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CASE SERIES
Other

Myocarditis in COVID-19 presenting with cardiogenic shock: a case series

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Background SARS-CoV2, also known as COVID-19, is a specific strain of coronavirus that is responsible for an ongoing global pandemic. COVID-19 primarily targets the respiratory system via droplet transmission, causing symptoms similar to influenza, including fever, cough, and shortness of breath. It is now known to impact other organ systems, causing significant cardiovascular and gastrointestinal illness, among others.

Case summary We describe two cases of COVID-19 induced myocarditis presenting with cardiogenic shock. These cases highlight the importance of understanding the lethal cardiac complications of COVID-19 infection, as well as its presentation, diagnosis, pathophysiology, and potential treatment options. These two cases involve patients without underlying cardiovascular disease risk factors who experienced prolonged symptoms of COVID-19 infection. Both patients presented with cardiogenic shock more than one week after symptom onset and diagnosis. These cases demonstrate the late presentation of myocarditis and cardiogenic shock, treated with corticosteroids and inotropes, with subsequent recovery of cardiac function.

Discussion The cases highlight the importance of recognizing late presentation viral myocarditis secondary to COVID-19 infection, even in patients without underlying cardiac disease.

Keywords COVID-19 • Myocarditis • Case series • Cardiomyopathy • Shortness of breath • Cardiogenic shock

Learning points

- COVID-19 myocarditis is a late complication of COVID-19 infection, which may affect those without underlying cardiovascular disease.
- It is imperative to be vigilant of late presentation cardiomyopathy and cardiogenic shock in patients diagnosed with COVID-19 infection, as mortality may be high without immediate support.

Introduction

COVID-19 virus is part of a large family of single positive-stranded, enveloped RNA viruses that initially presented in Wuhan, China in late 2019.[1] It is an extremely contagious respiratory illness that has led to a debilitating global pandemic. Common symptoms include fever, cough, fatigue, shortness of breath, and loss of smell and taste, among others. While the majority of COVID-19 victims have mild

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illness, others may develop acute respiratory distress syndrome, intense cytokine storm, and septic shock, leading to multi-organ failure and death. The potential long-lasting effects of this deadly disease are yet to be determined, but detrimental cardiovascular injury has been described.[2] Possible mechanisms for cardiac involvement include a cytokine storm affecting multiple organ systems, direct myocardial cell injury via angiotensin-converting enzyme 2 receptors, and myocardial oxygen supply/demand mismatch.[3] These mechanisms of injury may lead to cardiac manifestations, such as myocarditis, heart failure, and arrhythmia. Those patients presenting with myocarditis should be identified rapidly to avoid progression to fulminant myocarditis, which is associated with higher mortality.[4]

Timeline

Case 1	
Five weeks prior to presentation	Initial COVID-19 diagnosis, mild symptoms, treated with supportive therapy at home
Hospital Day 1	Presentation with cough, fever, shortness of breath, found to be in cardiogenic shock, started on milrinone therapy
Hospital Day 2	Transthoracic echocardiogram (TTE) with ejection fraction of 25% with diffuse hypokinesis and dilated right ventricle with reduced function
Hospital Days 2–5	Treated with corticosteroids, diuresis, and standard heart failure regime, repeat echocardiogram with improved ejection fraction of 50% on hospital Day 5
Hospital Day 6–10	Weaned off inotropes, transferred out of critical care
Hospital Day 11	Discharged from hospital
Ten weeks after discharge	Repeat TTE revealed improved ejection fraction of 60%
Case 2	
Nine days prior to presentation	Initial COVID-19 diagnosis, mild symptoms, treated with supportive therapy at home
Hospital Day 1 (9 days after initial COVID-19 diagnosis)	Presentation with worsening fatigue and shortness of breath, found to be in cardiogenic shock, started on inotropic therapy with milrinone
Hospital Day 2	Transthoracic echocardiogram with ejection fraction of 45%, diffuse hypokinesis, diastolic dysfunction, and moderate pericardial effusion
Hospital Days 2–4	Treated with corticosteroids, diuresis, and standard heart failure regime
Hospital Days 5 and 6	Weaned off inotropes, transferred out of critical care
Hospital Day 7	Discharged from hospital
Six weeks after discharge	Repeat TTE with ejection fraction of 55% and resolution of pericardial effusion

