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Case Report

Biventricular takotsubo syndrome with COVID-19 in an Asian male

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ABSTRACT

Coronavirus disease 2019 (COVID-19) has been shown to affect the cardiovascular system, and several cases of takotsubo syndrome (TTS) induced by COVID-19 have been reported. TTS predominantly affects postmenopausal women in western countries, but the prevalence in men is higher in Asian populations. It should be noted that male patients with either TTS or COVID-19 are associated with higher mortality. Despite the higher prevalence of TTS in Asian men, little is known about Asian men with TTS induced by COVID-19. This is a case report of a 60-year-old Asian male with biventricular TTS precipitated by COVID-19. He presented with acute respiratory distress syndrome, cardiogenic shock, and acute kidney injury. He required intubation, multiple vasopressors, and renal replacement therapy. The left ventricular ejection fraction was 15%, but it normalized in 5 weeks. The patient had a prolonged hospital stay in a critical condition, but was eventually discharged alive. The scarce literature about this condition in Asian male populations and the increasing number of COVID-19 cases in Asian countries highlight the rarity and importance of this case. Further studies are warranted to investigate the uneven sex distribution and outcomes of TTS triggered by COVID-19 in an Asian population.

<**Learning objective:** Takotsubo syndrome (TTS) can be provoked by coronavirus disease 2019 (COVID-19). Male sex, right ventricular dysfunction, and COVID-19 as a trigger, are important predicting factors for worse prognosis. It is unknown if there is a significant racial difference in the sex distribution and outcomes for this condition. Further studies are warranted to investigate TTS triggered by COVID-19 in an Asian population.>

Introduction

Coronavirus disease 2019 (COVID-19) has been shown to affect the cardiovascular system, and takotsubo syndrome (TTS) can be induced by COVID-19 [1]. TTS predominantly affects postmenopausal women in western countries, but the prevalence in men is higher in Asian populations [2,3]. It should be noted that male patients with either TTS or COVID-19 are associated with higher mortality [2,4]. A case series [5] showed men are associated with higher rate of significant cardiac dysfunction, death, acute respiratory distress syndrome (ARDS), and acute kidney injury (AKI). Despite the higher prevalence of TTS in Asian men, little is known about Asian men with TTS induced by COVID-19. Presumably due to the regional differences of COVID-19 pandemic status and uneven sex distribution of TTS, there is scarcity of reports about Asian men with TTS precipitated by COVID-19 in the literature.

Case report

A 60-year-old Asian male with a history of hypertension, dyslipidemia, and type 2 diabetes mellitus presented with a 2-week history of fever and dyspnea. His vital signs were blood pressure 145/88 mmHg, heart rate 148 beats/min, respiratory rate 30/min, oxygen saturation 75% on 15 L oxygen, and temperature 38.4 °C. Physical examination was significant for severe respiratory distress, with bilateral crackles and tachycardia. He was intubated for acute respiratory failure. He subsequently became hypotensive and required vasopressor support.

Chest X-ray demonstrated diffuse opacities throughout the lung fields (Fig. 1). His previous electrocardiogram (ECG) recorded 1-day prior at a clinic showed atrial fibrillation, poor R progression, and negative T waves in lead I, aVL, and V2-V6 (Online Fig. 1). At presentation, his ECG showed sinus tachycardia, poor

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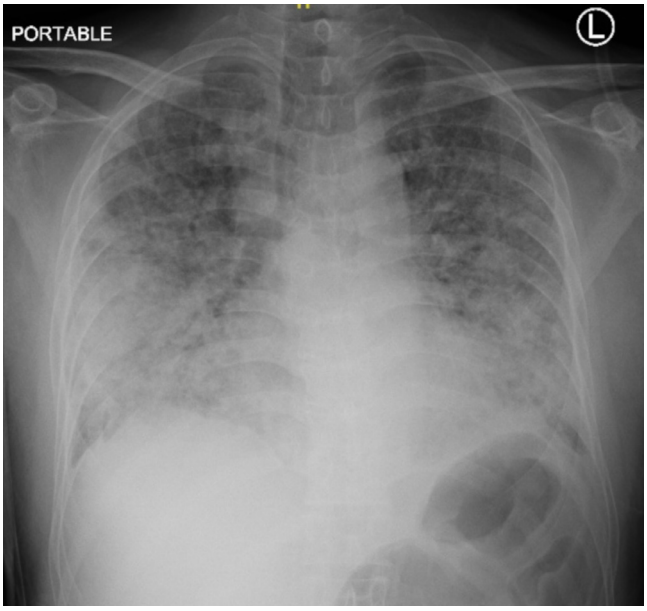

Fig. 1. Initial chest X-ray demonstrating diffuse ground-glass opacities throughout the lung fields.

