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Case report

How to manage thromboembolic risk in patient with SARS-CoV-2-related disease in the Emergency Department: A case report of cardiogenic shock due to massive pulmonary embolism

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ABSTRACT

Background: Although the most known feature of SARS-CoV-2 associated infection is a mild to severe pneumonia, increasing evidence suggests the existence of an infection-associated risk of both arterial and venous thromboembolism (VTE), but the exact magnitude of this phenomenon is still unknown.
Given that, it is important for the Emergency Physician to remember that a SARS-CoV-2 associated respiratory failure can be caused not only by the pulmonary parenchymal inflammation that characterizes the pneumonia, but also by an associated pulmonary thromboembolism.
Case report: A healthy 73-years old woman admitted to the ED for dyspnea, fever and thoracic pain. Cardiac ultrasound, electrocardiogram and clinical findings suggested a diagnosis of cardiogenic obstructive shock due to acute pulmonary embolism, successfully treated with thrombolysis. A CT angiography confirmed the pulmonary embolism (EP) diagnosis and showed bilateral pneumonia, caused by SARS-CoV-2 infection.
Conclusion: Considering the high prevalence of thromboembolic events in COVID-19 patients it is mandatory for the emergency physician to systematically evaluate signs of pulmonary thromboembolism, in order to perform the most patient-tailored therapy as soon as possible.

1. Introduction

Only a few months have passed since the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), causing the coronavirus disease 2019 (COVID-19), have spread all over the world, resulting in more than 17 million cases, more than 670,000 infection-related deaths [1] and a global health threat that has no comparison in the last decades.

The most known feature of SARS-CoV-2 is its ability to cause mild to severe pneumonia, with ground-glass opacity and bilateral patchy shadowing as the commonest radiologic equivalent [2]. However, more recent evidences suggest that SARS-CoV-2 can cause a multi-organ response, rather than only a pulmonary sepsis [3]. One of the most studied feature of COVID-19 is the effect on the cardiovascular system. In particular, it has been described a cardiovascular involvement, in terms of myocardial injury, in up to 22% of patients requiring Intensive Care Unit (ICU) [4]; it has been reported that up to 12% of patients without known cardiovascular disease had elevated troponin levels or cardiac arrest during hospitalization [5]; and there have been reported cases of COVID-19 with only a cardiac presentation [6]. Importantly, recent evidence shows that the course of the disease can be aggravated by a disseminated intravascular coagulation (DIC), which appears to have a prothrombotic character with high risk of thromboembolic events, both in deep venous circulation and pulmonary vessels [7].

2. Case report

A 73 years-old woman arrived in the Emergency Department (ED) for acute dyspnea, fever (38.5 °C), thoracic pain and cough in the previous five days, treated only with paracetamol. The patient was a healthy woman and had no medical history.

At the arrival in the ED she showed the characteristics of a low perfusion shock: she was in respiratory distress (sO2 75% in ambient air) with a respiratory rate of 40 breaths per minute, tachycardic, severely

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hypotensive (70/40 mmHg), with cold limbs and mottled skin; there were no pathological lung sounds and no clinical signs of peripheral venous thrombosis. ECG showed sinus tachycardia with incomplete right bundle block, S1Q3T3 pattern and negative T waves in inferior leads and in V2–V5. Arterial blood gas analysis revealed severe hypoxia and hypocapnia (pO2 40 mmHg, pCO2 32 mmHg), with an oxygen alveolar-arterial gradient of 70 mmHg. Bedside ultrasound showed a reduced inferior vena cava collapsibility index and a right ventricle (RV) distended and hypokinetic (mid diameter 55 mm; TAPSE 10 mm) with paradoxical interventricular septal motion and an estimation of right ventricular pressure of 70 mmHg; left ventricular function appeared normal (Fig. 1). Complete compression ultrasonography of the leg veins did not show any deep vein thrombosis (DVT).

Overall, although without signs of DVT, the most likely diagnosis was obstructive shock secondary to pulmonary thromboembolism. Given the perilous hemodynamic instability we performed immediately a systemic thrombolysis with alteplase, an besides fluid resuscitation. In the following 4 h the patient felt progressively better and both the respiratory and the hemodynamic parameters normalized; no complication of thrombolysis occurred. A second bedside ultrasound showed a decrease of the right ventricular pressure to 30 mmHg and a TAPSE of 20 mm. Finally, the CT pulmonary angiogram (Fig. 2) confirmed a bilateral pulmonary embolism and showed a modest ground glass lung consolidation: considering the lung pattern we performed a SARS-CoV-2 test, resulted positive.

