

Thrombo-embolic 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 level 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 ultrasound 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 thrombo-embolic events and their pharmacological treatment in infected patients.

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

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I. Introduction

The current SARS-CoV-2 pandemic, responsible for the COVID-19 disease, is a topic of concern to all healthcare professionals and learned societies. To better understand the pathophysiology of this disease and to optimize the medical management of the patients, regular updating and sharing of knowledge at a national and an international level is necessary for the advancement of scientific knowledge. Thromboembolic events such as pulmonary embolism, deep vein thrombosis and acute coronary syndrome represent the major complication of this infection. In this case report, we present a thrombo-embolic complication – a right ventricular thrombus - of the viral infection in a patient under a high-dose pharmacological thromboprophylaxis. We will also discuss the pharmacological modalities of thromboprophylaxis in infected patients and the therapeutic strategy of thrombo-embolic events.

II. Case presentation

We report the case of a 62-year-old male patient who was admitted to the emergency department for an acute respiratory distress. His past medical history consisted of an 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 prior to his admission showed a good left ventricular contractility with an ejection fraction of 63%. No left ventricular cavity dilation or wall hypertrophy were found. No anomaly was noted during the exploration of the right cavities. The patient weighed 62 kg.

Upon his admission, he was polypneic at 25 cycles/min and hypoxic (SpO_2 :70%). He was hemodynamically stable. Clinical examination noted a substernal and an intercostal indrawing. Pulmonary auscultation didn't reveal any rales or ronchi. On the electrocardiogram, a normal sinus rhythm was noted with a heart rate of 84 cycles/min. 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 (500mg, once daily), methylprednisolone (160mg, once daily), enoxaparin (6000UI, 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-hours sessions of prone position on the following days.

On day six, the patient suddenly developed a hemodynamic lability. He was hypotensive (7/4 cmHg) and tachycardic (140 cycles/min) with an irregular rhythm on the electrocardiogram monitor. After ruling out

septic and hemorrhagic etiologies, a TTE was performed and revealed a dilation of the right ventricle with a constricted left ventricle, a paradoxical septal motion and a right ventricular thrombus measured at 11mm. A CT pulmonary angiography couldn't be obtained due to his hemodynamic instability.



Figure 1 : Transthoracic echocardiogram of the patient, showing the thrombus (*) in the right ventricle.
(ZIANI Hicham, Ibn Sina Hospital)

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 ultrasound findings in favor of a massive pulmonary artery embolism, the decision of administrating a thrombolytic agent was made (Tenecteplase, 6000UI).

Unfortunately, no hemodynamic nor respiratory improvement were noted. The following TTE showed the persistence of the thrombus. The patient died 12 hours later with no hemorrhagic complication noted.

III. Discussion

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

Since march 2020, thrombo-embolic 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 of a fivefold increase of the 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 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, a hypercoagulable state caused by sepsis and endothelial activation due to the virus itself and the thrombophilic inflammation responsible of the increase of Von Willebrand factor and factor

VIII (6). The majority of deep vein thrombosis cases were diagnosed in bedridden patients who were put in a prone position which is known for altering venous return and promoting blood stasis. Acute coronary syndrome is thought to be caused by the hypercoagulable and inflammatory state (7), social isolation inducing a decrease of 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 ultrasound only to symptomatic patients, regardless of biological (D-dimer) modifications (9).

The place of TTE, compared to transesophageal echocardiogram, 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 80-90ms (10, 11). In some cases, direct signs are present such as a right intracavitary thrombus which is seen in 2% to 18% of patients diagnosed with a PE. This thrombus is located in the right atrium in 84% of cases and its size ranges from 2 to 10mm in 92% of cases (12, 13). 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 outcome in COVID-19 patients (14). Its increase can be explained by multiple mechanisms: the advanced age of the patients treated, the major inflammatory reaction, the acute pulmonary aggression associated with the deposition of intra-alveolar fibrin responsible for in situ D-dimer production (15). In addition to D-dimers, antiphospholipid antibodies (16), known for their thrombophilic effect, have been identified in some COVID-19 patients (17).

Regarding the anticoagulant treatment, many protocols have been proposed:

- The Société Française de Médecine Vasculaire (French society of vascular medicine) recommends to initiate 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 thrombo-embolic disease. If a TEE is suspected, patients can be treated if the clinical probability is high, even before obtaining paraclinical confirmation.

- 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 favor of respecting the usual thromboprophylaxis doses of LMWH in surveillance wards (63%) and in ICUs (54%). Only 30% were in favor of increasing the posology and less than 16% of them opted for curative doses in primary prevention of TEE (7).

- The European Society of Cardiology and the Société Française de Médecine Vasculaire recommends prescribing thromboprophylaxis treatment for discharged patients. In the other hand, the American College of Chest Physicians does not. In practice, a bedridden patient who was discharged from a 3-weeks stay in an ICU resulting in important neuropathy, will have a higher risk of developing a TEE over a patient who gained back his autonomy. In consequence, thromboprophylaxis treatment should be prescribed after a thorough evaluation of the patient and reassessed regularly.

- If a TEE is diagnosed, the treatment is based on LMWH or fondaparinux in patients admitted for a severe form of the infection (18). They can be switched to a direct oral anticoagulant (DOA) once they are out of the inflammatory phase of the infection.

- 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 (18) and stay on their initial treatment otherwise.

- Patients under a long-term treatment with platelet aggregation inhibitors should not halt it in case of SARS-CoV-2 infection. (9)

- A massive PE with hemodynamic repercussion is an indication to 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 administering the treatment (19). The TTE demonstrates a reduction of the right ventricle size from the third hour. By comparison, heparin has no effect within the same timeframe (20).

IV. Conclusion

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

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