Late manifestation of COVID-19 as aortic thrombus after failure of multiple anticoagulation therapies

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Introduction

SARS-CoV-2 (COVID-19) is a lethal pathogen that has quickly changed the healthcare landscape and quality of life for many people. The novel coronavirus is capable of a wide range of respiratory manifestations. One of the most unique characteristics of this disease process, however, is the tendency for hypercoagulability. Numerous journals have published findings regarding the correlation between COVID-19 and acute pulmonary embolisms or deep vein thrombosis.[1]

Few institutions, however, have documented the relationship with arterial hypercoagulability, specifically within the aorta. Increased propensity for thromboembolic disease has caused the medical community to construct various anticoagulation protocols. At the core of most protocols, it has been agreed upon that unfractionated heparin or low molecular weight heparin is the initial anticoagulant of choice that provides the lowest mortality risk.[2,3]

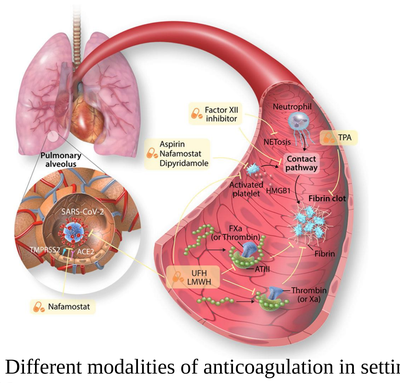

Image 1: Different modalities of anticoagulation in setting of COVID-19.

Case Presentation

A 45-year-old female with a history of COVID-19 pneumonia, atrial fibrillation, diabetes, hypertension, and obesity presented with chest pain and bilateral lower extremity weakness with exertion. She was diagnosed with COVID-19 at an outside facility one month prior to admission which had resolved at the time of presentation. Upon arrival, her right femoral pulse was 2+. Doppler of right dorsalis pedis and posterior tibial arteries were monophasic while left DP/PT were biphasic.

Computed tomography angiogram of the chest and abdomen with bilateral lower extremity runoff demonstrated 1 cm localized thrombus in the descending thoracic aorta, 12 cm thrombus in the right popliteal artery, and a 9 cm long deep vein thrombosis in the right popliteal vein. Patient was previously on apixaban for history of atrial fibrillation. Due to failure, the patient was discharged on rivaroxaban and a walking program.

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Case Presentation (con't)

- Repeat imaging 5 weeks later showed decreasing thrombus size in the descending thoracic aorta, no change in right popliteal artery thrombus, and complete resolution of right popliteal vein thrombus.
- CTA of the chest and abdomen was repeated 21 weeks later and showed continued improvement of the thrombus in the descending thoracic aorta, which was now barely visible.
- 11 days after that CTA, the patient re-presented to the emergency department with new onset left lower extremity pain. On physical exam, patient had non-palpable but dopplerable DP/PT bilaterally.
- Repeat CTA of the chest and abdomen with bilateral lower extremity runoff showed increased size of thrombus in descending thoracic aorta, now measuring 12 mm, increased occlusive thrombus of the right popliteal artery, and minimal visualization of bilateral dorsalis pedis arteries. The imaging was concerning for yet another failure of anticoagulation therapy and the patient was started on a heparin drip.

Due to multiple therapy failure, the patient was scheduled for a thoracic endovascular aortic repair (TEVAR). The operation was canceled after failure to place a lumbar drain. Imaging was repeated and showed the thrombus in the descending aorta had increased in size to 20 mm. As the patient now had failed heparin therapy, and endovascular repair was not feasible, open repair was pursued. A portion of the descending thoracic aorta was replaced with a 24 mm Dacron graft. The patient's postoperative course was relatively unremarkable, and on post-op day 8, she was able to be discharged on coumadin.

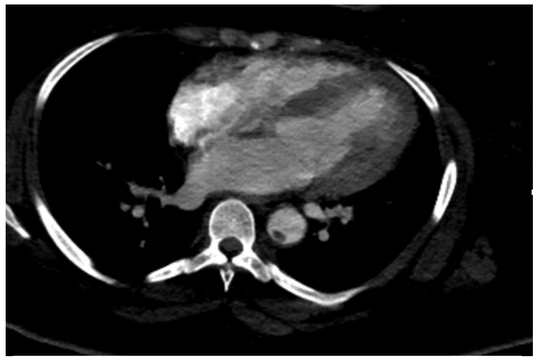

Image 2: CT image demonstrating aortic thrombus found at initial presentation on 4/28/2020.

