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# A Case of Multiple Large Left Ventricular Clots in a Patient with COVID-19

Azin Alizadehasl [1], MD; Soudeh Roudbari [2], MD; Pegah Salehi [2,*], MD; Alireza Sistani [3], MD; Atousa Mostafavi [4], MD; Hossein Kamranzadeh Fumani [5], MD; Alireza Yaghoubi [6], MD; Faranak Kargar [6], MD; Sara Adimi [7], MD

[1] Cardio-Oncology Department and Research Center, Rajaie Cardiovascular Medical and Research Center, Tehran, IR Iran
[2] Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran
[3] Emergency Department, Arak University of Medical Sciences, Arak, IR Iran
[4] Department of Cardiology, Tehran University of Medical Sciences, Shariati Hospital, Tehran, IR Iran
[5] Hematology-Oncology and Stem Cell Transplantation Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, IR Iran
[6] Heart Valve Disease Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran
[7] Department of Exercise Physiology, Central Tehran Branch, Islamic Azad University, Tehran, IR Iran

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**ABSTRACT**

**Introduction:** In January 2020, a new coronavirus was identified as the source of a newly developing type of pneumonia (COVID-19) in China. The number of infected people has been rising swiftly throughout the world since then and it has been reported to affect multiple systems apart from causing usual atypical pneumonia, one of which being the cardiovascular system. The underlying mechanism leading to cardiac injury has been hypothesized to be linked to a cytokine storm with unbalanced response to T-cell subtypes or secondary hemophagocytic lympho-histiocytosis, direct cardiac injury through viral myocarditis or cardiomyopathy through the ACE2 receptor, oxygen supply/demand imbalance with or without coronary artery disease, hypoxemia, and positive pressure ventilation leading to increased right ventricular afterload due to respiratory acidosis.

**Case Presentation:** A 49-year-old female with a non-notable medical history presented to the emergency department with the chief complaint of dyspnea, fever and chills, severe dry coughs, and diarrhea. COVID-19 was confirmed by chest Computed Tomography (CT) scan and Real-Time Polymerase Chain Reaction (RT-PCR). Due to high troponin levels, echocardiography was done, indicating that the patient had a reduced left ventricular ejection fraction with multiple large Left Ventricular (LV) clots, but she had no lesions in coronary angiography.

**Conclusions:** The pathological mechanism by which SARS-COV-2 causes viral myocarditis is still uncertain. However, it may result in cardiac injury via multiple mechanisms. COVID-19 may also predispose the body to thromboembolism in different ways. The current data suggested the existence of a hyper-coagulability state in patients with COVID-19 and endotheliitis could explain the reason why these patients seem more prone to venous and arterial thrombosis. However, further studies are needed to determine the other causes of the cardiovascular complications of COVID19.

## 1. Introduction

In January 2020, a new coronavirus was identified as the source of a newly developing type of pneumonia (COVID-19) in China. The number of infected people has been rising swiftly throughout the world since then. COVID-19 is the clinical manifestation of infection with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), a member of the family of Coronaviruses. The virus typically presents with significant respiratory symptoms that can progress into pneumonia, acute respiratory distress syndrome, or even shock. In the last few months, since the arising of the new virus, it has been reported to affect multiple systems apart from causing usual atypical pneumonia, one of which being the cardiovascular system (1-8).

*Corresponding author: Pegah Salehi, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran, Cellphone: +98-9133642258,
Email: p.salehi345711@gmail.com.

The underlying mechanism leading to cardiac injury is still unclear, but it has been hypothesized to be linked to a cytokine storm with unbalanced response to T-cell subtypes or secondary hemophagocytic lympho-histiocytosis, direct cardiac injury through viral myocarditis or cardiomyopathy (through the ACE2 receptor, since an animal model has shown that lung infection with SARS-COV-2 could cause ACE2-dependent myocardial infection), oxygen supply/demand imbalance with or without coronary artery disease, hypoxemia (which increases intracellular calcium and leads to myocyte apoptosis), and positive pressure ventilation leading to increased right ventricular afterload due to respiratory acidosis (3, 4, 6, 8-10).

This study aims to report a case of clinically suspected COVID-19-induced myocarditis with multiple large Left Ventricular (LV) clots.

## 2. Case Presentation

A 49-year-old female with a non-notable medical history, except for hyperlipidemia, presented to the emergency department with the chief complaint of dyspnea, fever and chills, and severe dry coughs since a few days ago. On the day of admission, diarrhea was added to her symptoms. She denied any recent travels, but confirmed having contact with a SARS-COV-2 positive patient who was a close relative.

