted healthcare worldwide. It can present with a variety of clinical manifestations including fever, cough, myalgia, dyspnea, headache, diarrhea, and vomiting [1]. Although respiratory symptoms predominate, COVID-19 is a high risk for arterial thromboembolism. Patients with severe COVID-19 infection can develop intravascular coagulopathy with endothelial dysfunction [2].

Multiple retrospective analyses have similar incidents from 12 to 31% of thrombotic complications in patients infected with COVID-19 [2]. A minority of these events are arterial (4%) [1, 3]. The mechanism of thromboembolic complications is multifactorial: a direct viral infection of the endothelial cell leading to diffuse endothelial inflammation increased pro-coagulant factors such as fibrinogen, factor VIII, and high inflammatory state associated with the cytokine storm leading to coagulation and fibrinolysis activation [4]. So, endothelitis and hypercoagulability, together with prolonged immobilization of critically ill COVID-19 patients complete the Virchow’s triad explains the mechanism of arterial thrombosis [3]. Elevated D-dimer was associated with high mortality [5]. The study of Tang et al showed that abnormal coagulation results, characterized by markedly elevated D-dimer and fibrin degradation products are common in patients who have died of this viral pneumonia [6]. In China, a study of 1099 covid-19 cases showed that 46.4% of patients had a high level of D-dimer (≥500μg/l), 60% of them had severe pneumonia [7].

Parminder K et al reported a similar case of a 43-year-old patient who had a severe form of COVID-19 infection. He had an elevated D-dimer and fibrinogen. He was found to have a thrombus of the proximal right superficial femoral artery and two days after admission, he had a cardiac arrest and died [8].

In a review, Cheruiyot I et al found that most patients with arterial thrombosis were elderly and had pre-existing co-morbidities [3], confirming the current evidence that pre-existing chronic disease increases the incidence and severity of COVID-19 [3, 9]. Pre-existing cardiac diseases have been known to prejudice vascular inflammation which could be exacerbated by the SARS-CoV-2 infection and the enhanced prevalence of arterial thrombosis in these particularly predisposed individuals [3]. An observation has been reported in the pediatric population where the presence of congenital cardiovascular disease predisposed affected children to severe COVID-19 infection and thrombotic complications [10].

We have two elderly patients with preexisting chronic illness in our cases, but the third case had 58 years, without medical history. The American Society of Hematology (ASH) recommends that all hospitalized patients with COVID-19 infection should receive anticoagulant thromboprophylaxis, in the absence of a contraindication [11].

The recommendations regarding therapeutic anticoagulation in patients with limb ischemia and SARS-CoV-2 infection are not well established yet [12, 13]. Bellosta R et al, in a study on 20 patients who underwent revascularization, showed that the usage of systemic heparin was associated with increased survival [5]. In this study, all the patients received LMWH after revascularization, and none of them required reintervention, which leads to the possibility that heparinization prevents recurrent thrombosis and improves the rate of survival and limb salvage [12].

However, in our case, a patient, treated with therapeutic LMWH after Fogarty artery embolectomy catheter, had a mid-leg amputation for a necrotic lower. This may be explained by the patient's comorbidities and the delay of the revascularization.

7. Conclusion

COVID-19 can be associated with an increased risk of limb ischemia. Our cases and review of the literature reveal that health care providers should be aware of life-threatening thromboembolic events. So, we should discuss therapeutic anticoagulation and laboratory values such as D-dimer may help with the decision.

References

9. M Zhao, M Wang, J Zhang, J Ye, Y Xu, Z Wang, et al. Advances in


