Reverse Takotsubo Cardiomyopathy After Casirivimab-Imdevimab Therapy in a Patient with COVID-19: A Case Report

**Patient:** Female, 24-year-old

**Final Diagnosis:** Reverse takotsubo cardiomyopathy

**Symptoms:** Shortness of breath

**Medication:** —

**Clinical Procedure:** —

**Specialty:** Cardiology

**Objective:** Rare disease

**Background:** Takotsubo cardiomyopathy, also referred to as apical ballooning syndrome (ABS), stress cardiomyopathy, or broken heart syndrome, initially described in Japan, is characterized by transient wall motion abnormalities involving the apical segment. Several variants have been described, including reverse type, mid-ventricular type, and the focal type. In the reverse type, there is basal hypokinesis and apical hyperkinesis. Stress cardiomyopathy is most likely to occur in middle-aged women and the underlying etiology is believed to be related to catecholamine release due to intense stress.

**Case Report:** We report an extremely rare case of reverse takotsubo cardiomyopathy (rTTC) in a young woman with COVID-19 who was treated with Casirivimab-Imdevimab therapy. Our report is the second to reveal rTTC in a patient with COVID-19 in which obstructive coronary artery disease was definitively ruled out by coronary CT angiography.

**Conclusions:** Cardiovascular involvement in COVID-19 has been linked to increased morbidity and mortality rates. Recent reports have suggested the occasional occurrence of TTC and the rare occurrence of reverse takotsubo cardiomyopathy (rTTC) in patients with COVID-19. In fact, to the best of our knowledge, this is only the fifth reported case of rTTC in a patient with COVID-19; importantly, 3 out of the 4 of the previous reported cases lacked definitive ischemic work-up to rule out obstructive coronary artery disease due to the critical condition of the patients.

**Keywords:** Casirivimab And Imdevimab Drug Combination • COVID-19 • Takotsubo Cardiomyopathy

**Full-text PDF:** [https://www.amjcaserep.com/abstract/index/idArt/936886](https://www.amjcaserep.com/abstract/index/idArt/936886)

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Background

The novel coronavirus SARS-CoV-2, which causes coronavirus disease 2019 (COVID-19), has now become the deadliest pandemic in the history of the United States, with a death toll surpassing that of the 1918 Spanish flu, as of September 2021, according to the COVID-19 Dashboard at Johns Hopkins University. In COVID-19, cardiac involvement manifests as cardiac myocyte injury, heart failure, arrhythmia, fulminant myocarditis, and pulmonary embolism (PE) [1,2]. Recent studies have suggested the occasional occurrence of TTC and the rare occurrence of reverse takotsubo cardiomyopathy (rTTC) in patients with COVID-19 [3]. In fact, to the best of our knowledge, this is only the fifth reported case of rTTC in a patient with COVID-19 [4-7]; importantly, 3 out of the 4 previously reported cases lacked definitive ischemic work-up to rule out obstructive coronary artery disease due to the critical condition of the patients [7].

Case Report

Our patient was a 24-year-old woman with history of uncomplicated C-section 7 weeks ago and recent diagnosis of COVID-19 confirmed by a positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR) for SARS-CoV-2 3 days prior to admission. She initially presented to the out-patient infusion clinic for Casirivimab-Imdevimab therapy. However, upon returning home, she developed respiratory distress 3 h after receiving monoclonal antibody infusion therapy, and subsequently lost consciousness, for which she was taken to the Emergency Department. She was only minimally responsive when she arrived and was intubated due to ongoing dyspnea and for airway protection. She was also given 2 doses of intravenous epinephrine and 1 dose of intravenous methylprednisolone for suspected anaphylactic reaction. Vital signs on admission were: temperature 37.5°C, pulse rate 123 beats per minute, respiratory rate 20 breaths per minute, blood pressure 141/106 mmHg, and oxyhemoglobin saturation of 100% on 15 L/min oxygen via bag valve mask. EKG (Figure 1A) showed new ST depression in leads V3-V6, suggestive of anterolateral wall ischemia, QTc of 450 ms, and sinus tachycardia with 103 beats per minute. Initial laboratory test results revealed troponin I elevation of 1.030 ng/ml (lab reference <0.034 ng/ml), which subsequently peaked at 6.8 ng/ml, elevated D-dimer of 0.77 µg/mL (lab reference <0.50 µg/mL), and elevated NT-proBNP of 1500 pg/ml (lab reference <125 pg/ml). A chest X-ray was grossly unremarkable (Figure 2). Empiric treatment with Remdesivir and Dexamethasone for COVID-19 pneumonia was commenced, as was aspirin (loading dose) plus heparin for possible non-ST elevation myocardial infarction (NSTEMI). The next day, transthoracic echocardiogram (TTE) revealed depressed left ventricular ejection fraction (EF) of 30-35%. The left ventricular basal to middle segments were severely hypokinetic while the distal segments and apex were hyperdynamic, consistent with rTTC (Figures 3, 4). An inferior vena cava (IVC) thrombus was noted as well. A repeat EKG 24 h later showed resolution of the ST depression (Figure 1B). A subsequent coronary CT angiogram ruled out obstructive coronary artery disease (CAD) and other coronary anatomical abnormalities, while CT pulmonary angiography ruled out pulmonary embolism, but did show subtle foci of inflammation in the superior segment of lower lobes, as evidenced by minimal ground-glass
changes. Patient was successfully extubated the next day. She was treated with Metoprolol, Lisinopril, and Furosemide while an inpatient for left ventricular (LV) systolic dysfunction and received a therapeutic dose of low-molecular-weight heparin for IVC thrombus. She was discharged on guideline-directed medical therapy for heart failure with reduced LVEF, as well as Apixaban, for a total of 3 months for IVC thrombus. TTE was repeated 2 days after the first TTE, just prior to discharge, and the findings were unchanged. TTE was again repeated 2 weeks after the first TTE, and showed resolution of wall motion abnormalities and complete recovery of LVEF.

