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# Malignant arrhythmia in a COVID-19 patient with a structurally normal heart

Clare Anne Yoke Kum <u>Fong<sup>1</sup></u>, MBBS, MRCP, Benjamin Wei Liang <u>Tung<sup>2</sup></u>, MBBS, MRCP, Weiqin <u>Lin<sup>2,3</sup></u>, MBBS, MRCP, Kay Choong <u>See<sup>1,3</sup></u>, MBBS, FRCPEd

<sup>1</sup>Division of Respiratory and Critical Care Medicine, Department of Medicine, National University Hospital, <sup>2</sup>Department of Cardiology, National University Heart Centre Singapore, <sup>3</sup>Yong Loo Lin School of Medicine, National University Singapore, Singapore

**Correspondence:** Dr Clare Fong, Senior Resident, Division of Respiratory and Critical Care Medicine, Department of Medicine, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074. <u>clare\_fong@nuhs.edu.sg</u>

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### **INTRODUCTION**

The coronavirus disease 2019 (COVID-19)<sup>(1)</sup> is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a positive-sense, single-stranded ribonucleic acid virus. Initially reported in Wuhan, People's Republic of China, COVID-19 has since spread to become a global pandemic.<sup>(2)</sup> Patients typically present with upper respiratory tract symptoms which can rapidly progress to severe respiratory, multi-organ failure and mortality.<sup>(3,4)</sup>

SARS-CoV-2 has multiple system effects, with one of the most important complications being cardiovascular.<sup>(3)</sup> These complications may be due to direct viral-induced myocardial injury<sup>(4)</sup> and myocarditis.<sup>(5)</sup> Additionally, underlying cardiac comorbidities may be exacerbated by hypercoagulability and extensive inflammation,<sup>(1)</sup> leading to acute myocardial infarction, myocardial infarction with non-obstructive coronary arteries,<sup>(6)</sup> heart failure and cardiac arrest.<sup>(7)</sup> Another major reason for sudden cardiovascular deterioration could be arrhythmias. Possible mechanisms include atrial<sup>(8)</sup> and ventricular<sup>(9)</sup> arrhythmias in the setting of cardiomyopathy. However, arrhythmias may occur even in a patient with structurally normal heart, which is illustrated by the following case.

#### **CASE DESCRIPTION**

A 65-year-old man of Indian ethnicity presented to the emergency department with five days of fever, non-productive cough and mild dyspnoea. He did not smoke and had well-controlled hypertension for which he was not on medication. At presentation, he had normal blood pressure (117/74 mmHg), mild tachycardia (102 beats/minute) and peripheral oxygen saturation of 95% on room air. Physical examination revealed normal heart sounds, right basal crepitations, absent elevated jugular venous pressure and absent lower limb oedema. Chest X-ray showed bilateral hilar and right mid-zone opacities (Fig. 1). Electrocardiogram (ECG) showed sinus rhythm of rate 97/minute, QRS duration of 74 milliseconds (ms), corrected QT

duration of 406 ms and no ST-segment deviation (Fig. 2). Pertinent laboratory findings included a white cell count of 4.87 x  $10^9$ /L (reference range:  $3.84 - 10.01 \times 10^9$ /L), haemoglobin of 15.9 g/dL (reference range: 13.1 - 16.6), platelet count of 169 x  $10^9$ /L (reference range:  $164 - 387 \times 10^9$ /L), creatinine of 101 umol/L (reference range: 60 - 107), sodium of 128 mmol/L (reference range: 134 - 145), potassium of 4.5 mmol/L (reference range: 3.5 - 5.0), calcium adjusted for albumin of 2.18 mmol/L (reference range; 2.15 - 2.55), magnesium of 0.82 mmol/L (reference range: 0.75 - 1.07), C-reactive protein of 90 mg/L (normal range: 0 - 10), lactate dehydrogenase of 872 U/L (normal range: 250 - 580) and a normal high-sensitivity troponin I of 17.0 ng/L (reference range: 0 - 17.8). COVID-19 was subsequently diagnosed, based on real-time reverse-transcriptase polymerase chain reaction of a nasopharyngeal swab sample.

