CARDIOVASCULAR MANIFESTATIONS OF COVID-19

Overview of cardiovascular manifestations of COVID-19 and echocardiographic features

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ABSTRACT

COVID-19 or SARS-CoV-2, a novel coronavirus, has rapidly spread across the globe, resulting in millions of infections and thousands of deaths. In this short review we describe the pathophysiology, clinical and echocardiographic manifestations of the virus, with specific reference to the cardiovascular system. We conclude with a case summary reflective of the most common cardiovascular presentation in severely ill patients.
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INTRODUCTION

Coronaviruses belong to the subfamily Orthocoronavirinae. They are enveloped viruses that comprise a single stranded RNA genome and a nucleocapsid.[1] The SARS-CoV-2 outbreak was first recognised in Wuhan, China, in late 2019.[2] It has since been declared a pandemic. As of 26 April 2020, over 2.9 million confirmed cases of SARS-CoV-2 and 203 917 deaths have been recorded worldwide.[3]

Most patients present with a respiratory illness.[4] Patients with pre-existing cardiovascular disease, especially the elderly, are at high risk of complications and poor outcomes, if infected with SARS-CoV-2. Studies from China have shown that there is a high prevalence of cardiovascular disease, hypertension and diabetes amongst symptomatic COVID-19 patients.[4]

PATHOPHYSIOLOGY

It is postulated that COVID-19 affects the cardiovascular system in a direct and indirect manner.

Direct effects

Direct effects are mediated by the binding of the SARS-CoV-2 to the angiotensin-converting enzyme (ACE2) receptor expressed in the lungs and the heart, among other organs. Binding of SARS-CoV-2 to this receptor results in activation of the renin-angiotensin system, resulting in endothelial dysfunction in various organs including the heart.[5]

Invasion of the host cell via CD147 spike protein has emerged as a novel mechanism of direct myocardial injury.[6] CD147, also called Basigin, is a transmembrane glycoprotein and is involved in viral infection, tumour development and invasion by the malarial parasite. It is expressed in haematopoietic, epithelial and endothelial cells and is upregulated in early erythroblasts, cardiac tissue, the placenta and thyroid.[7] Interaction of the spike protein and ACE2 promotes invasion of the virus into host cells.

It is unclear whether myocarditis is a result of direct viral invasion of the heart or whether it is secondary to the pro-inflammatory milieu.[8]

Indirect effects

Systemic inflammatory response to the virus results in a cytokine-mediated storm culminating in multi-organ failure, including the heart.[9]

Myocardial injury in the context of SARS-CoV-2 frequently results from impaired myocardial oxygen demand and supply ratio.[10] Injury to the myocardium results from a combination of hypoxia, sepsis with increased myocardial demand, and anaemia.

Myocardial infarction secondary to plaque rupture is attributed to inflammatory response from the virus and possibly a pro-thrombotic state.[11]

Arrhythmias have been noted – especially in patients hospitalised in intensive care units with severe disease. These may be attributed to effects of drugs and electrolyte imbalances.[12,13]

Stress-induced cardiomyopathy, or takotsubo cardiomyopathy, likely attributed to the acute stress response at the population level and/or severe respiratory infection, has been described in a recent case report.[14]

COMMON ECHOCARDIOGRAPHIC CHARACTERISTICS OF COVID-19

From the current literature review the following echocardiographic characteristics must be sought in patients afflicted with COVID-19:

Left ventricular (LV) systolic dysfunction due to SARS-CoV-2 results from wall motion abnormalities that can be either global or regional. This may be a result of myocarditis or coronary artery disease or stress-induced cardiomyopathy.[8,11] Regional wall motion abnormalities commonly tend to involve the infero-postero-lateral wall at the base of the heart in myocarditis but may also involve other regions of the LV. Coronary artery disease (CAD) must be considered as an important differential in the context of COVID-19, as patients may present with acute coronary syndrome. Therefore, the patient's clinical context and accompanying symptoms must be taken into account. Detection of wall motion abnormality in the typical distribution of a coronary artery favours the diagnosis of CAD.

