

## Paradoxical embolism subsequently pneumonia from the 2019 coronavirus disease. A Case report

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### ABSTRACT

In December 2019, the 2019 coronavirus disease, produced by the type 2 coronavirus causing severe acute respiratory syndrome, was identified for the first time. Increasingly investigations are reporting the occurrence of systemic complications, some of them in a mediate or even late phase of the disease, when the patient has left the hospital. A 30-year-old healthy female patient who came to the hospital fourteen days after being discharged due to viral pneumonia secondary to SARS-COV-2. She presented with intense pain and distal coldness in the right lower limb, dyspnea at rest and pain in the left hypochondrium. The diagnosis at discharge was paradoxical pulmonary thromboembolism. Thrombotic complications should be taken into account in all convalescent COVID-19 patients. An early diagnosis is important to establish anticoagulation.

**Keywords:** Coronavirus; Paradoxical embolism; Pulmonary embolism; Pneumonia.

In December 2019, the coronavirus disease 2019 (COVID-19), caused by the type 2 coronavirus that causes severe acute respiratory syndrome (SARS-COV-2), was identified for the first time in Wuhan city, capital of Hubei Province, Republic of China<sup>1</sup>. The main characteristic of patients with severe disease due to COVID-19, is the development of an acute lung injury<sup>2</sup>. However, increasingly investigations report the occurrence of systemic complications, some of them in a mediate and even late phase of the disease, when the patient has left the hospital<sup>3,4</sup>.

In the most severe form of COVID-19 disease, a hyperinflammatory response has been demonstrated, which contributes significantly to the pathophysiology

of the disease, together with multifactorial endothelial dysfunction and prothrombotic state.

For this reason, in critically ill patients with an exaggerated increase in inflammatory markers (IL-6, ferritin, TNF, D-dimer), corticosteroids and low molecular weight heparin (LMWH) have been used empirically at therapeutic doses. However, there is still no confirmation of effective treatment strategy, and the risk / benefit ratio of these empirical treatments is still unclear<sup>4,5</sup>.

Martínez Chamorro et al<sup>4</sup> reported in their study on thromboembolism in patients admitted for COVID-19 a prevalence of 26 % while Klok et al<sup>5</sup> demonstrated a prevalence of thrombotic complications in 31 % of their sample.

In 1877 Cohnheim described and defined paradoxical embolism as the passage of a venous thrombus into the systemic circulation through a right-to-left cardiac shunt through a patent ductus, atrial and/or inter-ventricular communications<sup>6</sup>.

The prevalence of paradoxical embolism is difficult to estimate, since the recurrence of its occurrence there must be an anatomical defect in the heart chambers that allows the passage of the embolus from the right chambers to the left. Prothrombotic diseases in patients with structural cardiac abnormalities increase the chances of suffering a paradoxical embolism<sup>7</sup>.

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### Conflicts of interest

The authors declare no conflicts of interest.

### CASE REPORT

A 30-year-old female patient, white skin color, with an apparent personal health history that fourteen days after

being discharged for viral pneumonia secondary to SARS-COV-2 suddenly began with intense pain and distal coldness in the lower limb right, associated with dyspnea at rest, persistent dry cough, aerogastria, palpitations and discomfort in the left upper quadrant. For this reason, she went to the Emergency Service of the Carlos J. Finlay Hospital. The patient did not report toxic habits or a history of recent trauma.

During her admission for pneumonia, the patient only had a fever of 38 °C, associated with a sporadic dry cough. She was tested for coronavirus antigen and Polymerase Chain Reaction (PCR) in real time, which confirmed her diagnosis. Physical examination revealed a decrease in vesicular murmur at the right lung base without any other alteration.

The tests carried out showed: hematocrit: 0.42; leukocytes:  $8.5 \times 10^9$  /L; neutrophils: 65 %; lymphocytes: 35 %; platelets:  $293 \times 10^9$ /L; erythrocyte sedimentation: 18 mm/h and the rest of the tests within normal values. The chest radiograph performed showed the presence of radiopaque lesions, with a reticular appearance in the right hemithorax, with greater intensity towards the pulmonary hilum.

Treatment with interferon alfa 2b was imposed at a rate of 3 million units, intramuscularly 3 times a week, and azithromycin (tab 500 mg) one tablet a day. She did not receive anticoagulation. After seven days of hospital admission, PCR was repeated for coronavirus, with negative result and it was decided to discharge the patient, finding that she was asymptomatic and in good general condition.

