Case Report

Multiple Arterial Thrombosis in a 78-Year-Old Patient: Catastrophic Thrombotic Syndrome in COVID-19

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ABSTRACT
We describe a patient with coronavirus disease 2019 (COVID-19) and multiple concomitant thromboses occurring on the 9th day of hospital stay. Thromboses were found in distinct zones of the aorta, as well as in the renal, humeral, and pulmonary arteries. The extensive biological workup performed following this catastrophic thrombotic syndrome found no evidence for underlying prothrombotic disease. In light of current evidence regarding endothelium abnormalities related to COVID-19, this extreme case of catastrophic thrombotic syndrome suggests that COVID-19 can induce severe arterial thrombosis following intense endothelial activation.

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Ethics Statement: The research reported in this paper adhered to relevant guideline.

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to the posterior wall of the abdominal supra-renal aorta, a small thrombus of the lateral wall of the aorta, and renal ischemia related to a complete occlusion of the right renal artery (Fig. 1A). The patient was diagnosed with intestinal occlusion due to paralytic ileus following the renal embolic event. The thoracic CT also showed an in situ pulmonary thrombosis of the posterobasal segment of the right lower lobe. The vascular CT of the left arm identified a distal thrombosis of the humeral artery. The Doppler exam of the carotids and lower limbs did not identify any other arterial or venous thrombosis. Transthoracic echocardiography identified neither intracardiac thrombus nor intracardiac shunt (negative for a right-to-left shunt using contrast). Transesophageal echocardiography was not performed. Intravenous unfractionated heparin was initiated (and rivaroxaban stopped). The patient underwent Fogarty embolectomy, which successfully removed the left humeral thrombosis (histopathology shown in Fig. 1B).

On day 10, while the patient had been on IV unfractionated heparin (with heparinemia within therapeutic range), the patient developed aphasia and motor deficit of the left lower limb. The brain magnetic resonance imaging scan showed an ischemic stroke in the territory of the left posterior inferior cerebellar artery (Fig. 1C). Major gastrointestinal bleeding occurred while heparinemia was ranging between 0.75 and 1.21 UI/ml. Concomitantly, an occlusion of the left palmar arch occurred. The oxygenation status did not worsen, and the patient did not undergo intubation. However, given the severity of the neurologic disorders, the coexistence of severe bleeding (which occurred after the ischemic stroke) and threatening thrombosis, the severe pain induced by digit ischemia, and the underlying frailty favoring rapid clinical worsening (sacral pressure ulcer and bronchial stasis), a

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**Figure 1.** (A) Images from the combined thoracic and abdominal computed tomography scan. The top arrows indicate a large aortic floating thrombus attached to the posterior wall of the abdominal supra-renal aorta. The middle arrows indicate the small aortic thrombus of the lateral wall. The bottom arrows indicate the proximal portion of the thrombus occluding the right renal artery. (B) Histopathology view (hematoxylin and eosin stain) of the humeral thrombus showing numerous altered neutrophils in its center (in blue—cell nucleus in deep blue; unaltered cells in pink). (C) Cerebral magnetic resonance imaging findings (FLARE sequence) showing multiple ischemic lesions in the brain stem, cerebellar vermis.
A thorough discussion with the patient’s family was undertaken. In line with the family’s wishes, palliative care was started on day 12. The patient died on day 19.

At admission, lab tests (Table 1) excluded COVID-19 coagulopathy according to the International Society on Thrombosis and Hemostasis definition (partial thromboplastin time 29.7 seconds). Platelet counts remained greater than 100 G/L despite daily hemograms. The extensive thrombophilia screening we performed was negative. Specifically, we found no evidence for antiphospholipid syndrome (2 negative tests, using 2 techniques, following the International Society on Thrombosis and Hemostasis guidelines).

Our patient suffered from a thrombotic storm/catastrophic thrombotic syndrome in the setting of COVID-19, with thrombus found in the aorta, and thromboembolic occlusion of pulmonary, renal, and humeral arteries. In contrast with 3 recently reported cases of embolic events in the setting of COVID-19, we found no evidence for antiphospholipid antibodies or other inherited thrombophilia. As our patient had a negative thrombophilia screening, and no atrial fibrillation and/or severe atherosclerosis, we believe that COVID-19 could represent a new etiology of catastrophic thrombotic syndrome. However, given that the patient had a history of previous pulmonary embolism, and thrombophilia screening can be falsely negative while under anticoagulants, we cannot completely rule out a concomitant other thrombotic risk factor. Nonetheless, the trigger for these extensive thromboses could well be the COVID-19—related endoceleitis described by Varga and colleagues. The intensity of this endothelial involvement related to severe acute respiratory syndrome coronavirus 2 prompted Ciceri and colleagues to describe COVID-19 disease as an “endothelial thromboinflammatory syndrome.” This intense endothelial thromboinflammatory syndrome could have been the trigger of the catastrophic case we are reporting herein, in the absence of “usual” procoagulant factors. Clinical trials (such as the Weight-Adjusted vs Fixed Low Doses of Low Molecular Weight Heparin For Venous Thromboembolism Prevention in COVID-19 [COVI-DOSE] trial—NCT04373707) investigating the best anticoagulation strategies in this setting are urgently needed.

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