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Coronavirus disease 2019 (Covid-19) presenting as purulent fulminant myopericarditis and cardiac tamponade: A case report and literature review

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ABSTRACT

The vast majority of patients in the ongoing coronavirus Disease 2019 (Covid-19) pandemic primarily present with severe respiratory illness. We report a Covid-19 patient who presented with findings of acute coronary syndrome and was found to have purulent fulminant myopericarditis and cardiac tamponade.
We compare our case to the previously reported instances of Covid-19-associated myocarditis. Through review of the available literature, we also highlight the potential mechanisms of cardiac injury in Covid-19. We hope to increase awareness amongst clinicians about this unusual presentation of Covid-19.

Introduction

In December 2019, the World Health Organization (WHO) was notified about multiple cases of pneumonia of unknown etiology originating in Wuhan city, Hubei province, China. The novel virus, named severe-acute-respiratory-syndrome-coronavirus-2 (SARS-Cov-2) was isolated on January 7th, 2020.[1] The acute respiratory disease, renamed Coronavirus Disease 2019 (Covid-19), was declared a pandemic on March 11th, 2020.[2]

SARS-Cov-2 has been seen to produce primarily respiratory symptoms, with evidence of ground-glass opacities on chest imaging.[3] However, the cardiovascular effects of SARS-Cov-2 have not been fully characterized.[4]

We report a patient with Covid-19 who presented with findings of acute coronary syndrome and was found to have purulent fulminant myopericarditis and cardiac tamponade, with subsequent circulatory shock.

Case report

A 50-year-old gentleman presented to an outside hospital with fevers, chills, generalized malaise, non-productive cough, dyspnea for 3–4 days and an episode of near-syncope on the day of presentation. In the emergency department, he was intubated for acute hypoxemic respiratory failure and SARS-Cov-2 testing was positive. ST-segment changes were noted on the electrocardiogram (ECG), so he was transferred to our hospital for acute coronary syndrome (ACS) management.

Past history was significant for hypertension and ischemic stroke. He was born in Honduras and immigrated to the United States at age twelve. There was no documented history of recent travel or sick contacts.

Admission labs were significant for leukocytosis with lymphopenia [white blood cell count 19,290/μL, absolute lymphocyte count 850/μL]; sodium 115 mEq/L; chloride 75 mEq/L; bicarbonate 13 mEq/L; anion gap 27; acute kidney injury (AKI) [blood urea nitrogen 44 mg/dL, creatinine 3.56 mg/dL]; elevated transaminases [aspartate transaminase (AST) 70 U/L, alanine transaminase (ALT) 48 U/L]; lactate dehydrogenase (LDH) 3332 U/L; arterial lactate 4 mmol/L. Arterial blood gas analysis revealed pH 7.21, pCO2 67mm Hg, pO2 213mm Hg on mechanical ventilator support (FiO2 80%, PEEP 10cm H_2O). Reverse-transcriptase-polymerase-chain-reaction test of a nasopharyngeal specimen reconfirmed SARS-Cov-2 infection.

Chest radiography revealed diffuse bilateral patchy opacities (Fig. 1). ECG showed sinus tachycardia, ST-elevation in leads II, III, aVF and ST-depression in I, aVL. Cardiac markers were elevated: high sensitivity troponin 544 ng/L, creatine kinase 2135 U/L, creatine kinase myocardial band 54.3 ng/mL. Other inflammatory markers

Abbreviations: SARS-Cov-2, severe-acute-respiratory-syndrome-coronavirus-2; Covid-19, coronavirus disease 2019

