Acute Coronary Syndrome Followed by Pulmonary Thromboembolism and Identification of a Large Fixed Thrombus between Atria in a Patient with Severe COVID-19: A Case Report

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Introduction

Patent foramen ovale (PFO) is a relatively frequent congenital heart defect; however, the identification of large thrombi between the atria through a PFO is a rare condition.\(^1\) When visualized, they represent a major clinical challenge and require emergency treatment.\(^2\)

The severity of this condition becomes even more accentuated when associated with other thrombotic events, such as pulmonary embolism.\(^3\) In turn, these events may have their genesis in hyperinflammatory states with high thrombogenic and angiopathic potential, as in the case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.\(^4\)

This study reports a rare case of a large fixed thrombus between the atria in a patient with severe condition caused by COVID-19, associated with the diagnosis of pulmonary embolism, which occurred days after an acute coronary syndrome (ACS) event.

Case description

We report the case of a 69-year-old female patient with grade III obesity, history of hypertension, hypothyroidism, and chronic venous insufficiency. On the sixth day of COVID-19 symptoms, the patient was hospitalized due to dyspnea and desaturation. At that time, isolation, bed rest, prophylactic anticoagulation with enoxaparin, supplemental oxygen, and non-invasive ventilatory support were required.

On the sixteenth day of evolution, the patient presented sudden-onset chest pain with tightness, radiating to the left upper limb, associated with sudden worsening of dyspnea. The electrocardiogram revealed an ST-segment elevation in the inferior wall, compatible with evolving acute myocardial infarction. The patient was referred to a tertiary hospital for diagnostic coronary angiography, which was performed more than 12 hours after the onset of symptoms, due to persistent chest pain, dyspnea and dependence on oxygen therapy. Coronary angiography showed tortuosity of the proximal segment of the right coronary artery (RCA) associated with a subocclusive stenosis of its middle segment, with an image suggestive of intracoronary thrombus (Figure 1A, 1B). No other coronary injury was observed. Primary angioplasty was carried out with drug-eluting stent implantation in the RCA, with satisfactory clinical and angiographic results (Figure 1C).

The patient was maintained on dual antiplatelet therapy with acetylsalicylic acid (ASA) and clopidogrel. On the day after angioplasty, she underwent a transthoracic echocardiogram that showed preserved cardiac chambers, left ventricular inferior wall hypokinesia, and preserved global ventricular systolic function. Moreover, the presence of a hypoechoic image with hypermobility in the left atrial cavity, measured at 60 mm × 10 mm, extending to the left ventricle, and a hypoechoic image with hypermobility in the right atrial cavity, measured at 55 mm × 10 mm, extending to the right ventricle were identified (Figure 2, Figure 3A, Video 1, Video 2), both suggestive of large intracavitary thrombi. In the diagnostic complementation by transesophageal echocardiography, a large filament image was confirmed, straddling the PFO, with mobile segments in the right and left atria (Video 3, Video 4, Video 5). No signs of pulmonary hypertension or right chamber overload suggestive of pulmonary embolism were identified.

Due to the risk of thrombus fragmentation and possible pulmonary or arterial embolization, the option of fibrinolysis was not considered. Once the characteristics and dimensions of the thrombus, the risk of pulmonary and systemic embolism, the recent infection status, the use of dual antiplatelet therapy and the increased risk of bleeding were known, surgical embolectomy was scheduled for the following days. Full anticoagulation with subcutaneous enoxaparin was initiated, and ASA was maintained.

In order to perform the embolectomy surgery, we opted to use tiroliban instead of clopidogrel, maintaining the triple therapy with enoxaparin, ASA, and tiroliban for 5 days before surgery. However, on the day immediately before surgery, a new control transthoracic echocardiogram showed that the interatrial thrombus was no longer present (Figure 3B). The presence of PFO was visualized, without associated thrombi, with left-right shunt. In view of this finding, surgical embolectomy was suspended.

Keywords

Patent Oval Foramen; Pulmonary Embolism; Case Reports

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To investigate possible thrombus fragmentation and secondary embolization, the patient underwent a pulmonary artery computed tomography angiography with iodinated contrast in cross-section. The exam demonstrated filling defects in the left pulmonary artery trunk and in segmental arterial branches to the left lower lobe, suggestive of acute pulmonary thromboembolism (Figure 4), in addition to lung parenchyma with sequelae of COVID-19. Carotid and venous Doppler results of lower limbs did not show significant changes.

Due to complete remission of the thrombus associated with PFO and clinical compensation, the patient was discharged from the hospital on day 33 of COVID-19 diagnosis, without requiring oxygen. Triple therapy (ASA, clopidogrel, and rivaroxaban) was indicated for 30 days due
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Videos 1 and 2 – Transthoracic echocardiogram with hypoechoic image with hypermobility in the left and right atrial cavity extending to the left and right ventricles, respectively.
- Link video 1: http://abcimaging.org/supplementary-material/2023/3601/ABC 351_RC_Vídeo1.mp4
- Link video 2: http://abcimaging.org/supplementary-material/2023/3601/ABC 351_RC_Vídeo2.mp4

Videos 3, 4 and 5 – Transesophageal echocardiography with hypoechoic large filament image, straddling the PFO, with mobile segments in the right and left atria.
- Link video 5: http://abcimaging.org/supplementary-material/2023/3601/ABC 351_RC_Vídeo5.mp4
to the high thrombotic risk, in addition to beta-blocker and statin therapy for coronary artery disease. After this period, ASA was suspended, and rivaroxaban and clopidogrel were administered for at least another 6 months, to optimize the risk-benefit ratio of prophylaxis of thromboembolic events versus prevention of bleeding events.

