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Three Cases of Severe SARS-CoV 2 Pneumonia Complicated by Combined Venous and Arterial Thrombotic Events

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Abstract

Several studies suggested that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is associated with a hypercoagulable state leading to multisystem organ dysfunction. The present article describes three cases of patients with SARS-Cov-2 pneumonia complicated by venous and arterial thromboembolism. Case1 is a 51 year-old-man not vaccinated with severe SARS-Cov-2 pneumonia who developed extensive arterial thromboses and pulmonary embolism after few days from symptoms onset. Laboratory panel at hospital admission showed sign of ongoing inflammation and a severe Hypercoagulable state. Case2 is a 58 year-old-man not vaccinated at low cardiovascular risk with severe SARS-Cov-2 pneumonia complicated by anterior STEMI due to acute thrombotic occlusion of left coronary artery and massive bilateral pulmonary thromboembolism. Subsequently the patient presented an acute ischemic stroke despite being treated with triple antithrombotic therapy low molecular weight heparin (LMWH), aspirin and clopidogrel. Case 3 is a 75 year-old man with an history of arterial hypertension that developed severe SARS-Cov-2 bilateral pneumonia. Doppler ultrasound of lower limb veins showed deep vein thrombosis of right main femoral vein. CT angiography of the chest ruled out sign of pulmonary embolization and underlined the presence of thrombus in the aortic arch. Physicians should be aware of these complications and remain vigilant for signs of VTE and ATE in the context of the current

Kew Words: arterial thromboembolic events; SARS-COV-2 pneumonia; venous thromboembolic events

Learning points

In Covid-19 we need to be aware of thromboembolic events in the healing phase of the disease. Patients with Covid-19 may benefit from long-term anticoaugulation.

Introduction

Several case reports [1-2] have demonstrated that venous thromboembolic events (VTEs) are prevalent in individuals hospitalized with SARS-Cov-2 pneumonia.

Few recent researches [3-5] have shown an increased incidence of arterial thromboembolic events in these patients, implying that systemic inflammation, long-established risk factors for VTE, as well as possible endothelial dysfunction predispose patients with severe SARS–CoV2 pneumonia to VTE and arterial thromboembolic events (ATE). Here, we describe three cases of male patients without pathological conditions who developed a severe form of SARS–CoV2 pneumonia complicated both by VTE and ATE.

Case Presentation

Patient 1

A 51-year-old male returned from Equador with no prior SARS-COV2 vaccinations and no history of cardiovascular disease presented to the Emergency Department/ED complaining of dyspnea and fever. The cardiac exam was unremarkable. A 12-lead electrocardiogram revealed sinus tachycardia with incomplete right bundle brunch. On admission, D-dimer was 28470 ng/ml (normal range 0-500 ng/ml) and serum C-reactive protein was 14.49 mg/dl (normal range 0-0.5 mg/dl). The nasofaringeal swab for SARS COV 2 was positive with subsequent genomic sequentation that validated the presence of equadoriant variant. Transtoracic echocardiography TTE revealed a left ventricular ejection fraction/LVEF of 55%, right ventricle enlargement (telediastolic diameter/DTD 42 mm), and two thrombotic stratifications spanning the right ventricle's apex and right

atrium (dimensions of 3 cm and 1 cm, respectively). Thoracic CT revealed bilateral interstitial pneumonia (visual score of 60%, figure n. 1a), and angio sequences confirmed the existence of right ventricular and atrial thrombi, as well as additional thrombotic apposition at the level of aortic istmus (figure n. 1b).

