Myocarditis Associated With COVID-19

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Abstract

Coronavirus disease 2019 (COVID-19) has rapidly evolved into a global pandemic, with affecting to-date over 23 million people and causing over 800,000 deaths around the globe. The major pathogenetic mechanisms include inflammation, vasoconstriction and thrombogenesis. Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) typically manifests as fever, cough, shortness of breath, and exhibits radiographic evidence of bilateral pneumonic infiltrates. Recent meta-analyses have shown that myocardial injury, including viral myocarditis, is prevalent among infected patients, especially in patients requiring ICU level care. Diagnosis of viral myocarditis is multifactorial and involves detection of elevated cardiac biomarkers and echocardiographic evidence of cardiomyopathy, in the absence of diseased coronary arteries. Endomyocardial biopsy with histopathologic examination provides definitive confirmation. We present a case of a previously healthy 52-year-old male who presented clinically with suspected myocarditis with new-onset dilated cardiomyopathy (DCM) and systolic dysfunction as a sequela of infection with SARS-CoV-2. In this report we highlight the clinical presentation of echocardiographic findings and proposed pathogenetic mechanisms of myocarditis associated with COVID-19 which has a varied presentation, ranging from clinically silent to life-threatening arrhythmias with hemodynamic compromise.

Keywords

1. Introduction

Coronavirus disease 2019 (COVID-19) was first reported to the World Health Organization (WHO) in late December 2019 as several isolated cases of cryptogenic pneumonia in Wuhan, China. [1,2] Three months later, the disease rapidly evolved into a global pandemic with putative pathogenetic mechanisms underlying the increased morbidity and mortality include acute inflammation, thrombogenesis, vasoconstriction, hemoglobin dysfunction and T-cell dysregulation [3]. These mechanisms are discussed in details and illustrated in a

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recently published paper by our group (Zhyvotovska A, Yusupov D et.al) [3] that also outlines some of the likely causes of the cardiac effects of COVID-19 that are, at least in part, due to reduction of angiotensin converting enzyme 2 (ACE2), acute inflammatory responses, hypoxia, and disruptions in the coagulation pathway [3] At present there are 22.6 million confirmed cases of COVID-19 worldwide with nearly 800,000 death attributed to the disease with the majority of documented cases in the United States (5.6 million and 174,000 death). [4]

Named according to genomic similarity to the virus responsible for the SARS pandemic, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been identified as the causal agent of COVID-19. [5] Infection with this novel pathogen typically manifests as fever, cough, shortness of breath, and radiographic evidence of bilateral pneumonic infiltrates. [1,2] Given the novelty of this viral outbreak, very few cases in literature have described the cardiac manifestations of COVID-19. According to a recent meta-analysis, the prevalence of myocardial injury in infected patients, as reflected by elevations in cardiac biomarkers, is 7.2 percent overall and 22 percent in patients requiring ICU level care. [6] Similarly, heart failure was identified as a complication in 49 percent of patients who died and in 3 percent of patients who recovered, in a retrospective study of 799 patients hospitalized for COVID-19. Among both groups, the overall prevalence of chronic heart failure was less than one percent. [7,8] Here we present a case of a previously healthy male who developed clinically suspected myocarditis with new-onset dilated cardiomyopathy (DCM) and systolic dysfunction as a sequela of infection with SARS-CoV-2.

2. Case Presentation

A 52-year-old healthy African American male with a 9-year history of well controlled hypertension, and no prior history of cardiovascular disease, presented to the emergency department with cough, subjective fever, shortness of breath, and a single episode of trace hemoptysis over the last 5 days. He initially presented 2 days earlier with similar symptoms and was subsequently discharged home for self-isolation with a presumptive diagnosis of COVID-19.

Physical examination revealed blood pressure of 161/109 mm Hg, heart rate of 118 beats per minute, respiratory rate of 20 breaths per minute, oxygen saturation of 87% on room air, and a body temperature of 98.0F (36.7C). On pulmonary auscultation the patient had trace bibasilar rales. Arterial blood gas analysis showed a pH of 7.49, carbon dioxide partial pressure of 27.9 mm Hg, oxygen partial pressure 93.3 mm Hg, bicarbonate level of 24.4 mm Hg, and a lactate level of 1.8 mmol/L. The patient was initially supplemented with 5L/min of oxygen via nasal cannula. However, he became progressively tachypneic, requiring 15L/min of supplemental oxygen by high flow nasal cannula (HFNC).

