

Case Report

Open Access

High Risk Pulmonary Embolism in a Patient with Covid-19 Pneumonia Treated With Tissue Plasminogen Activator in the Emergency Department: A Case Report and Literature Review

Silvia Pastor-Yvorra^{1*}, Ángeles Molina-Medina², Elena de Celis-Ruiz¹ and Nataly Cancelliere²

¹Neurology Department. La Paz University Hospital, Madrid, Spain

²Emergency Unit. La Paz University Hospital, Madrid, Spain

ABSTRACT

Introduction: SARS-CoV2, responsible for the current global pandemic, could predispose to a hypercoagulable state. Venous thrombosis is more frequent in COVID-19 associated coagulopathy than in bacterial sepsis-induced coagulopathy. Also, COVID-19 induces a hypercoagulation state that overlaps with a hemophagocytic syndrome, antiphospholipid syndrome, and thrombotic microangiopathy. It is not uncommon that patients with severe COVID-19 consult in the emergency department with embolisms that may result in life risk.

Materials and methods: a 77-year-old man, with a history of 4 days of dry cough and dyspnoea became hemodynamically unstable, with an RT-PCR assay of nasopharyngeal swab positive for COVID-19 and a high-risk pulmonary embolism in the CT pulmonary angiography. He received treatment with tissue plasminogen activator and dexamethasone. The patient evolved favorably, without the need for therapeutic management in the intensive care unit.

Results: We conducted a review of the literature regarding the COVID-19 associated coagulopathy and systemic thrombolysis.

Discussion: despite other published series, the treatment with fibrinolysis in our report resulted in better respiratory outcomes and survival. The European Society of Cardiology suggests that the treatment of COVID-19 patients with pulmonary embolism should be guided by risk stratifications according to the current guidelines. For that reason, patients with high-risk pulmonary embolism should receive systemic thrombolysis if there is not any contraindication.

*Corresponding author

Silvia Pastor-Yvorra, C/Paseo de la Castellana, 261, La Paz University Hospital (level 11), 28046, Madrid, Spain, E-mail: sylviamegara@hotmail.com

Received: November 06 2020; **Accepted:** November 12, 2020; **Published:** November 18, 2020

Introduction

SARS-CoV2 is a novel coronavirus recently detected and responsible of the current global pandemic that began in December 2019 in Wuhan, China. Although most patients have mild upper respiratory tract symptoms, others suffer pneumonia in different levels of severity. In the most severe cases, coagulopathy has been reported in several cases, mainly manifesting as an hypercoagulable state. Here we report a case of a patient with COVID-19 pneumonia and a high risk of pulmonary embolism (PE) treated in the emergency department (ED) with active tissue plasminogen (tPA) and dexamethasone without intensive care unit (ICU) management. We also conducted a review of the recent literature. Our aim was to share our good experience in terms of survival and improvement in the oxygenation rate (OR).

Materials and methods

We report a case of a 77 year-old man, with previous history of tobacco abuse, who consulted in the ED after 4 days of dry cough, and abrupt onset of dyspnoea in the last 24 hours. He had a blood pressure (BP) level of 89/59 mmHg, a heart rate of 120 bpm, a respiratory frequency of 36 breaths per minute, with no fever and a blood oxygen level of 85%.

We found a modest leucocytosis (1136 white cells/mm³) with lymphopenia (820 lymphocytes/mm³) in the complete blood count test. In his coagulation test, only slightly increased values of INR (1.3), and prothrombin activity (57%) were found, but levels of D-dimer were surprisingly high (14.000 ng/mL), with a normal level of fibrinogen and platelet count. A mild kidney failure with creatinine levels of 1.76mg/dL, glomerular filtration rate of 36mg/dL and urea of 83mg/dL was seen in the serum biochemistry, along with inflammation markers such as elevated ferritin (885ng/mL, C reactive protein (52.2mg/dL), IL-6 (22.1pg/mL), LDH (443UI/L), as well as troponin I (1472.1ng/L), with a normal level of procalcitonin.

