

# Splenoportal-mesenteric axis thrombosis and splenic artery occlusion as initial presentations of COVID-19 disease

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**Abstract.** – **OBJECTIVE:** Although pulmonary involvement represents the primary and most characteristic presentation of Sars-Cov-2 infection, due to its innate tropism for endothelium, it is also associated with systemic pro-coagulative changes and thromboses. This paper describes a COVID-19 atypical presentation with massive thrombotic occlusion of the splenoportal-mesenteric axis and the splenic artery in the absence of clinical or radiological manifestation of pulmonary involvement.

**PATIENTS AND METHODS:** Female patient, with no history of disease, trauma or fever in the last 30 days, was admitted to ER for persistent left subcostal pain. Laboratory exams, including inflammation, coagulation markers and Sars-CoV-2 serology, were requested. Whole-body CT with contrast media injection was performed.

**RESULTS:** Laboratory exams showed elevated reactive C-protein, bilirubin,  $\gamma$ -GT and D-dimer. Whole-body CT showed: splenic artery occlusion, thrombosis of splenic, mesenteric and portal veins with portal intra-hepatic branches ectasia, juxta-hilar portal cavernomatosis of probable acute onset (absence of signs of chronic hepatopathy and of varices), a hypodense area in the spleen indicating ischemic parenchymal suffering. The patient resulted positive for Sars-CoV-2 IgG, thus in the absence of typical clinics or pulmonary parenchymal abnormality at chest CT.

**CONCLUSIONS:** A case of acute venous thrombosis and arterial occlusion as primary manifestations of COVID-19.

*Key Words:*

COVID-19, Hypercoagulability, Thrombosis.

## Introduction

COVID-19 disease rapidly spread around the world and in March 2020, WHO declared the pandemic state<sup>1,2</sup>.

The virus is transmitted through respiratory droplets and enters target-cells through the Angiotensin-Converting Enzyme-2 (ACE-2), receptor particularly expressed in lung and in endothelium. The incubation lasts for 2-14 days, after which the symptomatic phase may appear with fever, coughing and short breath as most common presentations<sup>3</sup>.

Disease assessment and monitoring is mostly performed with chest CT that shows bilateral pulmonary abnormalities in  $\geq 75\%$  of cases. However, diagnosis is obtained with serological testing of Sars-Cov-2 DNA and of specific IgM and IgG<sup>3,4</sup>.

Although pulmonary involvement represents the primary and most characteristic presentation of the disease, Sars-Cov-2, due to its innate tropism for endothelial cells, demonstrated to cause systemic pro-coagulative changes and thrombotic events, as shown by the intense elevation of thrombosis markers such as D-dimer observed in patients with severe disease<sup>3</sup>.

This paper describes a case of COVID-19 atypical presentation with thrombotic occlusion of the splenoportal-mesenteric axis and acute occlusion of the splenic artery, in the absence of clinical and radiological signs of pulmonary disease.

## Patients and Methods

A female patient in her 70s was admitted to ER for a 7-days intense left subcostal pain par-

tially responding to oral paracetamol but rapidly recurrent, associated to absence of bowel movements for 8 days. The patient denied any history of fever in the past 30 days, no recent trauma, no gastro-intestinal or genital-urinary symptom and had no relevant pathological or surgical record. Vital parameters and glycemia were recorded. Clinical exam was obtained. Laboratory exams (haemachrome, cholangial-hepatic, coagulation and inflammation assets) were requested, and a blood gas analysis performed. A total body CT with contrast agent injection was then performed.

Based on the CT findings, the patient received an echocardiogram, an upper and lower limbs venous ultrasonography (US), Jak2/BCR/ABL dosing, thrombophilia screening (folic acid, B12 vitamin, LAC, Von Leiden polymorphisms, Factor II, coagulation C and S protein, APC resistance studies). She additionally received Sars-Cov-2 infection screening with two rhino-pharyngeal testing and 2019-n-COV IgM and IgG dosing, performed twice with chemo-luminescence technique.