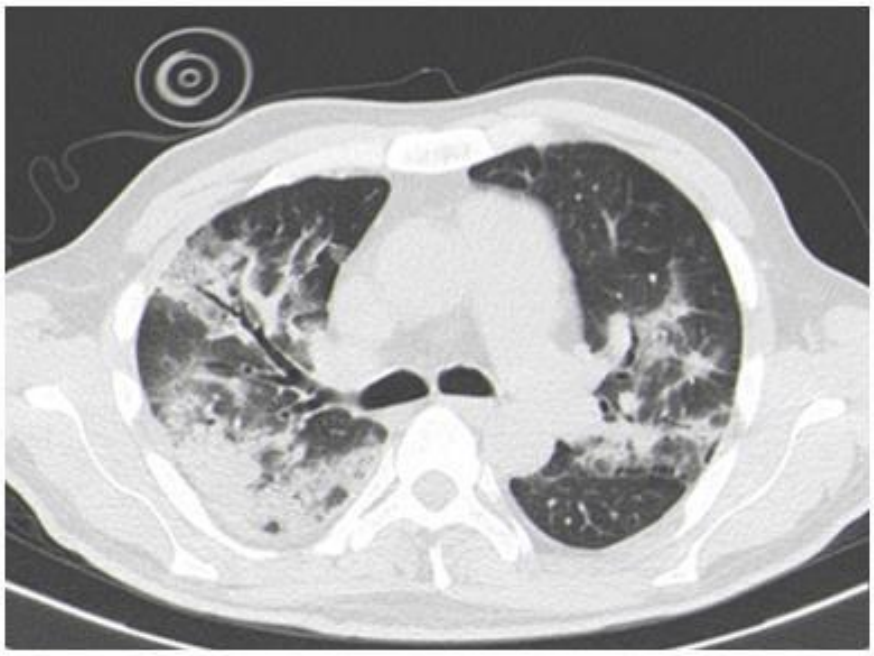

Figure 1a: HRCT at the time of pulmonary embolism.

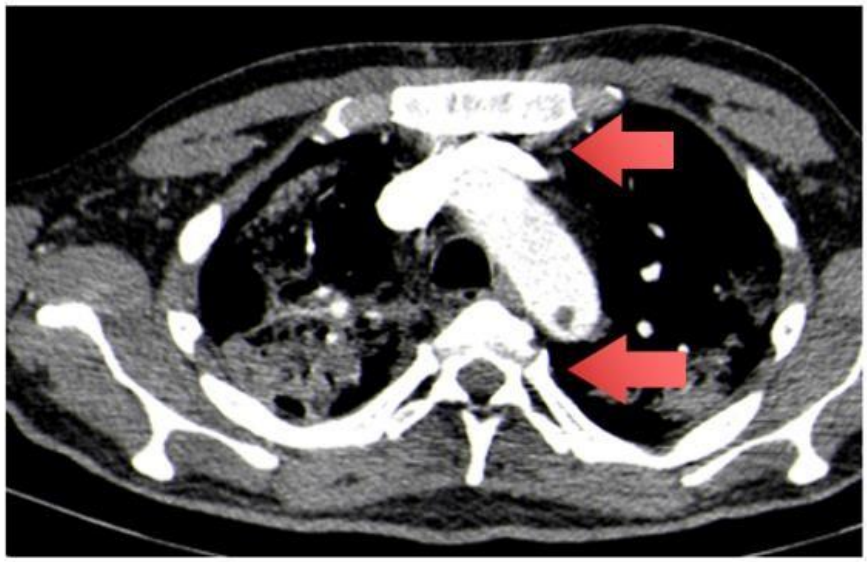

Figure 1b: Angio-CT showing thrombotic apposition at the level of aortic istmus

Due to the low risk of neurological embolization of aortic thrombus, the cardiac surgeon ruled out any invasive procedures. As a result, the patient was treated in the Intensive Care Unit/ICU with intravenous unfractionated heparin/UFH and a large dosage of steroids. During the hospitalization, the patient's ventilatory parameters progressively deteriorated, and he was intubated and pronated. Aspergillus was found in a broncoalveolar lavage/BAL. Unfortunately after few days the patient died.

