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Thromboembolic events in SARS-CoV-2 infection: A case report and review of the literature

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Abstract
Throughout the SARS-Cov-2 pandemic, multiple interrogations concerning the standard of care of infected patients were raised. Updating and regular sharing of knowledge at national and international levels has been the cornerstone of advancing knowledge and improving the care of these patients. In this case report, we present a thrombo-embolic complication of the viral infection, that manifested Itself with hemodynamic lability, in a patient with a history of ischemic cardiomyopathy treated with acetylsalicylic acid who received high-dose pharmacological thromboprophylaxis. Based on clinical and ultra Sound arguments, the patients received a thrombolytic treatment. Unfortunately, He died 12 hours later. No hemorrhagic complication of the thrombolytic treatment was noted.
In this article, we will also discuss the diagnostic modalities of thromboembolic events and their pharmacological treatment in infected patients.

Keywords: COVID-19, thromboembolic events, thromboprophylaxis, pulmonary embolism

Introduction
Throughout the SARS-Cov-2 pandemic, multiple interrogations concerning the standard of care of infected patients were raised. Updating and regular sharing of knowledge at national and international levels has been the cornerstone of advancing knowledge and improving the care of these patients. In this case report, we present a thromboembolic complication of the viral infection in a patient who received high-dose pharmacological thromboprophylaxis. We will also discuss the diagnostic modalities of thromboembolic events and their pharmacological treatment in infected patients.

Case presentation
We report the case of a 62-year-old male patient who was admitted to the emergency department for acute respiratory distress. His past medical history consisted of ischemic cardiomyopathy treated with acetylsalicylic acid and furosemide for the previous 3 years. He had no smoking history. A transthoracic echocardiogram (TTE) performed a month before his admission showed good left ventricular contractility with an ejection fraction of 63%. No left ventricular cavity dilation or wall hypertrophy was found. No anomaly was noted during the exploration of the right cavities.
Upon his admission, he was polygenic with a respiratory rate of 25 cycles/min and hypoxic with a SpO_2 at 70%. He was hemodynamically stable. Clinical examination noted sub sternal and intercostal in drawing and pulmonary auscultation didn't reveal any rales or Ronchi. On the electrocardiogram, a normal sinus rhythm with a heart rate of 84 cycles/min was noted. No repolarization abnormalities were found.
A SARS-CoV-2 PCR test was prescribed and returned positive. The chest CT scan ordered found peripheral ground glass lesions extending to 50% of the pulmonary parenchyma.
The patient was admitted to the intensive care unit for non-invasive ventilation and received azithromycin (500 mg, once daily), methylprednisolone (160 mg, once daily), enoxaparin (6000 UI, twice daily), ascorbic acid, cholecalciferol and zinc. On day three, the patient was intubated due to non-compliance with non-invasive ventilation and underwent two 16-hour sessions in a prone position the following days.
On day six, the patient abruptly developed hemodynamic lability. He was hypotensive (7/4 cm Hg) and tachycardia (140 cycles/min) with an irregular rhythm on the electrocardiogram monitor. After ruling out septic and hemorrhagic etiologies, a bedside TTE was performed and revealed a dilation of the right ventricle with a constricted left ventricle, paradoxical septal motion and a right ventricular thrombus. A CT pulmonary angiography couldn't be obtained due to his hemodynamic instability.