Stress-induced cardiomyopathy typically is characterised by apical ballooning with hyperkinesia of the base.[15] Cases of reverse takotsubo cardiomyopathy have been described in the context of COVID-19.[14] Reverse takotsubo cardiomyopathy results in ballooning or hypokinesia of the base with apical hyperkinesia. Rarely, it may be complicated by LV apical thrombus and myocardial rupture.[15]

LV diastolic dysfunction may result from increased afterload on the left ventricle from activation of the renin angiotensin system by SARS-CoV-2-mediated activation of ACE2 receptors.[5] Also in patients with acute respiratory distress syndrome (ARDS), right ventricular (RV) enlargement impedes LV filling in diastole due to paradoxical septal motion.[16]

ARDS results in pulmonary hypertension and causes pressure overload of the RV.[16] Furthermore, a pro-thrombotic state in COVID-19 predisposes to pulmonary embolism and thrombotic microangiopathy, which can further contribute to RV enlargement and dysfunction.[17] However, RV involvement can also occur as part of myocarditis in the absence of respiratory involvement.[18]

Pericardial effusion may occur as part of myopericarditis or decompensated heart failure, due to additional systemic inflammatory response from COVID-19 infection.[19]

CLINICAL VIGNETTE

A middle-aged, obese, hypertensive female presented with shortness of breath and suspected myocardial infarction. On arrival, she was in severe respiratory distress with bilateral crackles. She had a clinical diagnosis of pneumonia and was not in heart failure. There were bilateral patchy infiltrates on chest radiograph and computed tomography of the chest (Figure 1). Her 12-lead electrocardiograph showed right bundle branch block, left anterior fascicular block and sinus tachycardia (Figure 2). An echocardiogram revealed left

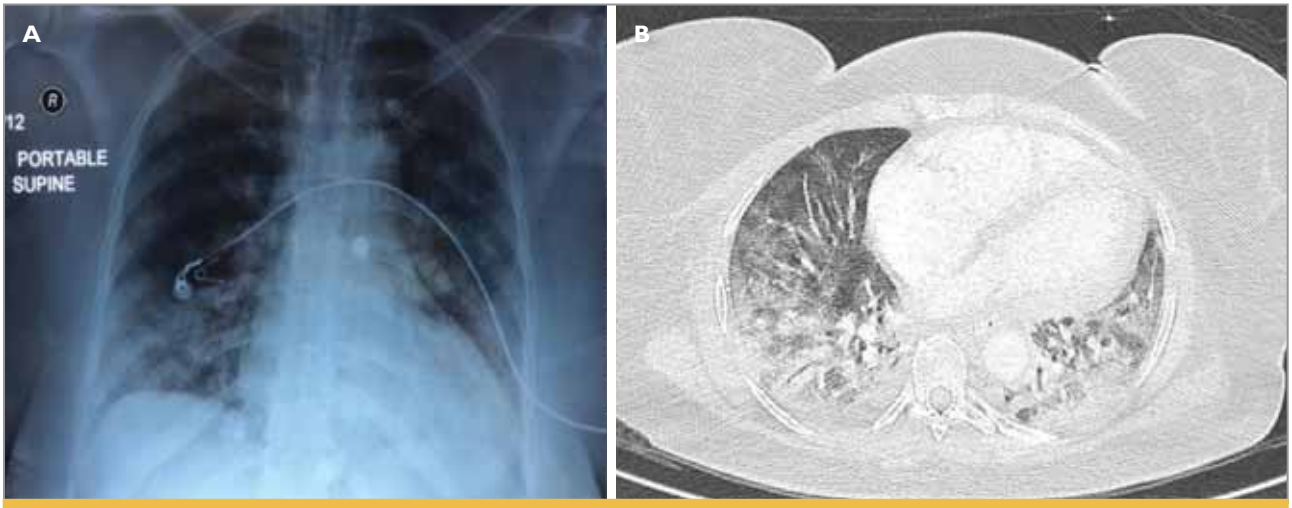

FIGURE 1: Chest X-ray (A) showing bilateral diffuse patchy infiltrates and computed tomography of the chest, (B) with typical ground glass opacification of the lungs consistent with SARS-CoV-2 pneumonia.