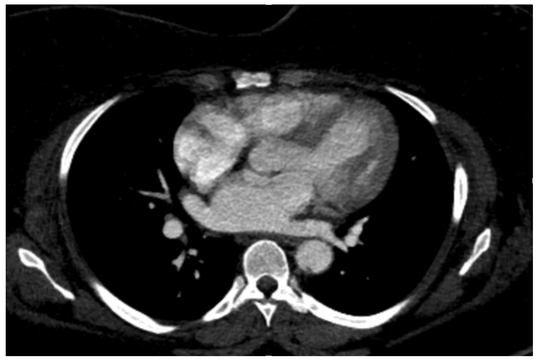

Image 3: CT image showing minimal aortic thrombus after treatment with rivaroxaban. Taken on 6/4/2020.

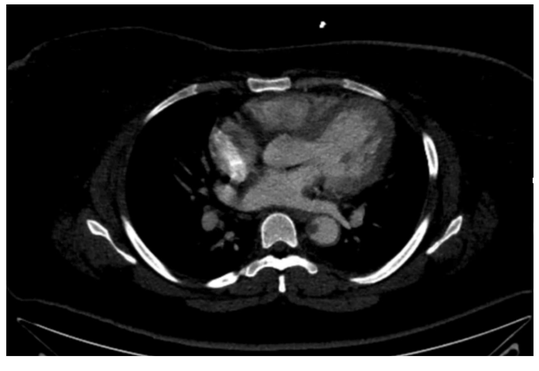

Image 4: CT image demonstrating reaccumulation of aortic thrombus after failure of anticoagulation therapy. Fourth CT taken on 11/9/2020.

Discussion

One widely documented complication of COVID-19 is hypercoagulability and the increasing incidence of venous thromboembolisms such as DVTs and PEs. The particular pathway behind coagulopathy in COVID-19 has not been established. Rather this disease seems to cause vascular hypercoagulability via a multi modal mechanism. A combination of immuno-thrombo-inflammatory process has been recently discussed in the literature.[4] Endothelial injury subsequently leads to inflammation within the vasculature.[5] In addition, the pro-inflammatory environment leads to an influx of cytokines and inflammatory markers such as TNF, IL-1, IL-6 causing a so-called "cytokine storm."[6] This disease process of inflammation also leads to rapid and extensive activation of macrophages and neutrophils, which has been reported as a characteristic of the virus.[4]

Discussion (con't)

One particular lab finding that has been outstanding in most COVID positive patients, is the elevation of D-dimer. This however has proven to be nonspecific in regards to severity of disease or long-lasting outcomes. Other significant lab values in patients with history of COVID reported by Calderon-Lopez showed 75% of patients had increase in fibrinogen and 86% of patients had increase in Factor VIII.[7] Post viral arterial thrombi have been of particular interest regarding the field of vascular surgery. One recent systemic analysis that included a total of 90 patients with history of COVID and arterial thrombi from 27 separate studies noted involvement of limb arteries (39%), cerebral arteries (24%), and great vessels (19%).[8] To our knowledge, very few cases of arterial thrombosis as the delayed manifestation of COVID-19 exist.

No consensus has been reached as to the specific therapies that should be used although a few guidelines have been released highlighting the significance of unfractionated heparin or low molecular weight heparin as primary inpatient treatment.[2,3] One of the preliminary guidelines released were from the International Society of Thrombosis and Hemostasis (ISTH) stating an initial dose of LMWH can be given to all patients needing hospitalization to decrease mortality and combat inflammatory cytokines. Furthermore, The American Society of Hematology has released interim guidelines on the management of venous thromboemboli and recommends the use of direct-acting oral anticoagulants over vitamin K antagonists.[9]

Conclusions and Implications

- COVID-19 is correlated with an increased risk of hypercoagulability and can even present in rare manifestations such as aortic and arterial thrombi.
- This case provides clear evidence that the late sequelae of COVID-19 are unknown.
- It would be beneficial to the medical community to devise a comprehensive plan on how to address the use of anti-coagulants in patients that have treatment failure.
- Lastly, there may be an advantage to check COVID status or IgM/G antibodies in newly diagnosed aortic thrombus with unknown etiology.

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