A 12-lead electrocardiogram (EKG) demonstrated sinus tachycardia, left ventricular hypertrophy, biatrial enlargement, and QTc 449. A chest radiograph showed diffuse bilateral multifocal opacities [Figure 1] with interval progression from the radiograph taken 2 days prior [Figure 2]. A bedside ultrasound of the lungs was positive for Kerley B lines, reduced lung sliding, and a localized pleural effusion of the right middle lung field. Initial blood tests

showed elevated cardiac biomarkers (Troponin T 0.017 ng/mL, pro B-type Natriuretic Peptide 1220 pg/mL), elevated inflammatory markers (high sensitivity C-Reactive Protein 104.97 mg/L, Procalcitonin 1.95 ng/mL, Ferritin 1492 ng/mL, Erythrocyte Sedimentation Rate 50 mm/hr), elevated Lactate Dehydrogenase (463 U/L), elevated quantitative D-Dimer (313 ng/mL), and lymphopenia. [9]

With radiographic evidence, clinical labs, and a high degree of suspicion for COVID-19, the patient was empirically treated with antibiotics, as well as anti-inflammatory and anti-malarial medications being used experimentally to treat SARS-CoV-2 infection. [7] The treatment regimen consisted of intravenous ceftriaxone (1 g once daily), intravenous azithromycin (500 mg once daily), and a loading dose of oral hydroxychloroquine (400 mg twice daily). In addition to antimicrobial therapy, the patient also received intravenous furosemide (60 mg once) for clinical hypervolemia. Within 24 hours of hospitalization the patient developed respiratory distress refractory to oxygen supplementation by HFNC and was febrile to 101.1F (38.4C). Due to worsening respiratory status he was admitted to the intensive care unit for Bilevel Positive Airway Pressure ventilation.

Transthoracic echocardiography (TTE) revealed an estimated left ventricular ejection fraction (LVEF) of 10–15%, reduced right ventricular systolic function, and global dilatation of all 4 chambers [Figure 3]. The right ventricle, right atrium and left atrium were moderately dilated, compared to mild left ventricular dilation. Specific measurements included: left ventricular internal diameter during end diastole (LVIDd) 5.8 cm, left ventricular internal diameter during end systole (LVIDs) of 5.1 cm, interventricular septum thickness (IVS) 1.3 cm and a Pulmonary Artery Systolic Pressure of 18 mm Hg. No significant valvular pathology was identified aside from mild regurgitation of the mitral and tricuspid valves. A pericardial effusion was not visualized.

Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay of a nasopharyngeal swab provided confirmation of SARS-CoV-2 infection. Thereupon, the patient was continued on a 5-day course of hydroxychloroquine (200 mg twice daily) in combination with azithromycin (250 mg once daily). [10] A presumptive diagnosis of viral myocarditis was made, and guideline directed medical therapy for heart failure was initiated. Repeat cardiac ultrasonography after completion of antimicrobial therapy, demonstrated persistent global hypokinesis, systolic dysfunction of the right ventricle, with an estimated LVEF of 20–25%, representing a modest improvement from presentation. Concurrent measurement of pro-BNP after completion of therapy also indicated improvement (802 pg/mL). At the time of writing, the patient was determined hemodynamically stable and discharged home with cardiology follow-up for a repeat TTE.
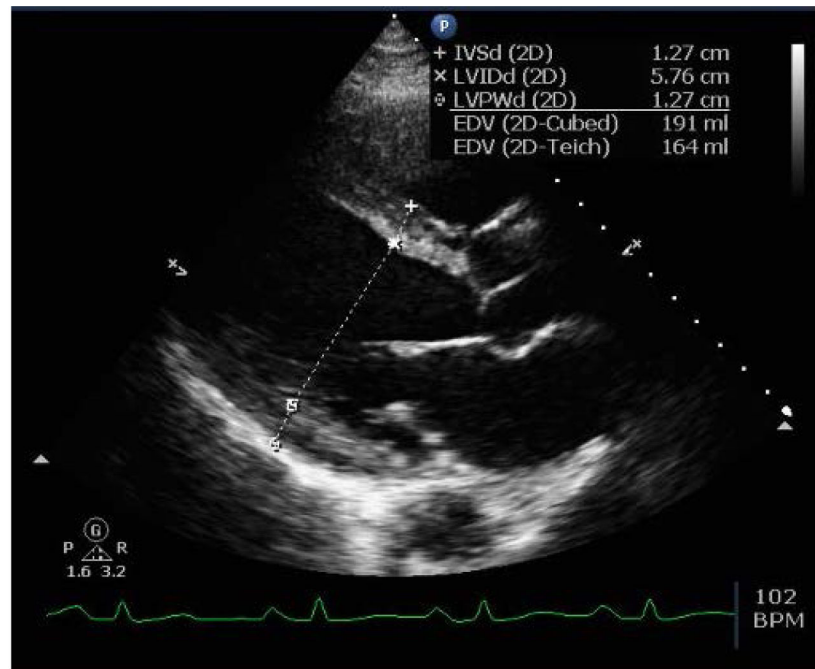
3. Imaging

