American Journal of Medical Case Reports, 2021, Vol. 9, No. 10, 485-488
Available online at http://pubs.sciepub.com/ajmcr/9/10/1
Published by Science and Education Publishing
DOI:10.12691/ajmcr-9-10-1

COVID-19 Pandemic Induced Stress (Takotsubo) Cardiomyopathy

Kyle Martin S. Alimurung[1], Darleen Sy[2], Benjamin N. Alimurung[2,*]

[1]Department of Medicine, Makati Medical Center, #2 Amorsolo Street, Legazpi Village, Makati, 1229, Philippines
[2]Section of Cardiology, Department of Medicine, Makati Medical Center, #2 Amorsolo Street, Legazpi Village, Makati, 1229, Philippines
*Corresponding author: Bnaoutpost@yahoo.com

Received April 20, 2021; Revised May 25, 2021; Accepted June 03, 2021

Abstract The COVID-19 pandemic has led to a diverse spectrum of medical conditions, including stress (Takotsubo) cardiomyopathy, which may be triggered by severe emotional or physical distress leading to reversible acute heart failure. This case highlights stress cardiomyopathy complicated by pulmonary edema and cardiogenic shock in an 86-year-old female, confirmed COVID-19 negative by RT PCR for SARS-CoV-2, brought about by intense emotional stress triggered by the ongoing pandemic.

Keywords: *COVID-19, pandemic, stress cardiomyopathy, Takotsubo cardiomyopathy, heart failure*

Cite This Article: Kyle Martin S. Alimurung, Darleen Sy, and Benjamin N. Alimurung, "COVID-19 Pandemic Induced Stress (Takotsubo) Cardiomyopathy." *American Journal of Medical Case Reports*, vol. 9, no. 10 (2021): 485-488. doi: 10.12691/ajmcr-9-10-1.

1. Introduction

Stress cardiomyopathy occurs in settings of heightened physical and emotional distress, with emotional stress more frequent in postmenopausal women. The condition commonly presents with chest pain, dyspnea, and diaphoresis along with ECG findings of ST-segment elevation, ST-segment depression, and T-wave inversion. [1] Its presentation may mimic acute coronary syndrome (ACS) and may be complicated by acute heart failure and/or cardiogenic shock. Therefore, an awareness by the practicing clinician of this entity is important in the differential diagnosis of ACS.

An increased incidence of stress cardiomyopathy has been observed during situations such as catastrophic natural disasters [2] and other severe global crises, including the ongoing COVID-19 pandemic. [3] There have been various reasons for the development of stress cardiomyopathy during the COVID-19 pandemic. These may be attributable to stress from physical and emotional isolation due to prolonged lockdown quarantines of communities, social distancing, [4] and emotional anxiety from being overly concerned for one's well-being during a global crisis. [5]

The aim of this case report is to raise awareness and enhance recognition among clinicians of stress (Takotsubo) cardiomyopathy as a potential etiology in the differential diagnosis of patients presenting with acute heart failure and cardiogenic shock, especially during periods of global crisis and upheaval.

2. Case Presentation

An 86-year-old female was admitted due to loose watery stools and fever. Medical history included end stage renal disease (ESRD) on regular hemodialysis, hypertension, dyslipidemia, and a myeloproliferative disorder. Vital signs were normal, except for a temperature of 38.5C. Patient was drowsy, easily arousable to verbal stimuli, with no motor or sensory deficits. Electrocardiogram (ECG) revealed normal sinus rhythm, an old anteroseptal wall myocardial infarction (MI) (unchanged from previous ECG), infero-lateral non-specific ST-T-wave changes, and QT interval prolongation with a QTc of 521 msec. Transthoracic 2-D echocardiogram (2-D echo) showed normal left ventricular dimension, wall motion and contractility, and a left ventricular ejection fraction (LVEF) of 71%. Pro-BNP was increased at 1132 pmol/L (ref. range: <14.78 pmol/L) and high sensitivity troponin-I (HS Trop-I) modestly elevated at 0.068 ng/mL (ref. range: < 0.015 ng/mL). CBC revealed moderate anemia, Hgb of 9.2 g/dL, and mild thrombocytopenia at 147 x 10^9/L. Serum electrolytes were normal. Serum creatinine was 7.95 mg/dL with an eGFR of 4.2 mL/min/1.73 m2. Procalcitonin was elevated, 2.42 ng/mL (ref. range: <0.50 ng/mL), consistent with bacterial infection. Blood cultures and testing for *Clostridium difficile* were negative. Urine culture and urinalysis were not done as the patient had minimal to no urine output due to her ESRD maintained on hemodialysis. A nasopharyngeal and oropharyngeal swab RT PCR for SARS-CoV-2 was negative.