Before this second admission, moist and normal-colored mucous membranes were verified on physical examination; non-infiltrated subcutaneous cellular tissue. Respiratory system: superficial polypnea, expiratory rate 29 breaths per minute, conserved vesicular murmur, the presence of rales was not found. Rhythmic heart sounds, heart rate 117 beats per minute, blood pressure 130/80 mmHg. The presence of a murmur or friction was not found. The examination of the peripheral vascular system showed distal coldness of the right lower limb, cyanosis and absence of the pedio, posterior tibial and right popliteal pulses. The limb ischemia time was less than 30 minutes, and the alterations in the affected limb were reestablished spontaneously; the rest of the physical examination without alterations.

Complementary tests were performed that yielded the following results: hematocrit: 0.42; leukocytes:  $5.8 \times 10^9$ /L; neutrophils: 68 %; lymphocytes: 32 %; platelets:  $240 \times 10^9$  /L; erythrocyte sedimentation (ESR): 64 mm/h.

Electrocardiogram: Sinus rhythm. Heart rate 120. No detected an alteration.

D-dimer: positive.

Lower limb arterial and venous Doppler: both arterial axes were explored in the iliac, femoral, popliteal,

posterior tibial and pediatric sectors, observing permeable vessels of normal caliber and the presence of negative diastoles. The iliac, femoral and pedic venous axes were explored, observing collapsible vessels, with a good increase in flow at distal compression.

Echocardiogram: contractile function of the preserved left ventricle. Discretely dilated and hyperdynamic right ventricle. No intracavitary mass or pericardial effusion, competent valves, aneurysm in the lower portion of the interatrialseptum of 4 mm with a left-right shunt. Fenestrated atrial septal defect. (Figure 1).

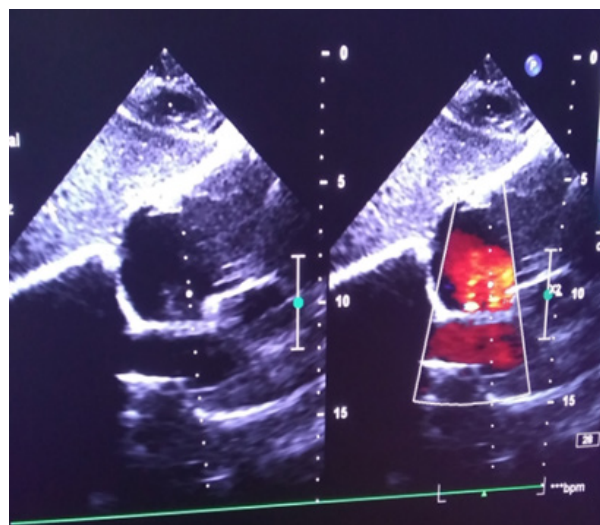


Figure 1. Transthoracic echocardiogram. A fenestrated atrial septal defect is observed.

Simple computed tomography of the chest: axial cuts were made at 5 mm. Ground glass images were observed at the level of the apicoposterior segment of the left upper lobe. A hyperdense image was visualized with densities ranging between -48 and -53 HU in a cottony shape with well-defined contours, adjacent to the great fissure of the right inferring lobe that corresponds to a vascular structure. (Figure 2). No alterations of the mediastinal structures were observed. Presence of a 39 x 89 x 57 mm hypocaptant image in splenic parenchyma, towards the superior pole and adjacent to the left hemidiaphragm that impresses with thin septa, in relation to splenic hematoma (Figure 3).

Immunological study: antinuclear antibodies and negative antiphospholipid antibodies.

Treatment with low molecular weight heparin (0.6 units of fraxiheparin per day subcutaneously), pentoxifylline (600 mg per day intravenously) and general measures was decided. A conservative and expectant treatment was chosen with respect to the splenic hematoma. The patient had a favorable evolution and it was decided to discharge after 14 days with treatment with fraxiheparin, a vial of

0.6 units per day subcutaneously for three months. She continues to progress satisfactorily at her home, without respiratory or peripheral vascular manifestations. Periodic ultrasound follow-up of the splenic hematoma shows a decrease in its size.



Figure 2. Simple chest tomography. Image suggestive of pulmonary embolism.

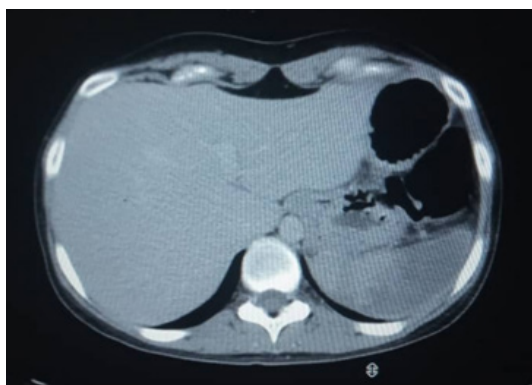


Figure 3. Simple abdominal tomography. Image suggestive of splenic hematoma.