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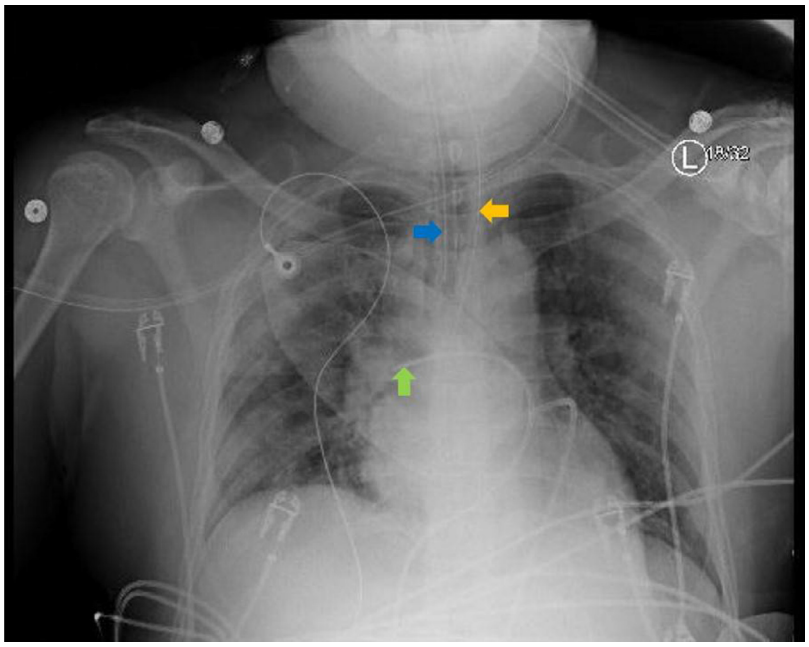

Fig. 1. Portable chest radiograph (Antero-posterior view) showing presence of diffuse bilateral patchy opacities within lung parenchyma. The cardiac silhouette appears normal in size. An endotracheal tube is visualized (blue arrow), with the tip above the carina. An enteric tube is noted (yellow arrow), with its distal end coursing below the diaphragm. A femoral approach Swan-Ganz catheter is noted (green arrow), with its tip overlying the right pulmonary artery. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

were also significantly elevated: erythrocyte sedimentation rate was 46 mm/hr, D-dimer 1068 ng/mL D-dimer units, procalcitonin 8.16 ng/mL, C-reactive protein 11.85 mg/dL, ferritin 66,165 ng/mL. T-cell subset analysis showed absolute CD4+ count 285/μL (26%) and CD8+ count 114/μL (10%).

On arrival, he was immediately taken to the cardiac catheterization laboratory (CCL). Coronary angiography revealed right dominant circulation with normal coronary vessels. Transthoracic echocardiogram (TTE) showed severe global left ventricular systolic dysfunction, right ventricular (RV) enlargement, RV systolic dysfunction. A moderate-to-large pericardial effusion was noted anterior to the RV with organizing material (suggesting an inflammatory process). There was evidence of intermittent RV impaired filling and collapse, suggestive of tamponade physiology (Fig. 2).