R progression, without other remarkable findings (Fig. 2). Laboratory tests were significant for leukocytosis with lymphopenia, troponin-I (2.69 ng/mL), brain natriuretic peptide (238 pg/mL), D-dimer (13.8 μg/mL Fibrinogen Equivalent Unit), and inflammatory markers (C-reactive protein 281 mg/L, interleukin-6 369 pg/mL). Troponin-I peaked at 2.77 ng/mL. His central venous oxygen saturation was 61%. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction test was positive.

Cardiovascular differential diagnosis included 1) type II myocardial infarction (MI) with septic shock and hypoxemia, 2) Non-ST elevation MI involving left anterior descending artery, 3) viral myopericarditis, 4) TTS, 5) pulmonary embolism, and 6) right ventricular (RV) dysfunction.

Transthoracic echocardiogram (TTE) showed severe hypokinetic biventricular apical and mid segments, while the bases of the left ventricle (LV) and the RV were contracting normally. The left ventricular ejection fraction (LVEF) was 15% (Fig. 3, Online Video 1). Findings were consistent with biventricular TTS.

The patient was admitted to the intensive care unit for his ARDS, septic shock, cardiogenic shock, and TTS. The patient required multiple vasopressors and mechanical ventilation. Hydroxychloroquine, azithromycin, and broad-spectrum antibiotics were administered for COVID-19 and septic shock. Intravenous corticosteroids were initiated for his severe inflammation. The patient was also given aspirin, atorvastatin, and therapeutic anticoagulation therapy.

His hospital course was complicated by AKI requiring hemodialysis, bacterial pneumonia, and gastrointestinal bleeding. The patient was extubated on day 12 of admission and subsequently transferred to the general medicine floor. His most recent ECG showed resolution of poor R progression but baseline pre-existing negative T waves remained, which suggests that the poor R progression, pseudo-normalized T waves, and atrial fibrillation seen at presentation were induced by TTS and the negative T waves were chronic findings (Online Fig. 2). TTE was repeated on day 37 of admission, and it exhibited resolution of the wall motion abnormalities and the LVEF was 55% (Online Video 2). Currently, he is undergoing subacute rehabilitation.

Discussion

Our case met the following international takotsubo diagnostic criteria [6]: 1) transient LV dysfunction with typical echocardiogram findings, 2) COVID-19 as a physical trigger, 3) new ECG abnormalities, and 4) elevated cardiac biomarkers. This patient did not undergo cardiac magnetic resonance imaging or endomyocardial biopsy given active SARS-CoV-2 infection. The pattern of transient wall motion abnormalities was supportive of TTS.

The current understanding of TTS remains limited. The role of sympathetic stimulation precipitating myocardial stunning, catecholamine toxicity, multi-vessel spasm, and microcirculatory dysfunction, have been debated as pathophysiological mechanisms [6]. A study performed in European countries and the USA showed that TTS predominantly affects women, but men account for only 10% of the patient population and tend to have a higher risk for catecholamine use, intubation, cardiogenic shock, and death compared to women [2]. On the other hand, the prevalence of TTS in men is reported to be higher in Asian populations [3].

TTS typically affects the LV, but the RV may also be involved [6]. It is known that RV involvement is an independent predictor of worse prognosis for TTS [7]. At the same time, RV dysfunction in patients with COVID-19 is also associated with worse prognosis [8]. In our case, RV involvement of TTS could have been aggravated by other etiologies such as pulmonary embolism or ARDS in the setting of COVID-19. Since the patient was hemodynamically unstable, chest computed tomography (CT) with contrast was not performed.

A study has shown 15% of patients with TTS had co-existing coronary artery disease, and its presence is not an exclusion criterion for TTS [2]. In this case, coronary angiogram and coronary CT angiography were deferred due to active SARS-CoV-2 infection. As shown in this case, clinicians need to keep in mind that diagnostic work-up for other differential diagnoses is limited in patients with COVID-19. Although he could have had atherosclerotic lesions, it was difficult to correlate the wall motion abnormality with any pattern of coronary artery disease. Furthermore, resolution of his cardiomyopathy did not support ischemic etiologies.

COVID-19 affects the cardiovascular system leading to a variety of conditions including myocardial injury, heart failure, and arrhythmias, which are associated with reduced survival [9]. The proposed mechanisms of cardiac involvement in SARS-CoV-2 infection include oxygen supply and demand imbalance with septic shock and hypoxia, direct myocardial injury, coronary microthrombosis in a hypercoagulable state, endothelial dysfunction, or instability of coronary plaque provoked by a cytokine storm [10]. These pathophysiologic insults induced by COVID-19 could have led to TTS in this patient. A recent study showed that there was a significant increase in the incidence of TTS during the COVID-19 pandemic (incidence proportion, 7.8%) when compared with pre-pandemic periods (incidence proportion range, 1.5−1.8%) among acute coronary syndrome patients without COVID-19, indicating underlying psychological stress response to the COVID-19 pandemic as a trigger [11]. A single center study from New York city exhibited that 118 patients with COVID-19 patient underwent a clinically indicated echocardiogram, and 5 (4.2%) patients were diagnosed with TTS [5]. A literature review yielded a summary of 16 patients with TTS induced by COVID-19, and all cases are reported from western countries suggesting case reports from Asian countries are scarce [12]. In terms of sex differences among patients with COVID-19, a study has demonstrated that men have significantly higher mortality than women [4]. In addition, a study showed higher rate of significant cardiac disfunction, death, ARDS, and AKI among men with TTS and COVID-19 [5].