Once stabilized, we transferred the patient in the Sub-Intensive Care Unit, where she was treated with therapeutic enoxaparin, hydroxychloroquine and antibiotic. Hypercoagulable state testing and malignancy screening were normal. At discharge her medical therapy included apixaban 5 mg twice a day. The heart ultrasound performed before the release from the hospital showed normal right ventricle dimensions and function.

3. Discussion

The relationship between SARS-CoV 2 infection and pulmonary embolism has been described in many patients [8,9].

Indeed, although reported only in case reports, it seems that SARS-CoV-2 has the potential to provoke pulmonary thromboembolism even

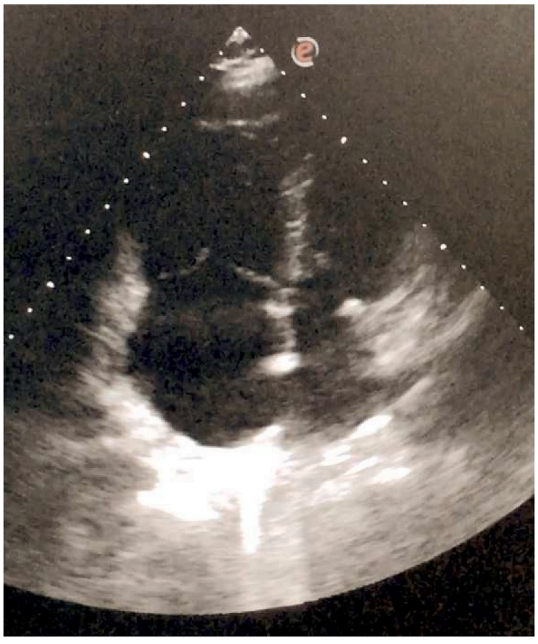

Fig. 1. Cardiac ultrasound, four-chamber view: right ventricular and atrium dilatation is visible.

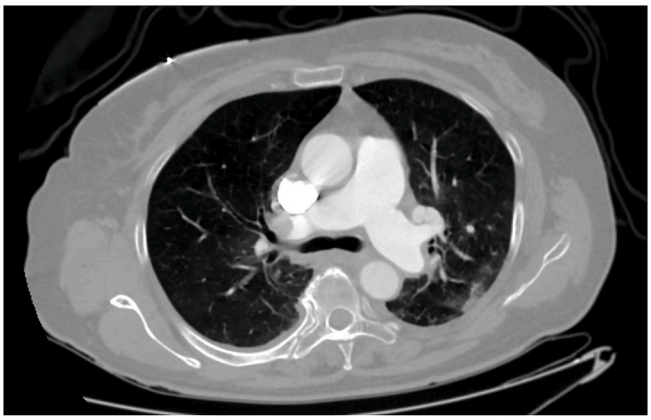

Fig. 2. CT pulmonary angiography: a modest ground glass lung pattern is visible in both lungs; thromboembolic occlusion is visible in the right branch of the pulmonary artery.

in patients without thromboembolic risk factors other than infection [10,11]. However, the actual prevalence of thromboembolic events among COVID-19 patients still remains unknown. In ICU settings the prevalence of non-COVID-19 PE and DVT is estimate to be 2–3% and about 30%, respectively, although there are very different results according to different studies [12].

The incidence of VTE events among COVID-19 patients also varies between different studies and settings, but appears to be higher than that of non-COVID-19 patients.

A study from Klok et al. found an incidence of VTE events of 31% in a group of 184 patients admitted to the ICU [13]; a retrospective study from Llitjos et al. found an impressive overall rate of 69%, although in a significantly smaller population [14].

In a study from Cui et al. the incidence of VTE events was 25% in a population of 81 patients. Levels of D-dimer higher than 1.5 μg/mL predicted VTE with a sensitivity of 85%, a specificity of 88.5% and had a negative predictive value of almost 95% [15].