Figure 1.
Chest X-ray 2 days prior to presentation

Figure 2.
Portable AP Chest X-ray from present hospitalization

Echo Measurements

Left Ventricle 1		Left Ventricle 2		Left Atrium	
Echo EF Estimated	10-15% %	LVIDd index	2.64 cm/m2 (Range: 2.2 - 3.0)	LA Volume Index	27.09 mL/m2 (Range: 16 - 34)
LVIDd (cm)	5.8 cm (Range: 4.2 - 5.8)	LVIDs index	2.32 cm/m2 (Range: 1.2 - 2.1)	LA volume	59.6 mL (Range: 18 - 58)
LVIDs (cm)	5.1 cm (Range: 2.5 - 4.0) ❗	PW (cm)	1.3 cm (Range: 0.6 - 1.0) ❗	LA diameter (cm)	3.7 cm (Range: 3.0 - 4.0)
IVS (cm)	1.3 cm (Range: 0.6 - 1.0) ❗			**Right Atrium**	
FS	12 % (Range: 28 - 41)			RA pressure	8 mmHg

Figure 3.
2D Echo showing diffusely dilated cardiac chambers

4. Discussion

Acute viral myocarditis is the inflammation of myocardium secondary to immune-mediated lymphocytic infiltration and/or pathogen-directed cytotoxicity resulting in myocyte degeneration and necrosis of nonischemic origin. Cardiac remodeling as a result of fibroblast deposition and formation of granulation tissue adversely affects cardiac output and leads to abnormalities of the conduction system. [11] In patients with COVID-19, viral myocarditis is an important cause of myocardial injury. It manifests with a pseudo-infarct presentation consisting of elevated cardiac biomarkers, echocardiographic evidence of cardiomyopathy, in the absence of diseased coronary arteries. [11,12] The exact mechanisms of cardiac injury in COVID-19 are not well established. Cardiac manifestations are partially due to the reduction of ACE2, increase of angiotensin II relative to angiotensin 1–7, hypoxia, and disruptions in the coagulation pathway. The inflammatory response plays a large role in myocarditis resulting from SARS-CoV-2 infection. Inflammatory infiltrates

including an abundance of macrophages and CD4+ T cells have been identified in several autopsy studies. [13] Diagnosis of viral etiology, requires endomyocardial biopsy with histopathologic examination. Identification of the SARS-CoV-2 genome in cardiac tissue or viral particles in cardiomyocytes is also imperative. [11,14] To date, most cases of SARS-CoV-2 myocarditis in literature have been reported under the premise of strong clinical suspicion without cardiac MRI or endomyocardial biopsy. [15,16,17,18,19,20]

We believe that the preceding viral prodrome, constellation of symptoms and confirmatory RT-PCR testing for SARS-CoV-2, strongly supports an infectious etiology of our patient's cardiac decompensation. Sinus tachycardia on presentation, which is the most common ECG change seen in myocarditis [21], laboratory evidence of myocardial injury, global DCM and diffuse hypokinesis on TTE, and sudden onset of symptoms, favors the diagnosis of myocarditis. In the absence of angina, risk factors for ischemic heart disease, clinical signs of chronic heart failure, or any other signs of end organ damage [preserved renal function (CrCl 115 mL/min by Cockroft-Gault), no evidence of pulmonary hypertension (PASP 18 mm Hg)], we also postulate that our patient's presentation was consistent with new-onset heart failure rather than decompensation of heart failure secondary to long standing hypertension. For a definitive diagnosis, ischemic cardiomyopathy should be excluded via coronary angiography, however given the pandemic resources were restricted at the time of the care.

A limited number of publications to date have reported on clinically suspected myocarditis secondary to SARS-CoV-2 infection. [15,16,17,18,19,20] A single report from Italy described a patient with COVID-19 in whom histopathologic examination of an endomyocardial biopsy identified viral particles in inflammatory cells within the myocardium but absence of virus within cardiomyocytes. [16] With respect to clinical status in the setting of presumed myocarditis, these reported cases describe significant troponinemia (>100 times the upper reference limit), severe acidosis (pH <7.1), high elevations in markers of cytokine storm, definitive ECG changes, profound hemodynamic compromise requiring resuscitative measures (ECMO, inotropic support), and the development of fulminant myocarditis.

By comparison to current literature, our patient had a clinically silent presentation; he was hemodynamically stable, with low levels of cardiac biomarkers, non-specific ECG and radiographic findings, mild elevations in inflammatory markers, and absence of shock. On the contrary, the degree of cardiac dysfunction measured by LVEF on TEE was most pronounced in our patient (LVEF 10–15%) compared to other reported cases. [15,16,17,18,19,20] In addition, our case is the first to describe clinically suspected myocarditis in an African American male, residing in a predominantly low socioeconomic neighborhood in the United States. It has been shown that COVID-19 disproportionately affects males, African Americans, and people with specific underlying comorbidities therefore this case provides insight into the manifestations of COVID-19 in high risk populations. [22,23].

5. Conclusion

Myocarditis associated with COVID-19 has widely variable presentations, which range asymptomatic to life-threatening arrhythmias and hemodynamic compromise [15,17]. A high index of suspicion is required to recognize the patient with cardiovascular manifestations of COVID-19 as there is evidence to show a negative impact on morbidity and mortality in such patients. Further research is needed to enhance our understanding of this disease process thus improving risk stratification in this high-risk group, especially in the acute setting since conventional work-up such as angiography and endomyocardial biopsy may not be readily available in pandemic circumstances.

Acknowledgements

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