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CASE REPORT

Repeat recurrence of takotsubo cardiomyopathy related to inhaled beta-2-adrenoceptor agonists

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Abstract

Takotsubo cardiomyopathy (also referred to as transient apical ballooning syndrome, broken heart syndrome or stress cardiomyopathy) is an increasingly recognized entity in the western world typically characterized by reversible left ventricular dysfunction that develops in the setting of acute severe emotional or physical stress. Increased catecholamine levels have been proposed to play a central role in the pathogenesis of the disease, although the specific pathophysiology of this condition remains elusive at the present moment. In recent times, there have been reports of takotsubo cardiomyopathy (TC) following medical interventions such as invasive or surgical procedures or specific medical regimens. In the current report, we present a patient with multiple recurrences of TC triggered by the same medical therapeutic intervention; in our particular case, repetitive exposure to inhaled beta-2-adrenoceptor agonist.

Key words: Takotsubo; Beta-2-adrenoreceptor agonist; Recurrence; Ventricular dysfunction; Heart failure

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INTRODUCTION

Takotsubo cardiomyopathy (apical ballooning syndrome or stress cardiomyopathy) is an increasingly recognized entity in the western world characterized by reversible left ventricular dysfunction that develops in the setting of acute severe emotional or physical stress. Increased catecholamine levels have been proposed to play a central role in the pathogenesis of this condition[1]. Recently, there have been reports of takotsubo cardiomyopathy (TC) following medical interventions[2]. We present a patient with multiple recurrences of TC triggered by the same medical therapeutic intervention; in our case, repetitive exposure to inhaled beta-2-adrenoceptor agonist.

CASE REPORT

A 76-year-old woman with a history of chronic obstructive lung disease, depression and hypertension presented to the emergency department after experiencing worsening dyspnea and wheezing. Upon arrival, she received continuous nebulization of terbutaline and intravenous dexamethasone. Despite continuous therapy and close follow-up, she failed to clinically improve. Six hours after her initial presentation, she reported an oppressive chest pain associated with worsening of her dyspnea. Electrocardiogram showed diffuse prominent T wave inversions that were not present upon admission. Initial set of cardiac enzymes were normal but rose after 6 h with a cardiac troponin I 0.91 ng/mL. An acute coronary syndrome was suspected, and intravenous heparin, aspirin, and beta-blocker were started. An echocardiogram performed at

the bedside showed depressed left ventricular function with an ejection fraction of 40% with apical dyskinesis. Urgent cardiac catheterization was performed demonstrating normal epicardial coronary arteries; left ventriculography showed depressed left ventricular function and an apical ballooning pattern. She was diagnosed with TC and was treated with furosemide, metoprolol and lisinopril that was continue as an outpatient. She soon thereafter recovered, and was discharged on her 4th hospital day. Subsequent echocardiogram 4 wk after discharge showed recovery of ventricular function with ejection fraction of 65% and normal wall motion.

Seven months after her initial presentation, she developed another episode of dyspnea and wheezing, which she described as her usual pulmonary exacerbation. She denied any acute stressors or active illnesses. Her beta 2-agonist rescue inhaler was used more than 20 times per day for 2 d achieving only partial relief. Once again, she presented to the emergency department and received serial treatments with inhaled short acting beta-2-agonists and intravenous steroids with subsequent improvement. Shortly after therapy, she experienced oppressive chest pain and new clinical and radiological signs of pulmonary congestion, leading to progressive hypoxia requiring intubation. A new electrocardiogram demonstrated new diffuse T wave inversions and repeat troponin I levels were now elevated (1.39 ng/dL, normal < 0.9 ng/dL). Cardiac catheterization found absence of obstructive coronary disease and ventriculography showed moderate systolic dysfunction with apical akinesis. She was started on loop diuretics, beta-blockers and an angiotensin-converting-enzyme-inhibitor, after which she markedly improved over the subsequent several days. She was discharged after 5 d in-hospital.

One year after her second episode, she experienced another acute exacerbation of her pulmonary disease, where she was admitted to an outside hospital. During her second hospital day, she developed recurrent chest pain and signs of volume overload with new electrocardiographic changes similar to her prior episodes along with abnormal cardiac enzyme elevations. She was taken urgently to the cardiac catheterization laboratory where no obstructive coronary disease was noted and similar ventriculographic findings were reported (moderate regional systolic dysfunction with apical akinesis).

After the third episode, her medical regimen was changed. Frequent use of beta-2-agonists was discontinued; she has been stable with a regimen of inhaled steroids, ipratropium bromide, lisinopril and metoprolol. As of her last follow-up 6 mo after the third presentation, she has developed mild pulmonary exacerbations but no further episodes of TC.