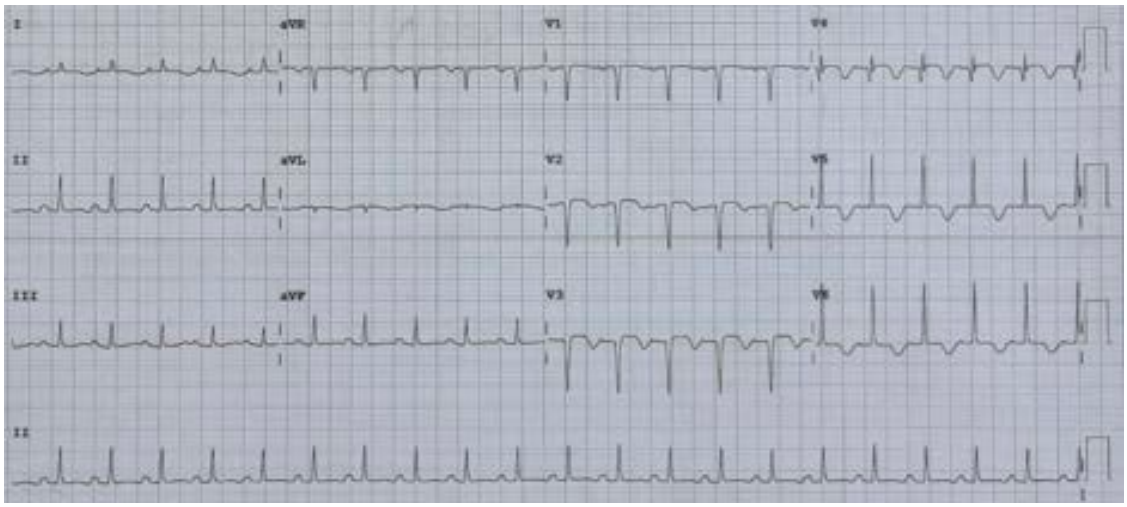

Figure 1. ECG: sinus tachycardia, old anteroseptal wall MI, new ST-segment elevation V2-V4, prolonged QT interval (QTc of 499), and new extensive T-wave inversion

During hospital stay, the patient repeatedly expressed worry and heightened concern for the worsening global pandemic and recent COVID-19 infection surges in the country. Moreover, she particularly worried for siblings who, because of their advanced age and pre-existing co-morbidities, were at high risk for severe COVID-19 disease, after several staff residing in the same household contracted COVID-19 infections. On day three, she was further alarmed by news of a devastating explosion in Beirut, Lebanon and a desire to help those affected by the tragic incident in the midst of the pandemic. Several hours later, she suddenly complained of low back pain, progressive breathing difficulty, oxygen desaturation, and hypotension. ECG showed sinus tachycardia, an old anteroseptal wall MI, new ST-segment elevation in V2-V4, prolonged QT interval (QTc of 499 msec), and new extensive T-wave inversion (Figure 1). Chest x-ray revealed pulmonary edema (Figure 2). A repeat 2-D echo demonstrated new hypokinesia to akinesia of mid to apical segments and apical ballooning of the left ventricle (LV). LVEF was reduced to 34% from baseline of 71% (Figure 3A). Importantly, left ventricular outflow tract (LVOT) obstruction was absent. Pro-BNP was significantly increased at 6973 pmol/L and HS Trop-I modestly elevated at 6.94 ng/mL. Repeat RT PCR testing for SARS-CoV-2 was negative.

