

An extensive arterial thrombosis with lower limb ischemia in a COVID-19 patient: a case report.

Johary Andriamamonjisoa¹, Etienne RAKOTOMIJORO¹, Volatiana Andriananja¹, Mihaja Raberahona¹, Radonirina Lazasoa Andrianasolo², Rivonirina Andry Rakotoarivelo³, and MAMY RANDRIA⁴

¹University of Antananarivo Faculty of Medicine

²Endocrinology Department, Joseph Raseta Befelatanana University Hospital Center, Antananarivo, Madagascar

³University of fianarantsoa, Faculty of medicine, Departement of Infectious Diseases

⁴Centre Hospitalier Universitaire Befelatanana Antananarivo

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An extensive arterial thrombosis with lower limb ischemia in a COVID-19 patient: a case report.

Johary Andriamamonjisoa Andriamizanaka¹, Etienne Rakotomijoro², Volatiana Andriananja³, Mihaja Raberahona⁴, Radonirina Lazasoa Andrianasolo⁵, Rivonirina Andry Rakotoarivelo⁶, Jean de Dieu Randria Mamy⁷

ABSTRACT:

Background: The COVID-19 pandemic is responsible for huge morbidity and mortality throughout the world. Several serious complications of this disease have been reported. It can cause hypercoagulability, which may lead to venous and arterial thromboembolic diseases. This hypercoagulability state is also associated with high morbidity and mortality. Arterial thrombosis in COVID-19 is poorly described compared to venous thrombosis and pulmonary embolism. We report a case of an extensive arterial thrombosis leading to a limb ischemia with extremely high D-dimer in a COVID-19 patient.

Case presentation: A 69-year-old man was hospitalized for febrile dyspnea. He is a hypertensive and diabetic patient. On admission, pulse oxygen saturation was 72% on room air. He had cyanosis of the left foot up to the mid-thigh. The left pedal, posterior tibial, popliteal and femoral pulses were abolished. Chest CT scan was in favour of COVID-19. He has a high D-dimer level of 257 344 ng/ml. Arterial Echo-Doppler found an extensive intraluminal thrombus along the arterial axes of the left lower limb, completely obstructing them, starting from the primitive iliac artery just after its bifurcation with the aorta and extending distally (external iliac; common femoral; superficial femoral; popliteal; anterior tibial; posterior tibial; fibular and pedal). The patient was diagnosed with COVID-19 critical form, associated with ischemia of the left lower limb secondary to an extensive arterial thrombosis. He was receiving anticoagulation, and underwent surgical amputation of the ischemic limb. The patient survived the event; however, he was on long-term oxygen therapy at home.

Conclusions: Arterial thrombosis may occur during COVID-19 and may be responsible for peripheral or central ischemia aggravating morbidity and mortality. The occurrence of these events is related to the D-dimer value. Anticoagulation is an important part of the management of COVID-19, especially in severe forms in order to limit the occurrence of these thromboembolic diseases.

Key words: COVID-19, D-dimer, ischemia, arterial thrombosis, case report

Background:

COVID-19 is a leading cause of morbidity and mortality worldwide. Apart from the respiratory complications which are responsible for most of the deaths, several serious complications have been reported including compressive emphysema or acute pancreatitis. COVID-19 can also induce a hypercoagulable state, at the origin of venous and arterial thromboembolic events. This hypercoagulability is associated with high morbidity and mortality [1,2]. The literature mainly describes venous thromboembolic events and pulmonary embolisms [3,4]. Arterial thrombosis during COVID-19 is poorly described compared to venous thrombosis. According to literature, it can occur with a prevalence of 0.13% in a hospitalized patient who tested positive for COVID-19 and 0.19% in patients who tested negative [5]. We report a case of an extensive arterial thrombosis with extremely high D-dimer level that resulted in a lower limb ischemia in a COVID-19 patient.

Case presentation:

A 69-year-old man was hospitalized with febrile dyspnea at the military hospital of Antananarivo. He reported a close contact with a confirmed case of COVID-19 5 days before the onset of symptoms. His history included hypertension treated with Losartan 100mg per day, type 2 diabetes treated with Metformin 1500mg/day, alcoholism and smoking cessation for 10 years (9.5 pack-years). He has no known history of peripheral artery disease. For 13 days prior to his admission, he presented with a dry cough, shortness of breath at rest without orthopnea, fever, asthenia and anorexia. Two days before hospitalization, he felt a spontaneous severe pain with swelling of the left lower limb. Physical examination revealed a body mass index of 28.7 kg/m², a pulsed oxygen saturation of 72% on room air, a respiratory rate of 23 per minute, a high temperature of 38.9°C, a heart rate of 117 beats per minute, a blood pressure of 135/80 mmHg and bilateral clinical signs of pneumonia. He presented a cyanosis of the left foot up to the mid-thigh (Figure 1), a hypoesthesia of the left lower limb and the skin was cool. The left pedal, posterior tibial, popliteal and femoral pulses were abolished.

