Takotsubo's Paradox

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Abstract

Introduction: Takotsubo cardiomyopathy is an emerging clinical entity characterized by a transient depression of the contractile function of mid and or apical segments of the left ventricle with compensatory hyper kinesis or preservation of the basal wall leading to ballooning of the apex in systole and accounts for 2% of all patients presenting with symptoms of acute myocardial infarction. The Pathophysiology of Takotsubo cardiomyopathy is unclear and several hypotheses include catecholamine induced myocyte toxicity or coronary micro-vascular dysfunction. Presentations usually follow an episode of intense emotional or physiological stress, most often a noxious stressor. Takotsubo cardiomyopathy has rarely been described in the context of a positive or pleasurable emotional stimulus.

Methods: A 69 year old Caucasian female presented to the Gold Coast University Hospital with central chest heaviness and pain in her lower jaw. The patient's symptoms began during preparations for a family reunion, having recently heard the good news of her Son's return home and daughter's latest pregnancy. The patient was nervously excited and joyous at the thought of the upcoming family festivities. Her medical history was relevant for treated hypercholesterolemia, hypertension and migraines. Electrocardiogram demonstrated sinus rhythm with early Q waves and ST elevation in the lateral leads without T wave changes and a QTc of 405. The patient's initial troponin-I level was 6.9 with normal renal function.

Results: The patient was managed as an ST elevation acute coronary syndrome and transferred for angiogram revealing minor coronary disease of the distal LAD with associated coronary spasm and minor left circumflex disease without obstructive plaque or thrombus. Echocardiogram showed mildly impaired left ventricular systolic function with severely hypo kinetic mid left ventricular segments with an akinetic apex and sparing of the basal left ventricular segments in a non-vascular pattern consistent with takotsubo cardiomyopathy.

Conclusion: Takotsubo cardiomyopathy is becoming more widely recognized as a differential diagnosis for acute coronary syndrome particularly in patients with a clear history of recent negative stressors. To date clinical case reports demonstrate associations between Takotsubo cardiomyopathy and strong negative emotional stressors however the unique presentation of this patient suggests strong positive emotional stimulus may also be implicated in the events leading to Takotsubo cardiomyopathy.

Keywords: Takotsubo cardiomyopathy; Acute coronary syndrome; Angiogram; Echocardiogram; Female

Introduction

Takotsubo cardiomyopathy or stress-induced cardiomyopathy, first described in Japan in 1990, is an emerging clinical entity commonly referred to as broken heart syndrome. The word takotsubo translates to "octopus pot", a fishing jar with a wide base used to trap octopus, a name used to describe the appearance of the heart on left ventriculography [1].

It is characterized by a transient depression of the contractile function of mid and or apical segments of the left ventricle with compensatory hyper kinesis or preservation of the basal wall leading to ballooning of the apex in systole [2].

The Pathophysiology of Takotsubo cardiomyopathy is unclear and several hypotheses have been postulated to explain the changes seen on electrocardiogram and imaging modalities. These include catecholamine induced myocyte toxicity, coronary micro-vascular dysfunction and multi-vessel epicardial coronary vasospasm [3].

Typically clinical presentations can mimic acute myocardial infarction with symptoms of chest pain, shortness of breath, back pain, nausea and fatigue [3]. Takotsubo cardiomyopathy accounts for 2% of all patient's presenting with symptoms of acute myocardial infarction [4] and the phenomenon is more commonly observed in postmenopausal women. Electrocardiogram changes including ST segment elevation with elevated cardiac enzymes [2]. Coronary angiogram typically does not show obstructive lesions and only minimal coronary artery disease. Echocardiogram is characterized by marked left ventricular contraction abnormalities, typically apical and mid-ventricular akinesis, hypo kinesis and basal hyper-kinesis with a reduced ejection fraction of 20% to 49%, which spontaneously resolves over a period of days to weeks [3]. However, mortality rates have been reported at 3.2% [1].