**Discussion**

Reverse takotsubo cardiomyopathy is a rare form of stress-induced cardiomyopathy and presents with apical hyperkinesis and basal/inferior hypokinesis with the regional wall motion abnormality (RWMA) extending beyond a single epicardial artery distribution (Videos 1-6). In contrast, classical TTC manifests as basal hyperkinesis with apical hypokinesis. Other criteria of reverse takotsubo are similar to its classical variety and include: exclusion of obstructive coronary artery disease; new EKG changes (including ST-segment changes, T-wave inversion, left bundle branch block, and/or prolongation of QTc); elevation of cardiac enzymes; and absence of myocarditis and pheochromocytoma. Recovery of systolic function is expected on repeat cardiac imaging at the follow-up visit [8-15].

![Electrocardiogram](image1.png)

**Figure 1.** Electrocardiogram on admission (A) showing ST depression in V3-V6 (anterolateral leads). Red arrows indicating ST depression. Repeat electrocardiogram 1 day after admission (B) showing normal sinus rhythm with resolution of ST depression in anterolateral leads (V3-V6). Green arrows indicate absence of ST depression.

![CXR](image2.png)

**Figure 2.** CXR demonstrating unremarkable cardiome diastinal silhouette. Lungs expanded and clear. No pleural effusion seen.
Figure 3. 2D Transthoracic Echocardiogram with contrast at end-diastole (A) and without contrast at end-diastole (B). LV – left ventricle; LA – left atrium; RV – right ventricle. The red arrow indicates the cardiac apex while the blue arrow indicates interventricular septum.

Figure 4. 2D Transthoracic echocardiogram with contrast revealing basal ballooning in this case of rTTC at end-systole (A) and without contrast at end-systole (B). LV – left ventricle; LA – left atrium; RV – right ventricle. The red arrow indicates the cardiac apex while the blue arrow indicates interventricular septum.

Although the chief imaging modality for TTC and rTTC is echocardiography, cardiac magnetic resonance imaging (CMR) can also be a useful tool to exclude other masquerading differential diagnoses, including myocarditis and myocardial infarction, which may otherwise mimic (r)TTC.

Pathophysiology

As previously mentioned, catecholamine surge is the central pathophysiologic mechanism of stress-induced cardiomyopathy. High concentrations of epinephrine trigger a switch in intracellular signal trafficking in ventricular cardiomyocytes from stimulatory Gs protein to inhibitory Gi protein signaling via the β2-adrenoceptor, which in turn protects against the proapoptotic effects of the intense activation of β1-adrenoceptors. However, this change also causes a negative inotropic effect. Because β1-adrenoceptor density is greatest at the apical myocardium, this effect is greatest in that region.

In older women, the apical variant of takotsubo occurs more frequently because the highest density of adrenoreceptors occurs in the cardiac apex in the postmenopausal age group. In younger females, the occurrence of reverse takotsubo cardiomyopathy may be due to the high density of adrenoreceptors at the cardiac base, as opposed to the apex in the elderly patients [4,5].

TTC and Thromboembolism

The potential risk of intraventricular thrombus formation and systemic embolization should be addressed in patients with LV...
Video 1. Transthoracic echocardiogram (TTE) with contrast showing regional wall motion abnormalities.

Video 2. TTE with contrast showing regional wall motion abnormalities.

Video 3. TTE with contrast showing regional wall motion abnormalities.

Video 4. TTE with contrast showing regional wall motion abnormalities.

Video 5. TTE without contrast showing regional wall motion abnormalities.

Video 6. TTE without contrast showing regional wall motion abnormalities.
thrombus or severe LV systolic dysfunction. Echocardiography should include evaluation for potential thrombus as well as assessment of the extent of wall motion abnormality. According to the International Takotsubo Registry study, ventricular thrombus was detected in 1.3% of the 1750 patients with stress cardiomyopathy [11].

In our case, the patient had an IVC thrombus. The main underlying risk factors of thromboembolism for this patient were recent pregnancy [16] and ongoing COVID-19 [17]. Recommended treatment includes anticoagulation for 3 months, with the duration of anticoagulation modified based on the rate of recovery of cardiac function and resolution of the thrombus.

**Follow-Up**

TTE was repeated 2 weeks after the first TTE, and showed resolution of wall motion abnormalities and complete recovery of LVEF.

**Conclusions**

Cardiovascular involvement in COVID-19 is associated with increased morbidity and mortality rates. Recent studies have suggested the occasional occurrence of TTC and the rare occurrence of reverse takotsubo cardiomyopathy (rTTC) in patients with COVID-19. In fact, to the best of our knowledge, this is only the fifth reported case of rTTC in a patient with COVID-19, and only the second case where definitive ischemic work-up was done to rule out obstructive coronary artery disease. Of note, it cannot be confirmed whether the reverse takotsubo cardiomyopathy was a direct result of COVID-19 or if it was due to Casirivimab-Imdevimab therapy. Regardless, it would be very prudent to keep in mind that cardiomyopathies are possible consequences, albeit rare consequences, of COVID-19.

**Declaration of Figures’ Authenticity**

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