In conclusion, this is a case report of an Asian male with biventricular TTS triggered by COVID-19, resulting in protracted hospital-

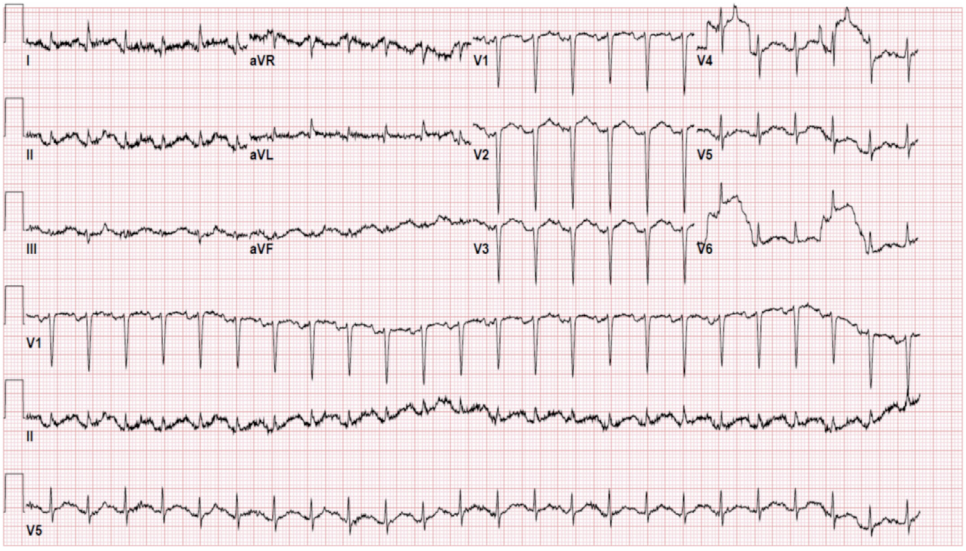

Fig. 2. Electrocardiogram at presentation demonstrating sinus tachycardia and poor R progression.

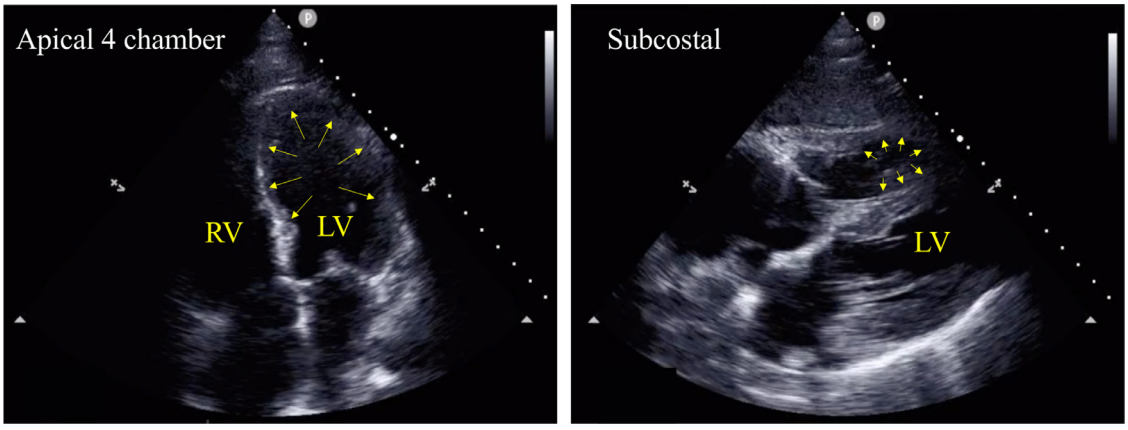

Fig. 3. Echocardiogram demonstrating left ventricular ejection fraction of 15%, with biventricular akinetic apical and mid segments.
LV, left ventricle; RV, right ventricle.

ization with multiple complications. Male sex, RV dysfunction, and COVID-19 as a trigger, were important predicting factors for worse prognosis. The scarce literature about this condition in Asian male populations and the increasing number of COVID-19 cases in Asian countries highlight the rarity and importance of this case. It is unknown if there is a significant racial difference in the sex distribution and outcomes for this condition. Further studies are warranted to investigate TTS triggered by COVID-19 in an Asian population.

Declaration of Competing Interest

None.

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None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jccase.2020.11.017.

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