Lesser Severity of Recurrent Takotsubo Cardiomyopathy While Taking Angiotensin II Receptor Blocker and Beta Blocker

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Abstract

Takotsubo cardiomyopathy (TC) is characterized by transient systolic and diastolic dysfunction, ventricular wall motion abnormalities and troponin elevation. The most common presenting symptoms are acute chest pain and dyspnea. The etiology is unknown but believed to be related to a surge in catecholamines as it is commonly associated with a preceding physical or emotional stress. Due to the lack of specific treatment, recurrence occurs in 2-12% of patients per year. We present a case of a patient with TC subsequently treated with an angiotensin II receptor blocker (ARB) and beta-adrenergic blocker (beta-blocker). A repeat TC episode 4 months later showed less severely abnormal cardiac enzymes, echocardiogram and overall hospital course. Because our patient experienced a classic episode of TC and a recurrent episode with milder symptoms and lower troponins, we hypothesize her medication regimen was a contributing factor to the milder manifestation of this cardiac syndrome.

Keywords: Takotsubo cardiomyopathy; Stress-induced cardiomyopathy; Angiotensin II receptor blocker; Beta-adrenergic blocker

Introduction

Takotsubo cardiomyopathy (TC) is a type of acute coronary syndrome (ACS) most commonly diagnosed in postmenopausal female patients that is characterized by transient systolic and diastolic dysfunction [1], wall motion abnormalities of the left ventricular apex and troponin elevations despite normal coronary arteries [2, 3]. There are four types based on cardiac catheterization findings including the apical type (> 80% of cases), midventricular type, basal type and focal type [4]. The most common presenting symptoms are acute chest pain and dyspnea while associated clinical findings include elevation in cardiac enzymes and electrocardiogram (ECG) changes [5, 6]. Other laboratory abnormalities include elevated brain natriuretic peptide (BNP) and BNP/peak troponin ratio when compared to ST-elevation myocardial infarction patients [7]. There are no randomized trials or expert consensus for medical management and treatment.

Although the etiology of TC is not clear, it is thought to be related to a catecholamine surge from a preceding physical or emotional stress. However, over 15-20% of TC episodes do not have clear triggers [8]. Catecholamine overload may also lead to chronic inflammatory states and oxidative injury as myocardial biopsies have demonstrated increased fibrosis and inflammatory cell infiltration in TC patients [9]. Estrogen may also play a role as meta-analysis has demonstrated about 80% of cases occur in women > 50 years [10] and women represent 90% of cases overall [8].

In 2012 over 6,000 cases of TC were reported in the United States with increasing annual incidence [11] representing 1-2% of all myocardial infarctions [12]. Roughly 2-12% of patients experience recurrent episodes [7, 8, 13]. Mortality is similar compared to patients with ACS from other causes [14, 15] and increased compared to control subject with reported chest pain [4]. Common complications include cardiogenic shock [16], arrhythmias [7] and death [5].

Case Report

A 59-year-old female with past medical history of hypertension and surgical menopause at age 35 secondary to bilateral oophorectomy presented to our clinic for follow-up evaluation of chest pain. Six months prior, she presented to the emergency department for new and severe epigastric pain which lasted for 12 h. ECG was significant for ST-depressions in the septal leads concerning for acute posterior myocardial infarction. Laboratory tests were significant for elevated troponin I (TnI) of 13 ng/mL and B-type natriuretic peptide (BNP) > 600 pg/mL. Transthoracic echocardiogram (TTE) demonstrated an estimated left ventricular ejection fraction of 35% with hypokinesis of the mid and distal segments and apical dyskinesis con-
quent increases in epinephrine and catecholamine levels also have a more protective property than females [18]. Mental stressors and subsequent increases in epinephrine and catecholamine levels also impact endothelial function and may result in catecholamine-related myocyte toxicity, coronary microvascular dysfunction and coronary microvascular spasm [19]. These theories are supported by the relationship between TC and estrogen withdrawal, as these patients lose the protective qualities of estrogen from catecholamine toxicity, calcium overload and oxidative stress. Fatty acid metabolism may also play a role as one retrospective study utilizing data from a national patient registry found patients with TC were less likely to be treated for hyperlipidemia at the time of presentation [15].