The chest X-ray showed subpleural opacities in upper and middle bilateral lobes, findings compatible with atypical pneumonia pattern (image 1a). The RT-PCR assay from the nasopharyngeal swab was positive for SARS-CoV2 infection.

According to the Wells and the Geneva scale for risk of presenting a PE, our patient scored 4.5 and 6 respectively, indicating a moderate risk (16.2% and 20-30% respectively) for presenting a PE. Taking into account the previous test results and the patients clinical and haemodynamic state, we conducted CTPA which

showed a central filling defect in both main pulmonary arteries with extension to the lobar arteries and the majority of segmental arteries, which corresponded to a diagnosis of acute bilateral PE. The ratio between the right ventricle (RV) and the left ventricle was increased in the CTPA, with a rectified ventricular septum and contrast reflux to suprahepatic veins, suggesting RV overload and insufficiency (image 1b). Nonetheless, his baseline electrocardiogram was normal. A non-rebreathing facemask was used to improve the patient's OR up to 93%. We conducted a transthoracic echocardiography (TTE), which showed signs of RV pressure overload: a moderate dilatation of the RV, a pulmonary ejection acceleration time lower than 60ms and a peak systolic tricuspid valve gradient lower than 60mmHg, without RV heart thrombi. According to the Pulmonary Embolism Severity Index (PESI) the patient ranked 177 points, which corresponded to a very high mortality risk [1].



Legends: 1a. Chest-ray which shows subpleural opacities in upper and middle bilateral lobes. 1b. CTPA with a central filling defect in both main pulmonary arteries.

Based upon these findings: elevated cardiac troponin levels, RV dysfunction on TTE, a PESI class of V and haemodynamic instability despite therapy with intravenous fluids, we initiated treatment with tPA: a bolus of 10mg followed by a 2h perfusion of 90mg. In order to try to reduce our patient's inflammatory condition, we initiated treatment with dexametasone. We used norepinephrine at a dose of 0.5 µg/kg/min to maintain BP values above 90/60mmHg. Intensive care management was finally not required because of the patient's good response. He was transferred to an Internal Medicine Hospital Ward, where he received treatment with anticoagulation therapy with low molecular weight heparin. He progressively experienced improvement in his OR (95% with non-rebreathing face mask) and his BP was normal (130/85mmHg) without further need of vasoactive treatments after the acute phase. Currently, he remains hospitalized, although he keeps improving day by day.

Results/Observations

Our patient shows the potential risk of acute PE without major predisposing factors besides SARS-CoV2 infection. One of the hallmarks of severe COVID-19 is coagulopathy. The most common pattern is characterized by fibrinogen and D-dimer increased levels, which correlates with a parallel rise in markers of inflammation. Unlike the classic DIC, prolongation of the partial thromboplastin time and prothrombin time is minimal, and thrombocytopenia is mild. The International Society of Thrombosis and Haemostasis (ISTH) proposed a new method to identify an earlier phase of sepsis-associated DIC called "sepsis-induced coagulopathy" (SIC) and has been used for Tang et al series to risk stratify patients who should receive anticoagulants for primary prevention [2,3].

Arterial and venous thromboses are more frequent in COVID-19 associated coagulopathy (CAC) than in bacterial sepsis-induced

coagulopathy [4]. The pathophysiology of CAC is complex. It appears to be a connection between inflammatory mediators and coagulation, and overlaps with a hemophagocytic syndrome, antiphospholipid syndrome (APS) and thrombotic microangiopathy [5]. A recently published case series have reported three affected patients with positive anticardiolipin, and antiB2 glycoprotein, they suggested that the viral infection could predispose to the development of reactive APS [6].