Case presentation

Case 1

We present the case of a 53-year-old African American male without significant past medical history who initially presented to the emergency room for evaluation of cough, fever, and shortness of breath. Five weeks prior, he had been diagnosed with COVID-19 and was treated with supportive therapy at home. In the emergency room, he was tachycardic and tachypnoeic with an oxygen saturation of 95% on 2 L/min nasal cannula. Distal pulses were 2+ and the patient was found to have cool extremities. His repeat COVID-19 nasopharyngeal polymerase chain reaction remained positive.

Serologic analysis was remarkable for a creatinine of 3.11 mg/dL (RR 0.6–1.3 mg/dL), aspartate aminotransferase 64 U/L (RR 5–45 U/L), alanine aminotransferase 70 U/L (RR 12-78 U/L), alkaline phosphatase 149 U/L (RR 46–116 U/L), total bilirubin 2.60 mg/dL (RR 0.2–1.0 mg/dL), as well as a lactic acidosis of 2.5 mmol/L (RR 0.5–2.0 mmol/L) and D-dimer of 2.85 μg/mL (RR < 0.5 μg/mL). Troponin was noted to be 5.68 ng/mL (peaked at 5.98 ng/mL) (RR < 0.04 ng/mL) and N-terminal-pro B-type natriuretic peptide 53 205 pg/mL (RR < 125 pg/mL). Electrocardiogram revealed sinus tachycardia with J-point elevation in the inferolateral leads. Chest X-ray showed mild pulmonary vascular congestion, but was otherwise clear. The patient was empirically anticoagulated with heparin and given intravenous diuretics.

He was admitted to the intensive care unit with the presumptive diagnosis of COVID-19 induced cardiomyopathy. Upon arrival, his cardiac output and cardiac index by Fick were found to be 3.1 L/min (RR 4–8 L/min) and 1.3 L/min/m^2 (RR 2.5–4 L/min/m^2), respectively, as calculated by concurrent arterial and venous blood gas analysis. A central line was placed and given a low SCVO2 with progression to cardiogenic shock, he was initiated on milrinone therapy. A complete transthoracic echocardiogram (TTE) was obtained demonstrating an ejection fraction of 25% (normal > 55%) with diffuse hypokinesis and moderately dilated right ventricle with reduced right ventricular function (*Figure 1*, *Video 1*).

He was given pulse dose steroids with methylprednisolone 1 g for 3 days. He was also treated with empiric antibiotics, which were discontinued 2 days after admission, as no source of infection was found and blood cultures remained negative. He did complete a 7-day course of hydroxychloroquine for COVID-19 infection, which was recommended therapy early in the COVID-19 pandemic. He was started on isosorbide dinitrate, hydralazine, carvedilol, and eplerenone. Further aetiologies of cardiomyopathy were ruled out with negative antinuclear antibodies, rheumatoid factor, scleroderma panel, HIV, hepatitis panel, mononucleosis panel, lyme, cytomegalovirus PCR, babesia.

Repeat TTE just 4 days after admission revealed an improved ejection fraction of 50%. IV steroids were tapered and given improvement in haemodynamics, he was weaned to room air and off inotropes. Inpatient left heart catheterization and cardiac magnetic resonance imaging (MRI) were deferred given the patient's rapid improvement and low suspicion for ischaemic cardiomyopathy, as well as to limit further exposure to the virus. He was discharged on a heart failure regime, including aspirin, atorvastatin, isosorbide