Presentations are usually following an episode of intense emotional or physiological stress, most often a noxious stressor and there may be higher prevalence in patients with known diagnosis of anxiety disorder. Studies have shown that acute emotional triggers can precipitate cardiovascular events such as myocardial infarction, cardiac arrhythmias and Takotsubo cardiomyopathy [5]. Literature reviews show 85% of takotsubo cardiomyopathy is triggered by an emotional stimulus that precedes the onset of symptoms by minutes to hours [6].

Emotional stressors have shown to include grief, fear, anger, relationship conflicts and financial problems and physical stressors include acute illnesses, surgery, chemotherapy, and stroke.

The link between positive emotional stressors and takotsubo cardiomyopathy is less well defined and has rarely been described in the context of a joyful or pleasurable emotional stimulus. This case report demonstrates that positive stressors and "joyful" emotional stimulus may in fact also be related to the "broken-heart" syndrome.

Case Presentation

A 69 year old Caucasian woman with a past medical history of hypertension, hyper-cholesterolemia and migraines presented to the emergency department of Gold Coast University Hospital with central chest heaviness and associated pain in her lower jaw. The patient's symptoms began after a long drive and boat ride to a family cabin, before beginning the preparations for a family reunion with family arriving from interstate and from the United Kingdom. In addition to the elation of the upcoming reunion, the patient had also received news of her daughter's latest pregnancy. Nervously excited and preparing the cabin for the upcoming festivities the patient noticed the gradual onset of a "brick" sitting across her chest, and felt breathless and extremely lethargic and fatigued. The patient's discomfort persisted to a lesser degree throughout the afternoon and evening and on presentation to the emergency department was responsive to sublingual glyceryltrinitrate. Thorough history taking indicated that the patient had no negative emotional or physical stressors preceding this event and the patient had no additional risk factors for acute coronary syndrome. The patient demonstrated no signs of cardiogenic shock or cardiac failure and physical examination was otherwise unremarkable.

Initial electrocardiogram demonstrated sinus rhythm with early Q waves and ST elevation in the lateral leads without T wave changes and a QTc of 405 (Figure 1). Chest x-ray did not demonstrate signs of other acute pathology. Laboratory results were remarkable for a troponin I level of 6.9ng/ml (normal, 0.00 - 0.04) with normal white cell count and normal renal function. The diagnosis of ST elevation acute coronary syndrome was made initially and the patient proceeded to be managed with aspirin, ticagrelor, and low molecular weight heparin and transferred immediately for cardiac catheterization. Coronary angiogram revealed normal coronary anatomy, minor coronary disease of the distal LAD with associated coronary spasm, and minor left circumflex disease without obstructive plaque or thrombus (Figures 2a, 2b, 2c & 2d).

Transthoracic Echocardiogram showed mildly impaired left ventricular systolic function with an ejection fraction of 47%, with severely hypo kinetic mid left ventricular segments with an akinetic apex and sparing of the basal left ventricular segments in a non-vascular pattern consistent with takotsubo cardiomyopathy (Figures 3a and 3b). Post-cardiac catheterization Troponin T level was 355ng/ml (normal <0.015ng/ml). The patient had an uneventful recovery post catheterization and was

Figure 1: Electrocardiogram.

Figure 2a: Angiogram showing Normal Right Coronary Artery in Right Anterior Oblique view.

Figure 2b: Angiogram showing normal Left anterior descending artery and circumflex artery in Right Anterior Oblique caudal view.

given the final diagnosis of takotsubo cardiomyopathy. Follow up transthoracic echocardiogram was planned for the patient and after monitoring was ceased the patient was discharged home in time for her long awaited family reunion.

Discussion

Takotsubo cardiomyopathy is an emerging clinical entity especially recognized in post-menopausal women after sudden

Figure 2c: Left ventriculography showing Hyper-contractile basal segment and apical ballooning in systole.

Figure 2d: Angiogram Diastole.

Figure 3a: Echocardiogram-Akinetic Apex in systole consistent with Takotsubo Cardiomyopathy.