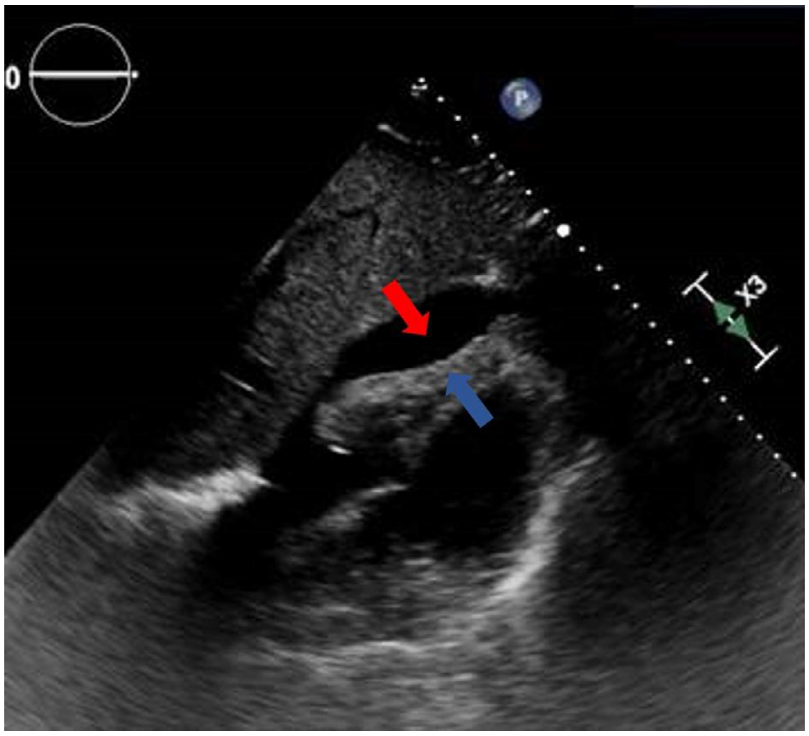

Fig. 2. Echocardiographic image (subcostal view) showing large pericardial effusion (red arrow) producing cardiac tamponade and collapse of right ventricle (blue arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

Table 1
Patient characteristics Key: AKI: acute kidney injury; ALC: absolute lymphocyte count; ALT: alanine transaminase; BALF: bronchoalveolar lavage fluid; BNP: brain natriuretic peptide; CRP: C-reactive protein; CK: creatine kinase 2135 U/L; CK-MB: creatine kinase myocardial band; CRRT: continuous renal replacement therapy; CVA: cerebrovascular accident; DDU: D-dimer unit; DOHS: day of hospital stay; ECMO: extracorporeal membrane oxygenation; ESR: erythrocyte sedimentation rate; HCQ: hydroxychloroquine; hsT: high sensitivity troponin; HTN: Hypertension; IABP: intra-aortic balloon pump; IVIG: intravenous immune globulin; LDH: lactate dehydrogenase; LV: left ventricle; LVEF: left ventricular ejection fraction; MP: methylprednisolone; MV: mechanical ventilator support; NP-PCR: nasopharyngeal polymerase chain reaction; ntBNP: n-terminal brain natriuretic peptide; PCR: polymerase chain reaction; RV: right ventricle; tropI: troponin I; WBC: white blood cell count.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age/Sex	50/M	63/M	64/F	53/F	37/M	47/F
Comorbidities	HTN CVA	Prior smoker Allergic cough	HTN Hyperlipidemia	None	None	Previous myocarditis
Travel History	Unknown	Hubei Province, China	Not reported	Unknown	Unknown	Unknown
Symptoms	1. Fever, chills 2. Generalized malaise 3. Non-productive cough 4. Dyspnea 5. Near-syncope	1. Fever 2. Productive cough 3. Dyspnea and chest tightness after exertion	Persistent chest pressure	1. Fever 2. Cough 3. Fatigue	1. Chest pain 2. Dyspnea 3. Diarrhea	1. Subjective fevers 2. Non-productive cough 3. Chest pain 4. Dyspnea
Radiographic findings	Diffuse bilateral patchy opacities	Ground-glass opacities	No acute abnormalities	No acute abnormalities	1. Enlarged heart 2. Pulmonary infection 3. Pleural effusion	Mild pulmonary congestion
Initial cell counts (/μL)	WBC: 19,290 ALC: 850	Not documented	Not documented	WBC: 8,900 ALC: 950	Not documented	Not documented
Initial Laboratory abnormalities	1. Hyponatremia 2. Hypochloremia 3. AKI 4. Metabolic acidosis 5. Elevated lactate 6. Transaminitis	1. Increased ALT 2. Increased creatinine 3. Hematuria	Elevated lactate	1. Hyponatremia 2. Hypochloremia 3. Hyperkalemia	Not documented	Not documented
Initial Inflammatory markers	1. ESR 46 mm/hr 2. CRP 11.85 mg/dL 3. D-dimer 1,068 ng/mL DDU 4. Procalcitonin 8.16 ng/mL 5. Ferritin 66,165 ng/mL 6. LDH 3,332 U/L	Not documented	1. CRP 54 ng/mL 2. D-dimer 166 ng/mL (normal) 3. Ferritin 967mcg/L	CRP 1.3 mg/dL	Not documented	Not documented
Initial Cardiac markers	1. hsT 544 ng/L 2. CK 2,135 U/L 3. CK-MB 54.3 ng/mL	1. tropI 11.37 g/L 2. Myoglobin 390.97 ng/mL 3. ntBNP 22,600pg/mL	tropI 7.9 ng/mL	1. hST 0.24 ng/mL 2. CK-MB 20.3 ng/mL 3. ntBNP 5,647pg/mL	1. Troponin T >10,000 ng/L 2. CK-MB 112.9 ng/L 3. BNP 21,025 ng/L.	Troponin T 225 ng/L
Electrocardiogram	1. Sinus tachycardia 2. ST elevation in II, III, aVF 3. ST depression in I, aVL	1. Sinus tachycardia 2. No ST-segment elevation	1. Sinus tachycardia 2. Low voltage QRS complexes in limb leads 3. ST elevation in I, II, aVL, V2-V6 4. PR elevation & ST depression in aVR	1. Low voltage in limb leads 2. Minimal diffuse ST elevation (more prominent in inferior & lateral leads) 3. ST depression with T-wave inversion in V1, aVR	ST elevation in III, aVF	1. Sinus tachycardia 2. Concave ST elevation in infero-lateral leads
Echocardiography	1. Severe global LV dysfunction 2. Enlarged RV 3. RV dysfunction 4. Moderate-large pericardial effusion 5. Intermittent RV impaired filling & collapse (s/o tamponade)	1. Enlarged LV 2. Diffuse myocardial dyskinesia 3. Low LVEF (32%) 4. Pulmonary HTN (44 mmHg)	1. Small LV 2. Severe concentric LV hypertrophy 3. Low LVEF (30%) 4. Dilated, severely hypokinetic RV 5. Small circumferential pericardial effusion	1. Increased LV wall thickness 2. Diffuse LV hypokinesis 3. Low LVEF (40%) 4. Mildly impaired LV diastolic function 5. Circumferential pericardial effusion (without s/o tamponade)	1. Enlarged heart 2. Marked decrease in LV systolic function 3. Low LVEF (27%) 4. Trace pericardial effusion	1. Normal LV function 2. Global pericardial effusion (without s/o tamponade)
Cardiac catheterization findings	Normal coronary vasculature	Not performed	Non-obstructive coronary artery disease	Normal coronary vasculature	Normal coronary vasculature	Not performed
Diagnosis	NP-PCR	PCR on sputum, BALF	NP-PCR	NP-PCR	NP-PCR	NP-PCR