## Results

Vital parameters showed temperature of 36.5°C, blood pressure 140/95 mmHg, cardiac frequency 80 bpm, oxygen saturation in ambient air of 99% and glycaemia of 106 mg/dL. Clinical exam showed tender abdomen with diffused pain at palpation, mostly elicited in the left superior-external quadrant. Laboratory exams showed neutrophilia ( $13.6 \times 10^3/\text{mmc}$ ), elevated reactive C Protein (10.8 mg/dL), hyperbilirubinemia (total 1.9 mg/dL, conjugated 0.71 mg/dL), hyper-alanine aminotransferase (ALT 39 U/L, AST 55 U/L), elevated  $\gamma$ -GT (52 U/L), alkaline phosphatase 176 U/L, lactic dehydrogenase 248 U/L, PT % 59, INR 1.30, APTT 43.40 sec, APTT ratio 1.40, fibrinogen 1307.00 mg/dL, D-dimer 4926.00 ng/mL. Blood gas analysis showed pH 7.52, PaCO<sub>2</sub> 30 mmHg, PaO<sub>2</sub> 99 mmHg, Hb and electrolytes in NR, HCO<sub>3</sub> 25.2 mmol/L and Lactates 0.8 mmol/L.

CT major findings:

- Complete occlusion of the splenic artery at its emergent from the tripod (Figure 1A).
- A non-homogeneously 3 cm hypodense area of parenchyma with non-homogeneous contrast enhancement localised at the inferior pole of the spleen, of probable ischemic aetiology (Figure 1B).
- Thrombosis of the extrahepatic and intrahepatic portal branches extending to the splenic and

superior/inferior mesenteric veins (with patency of intestinal perivisceral venous branches), these associated with portal juxta-hilar cavernomatosis of probable acute origin. No direct or indirect signs of chronic hepatopathy or gastro-esophageal varices (Figure 1C).

- No direct or indirect signs of intestinal ischemic sufferance, no intra-abdominal fluids (Figure 1D).
- No pulmonary parenchymal alterations (Figure 1E).

US exam was negative for deep venous thrombosis, Jak2/BCR/ABL dosing, thrombophilia screening resulted all negative. Sars-Cov-2 infection rhino-pharyngeal testing resulted negative, however, IgG dosing, resulted positive.

The echocardiogram showed no evidence of intra-cardiac thrombi, valve or muscle dysfunction, no shunts and normal dimensions of all chambers.

Based on the absence of signs of sufferance of the intestinal wall and of the liver and considering the limited extension of the ischemic alteration in the spleen, surgical and interventional radiology treatments were not indicated. The patient was admitted to the general surgery department where a therapeutic scheme with 8000 UI/die of low molecular heparin (LMWH).

## Discussion

The injury of the endothelium and the venous stasis represent two determining triggers for thrombus formation<sup>5</sup>. Similarly, systemic inflammation, induce the activation of pro-coagulative states, activate endothelial cells and predispose to thrombosis<sup>6</sup>.

SARS-Cov-2 infection not only induces the above-mentioned mechanisms but also, due to its innate tropism for endothelial cells, directly damages them and activates intravascular coagulation, predisposing to systemic thrombotic alterations<sup>3,7</sup>.

Portal thrombosis with cavernomatosis most frequently develops secondary to chronic hepatopathies due to the congestion or compression of the intra-hepatic portal branches induced by that may induce thrombosis of the splenoportal axis and the development of anomalous and serpiginous accessory drainage routs<sup>8</sup>. Thus, the presented patient had no clinical or radiological sign of chronic hepatopathy and/or cardiac-induced hepatopathy.

COVID-19 most frequently presents with upper airways and pulmonary symptoms but the patho-

logical involvement of different organs, especially the vascular one, are described<sup>9</sup>. Although less frequent, disease presentation with severe respiratory and vascular abdominal alterations is described in the literature<sup>10,11</sup>. In these case reports vascular thrombotic pathologies occurred in patients already hospitalised for severe COVID-19.

Thrombotic manifestations in the absence of either clinical or radiological sign of pulmonary involvement, as described in our case, are a very uncommon clinical presentation. The patient was admitted to our ER department without any referred respiratory symptoms or fever in the previous 30 days. These different clinical presentations could have warded off a prompt diagnosis of COVID-19, exposing healthcare providers to a high infection risk.