Discussion

The case reported here exemplifies an association between COVID-19 and ACS, already observed in some patients in recent years. Notably, it is not possible to state whether ACS occurred due to the classic rupture of an atherosclerotic plaque in the RCA or due to an embolus originating from the thrombus through the PFO, identified one day after the coronary event. Numerous recent reports in the literature indicate that, even without a previous atherosclerotic event, the pro-inflammatory and prothrombotic state related to COVID-19 may act as triggering factors for coronary thrombosis.

The increased metabolic demand caused by a viral infection can induce hypoxemia, hypotension, instability of atherosclerotic plaques, or some stress on the vascular system, thereby leading to the development of an occlusive thrombus and, consequently, ACS. Furthermore, the inflammatory injury caused by SARS-CoV-2 in vascular and cardiac cells is also capable of causing ischemia or myocardial infarction.

Another previously documented hypothesis is related to coagulation abnormalities, including increased prothrombin time, elevated D-dimer levels, platelet activation, and endothelial dysfunction during severe cases of COVID-19. This scenario favors thrombogenesis and corroborates the occurrence of thromboembolic complications. Besides that, immobilization secondary to prolonged hospitalization also contributes to the hypercoagulable state, given the thrombogenic potential of blood stasis. Additionally, obesity and chronic venous insufficiency are also risk factors for the occurrence of thromboembolic events, especially in patients with PFO.

Another relevant aspect was the visualization of a thrombus trapped in the PFO during the transthoracic echocardiogram, which is a rare event. Its identification requires immediate and timely treatment, especially due to the possible outcome of pulmonary or paradoxical systemic embolism. If that occurs, the brain is the most frequently affected organ, followed by the coronary arteries. It is not possible to state whether the identified interatrial thrombus was formed from the progression of a thrombus formed at the site or whether it was secondary to the expansion of an embolus from the lower limb or pelvis to the pulmonary artery, eventually “captured” by the PFO.

It is noteworthy that the transit of the thrombus in the interatrial septum, through the PFO, occurs when right atrial pressure exceeds left atrial pressure. This can happen in cases of acute pulmonary embolism and pulmonary hypertension. In this case, the patient underwent an angiotomography of the pulmonary arteries, which showed filling failures compatible with pulmonary thromboembolism, but it was not possible to confirm the date of its occurrence.

Treatment strategy of thrombus in transit is challenging and controversial, but three possible approaches include anticoagulation, fibrinolysis or cardiac surgery, which have particular benefits and risks. It is worth emphasizing that anticoagulation alone is primarily used in patients with comorbidities or patients who refuse invasive therapy.

Fibrinolysis should be considered in hemodynamically unstable patients with high surgical risk. In view of the stability of the patient, this therapeutic option was not considered. Furthermore, this approach may cause thrombus fragmentation with subsequent pulmonary and/or systemic embolization.

Currently, the treatment associated with a lower overall incidence of post-therapy embolic events and lower mortality is cardiac surgery for thrombus extraction. The recommended treatment is surgical embolectomy with exploration of the right heart and closure of the PFO using cardiopulmonary bypass. This was the conduct of choice for the patient in the reported case. However, surprisingly, the prescribed pre-surgical drug therapy (ASA, enoxaparin, and tiroliban for 5 days) resulted in complete disappearance of the thrombus.

Figure 4 – Pulmonary artery CT angiography. A: Filling defects in segmental arterial branches to the left lower lobe; B: Filling defects in the left pulmonary artery trunk.
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Considering the disappearance of the image of the interatrial thrombus and a possible pulmonary and systemic embolization, carotid, vertebral, and lower limb Doppler scans were performed, with normal results. Nevertheless, an angiotomography of the pulmonary arteries revealed an acute pulmonary thromboembolism. It is not possible to state whether the patient had already had an episode of pulmonary embolism before the occurrence of ACS. On the one hand, the previous occurrence of pulmonary thromboembolism could facilitate the understanding of the thrombus in transit through a PFO due to the increase in right atrial pressure. However, the absence of signs of pulmonary hypertension and right chamber overload on the first echocardiogram makes it difficult to defend this thesis to explain the pathophysiological mechanism. Thus, the occurrence of pulmonary embolism as a consequence of the dissolution of the interatrial thrombus through drug therapy used seems more plausible.

The uniqueness of the case reported, as a limitation of the study, makes it difficult to generalize the results and conclusions obtained in our analysis; furthermore, it supports the replication of the procedures used.

Author Contributions
Conception and design of the research and acquisition of data: Carrijo AMM, Brito VP, Santos GA, Silva SGT; analysis and interpretation of the data and writing of the manuscript: Carrijo AMM, Brito VP, Santos GA, Silva SGT, O’Connell JL; critical revision of the manuscript for intellectual content: O’Connell JL.

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This study was approved by the Ethics Committee of the Universidade Federal de Uberlândia under the protocol number 5.455.568. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References