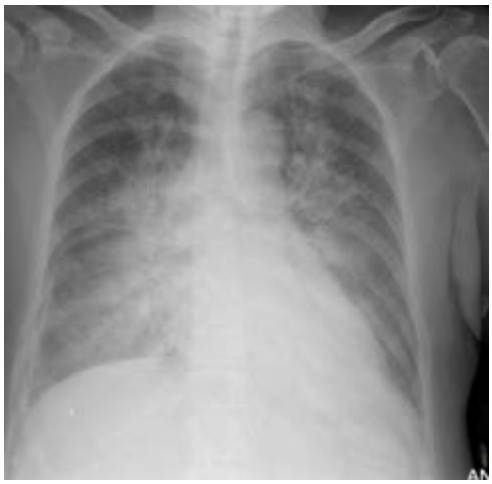

Figure 2. Chest X-ray: pulmonary edema

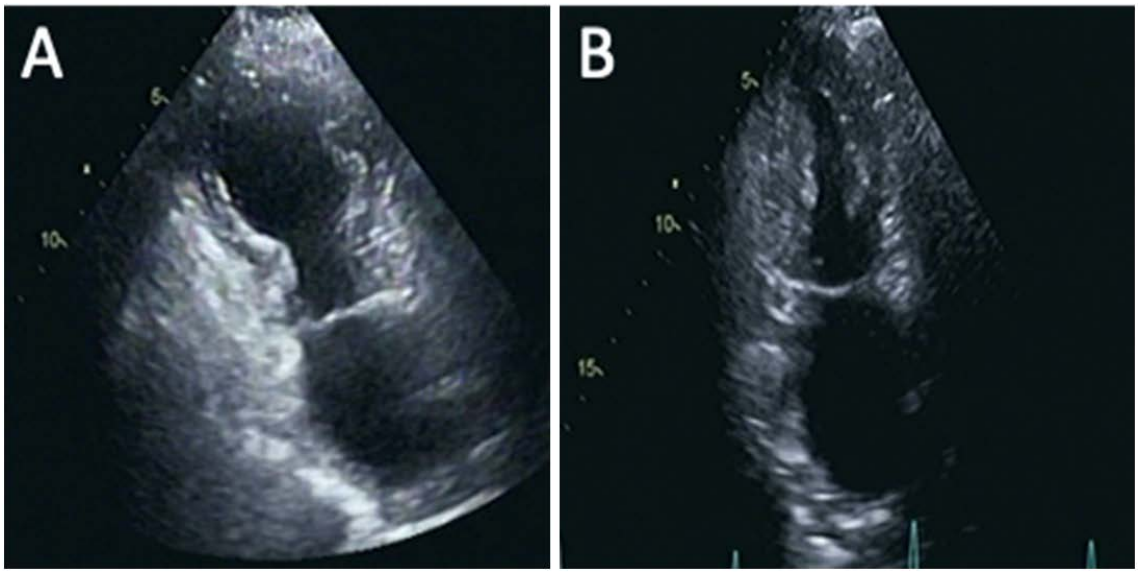

Figure 3. 2-D echo: 2 chamber view, systolic frames, (A) LV apical ballooning, day 3 (B) Normal, day 13

She was intubated, placed on mechanical ventilation, and transferred to the critical care unit. Continuous renal replacement therapy was initiated and procalcitonin had decreased to 1.46 ng/mL. Due to persistent hypotension, norepinephrine and dobutamine IV drips were started. She experienced episodes of paroxysmal atrial fibrillation, converted to sinus rhythm with IV amiodarone. Aspirin, clopidogrel, subcutaneous enoxaparin, and low dose metoprolol were administered. With aggressive heart failure management, the patient experienced clinical improvement with resolution of the pulmonary edema and cardiogenic shock. On day 8, repeat blood cultures were also negative. On day 13, repeat 2-D echo showed normal left ventricular wall motion and contractility with preserved LVEF of 76% and complete absence of the apical ballooning (Figure 3B). Coronary angiography was deferred due to limited cardiovascular services and personnel during the ongoing pandemic. She was discharged stable after a total hospital confinement of 24 days. Apixaban was prescribed for 3 months but discontinued after only 2 months, in light of a follow-up 2-D echo at 2 months, demonstrating sustained normal LV systolic function, normal LVEF, and no recurrence of LV apical ballooning.

3. Discussion

The ongoing COVID-19 pandemic worldwide has led to a diverse spectrum of medical conditions including myocardial injury complications such as acute myocarditis, acute coronary syndrome (ACS), and stress Takotsubo cardiomyopathy. [6] Takotsubo, first described in Japan in 1990, refers to the classic left ventricular apical ballooning seen in the majority of cases, resembling an inverted octopus trap used in Japan. Less frequent variants of LV systolic dysfunction localized to the mid-ventricular or basal regions have been described, with a prevalence of 10-20% and 5%, respectively. [7] On 2-D echo, the mid-ventricular variant exhibit hypo or akinesia of the mid portion of the LV with normal apical and basal contraction. Patients with this varant may also experience severe LV dysfunction and cardiogenic shock. The basal variant, on the other hand, presents with hypo or akinesia of only the basal segment of the LV. Patients with the basal variant experience less severe hemodynamic compromise. Rare variants include biventricular dysfunction, with a prevalence of <0.5% and a similar clinical presentation as the mid-ventricular variant. Finally, a generally benign variant with dysfuntion limited to only a focal LV segment has been observed in large cohort series of stress cardiomyopathy. [7]