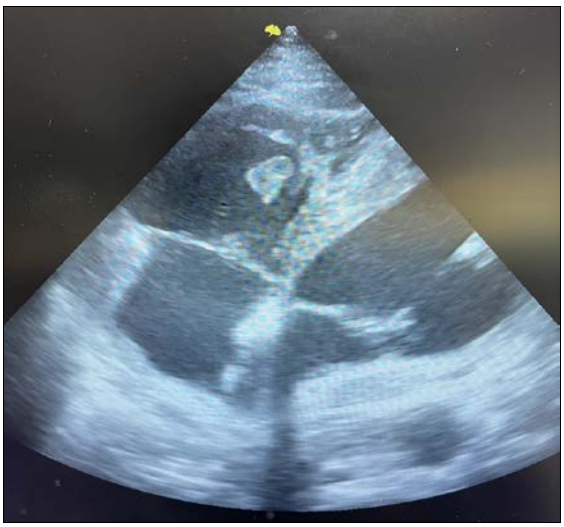

Fig 1: Transthoracic echocardiogram showing the thrombus in the right ventricle

Blood work revealed an increase in troponin and D-dimer levels respectively from 0, 05 ng/ml to 4 ng/ml and from 650 ng/ml to 3300 ng/ml. Arterial blood gas study showed an alteration in gas exchanges and an increased alveolar dead space.

Upon these findings, and based on clinical and echo graphic findings in favour of a massive pulmonary artery embolism, the decision of administrating a thrombolytic agent was made.

Unfortunately, no hemodynamic or respiratory improvement was noted. The following TTE showed the persistence of the thrombus. The patient died 12 hours later with no hemorrhagic complication noted.

Discussion

COVID-19 is a viral infection caused by the SARS-CoV-2 virus that originated in China at the end of 2019. The infection presented itself with respiratory symptoms associated with various manifestations like myalgia, headaches, anosmia, ageusia and peripheral ischemia.

Since March 2020, thromboembolic events (TEE) became more and more described in the literature, with an incidence reaching 14% of hospitalized patients in surveillance wards [1,2] and between 17% and 50% of patients hospitalized in ICUs [3,4].

Pulmonary embolism (PE) represents the main complication responsible for a fivefold increase in mortality compared to SARS-CoV-2-positive patients who didn't develop it [5]. It is followed by deep vein thrombosis and acute coronary syndrome, by order of frequency. The rise in the incidence of these complications can be explained by the presence of factors influencing the Virchow triad namely stasis of flow due to prolonged bed rest and obesity, intravascular vessel wall damage secondary to endothelial inflammation and the irritation caused by catheters, and hypercoagulable state caused by sepsis and endothelial activation; caused by the virus itself; and the thrombophilic inflammation responsible of the increase of Won Willebrand factor and factor VIII [6].

The majority of deep vein thrombosis cases are diagnosed in bedridden patients who have been put in a prone position which is known for altering venous return and promoting stasis of flow. The acute coronary syndrome is caused by the hypercoagulable and inflammatory state [7], social isolation inducing a decrease in physical activity and a change of eating habits [8], difficult access to anticoagulant treatment in outpatient care and potential pharmacological interactions with antiviral treatments.

Some authors recommended a systematic screening for pulmonary embolism using CT pulmonary angiography (CTPA) even in patients who didn't present any suggestive symptoms. This attitude is debatable knowing that only one PE will be diagnosed every 20 CTPA in patients treated for a mild form of COVID-19 infection, in contrast with one PE diagnosed in every 4 CTPA in patients hospitalized in ICUs for a severe infection. This prompted some authors to reserve the use of ambulatory explorations with CTPA and Doppler echography in symptomatic patients only, regardless of biological (D-dimer) modifications [9].

The place of TTE, compared to ttransesophagealechocardiogram, remains important in the orientation and diagnosis of pulmonary embolism by looking for indirect signs such as a dilation of the right ventricle, reduced size of the left ventricle, septal movement anomalies, alteration in left ventricle filling, no right ventricle wall thickening, pulmonary arteries and inferior vena cava dilation, tricuspid regurgitation with moderately high pulmonary arteries pressure and a pulmonary artery acceleration time below 80-90 ms. [10]. In some cases, direct signs are present such as a right intracavitary thrombus which is seen in 2% to 18% of patients diagnosed with PE. It is located in the right atrium in 84% of cases and its size ranges from 2 to 10mm in 92% of cases [11, 12]. It is virtually impossible to visualize a thrombus in the trunk of the pulmonary artery or in any of its branches by TTE.