DISCUSSION

TC usually presents after an identifiable trigger such as an emotional or physical stressor. Prior studies report an identifiable trigger in 66% of the retrospective series and up to 98% in the prospective series[3,4]. Common stressors include acute fear or panic after a natural catastrophe, death of a relative or a sense of self danger[5,6]. Recent reports have proposed acute exacerbations of multiple medical conditions such as asthma, pneumothorax, gastrointestinal bleeding or hypoglycemia as potential triggers[4]. Common medical interventions have also been found to elicit this phenomenon[2]. In our case, we hypothesized the use of excessive short acting beta-2-agonists such as albuterol or terbutaline as a possible trigger of this entity. Our patient only developed clinical and electrocardiographic evidence of TC after continuous exposure to beta-2-adrenergic agonists despite the partial improvement of her pulmonary status.

Increase beta-2-adrenoceptor activity in the setting of a high catecholaminergic state has been proposed as possible reproducible model for this entity, inducing cardiac dysfunction and myocyte injury though calcium leakage due to hyperphosphorylation of the ryanodine receptor 2[7]. Increased beta-2 concentration gradient from apex to base could play an important role in the apical myocardial dysfunction and ballooning commonly found in TC cases[8]. Furthermore, the characteristic apical contractile dysfunction has been attenuated with the administration of beta-2-adrenergic blockers[9] and other beta blockers[10]. Unfortunately, most of this evidence has been gathered from animal experimental studies and most of the presumed pathophysiologic mechanisms are a result of assumption and extrapolation from the animal to the human model.

Recurrence of a TC is a rare phenomenon but has been described previously[11-13]. Postulated recurrence rates range from 7.7% to 11.4%. To the best of our knowledge, we report for the first time multiple recurrences of TC triggered by the same therapeutic intervention. Our patient was diagnosed 3 times with TC based on the widely accepted Mayo guidelines for TC, notably in the absence of head trauma, intracranial bleeding, pheochromocytoma, hypertrophic cardiomyopathy or myocarditis. Prevention with medical surveillance, changes in her medical regimen and avoidance of proposed triggers, in this case short acting beta-2-agonist use, have been the key to prevent further exacerbations.

REFERENCES

1 **Wittstein IS**, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, Wu KC, Rade JJ, Bivalacqua TJ, Champion HC. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005; **352**: 539-548

2 **Abraham J**, Mudd JO, Kapur NK, Klein K, Champion HC, Wittstein IS. Stress cardiomyopathy after intravenous administration of catecholamines and beta-receptor agonists. *J Am Coll Cardiol* 2009; **53**: 1320-1325

3 **Gianni M**, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning syndrome or takotsubo cardiomyopathy: a systematic review. *Eur Heart J* 2006; **27**: 1523-1529

4 **Wittstein IS**. Acute stress cardiomyopathy. *Curr Heart Fail Rep* 2008; **5**: 61-68

5 **Cebelin MS**, Hirsch CS. Human stress cardiomyopathy. Myocardial lesions in victims of homicidal assaults without

internal injuries. *Hum Pathol* 1980; **11**: 123-132
6 **Cocco G**, Chu D. Stress-induced cardiomyopathy: A review. *Eur J Intern Med* 2007; **18**: 369-379
7 **Ellison GM**, Torella D, Karakikes I, Purushothaman S, Curcio A, Gasparri C, Indolfi C, Cable NT, Goldspink DF, Nadal-Ginard B. Acute beta-adrenergic overload produces myocyte damage through calcium leakage from the ryanodine receptor 2 but spares cardiac stem cells. *J Biol Chem* 2007; **282**: 11397-11409
8 **Mori H**, Ishikawa S, Kojima S, Hayashi J, Watanabe Y, Hoffman JI, Okino H. Increased responsiveness of left ventricular apical myocardium to adrenergic stimuli. *Cardiovasc Res* 1993; **27**: 192-198
9 **Izumi Y**, Okatani H, Shiota M, Nakao T, Ise R, Kito G, Miura K, Iwao H. Effects of metoprolol on epinephrine-induced takotsubo-like left ventricular dysfunction in non-human primates. *Hypertens Res* 2009; **32**: 339-346
10 **Ueyama T**, Kasamatsu K, Hano T, Yamamoto K, Tsuruo Y, Nishio I. Emotional stress induces transient left ventricular hypocontraction in the rat via activation of cardiac adrenoceptors: a possible animal model of 'tako-tsubo' cardiomyopathy. *Circ J* 2002; **66**: 712-713
11 **Maroules CD**, Linz NA, Boswell GE. Recurrent Takotsubo cardiomyopathy. *J Cardiovasc Comput Tomogr* 2009; **3**: 187-189
12 **Desmet WJ**, Adriaenssens BF, Dens JA. Apical ballooning of the left ventricle: first series in white patients. *Heart* 2003; **89**: 1027-1031
13 **Elesber AA**, Prasad A, Lennon RJ, Wright RS, Lerman A, Rihal CS. Four-year recurrence rate and prognosis of the apical ballooning syndrome. *J Am Coll Cardiol* 2007; **50**: 448-452

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