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COVID-19 complicated by acute arterial thrombosis: Therapeutic challenges

A 64-year-old Caucasian woman with a past medical history of hypertension, hyperlipidemia, morbid obesity, hypothyroidism, ovarian tumor in remission, presented to the emergency department (ED) with a day history of altered mental status, left upper extremity pain, weakness, dizziness, unsteadiness, and a fall. The patient had an onset of dry cough for one week and received outpatient azithromycin. In the ED, body temperature was 95.4 °F, oxygen saturation was 89% on room air, blood pressure of 134/76, and pulse of 87. Physical exam yielded a leathargic yet otherwise oriented to time, place, and person patient with left upper extremity weakness, coldness, diminished brachial, radial, and ulnar pulses. Initial lab work revealed normal complete blood counts, unremarkable metabolic panels, normal TSH and procalcitonin. A chest x-ray showed bilateral patchy infiltrates suggestive of COVID-19 pneumonia. Subsequently, the COVID-19 nucleic acid amplification test detected the virus. The patient underwent a series of imaging studies with Doppler arterial ultrasound that showed acute thrombosis of the left brachial artery. CT and MRI of the brain showed acute infarct within the posterior circulation involving the left cerebellum and left posterior-lateral medulla (Panel 1). A Transthoracic echo showed preserved systolic function with no intra-cardiac thrombi or evidence of intracardiac shunts. EKG was normal, with 431 msec QTc interval. Additional lab work revealed elevated D-Dimer 1896 ng/mL (<500 ng/mL), Fibrinogen 620 mg/dL (200–400 mg/dL), and C reactive protein 119 mg/L (<90 mg/L). The patient underwent urgent left upper extremity angiogram through the right common femoral artery, with difficulties due to presence of a pannus. A 25 cm 6 French sheath was inserted, a wire advanced into the aortic arch under fluoroscopic guidance, the left subclavian artery selected, and intravenous heparin infused. The angiogram demonstrated a significant filling defect at the junction of the left subclavian and brachiocephalic arteries (Panel 1) with no flow in the left vertebral artery. The catheter was advanced into the left axillary artery, then abruptly into the occluded left brachial artery at the level of the mid humerus with no collaterals supplying the forearm. The catheter was further advanced below the elbow, the ulnar artery was selected, a dedicated angiogram performed which showed a relatively normal ulnar artery with static contrast and no significant inflow. Selective radial angiogram demonstrated a diminutive and thrombosed radial artery (Panel 1). A 135 cm thrombolysis catheter was advanced with the distal tip within the radial artery and across the origin of the ulnar artery, with the proximal side hole within the patent segment of the left brachial artery, thrombolysis was initiated at a rate 0.5 mg of tPA per hour for a total of 12 h. Post thrombolysis angiogram showed successful thrombolysis with minimal residual thrombus within the left forearm and the left radial artery, blood flow was restored within the deep palmar arch, with perfusion of the fingers (Panel 2). In the interim, the patient was maintained on full-dose anticoagulation after neurology and neurosurgery assessment, oxygen therapy, hydroxychloroquine, and azithromycin, then admitted to the intensive care unit under the care of a multidisciplinary team. Given the unique presentation and overwhelming thrombosis, a comprehensive coagulopathy testing was implemented to underline any concomitant thrombophilia, which was unremarkable, that included anti-nuclear antibody, anticardiolipin antibodies, lupus anticoagulant, B2 Glycoprotein, anti-thrombin III, JAK2 (V617F), Protein C, Protein S activity. Factor 5 (V) Leiden, Prothrombin genes and there was no flow cytometric evidence of paroxysmal nocturnal hemoglobinuria. The clinical course was later complicated by neurologic deterioration due to expanding cerebral ischemia with hemorrhagic conversion despite therapeutic anticoagulation, hence the patient was eventually placed on comfort measures.

The novel coronavirus, identified in December 2019 in Wuhan, China, has rapidly spread and became a global pandemic [1]. The most common presentation of the COVID-19 is cough (79.4%), followed by fever (77%), and dyspnea (56.5%). In up to 33.1% of patients, the disease’s course ended with severe respiratory failure leading to invasive mechanical ventilation [2]. Furthermore, the patients can develop COVID-19 induced coagulopathy, which mandates appropriate evaluation, and interventions to prevent and treat thromboembolic complications [3]. The overall pathogenesis of COVID-19 induced thrombosis is incompletely understood. The proposed mechanisms include endothelial dysfunction due to direct viral invasion; critical care immobility and stasis; intravascular catheters related injury, and acute systemic inflammatory response (Cytokine, and Complement-mediated storm) [4,5]. Finally, elevated levels of circulating prothrombotic factors (factor VIII, fibrinogen, von Willebrand factor, and Neutrophil extracellular traps), reactive thrombocytosis, and antiphospholipid antibodies are all linked with severe COVID-19 [6–8]. D-dimer levels also correlate with morbidity and mortality; thus, supporting prophylactic anticoagulation when D-dimer levels are very high (e.g., >6 times the upper limit of normal) [3]. In a series of 184 ICU admitted COVID-19 patients, 31% cumulative incidence of thrombotic events was noted, of which 27% were confirmed VTE’s and 3.7% attributed to arterial thrombosis [9]. Another series reported twenty COVID-19 patients who developed acute limb ischemia at a single institution over three months, open surgical revascularization performed in 17, of which 12 (71%) were successful, postoperative systemic heparin infusion significantly associated with survival (0% vs. 57.1%, P = 0.042) [10]. Another report described four patients with acute limb ischemia, two of whom
were young and did not have any comorbidities who developed humeral artery and aortoiliac thromboses, treated with systemic anticoagulation only [11]. Our patient clinical presentation indicates a COVID-19–related hypercoagulable state as a plausible cause of acute limb ischemia and stroke. This case shines the light on a novel therapeutic approach when managing acute limb ischemia with a pharmacomechanical strategy using catheter-directed thrombolysis (CDT) in conjunction with systemic anticoagulation reported in many pieces of literature when treating massive venous and pulmonary embolism. Thus, further studies are needed to determine CDT’s efficacy and safety and the role of empiric intermediate or full-dose anticoagulation in high-risk patients with COVID-19 to prevent and treat thromboembolic complications.

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Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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