An increase in D-dimer levels was identified early in the pandemic to be a predictive factor of bad outcomes in COVID-19 patients [13]. Its increase can be explained by multiple mechanisms: The advanced age of patients treated, major inflammatory reaction, and acute pulmonary aggression associated with intra-alveolar fibrin deposition responsible for in situ d-dimer production [14]. In addition to D-dimers, antiphospholipid antibodies [15]; known for their thrombophilic effect; have been identified in some COVID-19 patients [16].

Regarding anticoagulant treatment, many protocols have been proposed

1. The Société Française de Médecine Vasculaire (French Society of vascular medicine) recommends initiating a 7 to 14 days prophylactic treatment using low-molecular-weight heparin (LMWH) or fondaparinux in patients treated in ambulatory care if there is a significant reduction of their mobility or if they meet at least one of the following factors: Over 70-years-old, obesity, active neoplasia, surgery in the previous 3 months, history of thromboembolic disease. If a TEE is suspected, patients can be treated if the clinical probability is high, even before obtaining paraclinical confirmation.
2. In hospitalized patients, considering the high incidence of TEE even with an effective thromboprophylaxis, multiple publications suggested raising empirically the posology of LMWH. An international consensus identified that most experts were in favour of respecting the usual thromboprophylaxis doses of LMWH in surveillance wards (63%) and in ICUs (54%). Only 30% were in favour of increasing the posology and less than 16% of them opted for curative doses in primary prevention of TEE [7].
3. The European Society of Cardiology and the Société Française de Médecine Vasculaire recommends prescribing thromboprophylaxis treatment for discharged patients. On the other hand, the American College of Chest Physicians doesn't. Pragmatically, a bedridden patient who was discharged from a 3-week stay in an ICU resulting in important neuropathy will have a higher risk of developing a TEE than a patient who gained back his autonomy. In consequence, thromboprophylaxis treatment should be prescribed after a thorough evaluation of the patient and reassessed regularly.
4. If a TEE is diagnosed, the treatment is based on LMWH or fondaparinux in patients admitted for a severe form of infection [17]. They can be switched to a direct oral anticoagulant (DOA) once they are out of the inflammatory phase of the infection.
5. Patients receiving oral anticoagulants for other etiologies (Vitamin K antagonists and DOA), should be

switched to LMWH if they present with a severe form of the viral infection [17] and stay on their initial treatment otherwise.

6. Patients under long-term treatment with platelet aggregation inhibitors should not halt it in case of SARS-CoV-2 infection.
7. A massive PE with hemodynamic repercussions is an indication of thrombolytic treatment. According to the reviewed studies, the mortality rate varies between 30% and 65%. Thrombolysis allows in these cases a rapid hemodynamic improvement with a remarkable reduction of 30% of mean pulmonary artery pressure and an increase of 15% of the cardiac index as early as in the second hour after administrating the treatment [18]. The TTE demonstrates a reduction of the right ventricle size from the third hour. By comparison, heparin has no effect within the same timeframe [19].

Conclusion

SARS-CoV-2 infection has now become a quintessential thromboembolic disease. The diagnosis, prevention and treatment of these thromboembolic events are the current priority of the medical community. Larger studies are needed to refine the treatment regimen and improve patient outcomes.