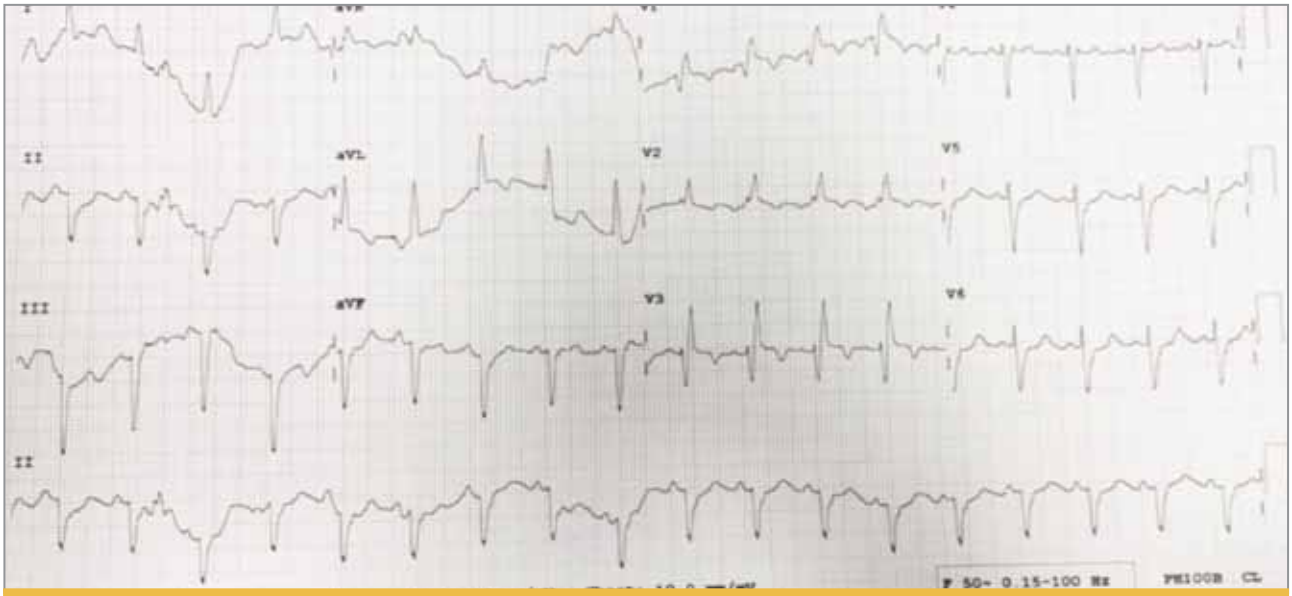

FIGURE 2: Twelve lead electrocardiogram done on an ill patient at index presentation, showing right bundle branch block, left anterior fascicular block and sinus tachycardia.