Initially regarded as a benign condition, Takotsubo cardiomyopathy may actually be associated with severe clinical complications, similar to our patient who experienced florid pulmonary edema and cardiogenic shock. A 12.4% incidence of cardiogenic shock among 1750 patients is cited in the International Takotsubo Registry. Another complication is LVOT obstruction and systolic anterior motion of the mitral valve due to hypercontractility of the basal portions of LV may lead to mitral regurgitation (MR) in 14-25% of patients. Acute MR, which worsens cardiac output, adds to the complexity of clinical management. [7] Arrhythmias during the acute phase of illness occur in 25% of patients, with atrial fibrillation seen in 5-15%, and ventricular arrhythmias occuring in 4-9%. Torsades de pointes among patients with a prolonged QT interval of >500 msec may further complicate management. [7] Rare complications include intramyocardial hemorrhage and left ventricular wall rupture, which are generally diagnosed postmortem. Risk factors associated with these two complications include older age, hypertension, prolonged ST-segment elevation, and less frequent use of beta blockers. [7]

Stress (Takotsubo) cardiomyopathy is a physically or emotionally induced, reversible left ventricular wall motion abnormality that exists beyond the territory supplied by a single coronary artery. [7] The precise pathophysiology is still unknown. However, one of the proposed mechanisms links physical or emotional stressors which lead to the extrusion of norepinephrine and neuropeptide Y from pre-synaptic terminals, and spillover on the myocardial level may induce direct toxic effects and/or myocardial microvascular dysfunction on these tissues in predisposed individuals. [7]

Jabri and co-investigators, in a recent retrospective survey in 2 hospitals in Cleveland, Ohio of COVID-19 negative patients presenting with ACS during the ongoing pandemic compared with 4 comparable timeline pre-pandemic cohorts, found an increased incidence of stress cardiomyopathy (4.58 incidence rate ratio). [3]

Among Southeast Asian individuals, similar to other patient populations, the syndrome is predominantly seen in elderly post-menopausal women, with a mean age 69.3 years, a higher incidence of physical triggers, and comparable in-hospital cardiovascular mortality of 4.1%. [1] Typical presenting symptoms are chest pain, dyspnea, and diaphoresis. On 2-D echo, left ventricular apical ballooning is the most commonly found variant observed in 89% of patients. [1]

Three commonly used major diagnostic criteria sets include: the Revised Mayo Clinic, the Heart Failure Association–European Society of Cardiology, and the International Takotsubo Diagnostic (InterTAK) criteria. [7] Our patient showed evidence of transient, reversible LV dysfunction on 2-D echo with hypokinetic to akinetic mid to apical segments and apical ballooning that resolved on repeat echocardiogram after 2 weeks. The ECG showed ST-segment elevation, extensive T-wave inversion and QTc prolongation, and modestly elevated HS Trop-I, which are all characteristic features described in the InterTAK diagnostic criteria. Moreover, her clinical presentation (female, emotional trigger, absence of ST-segment depression, and QTc prolongation) constitute 4 of 7 criteria, accounting for 67 out of a total 100-weighted points, of the InterTAK Diagnostic Risk Score (95% specificity), [7] a practical bedside tool for distinguishing Takotsubo cardiomyopathy versus ACS.

Although there are no randomized clinical trials to define the optimal management of patients with Takotsubo cardiomyopathy, the goal of treatment is supportive care to sustain life and minimize complications until there is full recovery of LV function. In patients with classic LV apical ballooning, it is critical to determine by 2-D echo the presence of LVOT obstruction as a result of hypercontractility of the basal segments because inotropic

agents may worsen obstruction and cardiogenic shock. Beta blockers may be added to lessen LVOT obstruction and improve cardiac output through reduction of basal hypercontractility. Likewise, they can be used to treat hypertension in those who are hemodynamically stable, may play a role in the prevention of malignant arrhythmias, and prevent cardiac rupture. [7] LV thrombus formation, particularly in patients with LV apical ballooning, is a recognized complication with a 2-9% risk of systemic embolism and stroke. The highest risk of thromboembolism is seen during the acute phase of heart failure and cardiogenic shock. [7] Thus, systemic anticoagulation is warranted until LV systolic function recovers, usually within several weeks, and documented with follow-up 2-D echo. In our case, anticoagulation was initially planned for 3 months. However, in light of sustained LV recovery documented by a normal 2-D echo at 2 months, it was decided that the apixaban could be safely discontinued earlier.