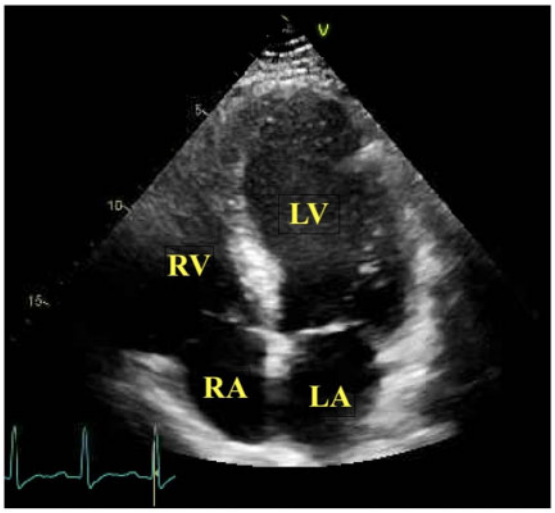
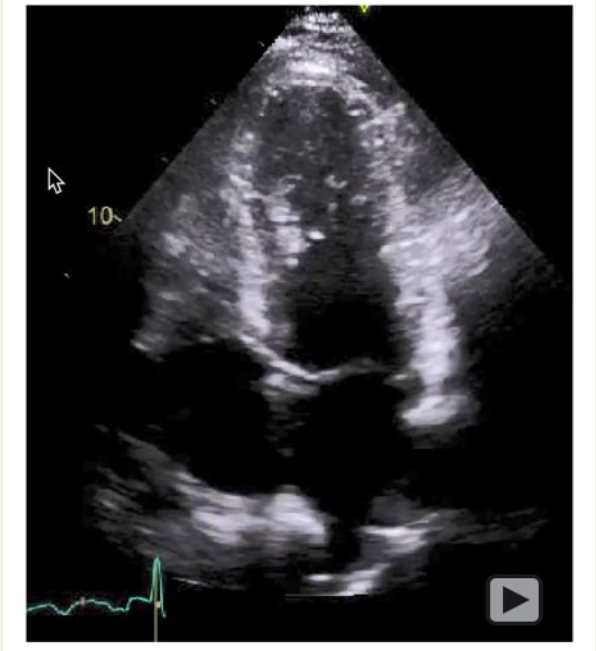
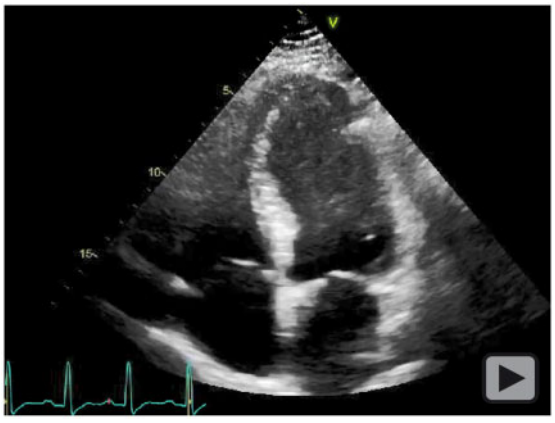


Figure 1 Transthoracic echocardiogram still and loop four-chamber view revealing an ejection fraction of 25% (normal > 55%) with diffuse hypokinesis, moderately dilated right ventricle, and reduced right ventricular function. Left ventricular internal diameter end diastole: 49 mm; left ventricular internal diameter end systole 46 mm (RR male 42–59 mm). Right ventricular internal diameter end diastole: 47 mm (RR 35–45 mm).



Video 2 Transthoracic echocardiogram loop four-chamber view ten weeks after hospital discharge revealing improved EF of 60% (normal > 55%).