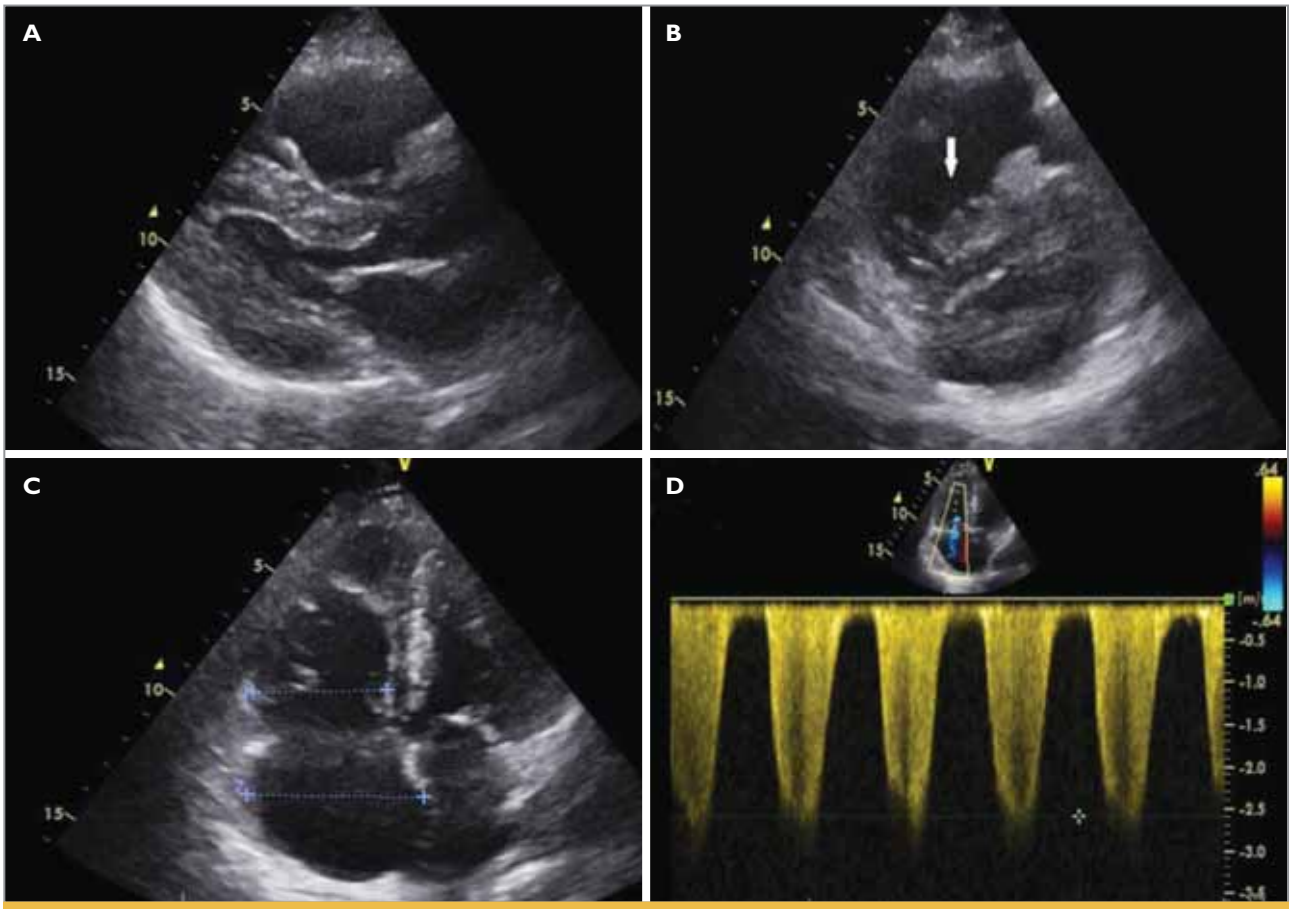

FIGURE 3: RV enlargement secondary to COVID-19 pneumonia complicated by moderate tricuspid regurgitation and mild pulmonary hypertension. (A) Parasternal long-axis view depicting LV hypertrophy and RV enlargement. (B) Parasternal short-axis view showing pressure overload of the RV with flattening of the interventricular septum (arrow). (C) Right atrium and ventricle measurements confirming enlarged chamber sizes. (D) Continuous wave Doppler showing RV systolic pressure of 26.8mmHg.

ventricular hypertrophy with preserved ejection fraction, no regional wall motion abnormality and right ventricular enlargement with pulmonary artery systolic pressure of about 36mmHg (Figure 3). Her troponin-T assay was elevated, and her blood chemistry was suggestive of sepsis complicated by disseminated intravascular coagulation and acute renal failure. She was HIV negative. She tested positive for COVID-19. She received intensive supportive care and made a remarkable recovery.

CONCLUSION

COVID-19 has a myriad of cardiovascular manifestations. Respiratory symptoms, with or without cardiac symptoms, tend to predominate – as in this case. As the COVID-19 pandemic continues to unfold, it is incumbent upon all clinicians to maintain a high index of suspicion for the disease, especially in a patient with comorbid conditions.

Conflict of interest: none declared.

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