(*continued*)

Management	1. MV 2. Pericardiocentesis 3. Vasopressors 4. Inotropes 5. HCQ 6. Azithromycin 7. Vancomycin 8. Cefepime 9. IVIG 10. MP 11. Methylene blue	1. MV 2. Vasopressors 3. Lopinavir-ritonavir 4. Interferon α-1b 5. MP 6. IVIG 7. Piperacillin-tazobactam 8. CRRT 9. ECMO	1. IABP 2. Inotropes 3. HCQ	1. Inotropes 2. HCQ 3. Lopinavir-ritonavir 4. IV Aspirin 5. MP 6. Diuretics 7. Beta-blockers	1. Vasopressors 2. Inotropes 3. IVIG 4. MP 5. Piperacillin-tazobactam 6. Diuretics	1. Vasopressors 2. Pericardiocentesis
Secondary infections	No	1. *Candida* (BALF) 2. Human α-herpesvirus and β-herpesvirus (BALF) 3. *Bacteroides ovalus* (blood cultures)	No	No	No	No
Outcome	Death (4th DOHS)	Death (33rd DOHS)	Recovery (7th DOHS – still hospitalized)	Recovery (6th DOHS – unclear if still hospitalized)	Recovery (7th DOHS – unclear if still hospitalized)	Recovery (unclear if still hospitalized)
Reference	Current case	[14]	[15]	[16]	[17]	[18]

Pericardiocentesis was performed and 600cc of serosanguinous fluid was drained, with the drain left in place. Pericardial fluid studies revealed 69 nucleated cells (6% granulocytes, 31% lymphocytes, 48% monocytes, 11% mesothelial cells, 4% reactive mesothelial cells). TTE performed post-pericardiocentesis revealed moderate improvement in hemodynamic parameters.