## DISCUSSION

Thromboembolic complications in the course of coronavirus infection are one of the variables to take into account in the course of the disease; both in the acute phase and the late phase, once the patient returns to her home.

COVID-19 patients are at high risk for arterial and venous thrombotic occlusions. Pulmonary histopathology often reveals fibrin-based occlusions in the small blood vessels of patients who succumb to the disease. One of the explanations given so far is that pathogenic antibodies that target phospholipids and phospholipid-binding proteins (aPL antibodies) have been detected in case series of patients with COVID-19<sup>8,9</sup>.

In a recent article in the Netherlands for the journal *Thrombosis Research*, it was noted that 31 % of 184 patients suffered thrombotic complications, a

figure that the researchers described as remarkably high, even though extreme consequences such as amputation are rare<sup>5</sup>.

The presence of hematomas at different levels has also been reported: deep muscular, retroperitoneal, splenic, subdural<sup>10,11,12</sup>. In the particular case of this patient, it was secondary to splenic embolism.

Paranjpe I et al<sup>13</sup>, demonstrated in their study greater survival in patients treated with therapeutic doses of anticoagulation. However, the data collected so far do not provide sufficient clarity on anticoagulation in discharged patients, especially in those in whom no complications were found during admission. Another issue would be related to the time required for anticoagulation<sup>14</sup>.

The patient who is being described here, had several episodes of embolic events at different levels of the economy: pulmonary embolism, splenic embolism and acute arterial insufficiency, equally embolic in nature. This forced her attending physicians to rule out the possibility of paradoxical embolism, which it was demonstrated in the echocardiogram, in the presence of an atrial septal defect. This malformation was not known to the patient.

Physiopathologically, the existence of pulmonary hypertension is necessary to allow the appearance of a right-left shunt; it can be transitory and is not always objectively verified. This hypertension is frequently caused by pulmonary thromboembolism<sup>15</sup>.

The definitive diagnosis of paradoxical embolism can only be made in those exceptional cases in which a thrombus is observed through a septal defect during the ultrasound study. However, the fulfillment of a series of criteria is admitted as a diagnosis: systemic arterial embolism, in the absence of atrial fibrillation, from an embolic source located in the left heart chambers or in a proximal arterial bed; right-left short circuit at any level; and venous thrombosis and / or pulmonary embolism<sup>15</sup>.

The review of the medical literature has revealed patients who have suffered embolic phenomena of a paradoxical nature, in the course of an infection by SARS-CoV-2<sup>16</sup>. The common denominators in these patients have been the existence of a structural heart condition and a prothrombotic state.

## CONCLUSIONS

Pulmonary embolism is an acute complication with a high risk of death. A high degree of suspicion is required for its diagnosis. For this reason, thrombotic complications must be taken into account in all convalescent COVID-19 patients. An early diagnosis is important to establish anticoagulation and measures to save the life of the patient.

## AUTHORSHIP:

ABC y YRR: conceptualization, data curation, formal analysis, research, in the provision of resources and in writing - review and editing of the work.

JDF: research, in the writing - revision and editing of the work.

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## Embolismo paradójico tras neumonía por la enfermedad por coronavirus de 2019. Informe de un caso

### RESUMEN

En diciembre de 2019 se identificó por primera vez la enfermedad por coronavirus de 2019, producida por el coronavirus de tipo 2 causante del síndrome respiratorio agudo severo. Son cada vez más las investigaciones que reportan la ocurrencia de complicaciones sistémicas, algunas de ellas en una fase mediata e incluso tardía de la enfermedad. Se presenta el caso de una paciente femenina de 30 años de edad, aparentemente sana, que acudió al hospital catorce días después de haber sido egresada por neumonía viral secundaria a SARS-CoV-2. La paciente aquejaba dolor intenso y frialdad distal en el miembro inferior derecho, disnea en reposo y dolor en hipocondrio izquierdo por lo cual fue ingresada para estudio, confirmándose el diagnóstico de embolismo pulmonar paradójico. Las complicaciones trombóticas deben tenerse en cuenta en todos los pacientes convalecientes de COVID-19. Un diagnóstico precoz es importante para instaurar la anticoagulación.

**Palabras Clave:** Coronavirus; Embolia paradójica; Embolia pulmonar; Neumonía.



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