Patient 2

A 58-year-old male with no prior SARS-COV2 vaccination and no history of cardiovascular illness presented to the emergency department with chest discomfort and dyspnea. The nasofaringeal swab tested positive for SARS COV 2, and further genomic sequencing confirmed the presence of the delta variant. A 12-lead electrocardiogram revealed anterior ST elevation consistent with STEMI. Coronary angiography revealed acute thrombotic occlusion of the left coronary artery/LAD (figure n. 2a), which was successfully treated by primary coronary angioplasty and stent implantation (Synergy 3,5 x 32 mm @ 18 atm). The final angiography was suboptimal because of a substantial thrombotic burden in the distal LAD with TIMI 0

flow. Across the procedure, a glycpprotein Iib/IIa inhibitor (tirofiban) and a loading dose of ticagrelor were provided. TTE revealed a 35% LVEF with apical, lateral, and anterior wall akinesia in the medio-distal segments in the presence of biatrial thrombotic apposition. Additionally, the patient received intravenous UFH and was intubated as a result of acute respiratory syndrome/ARDS. Thoracic computed tomography demonstrated bilateral interstitial pneumonia (visual score of 70%), and angiograms revealed severe bilateral pulmonary thromboembolism, indicating the presence of additional thrombotic apposition at the level of the left atrium and left pulmonary veins (figure n. 2b).

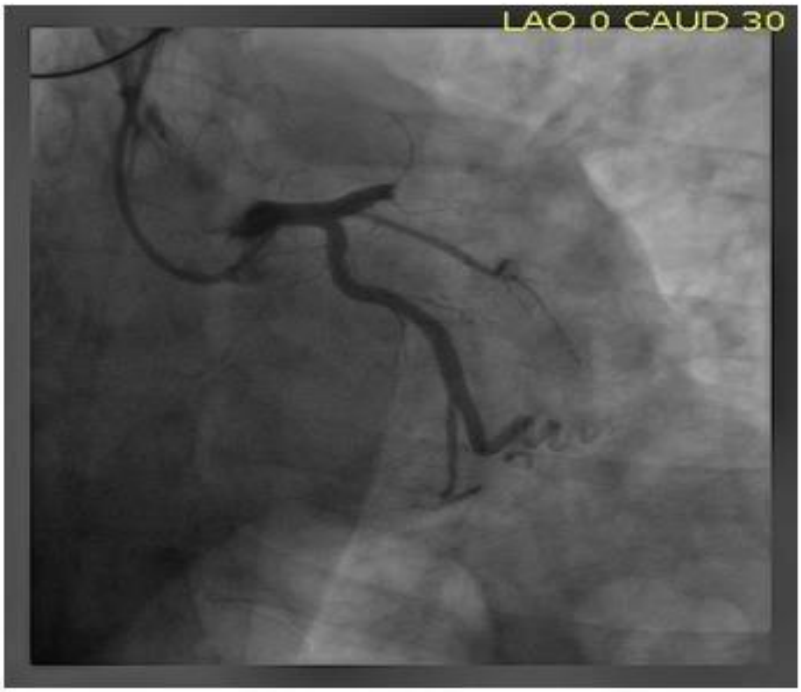

Figure 2a : Coronary Angiography showing acute thrombotic occlusion of LAD

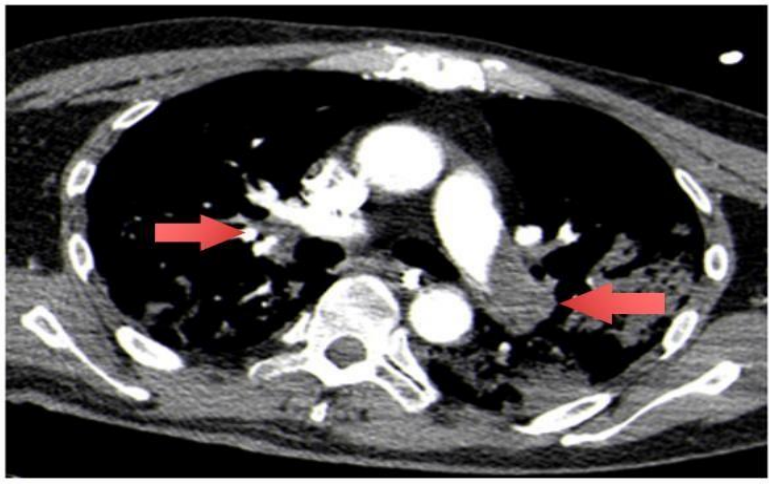

Figure 2b: Angio TC showing Filling defects at the level of right and left pulmonary artery

