Disseminated Thrombosis in COVID-19 Cases: The Role of Early Antithrombotic Treatments?

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Abstract
Many newly published articles have focused on the association between COVID-19 and thrombogenicity. Indeed, it has become a frequently observed phenomena. In this study, we report on a 45-year-old man with a COVID-19-positive test. His dramatic progression started 5 days after admission. He developed a right ventricular (RV) thrombus (rare condition) and multiple brain sites infarction. We discuss this phenomena by showing the extent to which the thrombosis can take place, the possible relation between inflammatory, D-dimer and case progression and suggest a treatment approach particularly in cases with multiple thrombogenicity organ involvement.

Introduction
Systemic coagulation activation and thrombotic complications are a well observed phenomena in COVID-19 cases. Thrombus can occur in heart, lung and brain and at peripheries. We report a unique case of COVID-19 which developed multiple thromboses at different organ sites.

Case Presentation
A 45-year-old man presented to the emergency department at the Dubai Hospital on May 1, 2020 at 1:20 p.m. with a 1-day history of fever, cough, sore throat and shortness of breath. His vital signs are shown in Table 1.

Physical Exam
He appears well developed and well nourished. Effort breathing with normal breath sounds. Tachypnea noted, no respiratory distress, and heart auscultation revealed tachycardia with no added sound or murmur.
The patient tested positive for COVID-19. He was managed in the AE COVID-19 isolation unit. In addition to 10–15 L/min oxygen mask, paracetamol (IV tablets) and IV fluid, he received medications, for details see Table 2. Unfortunately, the patient experienced dramatic progression and worsening of his condition.

Table 3 shows the progression of his lab markers.

He became more agitated and restless despite O2 saturation ranging between 95 and 98% on 15 L/min of oxygen. On May 6, 2020, the patient complained of weakness in his face since the morning and drooling of saliva. The patient was unable to talk properly, complaining of difficulty in talking with hoarseness of voice. Signs of UMN involvement of facial nerve were noted. Tone and power were normal in his upper arms. An urgent brain CT scan was ordered and reported the following: cortical and subcortical inhomogeneous hypodensities involving bilateral frontal, temporal bilateral cerebellar lobes, suggestive of recent ischemic insult (Fig. 5).

The patient was loaded with aspirin 300 mg and daily 75 mg enoxaparin, shifted from prophylactic dose into full therapeutic doses of 80 mg twice daily. Bedside echocardiography done on May 7, 2020 showed the following: preserved cardiac chamber dimensions, LVEF 60%, normal flow across the heart valves. There were relatively large mobile thrombus seen attached to the anterior cusp of tricuspid valve in the right ventricular inflow subcostal view (Fig. 6a, b).

The patient developed respiratory failure and desaturating SpO2 less than 90%. ABG: PH 7.4, PCO2 72.6, HCO3 28.7, SO2 94.2. He was electively intubated on May 7, 2020. His general condition worsened. He developed brady asystole, resuscitated as per ACLS protocol, but the trials were not successful. His death was declared on May 11, 2020.
Discussion

The reported case showed a disseminated hypercoagulable status. The case has low risk factors for developing thromboembolic phenomena. In the era of the COVID-19 pandemic outbreak, several pathological entities have been proposed by different researchers. Activation of the coagulation system has been observed in many cases. Preliminary data show that in patients with severe COVID-19, anticoagulant therapy appears to be associated with lower mortality in the subpopulation meeting sepsis-induced coagulopathy criteria or with markedly ele-
vated D-dimer [1, 2]. Reports of sepsis, DIC high D-dimer, raised inflammatory CRP, and procalcitonin [3, 4] can lead to the conclusion that the hypercoagulability criteria in Virchow’s triad is the leading thrombogenic factor in COVID-19.

Development of cardiac thrombus (RV) is a rare finding. Right ventricular thrombus formation is a potential complication of ARVC with impaired right ventricular function [5]. As in LV thrombus of formation, the conventional treatment is to receive a therapeutic dose of heparin (either conventional or LMWH). In acutely formed right ventricular thrombus as in this case, we consulted a neurologist for further management with a dose of enoxaparin. He suggested that we should start on a prophylactic dose of 40 mg s.c. b.i.d., repeat CT scan after 24 h, and if no progression occurs, then to consider a full therapeutic dose of enoxaparin.

Right heart thrombus (RHT) typically represent mobilized deep vein thromboses that have become lodged temporarily in the right atrium or right ventricular [6, 7]. This can add more to our understanding of the disseminated nature of thrombogenicity of COVID-19 disease. Although in this case DVT was not looked at even with the presence of high lab results of D-dimer (Table 3), we should highly suspect DVT in high D-dimer and perhaps start a therapeutic dose of heparin as soon as possible to avoid further embolic phenomena.

Furthermore, the natural history of pulmonary embolism (PE) is incompletely characterized because most episodes of PE go undetected [8]. In this case with an appropriate ventilation setting and oxygenation, we should not ignore the pulmonary embolic phenomena which can happen and pass undetected clinically perhaps due to small emboli showers.

The development of cerebrovascular accident (CVA) has dramatic clinical consequences in a COVID-19 patient and a huge impact on medical services. It seems to carry a very high mortality rate. In our hospital, COVID-19 patients who developed CVA have 100% mortality rate.

Conclusion

COVID-19 cases can develop hypercoagulability status. This hypercoagulability and involvement of major organs, like the heart and brain, can have a significant mortality outcome. Introduction of therapeutic antithrombotic treatments such as heparin, antiplatelet and or new oral anticoagulants for these patients as much earlier as possible in the disease may reduce the severity of the disease outcome. Further studies with controlled trials for medical evidence are needed.

Statement of Ethics

According to the Dubai Scientific Research Ethics Committee (DSREC), Dubai Health Authority, no consent from the patient is needed to publish this case report (Ref. DSREC-GL12-2020, of October 15, 2020).

Conflicts of Interest Statement

The authors have no conflicts of interest to disclose.
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Author Contributions

All authors contributed equally.

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