There is some evidence that tPA inhibits interleukin-1, which could be related with the COVID-19 cytokine storm [7]. As suggested by the European Society of Cardiology and an American consensus paper, the treatment of COVID-19 patients with PE should be guided by risk stratifications according to the current guidelines. For that reason, hemodynamically unstable patients should receive tPA in the absence of contraindications [8]. It has been published a case series of 5 systemic fibrinolysis in patients with suspected PE (on the basis of a combination of obstructive shock, unexpected cardiac arrest and acute cor pulmonale on transthoracic echocardiography) in the context of severe SARS-CoV2 pneumonia, with 4 deaths. The authors concluded that the treatment with tPA in suspected PE was associated with poor outcome, and that PE could also be over suspected [9]. In the Faggiano series, 1 out of 7 patients with PE and concomitant COVID-19 pneumonia was treated with systemic thrombolysis (death for haemorrhagic complication) [10]. It has also been proposed treatment with catheter directed thrombectomy, as an additional therapeutic option in patients who are receiving full anticoagulation and present with rapid clinical collapse [11].

Discussion

Clinicians should consider the possibility of PE in patients with sudden onset of oxygenation deterioration, respiratory distress and reduced BP as in our case. Closely monitoring patient vital signs and coagulation parameters is mandatory in this COVID-19 pandemic, since SARS-CoV2 infections appear to have a thrombogenic and inflammatory effect. Despite other published series, the treatment with fibrinolysis in our report resulted in better respiratory outcomes and survival.

The limitations of the study are: lack of ability to generalize, publication bias because of good response of the treatment, retrospective design and absence of a control group. More studies are needed with an adequate methodology and comparisons between different anticoagulants to establish faithfully conclusions about efficacy and safety of these drugs, that will lead to algorithms of therapeutic decision.

Acknowledgements

To the emergency department of La Paz University Hospital, specially to the emergency coordinators Rosario Torres and Angelica Rivera.

References

1. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing G-J, et al. (2020) ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *European Heart Journal* 41: 543-603.
2. Iba T, Levy JH, Warkentin TE, Thachil J, Poll T, et al. (2019) Diagnosis and management of sepsis-induced coagulopathy and disseminated intravascular coagulation. *J Thromb Haemost* 17:1989-94.
3. Tang N, Bai H, Chen X, Gong J, Li D, et al. (2020) Anticoagulant treatment is associated with decreased

- mortality in severe coronavirus disease 2019 patients with coagulopathy J Thromb Haemost. 18:1094-1099.
4. Amgalan A, Othman M (2020) Hemostatic laboratory derangements in COVID-19 with a focus on platelet count Platelets 1: 6. doi:10.1080/09537104.2020.1768523
5. Iba T, Levy JH, Connors JM, Warkentin TE, Thachil J, et al. (2020) The unique characteristics of COVID-19 coagulopathy. Crit Care 24: 360.
6. Zhang Y, Xiao M, Zhang S, et al. (2020) Coagulopathy and antiphospholipid antibodies in patients with Covid-19. N Engl J Med. April. <https://doi.org/10.1056/NEJMc2007575>
7. A Stringer, BM Hybertson, OJ Cho, Z Cohen, JE Repine (1998) Tissue plasminogen activator (tPA) inhibits interleukin-1 induced acute lung leak. Free Radic Biol Med 25: 184-188.
8. Roncon L, Zuin M & Zonzin P (2020) Fibrinolysis in COVID-19 patients with hemodynamic unstable acute pulmonary embolism: yes or no?. J Thromb Thrombolysis 50: 221-222.
9. Ly A, Alessandri C, Skripkina E, et al. (2020) Rescue fibrinolysis in suspected massive pulmonary embolism during SARS-CoV2 pandemic. Resuscitation 152: 86-88.
10. Faggiano P, Bonelli A, Paris S, et al. (2020) Acute pulmonary embolism in COVID-19 disease: Preliminary report on seven patients. Int J Cardiol 313:129-131.
11. Galastri FL, Valle LGM, Affonso BB, et al. (2020) COVID-19 complicated by pulmonary embolism treated with catheter directed thrombectomy. Vasa 49: 333-337.