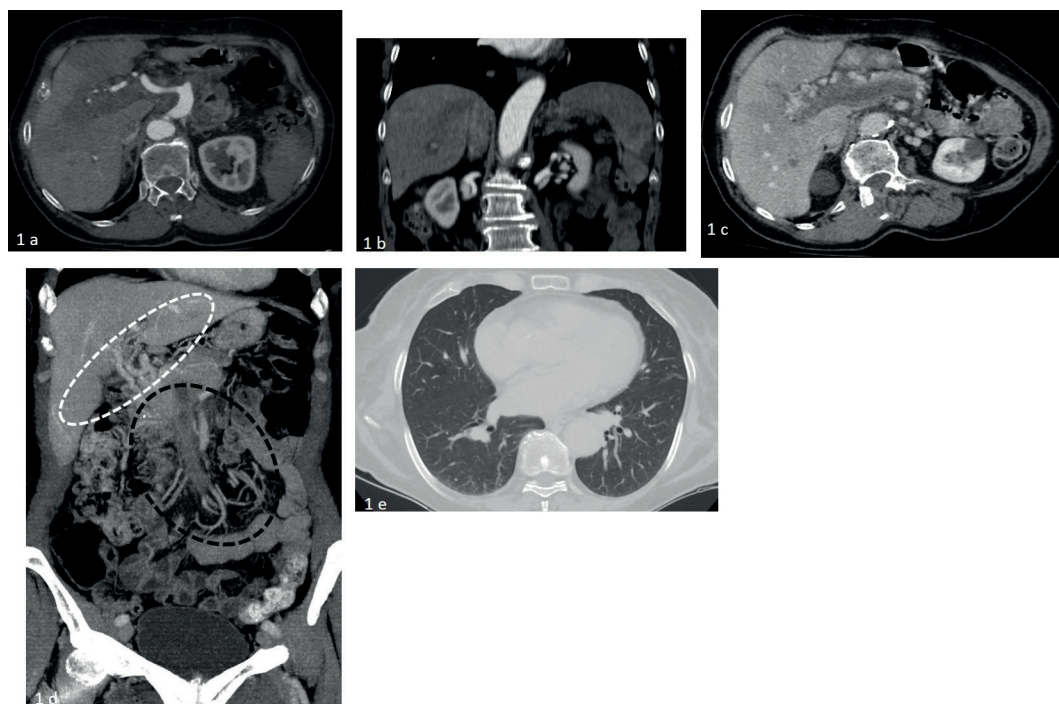
Based on the increasing and consisting evidence on Sars-Cov-2, endothelial tropism and correlation of the infection with systemic thrombotic events, together with the absence of evidence of hepatopathy, it could be hypothesised that the thrombosis of the spleno-portomesenteric

axis with cavernous transformation of the portal vein observed in the patient is a manifestation of COVID-19 disease.

Concerning the thrombosis of the splenic artery, a pro-thrombotic activity of Sars-CoV-2 on arterial systems has been described<sup>11</sup>. Moreover, all potential causes of arterial thromboembolism had been excluded and also, splenic artery thrombosis is an uncommon site of thromboembolism and its embolic aetiology can be considered improbable: therefore, we can speculate the arterial occlusion to be linked to COVID-19 disease.

## Conclusions

To conclude, in case of thrombotic venous and arterial disease in patients with no detectable predisposing factor, it is important to evaluate the possibility of Sars-CoV-2 infection and serologically exclude it, in order to safeguard caregivers and correctly address treatment plans.



**Figure 1.** Female, 70s, intense left subcostal pain. Complete occlusion of the splenic artery at its emergent from the tripod (A). A non-homogeneously 3 cm hypodense area of parenchyma with equally non-homogeneous contrast enhancement localised at the inferior pole of the spleen, of probable ischemic aetiology (B). Thrombosis of the extrahepatic and intrahepatic portal branches associated with portal juxta-hilar cavernomatosis no direct or indirect signs of chronic hepatopathy, intestinal ischemic sufferance and intra-abdominal fluids (C). Thrombosis of the extrahepatic and intrahepatic portal branches associated with portal juxta-hilar cavernomatosis (*white circle*); thrombosis extending to the splenic (*arrow*) and to superior/inferior mesenteric veins with patency of intestinal perivisceral venous branches (*black circle*); no direct or indirect signs of chronic hepatopathy, intestinal ischemic sufferance and intra-abdominal fluids (D). No pulmonary parenchymal alterations detectable (E).

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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