Stress cardiomyopathy is a reversible syndrome, but recurrences may occur with an incidence of 2-4% per year. [7] There is no consensus on long-term management, although some experts advocate the use of beta blockers in patients with ongoing symptoms, recurrent episodes, or persistent anxiety. Angiotensin-converting enzyme inhibitors (ACEI) or angiotensin-receptor blockers (ARB) have shown a marginal 1-year survival benefit on retrospective analysis and are reasonable therapies for patients with stress cardiomyopathy. [7] Heightened emotional distress brought about by the COVID-19 pandemic, aggravated by news of a factory explosion in Beirut, Lebanon, [9] mentioned explicitly by our patient, taken together, were the apparent triggers for her stress cardiomyopathy. Published literature suggest that intense emotional stress caused by the pandemic is significant enough to activate the brain-heart axis and serve as a stressor for the development of stress cardiomyopathy. [10,11] Other studies have found a similar presentation of stress cardiomyopathy brought about by emotional distress triggered by natural disasters, [2] anxiety of social isolation [4] and being overly concerned for one's health during the COVID-19 pandemic. [5]

To our knowledge, this is the first reported case of stress Takotsubo cardiomyopathy during the ongoing COVID-19 pandemic in the Philippines.

4. Conclusion

Stress cardiomyopathy, triggered by heightened emotional distress as a result of a serious global crisis, should be considered in the differential diagnosis of patients presenting with acute heart failure and/or cardiogenic shock.

Acknowledgements

Role of the funding source: no funding.

Declarations of Interest: the authors have no competing interests.

The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

References

[1] Kow K, Watson TJ, Foo D, Ho HH. Clinical characteristics and outcomes of South-East Asian patients with Takotsubo (stress-induced) cardiomyopathy. IJC Heart & Vasculature. 2018; 21: 29-31.

[2] Wong CK. Takotsubo (stress) cardiomyopathy: insights gleaned from the Christchurch Earthquake experience. N Z Med J. 2014; 127(1396): 5-9.

[3] Jabri A, Kalra A, Kumar A, Alameh A, Adroja S, Bashir H, et al. Incidence of Stress Cardiomyopathy During the Coronavirus Disease 2019 Pandemic. JAMA Network Open. 2020; 3(7): e2014780.

[4] Rivers J, Ihle JF. COVID-19 social isolation-induced takotsubo cardiomyopathy. Med J Aust. 2020; 213(7): 336-. e1.

[5] Chadha S. 'COVID-19 pandemic' anxiety-induced Takotsubo cardiomyopathy. QJM: An International Journal of Medicine. 2020; 113(7): 488-90.

[6] Giustino G, Pinney SP, Lala A, Reddy VY, Johnston-Cox HA, Mechanick JI, et al. Coronavirus and Cardiovascular Disease, Myocardial Injury, and Arrhythmia. Journal of the American College of Cardiology. 2020; 76(17): 2011-23.

[7] Medina de Chazal H, Del Buono MG, Keyser-Marcus L, Ma L, Moeller FG, Berrocal D, et al. Stress Cardiomyopathy Diagnosis and Treatment: JACC State-of-the-Art Review. J Am Coll Cardiol. 2018; 72(16): 1955-71.

[8] Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M, et al. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. New England Journal of Medicine. 2015; 373(10): 929-38.

[9] World Health Organization. Lebanon emergency appeal 20202020 October 29, 2020. Available from: https://www.who.int/emergencies/funding/appeals/lebanon-explosion-2020.

[10] Giannitsi S, Tsinivizov P, Poulimenos LE, Kallistratos MS, Varvarousis D, Manolis AJ, et al. [Case Report] Stress induced (Takotsubo) cardiomyopathy triggered by the COVID-19 pandemic. Exp Ther Med. 2020; 20(3): 2812-4.

[11] Desai HD, Sharma K, Jadeja DM, Desai HM, Moliya P. COVID-19 pandemic induced stress cardiomyopathy: A literature review. IJC Heart & Vasculature. 2020; 31: 100628.