He initially received supportive treatment in the general ward under Medicine and was kept under airborne precautions. However, he developed hypoxemic respiratory failure on day 2 of hospitalization (day 6 of illness) and was transferred to the intensive care unit (ICU). On arrival to the ICU, his blood pressure was 131/95 mmHg, heart rate was 100 beats per minute, and oxygen saturation was 99% on 4 litres/min nasal prongs. Physical examination revealed bilateral basal crepitations, dual heart sounds with no murmurs or added sounds and no pedal oedema. Bedside ultrasound revealed normal heart structure and preserved left ventricular ejection fraction. There was no pericardial effusion. His C-reactive protein rose to 193 mg/L and 937 U/L respectively. On day 3 of hospitalisation (day 7 of illness), the patient developed acute respiratory distress syndrome requiring invasive mechanical ventilation and paralysis (chest X-ray, Fig. 3), oliguric acute kidney injury requiring continuous renal replacement therapy and vasodilatory shock requiring the use of noradrenaline (0.2 micrograms/min) and vasopressin (0.03 units/min).

On Day 5 of hospitalisation (Day 9 of illness), despite cardiorespiratory stability, the patient unexpectedly developed ventricular tachycardia (VT) resulting in cardiac arrest. Prior to the arrest, he had been on noradrenaline of 0.06 micrograms/min and off vasopressin. Pertinent laboratory values just before the onset of VT include a sodium of 127 mmol/L (reference range: 134 - 145), potassium of 4.5 mmol/L (reference range: 3.5 - 5.0), calcium adjusted for albumin of 2.36 mmol/L (reference range; 2.15 - 2.55), magnesium of 0.82 mmol/L (reference range: 0.75 - 1.07) and a phosphate of 1.60 mmol/L (0.85 - 1.45). He received immediate cardiopulmonary resuscitation, defibrillation and intravenous amiodarone. There was return of spontaneous circulation after six minutes of resuscitation. Retrospective review of his continuous ECG monitoring record revealed sudden deterioration of baseline sinus rhythm into an idioventricular rhythm (rate 60 beats/minute) (Fig. 4A). Subsequently a run of VT was started by a premature ventricular complex (PVC) falling on the preceding T wave (Fig. 4B). Upon successful resuscitation and return of spontaneous circulation, the ECG returned to sinus rhythm with narrow QRS complexes (Fig. 4C). There was no evidence of atrioventricular nodal block, QT duration prolongation or ST-segment deviation suggestive of ischemia. Post-resuscitation, his serial troponin I levels were mildly elevated at 41.3 and 85 ng/L (normal range 0.0 – 17.4 ng/L). His N-terminal-pro hormone BNP (NT-proBNP) was 223 pg/mL (normal range: 0 - 241). Repeat echocardiogram revealed preserved left ventricular function and strain imaging confirmed normal deformation (global longitudinal strain -16%, Mindray M9, Shenzhen, China). He had no recurrence of arrhythmia, was weaned off renal replacement therapy and was successfully extubated after eight days of mechanical ventilation. He was transferred to the general floor and discharged after undergoing rehabilitation.

#### DISCUSSION

COVID-19 infection has been associated with cardiovascular complications, including myocardial injury as evidenced by elevated troponin levels. SARS-CoV-2 appears to involve

the myocardium and sporadic autopsy cases suggest an infiltration of interstitial mononuclear inflammatory cells within the myocardium.<sup>(10)</sup> The virus has an affinity for the host angiotensin-converting enzyme 2 receptor, which raises the possibility that it may directly infect the myocardium and vascular endothelium.<sup>(11)</sup> Although acute myocarditis with depressed left ventricular function has been described in patients diagnosed with COVID-19,<sup>(6)</sup> our patient highlights the potential of COVID-19 to cause malignant arrhythmias despite a normal ejection fraction, electrocardiogram and troponin levels.