A study from Lodigiani et al. considering 388 patients admitted in ICU and General Ward showed an incidence of venous thromboembolism of 6.4% in General Ward and of 16.7% in the ICU; remarkably, 100% of the ICU patients received thromboprophylaxis, while the patients in the General Ward did not. In this study more than a half of venous or arterial thromboembolic events were diagnosed within the first 24 h of hospital admission [16]. In the study by Klok et al. aforementioned [13], all patients received at least thromboprophylaxis and the cumulative incidence of their composite outcome (acute pulmonary embolism, deep-vein thrombosis, ischemic stroke, myocardial infarction or systemic arterial embolism), as said, was 31%. In both studies the most frequent thromboembolic event was isolated pulmonary embolism. In the ICU population studied by Llijtos et al. the incidence of VTE was even higher, consisting in 100% in the prophylaxis group and 56% in the complete anticoagulation group (overall rate, as said, was 69%) [14]. The most important difference between these three studies is that in the last one VTE was searched systematically, while in the other two VTE was searched only if clinically suspected [13,14,16].

The proposed physiopathology behind the prothrombotic risk in COVID-19 patients is a complex pathway consisting in a sort of modified, sepsis-induced DIC: this so-called “sepsis-induced coagulopathy (SIC)” is characterized by suppression of fibrinolysis caused by excessive production of plasminogen activator inhibitor-1 (PAI-1), an alteration that is rarely seen in malignancy-associated DIC: as a result, the bleeding phenotype is more common in non-septic DIC, while SIC can have a prothrombotic effect, at least at the beginning [17,18].

All thing considered it seems reasonable, for every COVID-19 patient coming in the Emergency Department with severe hypoxia, to consider not only the pulmonary parenchymal involvement, but also an acute,

hidden cor pulmonale secondary to pulmonary thromboembolism as the main cause of the disease.

Therefore it could be important, especially for the Emergency Physicians, to be familiar with the most common echocardiographic sign of acute pulmonary embolism. These are usually indirect and consist mainly in the criteria for right ventricular overload, seen in 30–40% of patients with PE: diastolic right ventricular mid diameter >35 mm or >41 mm at the base [19], right ventricle/left ventricle ratio >1, systolic flattening of interventricular septum or right ventricular outflow acceleration time <105 ms or tricuspid incompetence (TI) gradient >30 mmHg in absence of right ventricular hypertrophy (RVH). The 60/60 sign, consisting in a right ventricular outflow tract acceleration time ≤60 ms in presence of a pulmonary arterial systolic pressure ≤60 mmHg, and McConnell sign, consisting in a right ventricular akinesia of the mid free wall with normal motion at the apex, are highly specific for PE [20,21]. We believe that in patients with severe hypoxia these signs should be evaluated systematically, in order to perform an early diagnosis of acute pulmonary embolism.

Finally, a few concerns have been raised about the thrombolytic therapy in COVID-19 patients. In fact, no guidelines about the management of PE in COVID-19 patients exists. The current 2019 ESC guidelines about the management of PE [21] recommend the use of systemic thrombolytic therapy in high-risk PE, and catheter-directed thrombolysis (CDT) and surgical embolectomy in whom thrombolysis is contraindicated or has failed. The most relevant criticism about systemic thrombolysis relates to the bleeding risk; that is the reason why some physicians may prefer the catheter-guided procedure, considering the lower dose of thrombolytic required [22]. It should be considered, anyway, that CDT and surgical embolectomy are not always available, including in our Hospital; luckily, the patient did not have any contraindication to systemic thrombolysis and we performed it effectively. Other case series, anyway, shows good outcomes both with the CDT and the surgical embolectomy [8,9], and one major hemorrhagic complication leading the patient to death has been reported in a case series of seven patients [8]. In a recent study [23] the CDT resulted better than the systemic thrombolysis in terms of major bleeding complications and hospital mortality. Whether the CDT is superior to the systemic approach in the COVID-19 framework is unknown.

4. Conclusion

The thromboembolyc risk in COVID-19 patients, together with the high prevalence of thromboembolic events, particularly EP, should be taken into account in every patient coming in the ED with severe dyspnea. For this reason, in order to achieve an early diagnosis of acute cor pulmonale, could be useful in these patients to perform a systematic investigation of right ventricular overload.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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