The nasopharyngeal swab for SARS-CoV-2 reverse transcriptase-polymerase chain reaction (rt-PCR) performed on admission was negative. The complete blood count showed a haemoglobin level of 13.3 g/dl (13.5-17.5 g/dl) a white blood cells count of 11.81 G/L (5-10 G/L) and a platelet count of 81 G/L (150-400 G/L). The C-reactive protein was 82.6 mg/L (<6 mg/l). The creatinine was 187 µmol/L (65.4-119.3 µmol/L). The blood sodium level was 141 mmol/L (135-145 mmol/l) and the blood potassium level was 4.9 mmol/L (3.6-5.2 mmol/l). The glycated haemoglobin was 7.5% (<6%). The D-dimer was 514 times the upper normal limit (220-500 ng/mL). The troponin was normal. The electrocardiogram showed a regular tachycardia with a heart rate of 103 bpm. Chest CT scan was in favour of COVID-19 showing ground glass images with 50-75% involvement, without pulmonary embolism (Figure 2). The arterial doppler ultrasound showed an extensive intraluminal thrombus along the arterial axes of the left lower limb, completely obstructing them, starting from the common iliac artery just after its bifurcation with the aorta and extending distally (external iliac, common femoral, superficial femoral, popliteal, anterior tibial, posterior tibial, fibular and pedal), without any detectable collateral circulation (Figure 3 a, b, c). The patient was diagnosed with a severe COVID-19 associated with acute ischemia of the whole left lower limb secondary to an extensive arterial thrombosis. He was receiving oxygen therapy with a high concentration oxygen mask at 15 L/min, corticosteroid therapy with intravenous dexamethasone (12 mg/day), subcutaneous therapeutic anticoagulation with enoxaparin at a curative dose (8000UI x2/day), oral antibiotic therapy with levofloxacin (1g/day) and insulin therapy (rapid-acting insulin 14UI x3/day and long-acting insulin 20 UI/day). The patient was transferred to the surgical ward due to aggravation of the ischemia with skin necrosis of extremities and underwent an amputation of the ischemic left lower limb. The post-operative follow-up was simple. The patient was discharged after 28 days of hospitalization and was under long-term oxygen therapy at home. At one month follow-up, he remained well and there was no recurrence of other ischemia.

Discussion and conclusion:

We report here a case of a hypertensive and diabetic patient presenting a severe form of COVID 19 associated

with an ischemia of the left lower limb with an extremely high d-dimer level.

High D-dimer value is associated with severe infection and high risk of thromboembolic events during COVID-19 [6]. Arterial occlusion can be life threatening or can lead to significant disabilities. Our patient had a history of hypertension, previous smoking and type 2 diabetes. According to the literature, these comorbidities are significantly associated with the occurrence of arterial thrombosis during COVID-19 [5]. He was diagnosed with a severe form of COVID-19 and presented at the same time an ischemia of the left lower limb secondary to an extensive thrombosis of several arteries in the left lower limb. Our patient had a D-dimer up to 514 times the upper normal level. The d-dimer level correlates with the severity of the disease and is a reliable prognostic marker of in-hospital mortality in those admitted with COVID-19 [6–8]. The risk of death is therefore high for our patient. In COVID-19, arterial thrombosis mainly involves the heart, the brain, the kidney and the bowels. There were only few reported cases of arterial thrombosis involving limbs including the left arm, the left leg, the right arm and the right leg [5]. However, our case involved the entire left lower limb (thigh, leg, foot).

Gold DD. et al. reported a series of cases of arterial thrombosis. The first case had a thrombosis of the two renal arteries, the superior mesenteric artery and the celiac trunk. The second case had a thrombosis of the aorta, the celiac trunk, hepatic and the splenic arteries. The third case had a cerebral, pulmonary, splenic and renal thrombosis. The fourth case had a thrombosis of the lung, the spleen and the kidney. The last case was a peripheral thrombosis with an occlusion of the radial and ulnar arteries [9]. All five patients had arterial occlusions that were life-threatening or disabling, and four of the five patients did not survive. Despite the severity of the COVID-19 and the arterial occlusion, our case had survived. However, the delay in the management led to a total obstruction of the artery causing ischemia which resulted in amputation. The outcome was unexpected given the severity of COVID-19 and the extensive arterial occlusions in a country like Madagascar with limited technical platform and resources.

One limitation associated with this case report is that we have not been able to perform any serology test for covid 19 to strengthen the diagnosis made by chest CT scan, due to unavailability of this test.

We report a case of an extensive peripheral arterial thrombus with an extremely high D-dimer during COVID-19. Arterial thrombosis can occur during COVID-19, causing peripheral or central ischemia with increased morbidity and mortality. The occurrence of these events is related to the D-dimer value [10]. Thus, this report underlines the potential role of anticoagulation in COVID-19 especially in severe forms and furthermore in patient with cardiovascular comorbidities, or in the case of a high D-dimer value in order to limit the occurrence of thromboembolic diseases.