In terms of myocardial injury, Shi *et al* studied a cohort of 416 hospitalised patients with COVID-19, of whom 82 (19.7%) had elevated troponin I levels.<sup>(4)</sup> Similarly, Guo et al reported that among 187 patients with COVID-19, 52 (27.8%) had elevated troponin T levels.<sup>(9)</sup> Both studies demonstrated that patients with myocardial injury had a significantly higher inhospital mortality rate compared to those without. They tended to be older and have existing coronary artery disease, heart failure, hypertension and diabetes. They also had higher leukocyte counts, C-reactive protein and procalcitonin levels. Previous SARS coronavirus infections have been known to be associated with tachyarrhythmias<sup>(12)</sup> and specifically to COVID-19, Wang et al has described the occurrence of arrhythmias in 23 patients (16.7%) out of a cohort of 138 patients with COVID-19 infection for which the prevalence increased to 44.4% in the 16 patients who were admitted to the ICU.<sup>(3)</sup> Separately, Guo et al reported that out of 187 patients, 11 patients (5.9%) had VT or ventricular fibrillation, two of whom had normal troponin T.<sup>(9)</sup>

To our knowledge, no prior study has demonstrated the occurrence of malignant arrhythmia in COVID-19 patients who had no abnormality found on echocardiography, electrocardiogram or initial troponin assay. Our patient demonstrated that COVID-19 could lead to arrhythmic collapse in the absence of any conventional risk factors. Given complete normalization of his ECG and normal post-resuscitation heart function, it is unlikely that acute myocardial infarction, septic cardiomyopathy<sup>(13)</sup> or acute myopericarditis<sup>(14)</sup> had led to VT. Furthermore, as the pre-collapse heart rate was only 60 beats/minute, it is unlikely that autonomic imbalance triggered VT.<sup>(15)</sup> In addition, as VT did not recur, we propose that COVID-19 infection could transiently and focally affect the cardiac conduction system, through a mechanism that is currently unknown.

The vulnerable period for malignant arrhythmia appears to be during that of COVID-19 associated inflammation, as marked by the increase in C-reactive protein and ferritin levels prior to our patient's VT collapse. During this period, COVID-19 can induce multi-organ failure including acute respiratory distress syndrome, acute kidney injury and septic shock,<sup>(3)</sup> which is also the time when heightened alertness for complications and increased monitoring should be implemented.

In conclusion, our patient's experience shows that COVID-19 has the potential to cause sudden death, via the development of malignant arrhythmia. Even though VT occurred during the phase of multi-organ dysfunction in our patient, his cardiac function on echocardiography and electrical rhythm on ECG were not affected. It seems possible that malignant arrhythmia could also occur in patients with less severe non-cardiac manifestations, including patients with mild respiratory failure nursed on the general ward. Without continuous ECG monitoring, sudden cardiovascular collapse could be erroneously ascribed to cardiomyopathy or rapidly worsening respiratory failure. Conversely, if malignant arrhythmia could be detected and defibrillated promptly, clinical outcomes can be excellent. Learning from our case, we therefore propose that ECG monitoring and defibrillator units be made readily available for COVID-19 patients, especially those in the inflammatory phase of their disease.

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Fig. 1 Chest radiograph showing bilateral hilar and right lower zone opacities.



Fig. 2 Electrocardiogram on admission showing sinus rhythm



Fig. 3 Chest radiograph on transfer to ICU showing worsening bilateral infiltrates.



Fig. 4A Telemetry strip before cardiac arrest: idioventricular rhythm prior to collapse



Fig. 4B Telemetry strip showing initiation of VT by PVC falling on preceding T wave



Fig. 4C ECG post spontaneous return of circulation