There was even an intercurrent sepsis caused by Staphylococcus aureus with parossistic atrial fibrillation/FAP. Following weaning from mechanical ventilation, the patient complained of right hemisome weakness. Without contrast agent, head CT revealed two ischemic lesions in the left parietal lobe and right cerebellar lobe, both of which were cardioembolic in origin and were treated conservatively. The patient presented with a minor muscle deficit in the right hemisphere upon discharge, and contrast echocardiography demonstrated full clearance of cardiac thrombotic apposition. Because the patient declined warfarin-based anticoagulation, dabigatran was administered in conjunction with dual antiplatelet treatment (cardioaspirin + clopidrogel) [6].

Patient 3

A 75-year-old male with a history of arterial hypertension who had previously been vaccinated against SARS-COV2 (Vaxzevria, two injections) went to the emergency department complaining of dyspnea. Cardiac examination revealed no abnormalities. A 12-lead electrocardiogram exhibited a sinus rhythm. The D-dimer level was 1897 ng/ml (normal range:

0-500 ng/ml), while the serum C-reactive protein level was 4.91 mg/dl (normal range: 0-0.5 mg/dl). Doppler ultrasonography of the lower limb veins detected right main femoral vein thrombosis. The nasofaringeal swab for SARS COV 2 was positive, and a CT pulmonary angiography revealed bilateral interstitial pneumonia (visual score of 45%, figure n. 3a) and thrombus (maximal diameter of 10 mm) in the aortic arch, lower than the origin of the left subclavian artery (figure 3b). Any invasive treatments have been ruled out by the cardiac surgeon. Additionally, the patient received low molecular weight heparin/LMWH, as well as a high dosage of steroids and remdesivir. Warfarin was prescribed upon discharge.

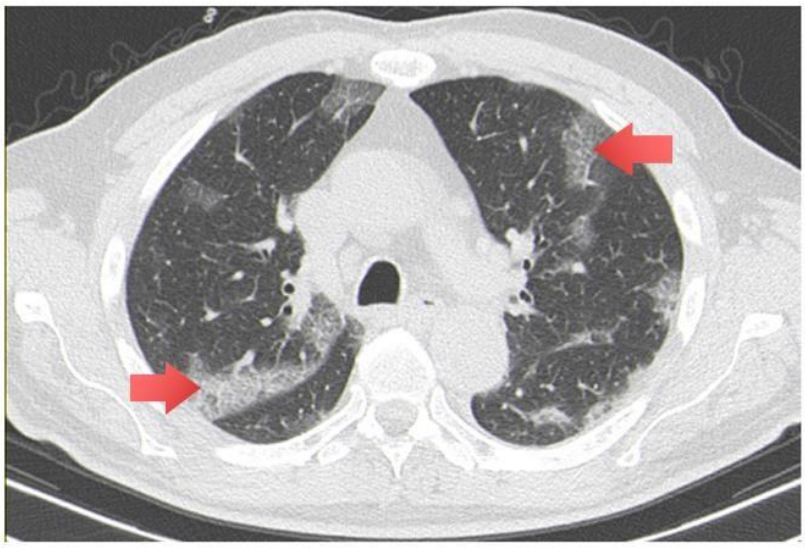

Figure 3a: HCRT on admission showing a diffuse bilateral“crazy paving” pattern with subpleural and peribronchial consolidation