Electrocardiogram (ECG) showed non-specific ST-T changes and chest Computed Tomography (CT) scan revealed bilateral ground glass opacities in favor of COVID-19 viral pneumonia (Panels A, B). The Real Time Polymerase Chain Reaction (RT-PCR) test also turned out to be positive. Other notable laboratory results included positive troponin = 181ng/L (normal value < 50 ng/L), white blood cells count = 7800/mL (13% lymphocytes), and elevated C-Reactive Protein [CRP, 5 mg/dL (normal value < 1 mg/dL)] and Erthyrocyte Sedimentation Rate [ESR, 45 mm/hr (normal value < 20 mm/hr)]. Due to the high troponin levels, a cardiology consult was requested and the patient underwent echocardiography, which showed a Left Ventricular Ejection Fraction (LVEF) of 40%, normal Right Ventricular (RV) size and function, no significant valvular disorder, no pericardial effusion, and multiple large apical and lateral wall clots (Panels C, D). Coronary catheterization was also performed, revealing normal coronary arteries and, consequently, confirming the diagnosis of COVID-19-induced myocarditis. Thus, treatment based on the guideline's drugs was initiated for the patient (figure 1).

## 3. Discussion

In January 2020, a new coronavirus was identified as the source of a newly developing type of pneumonia (COVID-19) in China and it rapidly began to spread worldwide, becoming an international health concern. The responsible pathogen has been identified as a novel single-stranded enveloped RNA similar to the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and has thus been named as SARS-CoV-2. The clinical course of SARS-CoV-2 infection has been characterized mainly by respiratory symptoms, such as fever, dry cough, and shortness of breath, which rapidly developed into Acute Respiratory Distress Syndrome (ARDS), multi-organ failure, and secondary bacterial infections in some patients. With the increasing number of confirmed cases of COVID-19 and the gathering of worldwide clinical data, in addition to the common clinical presentations of respiratory failure caused by COVID-19, there has been a considerable amount of concern regarding the cardiovascular manifestations induced by the virus. Cardiovascular complications of viral infections might include arrhythmias, myocarditis, pericarditis, heart failure,

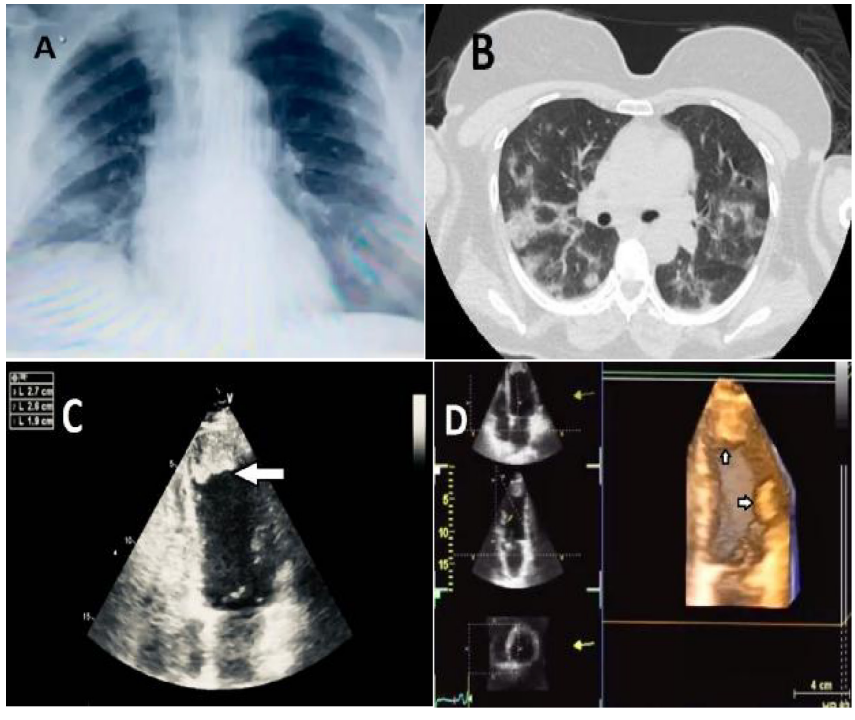


**Figure 1 (A-D).** A, the Patient's Chest X-ray Revealing Multiple Peripheral Opacities; B, Chest CT Scan Confirming the Findings of X-ray; C, Apical LV Clot in Trans-Thoracic Echocardiography; D, Apical and Lateral LV Clots in 3D Echocardiography.

myocardial ischemia, and type 1 and type 2 myocardial infarction. Evidence of myocardial damage has been proven by an increase in cardiac biomarkers, ECG changes, and echocardiographic abnormalities in up to 7.2% of patients without underlying cardiac disease and 22% of ICU patients in some studies. Additionally, increase in cardiac biomarkers was higher in patients with underlying cardiac disease and was associated with a higher mortality rate (1-8).

