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Takotsubo Cardiomyopathy in a Vaccinated Patient with Severe COVID-19

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INTRODUCTION

This case illustrated coronavirus disease-19 (COVID-19) induced interlukin-6 (IL-6) activation resulting in Takotsubo Cardiomyopathy (TCM) in a vaccinated patient. As noted by Kurowski et al.[1], the pathogenesis of TCM includes a high inflammatory state leading to increased myocardial stress and eventual transient dysfunction. As such, the patient may present with cardiac chest pain mimicking acute coronary syndrome and signs of clinical heart failure. This complication should be part of the differential in patients who present with acute ST-elevation myocardial infarction (STEMI), with no cardiac risk factors and suspicion for severe inflammation. The RECOVERY Collaborative Group[2] showed that the high inflammatory state seen in severe COVID-19 pneumonia can lead to major organ dysfunction, including TCM, and these patients also should be evaluated for immunomodulatory therapy targeting IL-6 as they may reduce mortality.

CASE REPORT

The patient was a 67-year-old female with a past medical history of chronic obstructive pulmonary disease, hypertension, and obesity who presented with 10 days of shortness of breath, fever, and fatigue. The patient received her second dose of the mRNA-1273 COVID-19 vaccine four days prior to admission, curiously while dyspneic, and when questioned further she was exposed by a family member who lives with her and subsequently tested positive for COVID during this period.

Physical exam was notable for irregular tachycardia and scattered rhonchi. Vitals were documented as blood pressure of 127/73 mmHg, heart rate of 127 beats/min, respiratory rate of 33 breaths/min, and oxygen saturation of 60% on room air improved to 92% on Bi-level Positive Airway Pressure. A computerized tomography chest scan with contrast was negative for an acute pulmonary embolism, but found bilateral interstitial opacities. Nasal swab polymerase chain reaction (PCR) testing was positive for COVID-19. Given this, she was admitted to the hospital for respiratory failure and management of her COVID. She was started on dexamethasone 10 mg once a day, with the intention of treating for 10 days, and a five day course of remdesivir. The patient was evaluated for tocilizumab, but she was not deemed a candidate due to hepatitis C antibody reactivity, positive methicillin-resistant Staphylococcus aureus respiratory culture with increasing oxygen requirements, and a large recent area of infarct in the left cerebellar hemisphere, as well as the left aspect of the brain stem.

On hospital day two, the patient complained of chest pain with an exam showing increasing respiratory effort, irregular tachycardia, no significant murmurs, and warm extremities. Vitals notable for blood pressure (147/75 mmHg) and heart rate (127 beats/min). Electrocardiogram (ECG) showed 1-mm upsloping ST elevations in leads II, III, and avF with a high sensitivity troponin found to be greater than 3000 ng/L (admission high sensitivity troponin less than 60 ng/l). Notable laboratory anomalies included IL-6 levels of 54.9 pg/mL, D-dimer levels of 28.45 mcg/mL, and C-reactive protein levels of 91.4 mg/L. Given the acute presentation, ECG findings, and troponin elevation, the differential diagnosis included STEMI, TCM, and myopericarditis.

The patient was intubated electively to reduce transmission and urgently taken for cardiac angiography. She was found to have no significant coronary artery stenosis with good thrombolysis in myocardial infarction (TIMI) 3 flow and a left ventriculogram with apical ballooning (Figure 1). A transthoracic echocardiogram with contrast showed ejection fraction 20-25%, normal left ventricular chamber size with basal wall hyperkinesis, and apical wall hypokinesis. The patient was admitted to the intensive care unit for her underlying COVID-19 pneumonia with findings consistent with TCM.

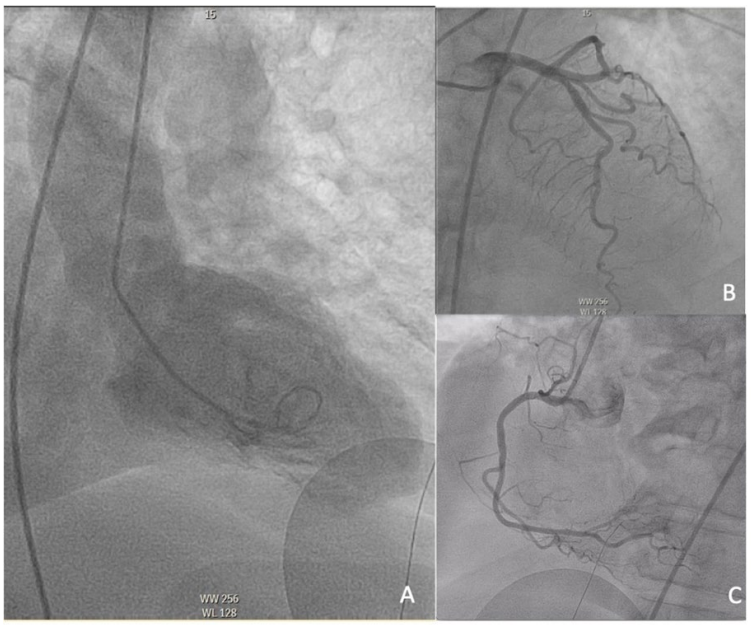

Figure 1. (A) Left ventriculogram consistent with apical ballooning. Angiogram showing good TIMI 3 flow in both the left (B) and right (C) coronary system.