List of abbreviations:

- COVID-19: coronavirus disease 2019
- SARS-CoV-2: severe acute respiratory syndrome-coronavirus-2
- ECG: electrocardiograph

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AAJ, RE, AV: Patient management, data collection and manuscript drafting

RM, ARL, RRA, RMJD: Manuscript revision

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Declarations

Ethical approval and consent to participate: not applicable.

Consent for publication : The patient was informed about the case report, why the case was peculiar and the authors' interest in publishing his case. The patient willingly gave informed consent to allow the authors to use the CT scan and arterial Doppler images for this case report. The patient's anonymity is well respected.

Competing interests: none.

Authors' information :

(1)Faculty of Medicine Antananarivo, Joseph Raseta Befelatanana University Hospital Antananarivo, Antananarivo 101, department of Infectious Diseases, Madagascar. (2)Faculty of Medicine Antananarivo, Joseph Raseta Befelatanana University Hospital Antananarivo, Antananarivo 101, department of Infectious Diseases, Madagascar. (3)Faculty of Medicine Antananarivo, Joseph Raseta Befelatanana University Hospital Antananarivo, Antananarivo 101, department of Infectious Diseases, Madagascar. (4)Faculty of Medicine Antananarivo, Joseph Raseta Befelatanana University Hospital Antananarivo, Antananarivo 101, department of Infectious Diseases, Madagascar. (5)Faculty of Medicine Antananarivo, Joseph Raseta Befelatanana University Hospital Antananarivo, Antananarivo 101, department of Infectious Diseases, Madagascar. (6)Faculty of Medicine, University of Fianarantsoa, University Hospital Tambohobe Fianarantsoa, Fianarantsoa 301, Madagascar. (7)Faculty of Medicine Antananarivo, Joseph Raseta Befelatanana University Hospital Antananarivo, Antananarivo 101, department of Infectious Diseases, Madagascar.

Legend of figures:

Figure 1: Photo of the patient's lower limbs showing the cyanosis from the left foot to the middle of the left thigh

Figure 2: Chest CT scan without injection of contrast medium, axial section showing multiple extensive ground-glass areas occupying 50-75% of the lung parenchyma, peripherally and centrally distributed, bilaterally subpleural, associated with fine intralobular reticulations giving a crazy paving appearance and areas of condensation especially in the posterior basal segments of the lower lobe bilaterally.

Figure 3 a: Arterial Doppler ultrasound of the arterial axes of the left lower limb showing an extensive intraluminal thrombus along the arterial axes of the left lower limb, totally obstructive, starting from the primitive iliac artery just after its bifurcation with the aorta and extending distally (external iliac; common femoral; superficial femoral; popliteal; anterior tibial; posterior tibial; fibular and pedal)

Figure 3 b, c: Arterial Doppler ultrasound, other view of the left lower limb arterial thrombosis

References :

- 1 . Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. *Intensive Care Med.* 2020;46: 1089–1098. doi:10.1007/s00134-020-06062-x
2. Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. *J Thromb Haemost JTH.* 2020;18: 1559–1561. doi:10.1111/jth.14849
3. Helms J, Severac F, Merdji H, Schenck M, Clere-Jehl R, Baldacini M, et al. Higher anticoagulation targets and risk of thrombotic events in severe COVID-19 patients: bi-center cohort study. *Ann Intensive Care.* 2021;11: 14. doi:10.1186/s13613-021-00809-5
4. Jenner WJ, Kanji R, Mirsadraee S, Gue YX, Price S, Prasad S, et al. Thrombotic complications in 2928 patients with COVID-19 treated in intensive care: a systematic review. *J Thromb Thrombolysis.* 2021;51:

595–607. doi:10.1007/s11239-021-02394-7

5. Guber N, Stewart L, Seo J, Kabrhel C, Nordenholz K, Camargo C, et al. Incidence and characteristics of arterial thromboemboli in patients with COVID-19. *Thromb J*. 2021;19: 104. doi:10.1186/s12959-021-00357-9
6. Yao Y, Cao J, Wang Q, Shi Q, Liu K, Luo Z, et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. *J Intensive Care*. 2020;8: 49. doi:10.1186/s40560-020-00466-z
7. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020;584: 430–436. doi:10.1038/s41586-020-2521-4
8. Ganesan R, Mahajan V, Singla K, Konar S, Samra T, Sundaram SK, et al. Mortality Prediction of COVID-19 Patients at Intensive Care Unit Admission. *Cureus*. 13: e19690. doi:10.7759/cureus.19690
9. Gold D, Kurd R, Einav S. Don't forget arterial thrombosis in patients with COVID-19: A case series. *Thromb Update*. 2021. doi:10.1016/j.tru.2021.100065
10. Garg K, Barfield ME, Pezold ML, Sadek M, Cayne NS, Lugo J, et al. Arterial thromboembolism associated with COVID-19 and elevated D-dimer levels. *J Vasc Surg Cases Innov Tech*. 2020 Jun 17;6(3):348–51.