The pathological mechanism by which SARS-CoV-2 causes viral myocarditis is still uncertain. Yet, it may result in cardiac injury via multiple mechanisms. 1. SARS-CoV-2 could cause direct viral invasion of cardiomyocytes and lead to myocarditis via this process. However, this has not been proven in pathological studies. In one case of endomyocardial biopsy, low-grade inflammation of the endocardium was detected with vacuolated macrophages, in which Coronavirus particles were seen in cytopathic, structurally damaged interstitial cells, while no viral particles were observed in the myocytes and endothelium and no myocardial necrosis was detected. 2. COVID-19 might cause cardiac injury indirectly by triggering an overwhelming immune inflammatory response, leading to the release of a profound systemic inflammatory activation (cytokine storm), which in turn might lead to a severe immunologic reaction in patients with a susceptible genetic predisposition, causing multi-organ dysfunction, one of the affected organs being the cardiac system. 3. Severe hypoxia from acute respiratory damage or oxygen supply/demand imbalance with or without coronary artery disease caused by the virus might result in oxidative stress and myocardial injury from increased myocardial oxygen demand in the presence of severe hypoxia due to acute lung injury (9-15). 4. Stress, or takotsubo, cardiomyopathy primarily occurs in females and can be preceded by emotional or physical triggers. A review of published reports suggested that coronary artery vasospasm, coronary microvascular dysfunction, LV outflow tract obstruction, and catecholamine surge might be the potential mechanisms of development of stress cardiomyopathy, which have also been reported in viral infections. Interestingly, it has been reported in patients with COVID-19, as well. This requires further investigation as a cause of cardiomyopathy in patients with COVID-19 (16). COVID-19 might also predispose the body to thromboembolism in different ways. The physiopathology has not been fully understood yet, but the current data have suggested the existence of a hyper-coagulability state in patients with COVID-19. Coronavirus infection might be a trigger for the activation of the coagulation system via several different pathogenetic mechanisms, including endothelial dysfunction characterized by increased levels of von Willebrand factor, systemic inflammation by toll-like receptor activation, and a pro-coagulatory state by tissue factor pathway activation (17). In more recent studies, there has been evidence of COVID-19 endothelial cells entering through the ACE2 receptor leading to endothelitis, which made patients susceptible to arterial and venous thrombosis. Patients with other risk factors of endothelial lesions, including male sex, high blood pressure, smoking, and diabetes, were more prone to the adverse effects of the virus on endothelium (18-20). Another recent research (21) showed a remarkably high prevalence of Deep Vein Thrombosis (DVT) (46%) and revealed the rapid time-course of thrombus formation despite prophylactic anti-coagulation. Importantly, 50% of the DVT was popliteal or femoral and was most often associated with thromboembolic events. This was consistent with the unexpectedly large number of pulmonary embolisms (21%) reported in SARS-CoV-2 pneumonia patients admitted to the ICU. Data obtained from China and Europe also suggested that COVID-19 might be associated with a hypercoagulable state and increased risk for venous thromboembolism. In addition, clots have been reported in the right ventricle in several other case reports (22-26).

A current research reported three cases with severe COVID-19 and cerebral infarction, one associated with bilateral limb ischemia, in the setting of elevated anti-phospholipid antibodies. Whether anti-phospholipid antibodies play a major role in the pathophysiology of thrombosis associated with COVID-19 requires further research (27). Furthermore, four cases of aortic thrombosis in patients admitted with COVID-19 were described in another study (28). Moreover, in a biopsy from the lungs of COVID-19 patients, distinctive vascular features were shown, consisting of severe endothelial injury associated with the presence of intra-cellular virus and disrupted cell membranes. Histologic analysis of pulmonary vessels in patients with COVID-19 revealed widespread thrombosis with microangiopathy. Alveolar capillary microthrombi was nine times as prevalent in patients with COVID-19 as in those with influenza and the amount of angiogenesis was 2.7 times as high as that in the lungs of the patients with influenza (29). Therefore, recent recommendations have emphasized prophylactic anti-coagulation measures in COVID-19 patients to prevent thromboembolism.

### *3.1. Conclusion*

In the recent publications, evidence of myocardial damage has been proven by an increase in cardiac biomarkers, ECG changes, and echocardiographic abnormalities in many patients without underlying cardiac diseases. The pathological mechanism by which SARS-CoV-2 causes viral myocarditis is still uncertain. Yet, it may result in cardiac injury via multiple mechanisms, which needs further research via biopsy or autopsy. COVID-19 may also predispose the body to thromboembolism in different ways. The physiopathology of the susceptibility to thromboembolism is not fully understood, but the current data have suggested the existence of a hyper-coagulability state in patients with COVID-19 and endotheliitis could explain the reason why COVID-19 patients seemed more prone to venous and arterial thrombosis. This requires further research on larger sample sizes throughout the world in order to help understand the underlying mechanisms in the near future.

### *3.2. Ethical Approval*

Not applicable.

### *3.3. Informed Consent*

The informed consent file has been uploaded in the files section.

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**Authors' Contribution**

Study concept and design: A.A., A.M., and A.S.; drafting of the manuscript: P.S. and S.R.; critical revision of the manuscript for important intellectual content: A.Y., F.K., and S.A.; statistical analysis: H.E.

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