Figure 3b: Echocardiogram Diastole.

exposure to emotional or physiological stress. The acute presentation is similar to that of acute coronary syndrome with apical ballooning on echocardiogram, normal coronary anatomy on angiogram and usually with return of normal cardiac function within weeks of the initial event. The aetiology remains tentative with several mechanisms being proposed such as multi-vessel coronary artery spasm, impaired cardiac microvascular function and catecholamine triggered myocardial stunning [1]. The presentation of stress cardiomyopathy is identical to acute coronary syndrome and as such patients are triaged and managed as an acute coronary syndrome until cardiac catheterization suggests otherwise. Recent use of optical coherence tomography has shown that takotsubo cardiomyopathy may occur in patients with structurally normal coronary arteries [7].

The proposed criteria for diagnosis of takotsubo include transient hypo-kinesis, akinesis, or dyskinesis of the LV apical and midsegments that extend beyond a single epicardial coronary artery, absences of obstructive coronary artery disease, ST elevation or T wave inversion on electrocardiogram with a rise in cardiac enzymes such as troponin-I and finally absence of recent head trauma, intracranial bleeding, pheochromocytoma, obstructive epicardial coronary artery disease, myocarditis and hypertrophic cardiomyopathy [3]. Previous studies have shown that patients undergoing stressful events undergo physiological changes including endothelial damage, increased coagulation, increased sympathetic tone, and increased blood pressure, blood viscosity and a release of inflammatory mediators. These changes ultimately lead to plaque rupture and adverse cardiovascular events. Studies have shown that negative emotional stressors trigger cardiovascular events [8].

The rise in catecholamine levels during a stressful event results in cardiac stunning [9]. Several hypotheses suggest that this may be through epicardial spasm, microvascular dysfunction hyperdynamic contractility, midventricular or outflow tract obstruction or the effect of catecholamine on cardiac myocytes[9].

Patients with stress-induced cardiomyopathy have statistically higher levels of catecholamines including dopamine, nor-epinephrine and epinephrine than patients with myocardial infarctions. Research in the area of positive stimuli, joyous occasions and positive stimuli and its possible association to takotsubo cardiomyopathy is lacking. This case report exemplifies the possible link between positive stressors and catecholamine release and takotsubo cardiomyopathy. Previous studies have shown that stress cardiomyopathy as the name suggests is linked to a negative stressor and patients usually present after traumatic events or circumstances.

It is well understood that states of excitement lead to a release in catecholamines. Whether they are positive or negative a surge in catecholamine is a natural response to sudden shock, fright, danger or excitement. It is possible that positive emotional stimulus through the same mechanism could lead to a presentation of takotsubo cardiomyopathy and in this case. A link between vulnerable personalities and the incidence of stress cardiomyopathy has been suggested, indicating that takotsubo

may in fact result from a combination of both a stressful event and a person's coping mechanisms [10].

This case report explains the importance of not limiting the causative events of stress cardiomyopathy to negative stimuli as it shows that positive stimuli "joyful and happy triggers" may also result in takotsubo.

Our understanding of the neurophysiology of the state of happiness is still in its infancy. Happiness is a tricky state to define from a neuropsychological point of view however might be thought of in terms of a balance between pleasure, meaning, and engagement or participation in life [11]. Studies have shown increased levels of dopamine, vasomotor sympathetic activity, secretory IgA levels and decreased salivary cortisol levels during states of happiness [12]. Significant activity after joyous stimulus was noted in the medial prefrontal cortex, thalamus, hypothalamus, subcallosal gyrus, posterior cingulate cortex, and superior temporal gyrus [13]. It seems likely given the association between catecholamines and takotsubo cardiomyopathy that is an extremely joyous or pleasurable event could result in the presentation of the cardiomyopathy through both higher levels of Dopamine and increased sympathetic activity and neuromediator release. As our understanding of this emerging clinical entity evolves, perhaps associations and causative agents for stress cardiomyopathy should be extrapolated to any events that cause a sudden release in catecholamine.

Future documentation showing a link between positive or pleasurable stimuli and stress cardiomyopathy will help further understanding of the pathophysiology and triggering events that result in takotsubo, hopefully translating into larger awareness of the condition amongst the medical fraternity, patient management strategies and improved outcomes.

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