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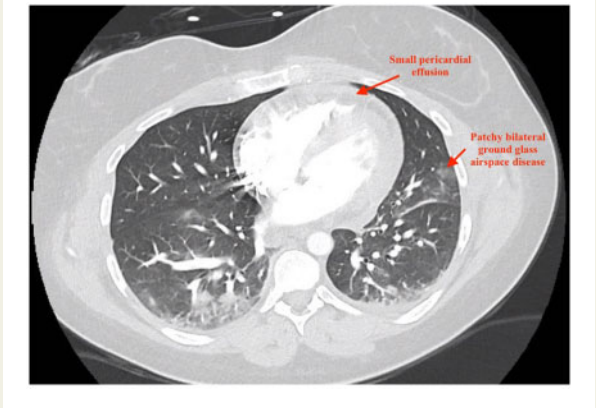


Figure 2 Computed tomography chest (axial cut), depicting bilateral, peripheral-basal predominant ground-glass opacities, and small pericardial effusion.

dinitrate, hydralazine, carvedilol, and eplerenone, as well as a prolonged prednisone taper. Repeat TTE 10 weeks after discharge showed an ejection fraction of 60% (*Video 2*).

Case 2

We present the case of a 30-year-old Caucasian female with past medical history of obesity who presented to the emergency department with complaints of fatigue and shortness of breath. She had been seen as an outpatient nine days prior, testing positive for COVID-19. On presentation, she was found to be tachycardic, tachypnoeic, and hypotensive with an oxygen saturation of 98% on room air. Physical exam was only remarkable for trace lower extremity oedema.

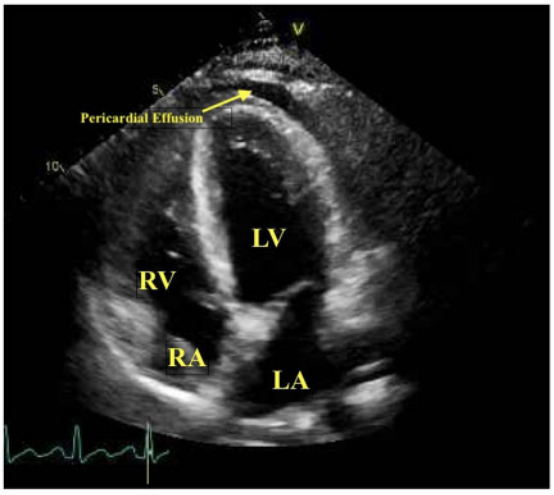
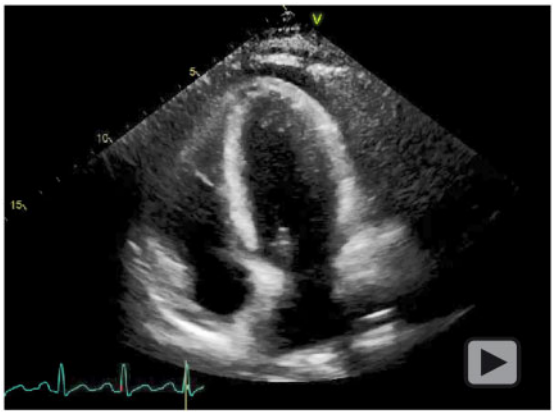


Figure 3 Transthoracic echocardiogram still and loop four-chamber revealing an ejection fraction of 45% (normal > 55%) with moderate diffuse hypokinesis, grade I diastolic dysfunction, and moderate pericardial effusion. Left ventricular internal diameter end diastole: 50 mm; left ventricular internal diameter end systole 37 mm (RR female 39–53 mm). Right ventricular internal diameter end diastole: 31 mm (RR 35–45 mm). Pericardial effusion 10 mm in size.



Video 3 Transthoracic echocardiogram still and loop four-chamber revealing an ejection fraction of 45% (normal > 55%) with moderate diffuse hypokinesis, grade I diastolic dysfunction, and moderate pericardial effusion. Left ventricular internal diameter end diastole: 50 mm; left ventricular internal diameter end systole 37 mm (RR female 39–53 mm). Right ventricular internal diameter end diastole: 31 mm (RR 35–45 mm). Pericardial effusion 10 mm in size.

Laboratory studies revealed lactic acidosis of 7.5 mmol/L (RR 0.5–2.0 mmol/L), troponin of 1.38 ng/mL (peak of 1.69 ng/mL) (RR < 0.04 ng/mL), NT-proBNP of 6022 pg/mL (RR < 125 pg/mL), and D-dimer of 1.05 μg/mL (RR < 0.5 μg/mL). Electrocardiogram showed sinus tachycardia with rate 140 b.p.m. Computed tomography chest showed patchy airspace disease, as well as a small pericardial effusion (*Figure 2*).