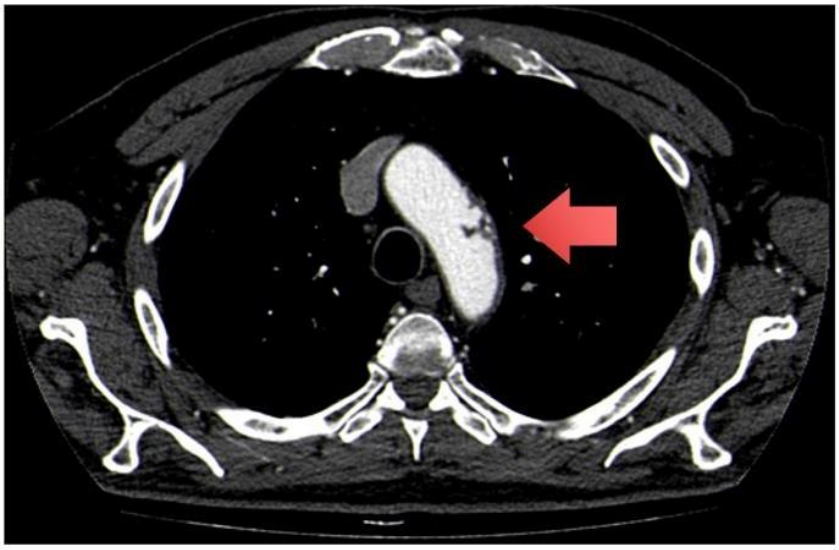

Figure 3b: AngioTc showing thrombus (diameter of 10 mm) at the level of aortic arch, lower than left subclavian artery origin

Discussion

Severe SARS-CoV-2 infection is associated with arterial and venous thrombotic complications including myocardial infarction (MI), ischemic stroke, and venous thromboembolism (VTE) [7].

The majority of studies have focused on venous thromboembolism, with the pulmonary circulation having substantially greater event rates than arm or leg veins [8].

Venous thrombotic complications occurred in 2.6 percent of 229 non-critically hospitalized patients and 35.3 percent of 170 critically ill hospitalized patients in a US registry of COVID-19 patients [9].

In two recent prospective researches from Italy, arterial thrombotic events had an incidence of roughly 10% [10].

Many patients with severe COVID19 have an earlier stage of sepsis-associated disseminated intravascular coagulation (DIC) characterized as "sepsis-induced coagulopathy," according to the International Society of Thrombosis and Haemostasis (ISTH) (SIC) [11].

Thrombotic complications have been shown to have a significant impact in determining a patient's prognosis. Microthrombi seen in the lungs, heart, and

kidneys after autopsy show that severe COVID-19 patients may suffer from multisystem organ failure due to thrombosis [12].

This disease-specific hypercoagulable state is thought to be caused by cytokine-mediated diffuse microvascular damage and, in some circumstances, reactive thrombocytosis. Obesity, advanced age, and hospitalization-related immobilization can all increase the risk of thrombosis and pulmonary embolism [13].

Furthermore, Stress-induced cardiomyopathy (Takotsubo cardiomyopathy), paroxysmal atrial fibrillation, or paradoxical embolization through a patent foramen ovale in the context of pulmonary hypertension caused by acute lung injury could all be sources of embolism to the brain, splanchnic circulation, or peripheral arteries. In these critically ill individuals, vasospasm caused by pressor treatment, iatrogenic artery damage, or spontaneous dissection are all possible explanations [14].

Moreover, elevated D-dimer levels levels have been found in COVID-19 patients, with a strong relation between elevated D-dimer levels on admission and in-hospital mortality, raising concerns about potentially undetected pulmonary embolism in these patients [15].

Pulmonary embolism can also occur late in the course of the disease raising the possibility that the hypercoagulable state persist over theactive inflammation phase and cytokine storm [1].

Conclusion

In conclusion, our case studies highlight important cardiovascular consequences associated with COVID-19 pneumonia. The occurrence of arterial and venous thrombosis at the same time increases the risk of poor survival due to multisystem organ failure. The cytokine storm-related mechanism for this disease-specific hypercoagulable condition has been highlighted, and it may persist in the late stages of infection. Anticoagulant and antiplatelet therapy are required in this situation, however the time though they must be discontinued is unclear. Close radiologic (angio-CT, transtoracic echocardiography) and laboratory (dosage of D-dimer and C-reactive protein levels) follow-up is required after discharge in good clinical practice.

Declarations

Ethics approval and consent to participate:

Not applicable

Consent for publication

All the patients involved in the current manuscript gave their consent for publication

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing interests

None

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Authors' contributions

GH, FDS, MV, FP collected the data and draft the manuscript. MP revised the final manuscript and contributed substantially to the study manuscript design. All authors read and approved the final manuscript."

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None

Conflict of Interest

None declared.

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