JACC: CASE REPORTS VOL. 2, NO. 2, 2020

EDITORIAL COMMENT

Stress Remains in the Eye of the Beholder*

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Stress cardiomyopathy is a unique syndrome of cardiac dysfunction that is gaining more recognition over time as awareness of this syndrome increases. Often, an intense stressor to the system is considered a catalyst leading to severe and often reversible cardiac dysfunction, originally termed "Takotsubo cardiomyopathy," named after the Japanese fishing pot with a narrow neck and wide base (1). The pattern seen of the left ventricle in this syndrome is often described to resemble the shape of the aforementioned pot (2). Importantly, the diagnosis of this syndrome remains one of exclusion in which common causes of acute cardiac dysfunction, including acute coronary syndromes, are excluded. Historical teaching included the consideration of an emotional trigger such as the loss of a loved one or a possible psychiatric illness as a comorbidity. In this issue of *JACC: Case Reports,* Gionfriddo et al. (3) have demonstrated the importance of identifying that acute stressors can also come in the form of withdrawal of a steady-state medication, which can lead to morbid consequences.

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In their case, a 67-year-old woman with a history of scleroderma-associated pulmonary arterial hypertension developed stress cardiomyopathy after cessation of an epoprostenol infusion that resulted from catheter malfunction. Appropriate diagnostic testing included an echocardiogram and subsequent coronary angiography to exclude obstructive coronary artery disease. After the diagnosis was suspected, the first step was reinstitution of the medication that was withheld because of the catheter malfunction. Contemporary medical therapies for heart failure were considered, but they could not be started as a result of her low blood pressures. Importantly, 1 month after this intervention, cardiac dysfunction had resolved on follow-up echocardiography.

Stress cardiomyopathy is a relatively recently acknowledged entity, and we are increasingly recognizing and understanding its existence. Original descriptions of this syndrome were typically associated with intense emotional stressors (leading to the name "broken heart syndrome"). However, contemporary research has demonstrated that emotional triggers are not as common as physical triggers, and many patients have no evident trigger (4) (**Figure 1**). However, given the original associations with psychiatric illness, as well as emotional lability, this has led to a gap in which some patients with stress cardiomyopathy believe that they are less likely to receive educational support for their condition (5). The critical consideration that a physical stressor may come not only in the form of a de novo insult, but also by removal of a steady-state therapy, can potentially lead to the recognition of more cases of stress cardiomyopathy. The present case of stress cardiomyopathy after epoprostenol withdrawal is only the second description of the syndrome with this class of drugs (6). The pathomechanisms of this syndrome are not fully understood. In the presented case, acute epoprostenol withdrawal could have led to both emotional and physical stress that could have explained the stress cardiomyopathy. The pump alarm (emotional stress) for a vital drug infusion could have triggered the traditional pathway of central nervous system activation with subsequent cathecholaminergic release. However, Gionfriddo et al. (3) also propose

*Editorials published in *JACC: Case Reports* reflect the views of the authors and do not necessarily represent the views of *JACC: Case Reports* or the American College of Cardiology.

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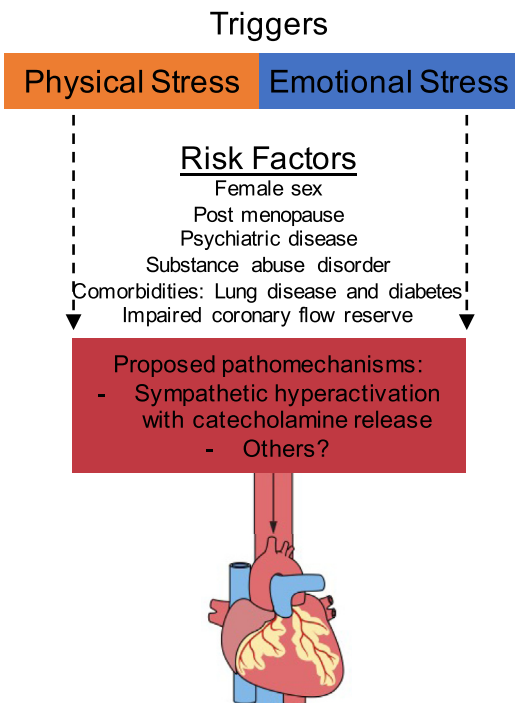
ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2019.11.044

FIGURE 1 Overview of Stress Cardiomyopathy



that acute pulmonary vasoconstriction following epoprostenol withdrawal could have led to right ventricular congestion with right atrial baroreceptor hyperactivation. Baroreceptor activation could have caused reflex sympathetic hyperactivation with the downstream effect of stress cardiomyopathy.

It light of the present case, it is critical to be aware of the broad class of agents that have been implicated as the causative agents of stress cardiomyopathy. They include exogenous catecholamines (most commonly epinephrine), drugs that activate the adrenal axis (e.g., midodrine), and withdrawal of alcohol, opioids, and beta-blockers (7). Some evolutionary biologists have theorized an association of Takotsubo cardiomyopathy with capture myopathy syndromes (seen in the wildlife), in which damage to muscle subsequent to the pursuit, capture, holding, handling, and manipulation of an animal has systemic consequences (8). It is possible there exists an evolutionary benefit for the species with capture myopathy and an advantage for escaping predators.

It is clear there remains much to learn about stress cardiomyopathy. This includes the following questions: Why is the prevalence so much greater in women? What is the true mechanism of the myocardial stunning observed? We will likely see more cases of stress cardiomyopathy with the rise of point-of-care ultrasound and bedside imaging. The consideration of a broad list of potential stressors will likely help in its recognition. As we identify more cases, we hope to learn more about this unique cardiomyopathy, with the goals of treating the condition and preventing its recurrence.

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REFERENCES

1. Lyon AR, Bossone E, Schneider B, et al. Current state of knowledge on Takotsubo syndrome: a position statement from the Taskforce on Takotsubo Syndrome of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail 2016;18:8–27.

2. Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J 2008;155:408–17.

3. Gionfriddo WJ, Ahmed HN, Farber HW. Stress cardiomyopathy precipitated by withdrawal of epoprostenol. J Am Coll Cardiol Case Rep 2020;2:289–93.

4. Templin C, Ghadri JR, Diekmann J, et al. Clinical features and outcomes of Takotsubo (stress) cardiomyopathy. N Engl J Med 2015;373:929–38.

5. Schubert SC, Kucia A, Hofmeyer A. The gap in meeting the educational and support needs of women with takotsubo syndrome compared to women with an acute coronary syndrome. Contemp Issues Educ Res (Littleton) 2018;11:133–44.

6. Cork DP, Mehrotra AK, Gomberg-Maitland M. Takotsubo cardiomyopathy after treatment of pulmonary arterial hypertension. Pulm Circ 2012;2:390–4.

7. Amariles P, Cifuentes L. Drugs as possible triggers of Takotsubo cardiomyopathy: a comprehensive literature search - update 2015. Curr Clin Pharmacol 2016;11:95–109.

8. Blumstein DT, Buckner J, Shah S, et al. The evolution of capture myopathy in hooved mammals: a model for human stress cardiomyopathy? Evol Med Public Health 2015;2015:195–203.

KEY WORDS acute heart failure, cardiogenic shock, epoprostenol, pulmonary arterial hypertension, stress cardiomyopathy