Several treatment strategies have been explored. As a result of the proposed mechanism involving catecholamine surge, beta-blockers have been explored as a potential treatment. To date, large prospective observational studies have found no improvement in recurrence rates or mortality when treating patients with normal doses of beta-blockers [8]. However, patients with left ventricular outflow obstruction [7] or interventricular pressure gradients may experience greater benefit [20]. Current understanding is that clinicians should choose combination alpha and beta-blockers such as carvedilol to minimize vasoconstriction due to alpha effects [7]. In addition, beta-blockers have been found to assist in associated complications of TC including cardiogenic shock, ventricular arrhythmias and death [16].

Overall, a reduced ejection fraction is noted in 86.5% of patients with TC [8] and therefore ACEI and ARBs may play a role in treatment [2]. A retrospective analysis in a large multi-center international registry including 1,118 patients with medications prescribed at hospital discharge found that patients taking ACEI and ARBs but not beta-blockers [8]. A systematic review also found that ACEI/ARB prescriptions are associated with decreased recurrence rates, but not beta-blocker prescriptions. However, both studies did not distinguish between types of beta-blockers (selective vs. non-selective) or combined beta-blocker and ACEI/ARB therapy [21]. Another retrospective review including 66 patients at two hospitals found that patients taking ACEI prior to admission did not develop critical complications including arrhythmia, cardiogenic shock and death [16]. Long-term clinical management to minimize recurrence rates and optimize overall prognosis is less clear. We substituted an ACEI for the ARB in this patient because large multi-center registries have found an associated decreased mortality and recurrence of TC [8, 16]. Information surrounding recurrent episodes of TC is limited. Some estimates have found recurrent episodes to occur between 3 weeks to 3.8 years and are associated with consistently poor left ventricular ejection fractions of ≤ 40% [14]. There are no clinical trials exploring medical management for effectively minimizing recurrent episodes. Therefore, assessing the efficacy of medical interventions including ACEI/ARBs and beta-blockers in relation to recurrent episode severity represents a potential point of interest for future exploration [13].

**Conclusions**

TC is a form of ACS where pathophysiology and optimal treatment is unknown. Recurrence is observed in 2-12% and...
there is little information surrounding medical interventions to optimize outcomes within this subpopulation. Because the condition is associated with increased morbidity and mortality, further exploration into management and treatment plans is warranted. We present a case where ARBs and beta-blockers dampened the symptoms of recurrent TC.

Grant Support

This work was supported by contracts from the National Heart, Lung and Blood Institutes nos. N01-HV-68161, N01-HV-68162, N01-HV-68163, N01-HV-68164, grants U0164829, U01 HL649141, U01 HL649241, K23HL105787, T32HL69751, R01 HL090957, IR03AG032631 from the National Institute on Aging, GCRC grant MO1-RR00425 from the National Center for Research Resources, the National Center for Advancing Translational Sciences Grant U1TR000124 and UL1TR000064, and grants from the Gustavus and Louise Pfeiffer Research Foundation, Danville, NJ, The Women’s Guild of Cedars-Sinai Medical Center, Los Angeles, CA, The Ladies Hospital Aid Society of Western Pennsylvania, Pittsburgh, PA, and QMED, Inc., Laurence Harbor, NJ, the Edythe L. Broad and the Constance Austin Women’s Heart Research Initiative, Cedars-Sinai Medical Center, Los Angeles, California, the Barbra Streisand Women’s Cardiovascular Research and Education Program, Cedars-Sinai Medical Center, Los Angeles, California, the Society for Women’s Health Research (SWHR), Washington, D.C., The Linda Joy Pollin Women’s Heart Health Program, and the Erika J. Glazer Women’s Heart Health Initiative, Cedars-Sinai Medical Center, Los Angeles, California.

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