The patient was transferred to the intensive care unit (ICU) from the CCL. The working diagnosis was SARS-Cov-2 infection causing purulent myopericarditis, leading to cardiogenic and distributive shock, with multi-organ failure (transaminitis, lactic acidosis, metabolic acidosis and acute kidney injury) and possibility of bacterial co-infection. He was started on intravenous (IV) inotrope (dobutamine), IV vasopressors (vasopressin, norepinephrine), enteral hydroxychloroquine (400 mg every 12 h on day one, followed by 200 mg every 12 h for 8 doses), IV azithromycin, IV cefepime and IV vancomycin.

He was evaluated by the Infectious Diseases service. Due to multi-organ failure (vasopressor support, elevated transaminases) and suspected bacterial co-infection, he was not eligible for investigational immunosuppressive therapies. The presence of acute kidney injury excluded enrollment in the antiviral Remdesivir trial. The heart failure and nephrology services actively assisted in his care.

Intravenous immunoglobulin (IVIG) was started (20 mg/kg/dose) on hospital day two, with increasing pressor requirements. He was noted to have melena on hospital day three, with further increase in vasopressor support – epinephrine IV infusion, methylene blue IV infusion and IV methylprednisolone (200 mg/d IV) were subsequently added. Cardiothoracic surgery was consulted for extracorporeal membrane oxygenation (ECMO) therapy, but it was not initiated due to evidence of gastro-intestinal bleeding and multi-organ failure.

Cytologic analysis of pericardial fluid revealed reactive mesothelial cells. Pericardial fluid cultures revealed no growth of bacteria, acid-fast bacilli or viruses. Blood cultures revealed no bacterial growth. He had worsening hemodynamics, with concomitant worsening laboratory parameters (peak AST 2567 U/L; peak ALT 997 U/L; peak creatinine 4.37 mg/dL and peak lactate 13.3 mmol/L) and lymphocyte counts [CD4+ 148/μL (18%); CD8+ 48/μL (6%)]. He succumbed to multi-organ failure on hospital day four, despite maximal vasopressor support and supportive care.

Discussion

SARS-Cov-2 exists in a different clade from other β-Coronaviruses – severe-acute-respiratory-syndrome-coronavirus (SARS-Cov) and Middle-East-respiratory-syndrome-coronavirus (MERS-Cov) .[3] Both SARS-Cov and MERS-Cov have been associated with myocardial injury, myocarditis, and heart failure.[5–7] Additionally, comorbidities like diabetes mellitus (DM) and hypertension in these patients were associated with increased mortality.[8,9]

A recent meta-analysis found that the prevalence of hypertension, cardiac/cerebrovascular disease and DM in Covid-19 patients was 17.1%, 16.4%, and 9.7%, respectively.[10] Patients needing ICU admission were also more likely to have these comorbidities.[10] Covid-19 patients with these comorbidities also had higher mortality rates.[11] A spectrum of cardiac complications [myocarditis, heart failure, cardiac arrhythmias, myocardial infarction (MI)] are being increasingly reported in Covid-19 patients.[3,4,12,13] A higher incidence of complications [acute respiratory distress syndrome (ARDS), malignant arrhythmias, AKI] and higher mortality rates were seen in Covid-19 patients with myocardial injury.[13]

There have been few well-described case reports of SARS-Cov-2 causing focal myocardial and/or pericardial involvement[14–18] (Table 1). Like our patient, they had elevated cardiac markers, with ECG changes and signs of ventricular dysfunction. Two patients had predominant symptoms of ACS without viral symptoms[15,17] – this correlates with reports of Covid-19 presenting with predominantly cardiovascular symptoms in some patients.[19] Despite their presentation, no significant findings were noted in those who underwent cardiac catheterization. Different treatment regimens were instituted – however, apart from our case, one other patient expired.[14]