Clinically, the patient continued to require high levels of oxygen via the ventilator with supportive care. Her inflammatory markers eventually trended down, as did her oxygen demand. A follow-up transthoracic echocardiogram showed return of normal cardiac function, ejection fraction of greater than 55%, and no regional wall abnormalities (Figure 2). Due to her lack of significant improvement and continued ventilator dependence, the multidisciplinary decision with the family was to have the patient undergo tracheostomy and percutaneous gastrostomy tube placement for long term convalescence.

Given the improvement of her cardiomyopathy with the improvement of her infection and the negative coronary findings on angiogram, the diagnosis of Takotsubo cardiomyopathy was believed to be most consistent.

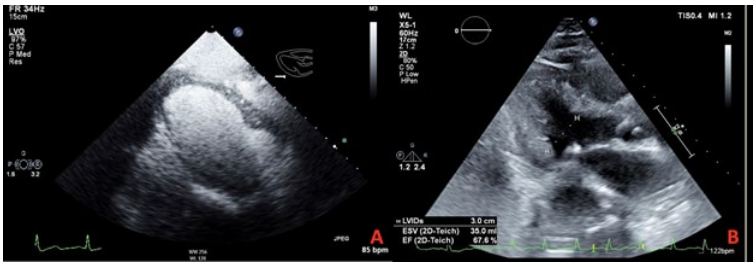

Figure 2. (A) Hospital day 2 ECHO with contrast showing an ejection fraction of 20-25%, normal left ventricular chamber size with apical hypokinesis and basal hyperkinesis consistent with TCM. (B) Hospital day 22 ECHO with contrast showing return of normal left ventricular function with no regional wall abnormalities. LVID: left ventricular internal dimension; ESV: end systolic volume; EF: ejection fraction.

DISCUSSION

Patients with Takotsubo cardiomyopathy classically present with typical chest pain and ECG findings of anterolateral ischemia. Of note, 1-2% of patients present with troponin positive suspected acute coronary syndrome or STEMI.[1] This finding was postulated to be due to direct left ventricular myocardial injury and resultant troponin leak appearing as ST elevations in the anterolateral precordial leads.[3] On ultrasound, the myocardial wall dyskinesis occurs over multiple coronary territories with no significant coronary stenosis seen on cardiac angiography further supporting a non-ischemic cardiomyopathy etiology.[1]

Stress, either psychological or physical, was thought to be a major contributor to TCM, with an 89.9% predominance for female patients.[3] A postulated theory includes increased levels of circulating catecholamines causing direct myocardial injury leading to classical left ventricular apical hypokinesis with basal hyperkinesis.[4] One such stressor may be the extensive inflammatory disease that occurs during an acute COVID-19 infection. It was believed to be a response to IL-6 activation through either the classical or trans signaling pathways.[2] IL-6 is produced transiently in response to infection and tissue injury, but prolonged inflammation can lead to continual synthesis leading to chronic inflammation and stress. A recent multicenter randomized control trial found a 4% reduction in all-cause mortality within the first 28 days for critically ill patients on tocilizumab with steroids against steroids alone.[2] In our case, the presentation with angiography and echocardiogram correlates with TCM, but the patients' comorbidities contraindicated tocilizumab.

Although novel therapies can be effective, the current strongest recommendation to prevent disease is vaccination. The two-part mRNA-1273 series provided viral protection with greater than 92% efficacy 14 days after the initial dose with greater than 94% efficacy two weeks after the second dose.[5] Although there have been reported cases of post-vaccine TCM, the timing and exposure with positive PCR seen in this case points to natural viral transmission leading to TCM.[6] Given the post-vaccination severe IL-6 mediated presentation by our patient, the importance of maintaining precautions prior to full vaccine series completion remains of utmost importance.

Although COVID-19 vaccinations have led to a significant decrease in severe disease, this case clearly demonstrated that vaccination, even complete vaccination, is not fully protective against severe disease. The patient had a severe IL-6 mediated disease despite the 92% efficacy rate with the vaccine after the first dose. Despite the high efficacy rate of these vaccines, it was essential to follow proper precautions as there was still a subset of those vaccinated who can develop severe COVID-19 pneumonia and can experience further complications due to the infection.

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