References

1. Grillet Franck, Behr Julien, Calame, Paul, Aubry, Sébastien, Delabrousse Eric. 2020 Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected with Pulmonary CT Angiography. Radiology. 2020;296:201544. DOI: 10.1148/radiol.2020201544.
2. Leonard-Lorant Ian, Delabranche Xavier, Severac, François, Helms Julie, Pauzet Coralie, *et al.* Acute Pulmonary Embolism in COVID-19 Patients on CT Angiography and Relationship to D-Dimer Levels. Radiology. 2020;296:201561. DOI: 10.1148/radiol.2020201561.
3. Middeldorp Saskia, Coppens, Michiel, Haaps Thijs, Foppen Merijn, Vlaar Alexander. Incidence of venous thromboembolism in hospitalized patients with COVID-19. Journal of Thrombosis and Haemostasis. 2020;18:10.1111/jth.14888.
4. Klok FA Kruip MJHA, van der Meer NJM, *et al*. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thrombosis Research. 2020;191:145-147.
5. DOI: 10.1016/j.thromres.2020.04.013
6. Klok FA, Kruip MJHA, van der Meer NJM, *et al*. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: An updated analysis. Thrombosis Research. 2020;191:148-150.
7. DOI: 10.1016/j.thromres.2020.04.041
8. Ackermann M, Verleden SE, Kuehnel M, *et al*. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in COVID-19. New England Journal of Medicine. 2020;383(2):120-128. DOI: 10.1056/NEJMoa2015432
9. Bikdeli B, Madhavan MV, Jimenez D, *et al*. COVID-19 and thrombotic or thromboembolic disease: Implications for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art Review. Journal of the American College of Cardiology. 2020;75(23):2950-2973. DOI: 10.1016/j.jacc.2020.04.031
10. Niccoli G, Luescher TF, Crea F. Decreased myocardial infarction admissions during COVID times: What can we learn? Cardiovascular Research. 2020;116(10):e126-e128. DOI: 10.1093/cvr/cvaa146
11. Khider L, Soudet S, Laneelle D, *et al*. Proposal of the French Society of Vascular Medicine for the prevention, diagnosis and treatment of venous thromboembolic disease in outpatients with COVID-19. Journal de Médecine Vasculaire. 2020;45(4):210-213. DOI: 10.1016/j.jdmv.2020.04.008
12. Jardin F, Dubourg O, Bourdarias JP. Echocardiographic pattern of acute cor pulmonale. Chest 1997 Jan;111(1):209-17. PMID: 8996019. DOI: 10.1378/chest.111.1.209.
13. Casazza F, Bangazoni A, Centonze F, Morpurgo M. Prevalence and prognostic significance of right-sided cardiac mobile thrombi in acute massive pulmonary embolism. Am J Cardiol. 1997;79:1433-5.
14. Chartier L, Béra J, Delomez M, Asseman P, Beregi JP, Bauchart JJ, *et al*. Free-floating thrombi in the right heart: Diagnosis, management, and prognostic indexes in 38 consecutive patients. Circulation. 1999;99:2779-83.
15. Zhou F, Yu T, Du R, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study [published correction appears in Lancet. 2020 Mar 28;395(10229):1038], Lancet. 2020;395(10229):1054-1062. DOI: 10.1016/S0140-6736(20)30566-3
16. Hunt BJ, Levi M. Re The source of elevated plasma D-dimer levels in COVID-19 infection. British Journal of Haematology. 2020;190(3):e133-e134. DOI: 10.1111/bjh.16907
17. Harzallah I, Debliquis A, Drénou B. Lupus anticoagulant is frequent in patients with COVID-19. Journal of Thrombosis and Haemostasis. 2020;18(8): 2064-2065. DOI: 10.1111/jth.14867
18. Devreese KMJ, Linskens EA, Benoit D, Peperstraete H. Antiphospholipid antibodies in patients with COVID-19: A relevant observation?. Journal of Thrombosis and Haemostasis. 2020;18(9):2191-2201. DOI: 10.1111/jth.14994
19. Moores LK, Tritschler T, Brosnahan S, *et al*. Prevention, diagnosis, and treatment of VTE in Patients with coronavirus disease 2019: CHEST Guideline and Expert Panel Report. Chest. 2020;158(3):1143-1163. DOI: 10.1016/j.chest.2020.05.559
20. Dalla-Volta S, Palla A, Santolicandro A, Giuntini C, Pengo V, Visioli O, *et al*. PAIMS 2: Alteplase combined with heparin versus heparin in the treatment of acute pulmonary embolism. Plasminogen Activator Italian Multicenter Study. J Am Coll. Cardiol. 1992;20:520-6.
21. Goldhaber SZ, Haire WD, Feldstein ML, Miller M, Toltzis R, Smith JL, *et al*. Alteplase versus heparin in acute pulmonary embolism: Randomised trial assessing right-ventricular function and pulmonary perfusion. Lancet. 1993;341:507-1.