Our patient, like other cases,[14,17] met several criteria for fulminant myocarditis. These include acuity of onset; premonitory symptoms of viral infection; rapidly developing severe hemodynamic dysfunction; evidence of severe myocardial injury & diffuse decreased ventricular wall movement; and symptoms of injury to other organs.[20] The reported mortality rate of this rare syndrome is between 40–70%.[21] The current management of viral myocarditis involves use of immunomodulatory therapy (steroids, IVIG); supportive therapy (including mechanical ventilation); and circulatory assist devices (Impella heart pump, intra-aortic balloon pump) to reduced wall stress and inflammation.[20,22] The role of ECMO and continuous renal replacement therapy (CRRT) in Covid-19 is unclear. It may help remove circulating cytokines and increase blood oxygen saturation, reducing the immune response and further reducing myocardial damage.[14] ECMO therapy has been useful in some Covid-19 patients with cardiogenic shock,[15] but more data is needed. It is unclear at this time what factors contribute to increased mortality in Covid-19 patients with myocarditis. Worse outcomes have been noted in those with co-infections.[12] In one case, worsening of certain hemodynamic parameters (such as pulmonary artery systolic pressure) indicate functional decline and may help as markers of mortality.[14]

The exact mechanism of SARS-Cov-2-induced cardiac injury is not yet known. There are different theories:

(a) Direct injury by viral replication. SARS-Cov has been detected in the heart on autopsy.[23] One study documented the concurrent presence of a high SARS-Cov-2 viral load in patients with fulminant myocarditis.[24] However, autopsies of Covid-19 patients revealed mononuclear cell inflammatory infiltrates without viral inclusions.[25]
(b) Exaggerated and dysregulated immune response ("cytokine storm") seen with other coronavirus infections. This leads to increased vascular permeability, cell apoptosis, suboptimal T-cell and antibody responses and ARDS.[26] Higher levels of inflammatory markers were noted in Covid-19 patients in the ICU.[27] Additionally, a concomitant rise in cardiac markers and other inflammatory markers seen in Covid-19 patients (some of whom eventually died) supports this hypothesis.[4,11,13,21]
(c) Hypoxia (due to SARS-Cov-2-induced ARDS) can lead to inflammation, cell injury and subsequent cardiac damage.[28] It can also lead to increased intracellular calcium deposition and apoptosis.[19]
(d) Systemic inflammation potentiating localized inflammation in advanced atherosclerotic coronary vessels has been seen in other viral illnesses.[29] Lymphopenia[3,27] has been noted in Covid-19 patients and has previously been linked to the development of atherosclerosis.[30]
(e) Direct myocardial involvement mediated via Angiotensin-converting-enzyme-2 (ACE2). ACE2 is an endothelium-bound enzyme that converts angiotensin I & II to inactive metabolites.[31] Its expression was necessary for pulmonary infection by SARS-Cov.[32] In murine models, SARS-Cov precipitated an ACE2-dependent MI after pulmonary infection.[23]

Our patient was diagnosed with a purulent myopericarditis and tamponade, causing circulatory shock with fatal multi-organ failure. His clinical picture, radiographic and laboratory findings fit the diagnosis of Covid-19. There were no other identified causes of myopericarditis. The rapidity of disease progression, combined with findings of purulent myopericarditis (previously unreported in the literature) contributes to the unique presentation of our case.

Conclusion

In the current pandemic scenario, clinicians must keep SARS-Cov-2 infection in the differential of patients presenting with acute coronary syndromes and findings of purulent myopericarditis, cardiac tamponade and circulatory shock. Further research is needed to define the optimal management of such complex clinical scenarios.

Declaration of Competing Interest

None
Both authors declare that they have no pertinent conflicts of interest.

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