The Potential Involvement of SARS-CoV-2 in the Immuno-Pathogenesis of a Type A Aortic Dissection Case

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Abstract
The novel coronavirus disease 2019 (COVID-19) may represent different clinical manifestations with different severities, from mild to severe. Even though the respiratory system is the mainly involved organ, numerous reports have mentioned cardiovascular complications in COVID-19. Herein, we report a case of type A aortic dissection in a COVID-19 patient.

KEYWORDS
aortic dissection, cardiovascular complications, COVID-19

1 | INTRODUCTION

Since the first emergence of the novel coronavirus in December 2019 in Wuhan, China, and the subsequent pandemic, the disease has become a major matter of concern for global health and affected millions of people all over the world. SARS coronavirus 2 (SARS-CoV-2), the virus responsible for COVID-19, targets the upper and lower respiratory tracts in most cases. Their involvement would cause pneumonia with symptoms such as dry cough, dyspnea, fever, sputum production, and rhinorrhea. One of the significant complications related to this virus is the ability of the disease to affect other organs with a wide range of signs and symptoms. Gastrointestinal manifestations (e.g., nausea, vomiting, diarrhea, anorexia, etc.), neurological manifestations (e.g., anosmia, ageusia, headache, altered mental status, dizziness, etc.), and multiorgan dysfunction (e.g., metabolic or electrolyte imbalance, etc.) may occur in COVID-19 patients.

In this case presentation, we aim to focus on the cardiovascular complications of COVID-19. They can present in different forms and severities, from nonspecific palpitations and chest tightness to life-threatening events such as left ventricular dysfunction (heart failure), acute
coronary syndrome (ACS), acute pericarditis, thromboembolic events (i.e., deep vein thrombosis [DVT], pulmonary embolism [PE], etc.), and sudden cardiac death. On the contrary, a worse prognosis and disease course have been reported in COVID-19 patients with a history of cardiovascular disease.

2 | CASE REPORT

A 67-year-old overweight man, a known case of hypertension and hyperlipidemia, with a history of aortic valve replacement (AVR) 7 years ago presented with dyspnea and epigastric pain. On admission, he was afebrile with tachycardia. The oxygen saturation in room air was 93%. Blood pressure was 150/90 mmHg on admission but decreased gradually and finally ended up in shock and acidosis. The patient's drug history included losartan 50 mg twice daily and atorvastatin 20 mg daily.

To rule out COVID-19, a chest CT scan was requested (the patient was hemodynamically stable at that time), which showed the parenchymal involvement suggestive of COVID-19 pneumonia (Figure 1). Furthermore, a chest CT scan revealed dilation of the ascending aorta. To evaluate for acute aortic syndromes, the patient was scheduled for emergency CT-angiography (CTA). CTA showed a flap dissection from the sinus of Valsalva extending to both common iliac arteries in favor of type A aortic dissection. Aortic arch branches originated from the true lumen and were patent. The coronary arteries originated from a false lumen with no flap of dissection within them. Celiac artery, superior mesenteric artery, and left renal artery originated from the true lumen. Inferior mesenteric artery originated from a false lumen. Right renal artery, even though originating from the true lumen, had small flaps of dissection (Figure 2). Ultra-sonography of the urinary system demonstrated increased cortical and pyramidal echo density with decreased cortico-medullary differences in both kidneys.

The laboratory results were as follows: Hb = 13.1 g/dl, WBC = 11,600 cells/mm³, ESR = 41 mm/h, LDH = 1039 IU/L, AST = 171 IU/L, ALT = 160 IU/L, ALP = 243 IU/L, Amylase = 95 IU/L, and the Troponin level was higher than normal.

The initial electrocardiogram (ECG) showed sinus tachycardia at the rate of 110 bpm, low voltage QRS complex in limb leads with no ischemic changes (Figure 3).

Transthoracic echocardiography in the emergency room showed a flap dissection in the ascending aorta interfering with aortic valve closure, resulting in moderate to severe aortic regurgitation. Functions of both ventricles were preserved with no pericardial effusion.

Regarding severe acidosis, elevated LDH level, and severe abdominal pain, an emergency surgery consult was requested with an impression of acute mesenteric ischemia. Despite intensive medical treatment (i.e., hydration, antibiotic therapy, etc.), the patient did not make it to the operating room and passed away before any surgical intervention. The PCR test result came positive for COVID-19 following the patient’s death.

3 | DISCUSSION

Herein, we report a COVID-19 patient with type A aortic dissection. This is not the first case of aortic dissection in
COVID-19 patients, and similar cases have been reported in the literature.\textsuperscript{5} Considering that aortic dissection is a severe life-threatening condition, these cases must be noticed to look for any association between these two conditions. This may help clinicians to give the optimal response in case of emergency conditions.

The relationship between viral infections and aortic dissection is now a substantial concern. Higher rate of aortic dissection admissions and increased in-hospital mortality were reported during influenza season.\textsuperscript{6} Factors such as inflammation and further immune-mediated injury, increased sympathetic activity, and adverse effects of medications may explain this relationship.

The pathophysiology of SARS-CoV-2 mainly involves the host inflammatory response, rather than viral infection. It has been shown that cytokine storm (CS), which is an exaggerated immune response to infection, is responsible for the deterioration of severe COVID-19 patients.\textsuperscript{7}
These immunopathologic pathways in COVID-19 infection may explain the higher rate of aortic dissection in these patients.

Recent studies have pointed out that the inflammatory response and apoptosis play a substantial role in aortic dissection pathogenesis. To explain the pathophysiology more profoundly, it is good to mention a 2020 study conducted by Ito et al. They showed that myocardin-related transcription factor A (MRTF-A) (i.e., a signal transducer of mechanical and hormonal stress) is one of the inducers of aortic dissection in mouse models. In their study, MRTF-A was induced by angiotensin II (Ang II). Angiotensin-converting enzyme 2 (ACE2) is the main receptor for SARS-CoV-2 entry to host cells. Following internalization of virus-ACE2 complex, the ACE2 level becomes downregulated and, therefore, Ang II level increases. According to Ito et al, this increased level of Ang II may induce aortic dissection via MRTF-A. Furthermore, increased levels of ACE2 can cause inflammation that is considered as another pathophysiology for aortic dissection. According to these findings, the occurrence of aortic dissection in COVID-19 patients does not seem very odd anymore.

**Figure 3** Initial electrocardiogram (ECG) showing sinus tachycardia at the rate of 110 bpm, right bundle branch block low voltage QRS complexes in limb leads with no ischemic changes
AUTHOR CONTRIBUTIONS
Azin Alizadehas involved in conceptualization, data curation, and writing—review and editing. Samira Eslami involved in supervision, data curation, and writing—original draft. Kimia Vakili involved in writing—original draft. Shirin Habibi Khorasani, Hamidreza Pour Aliakbar, Hanieh Nezhadbahram, and Mehrdad Haghazali involved in writing—review and editing.

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CONFLICT OF INTEREST
The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT
No data are available.

ETHICAL APPROVAL
Written informed consent was obtained from the relatives of the patient to publish this report in accordance with the journal's patient consent policy.

CONSENT
Written informed consent was obtained from the patient to publish this report in accordance with the journal’s patient consent policy. None of the authors listed on the manuscript are employed by a government agency that has a primary function other than research and/or education. None of the authors are submitting this manuscript as an official representative or on behalf of the government.

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