She was started on hydroxychloroquine, vitamin C, zinc, and atorvastatin. She was given empiric antibiotics and admitted to the intensive care unit. Transthoracic echocardiogram revealed an ejection fraction of 45% (normal > 55%) with moderate diffuse hypokinesis and a moderate pericardial effusion (*Figure 3*, *Video 3*). She was diagnosed with cardiogenic shock and was started on milrinone therapy and methylprednisolone.

During admission, her haemodynamics improved and milrinone was subsequently weaned off. She completed seven days of hydroxychloroquine and 2 days of antibiotics. She was hospitalized for a total of 7 days and was discharged home on atorvastatin, vitamin D, metoprolol tartrate, and a prednisone taper. Six weeks after discharge, repeat TTE showed an improved ejection fraction of 55% and resolution of pericardial effusion (Supplementary material online, *Video S4*).

Discussion

Although COVID-19 primarily targets the respiratory system, it has become increasingly associated with damage to other organs. In this case series, we discuss the cardiovascular effects of COVID-19 infection in two patients without prior cardiovascular disease. Both patients experienced worsening shortness of breath and continued fatigue after initial COVID-19 diagnosis, leading to their hospital presentations, at which time they were both found to be in cardiogenic shock.

Myocarditis can be defined as an inflammatory disease of the heart causing myocardial injury without an ischaemic cause. The most common aetiology of myocarditis in the USA is viral. The pathophysiology of viral myocarditis is thought to be direct cell injury and T-lymphocyte mediated cytotoxicity, which can be augmented by a cytokine storm syndrome.[5] Human coronaviruses prior to novel COVID-19 have been linked to myocarditis in all age groups, including MERS-CoV and SARS-CoV, both of which are closely linked to COVID-19. The specific pathophysiology of COVID-19 induced myocarditis is not well understood, but is thought to be closely related to its cell-entry mechanism. The virus enters human cells by binding its spike protein to the membrane protein angiotensin-converting enzyme 2 receptors, which can be found on ciliated columnar epithelial cells of the respiratory tract, type II pneumocytes, and cardiomyocytes.[6]

Clinical presentations of COVID-19 induced myocarditis can vary dramatically. Some patients may present with mild fatigue and dyspnoea, while others may present in fulminant cardiogenic shock, as was the case in these two patients. Typically, fulminant heart failure presents later in the course of viral infections, 2–3 weeks after contracting the disease. The early signs of fulminant myocarditis may resemble those of sepsis, but clues to suspect cardiac dysfunction include cold or mottled extremities, raised jugular venous pressure, peripheral oedema, and raised troponin and N-terminal pro-B-type natriuretic peptide levels. Electrocardiogram abnormalities can be seen in viral myocarditis, but these findings are not sensitive in detecting the disease and their absence is not exclusionary. The cardinal signs of myocarditis on echocardiogram are chamber dilation,

increased wall thickness, and pericardial effusion, along with ventricular systolic dysfunction.[7] Cardiovascular MRI, invasive catheterization, and endomyocardial biopsy may be considered for more definitive diagnosis, but are rarely required due to limited availability and their invasiveness.

Treatment of COVID-19 induced myocarditis should follow cardiogenic shock protocol, including liberal use of inotropes and vasopressors.[8] Depending on the severity of illness, patients may require mechanical circulatory support.

Lead author biography

Dr Adam Purdy is a pulmonary and critical care fellow at St. Luke's University Hospital in Bethlehem, Pennsylvania. A graduate of the University of Delaware and St. George's University School of Medicine, he completed his Internal Medicine training at Overlook Medical Center in New Jersey. Among others, his interests include critical care and undifferentiated shock.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case series including images and associated text has been obtained from both patients in line with COPE guidance.

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