Delayed Takotsubo Cardiomyopathy after Long-term Pacemaker Implantation

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Abstract

Takotsubo cardiomyopathy (TTC) is a transient and self-limiting left ventricular systolic dysfunction. Whilst the exact pathophysiology remains undetermined, emotional and physical stress are triggers for TTC, which has led researchers to speculate that neurohormones and the central autonomic nervous system play an important role in the development of TTC. Previous reports have recognized TTC as an acute complication of pacemaker deployment. We herein present two cases of TTC developing several years after permanent pacemaker implantation.

Keywords: Takotsubo cardiomyopathy, broken heart syndrome, pacemaker, post-menopause, catecholamine

Introduction

Takotsubo cardiomyopathy (TTC) was first discovered in 1990.[1] Manifestations of TTC and acute myocardial infarction can easily be confused. Both share characteristics of acute chest pain, dyspnea, pulmonary edema, elevated cardiac markers, ST-elevation or T-wave inversion on electrocardiography. Emotional or psychological triggers and newly implanted pacemaker have been identified as preceding the onset of TTC.[2-5] Occurrence of TTC has seldom been reported in patients after long-term pacemaker implantation. Here, we present two patients who developed TTC years after pacemaker implantation.

Case 1

A 69-year-old female presented to the emergency department (ED) with severe chest pain. She had a history of complete atrioventricular block and had received dual-chamber pacemaker implantation 3 years prior. Echocardiogram follow-up one year later showed normal left ventricular size, thickness and contractibility. Upon admission to the ED, one significant vital sign was her blood pressure of 169/94 mmHg. Troponin I was mildly elevated with a value of 0.31 ng/dl. The electrocardiogram showed pacemaker rhythm, no ST elevation. Her chest tightness was relieved by sublingual nitroglycerin. However, another attack of chest tightness followed two hours later, after which troponin I was elevated to 3.03 ng/dl. Coronary angiography was performed, revealing no significant coronary

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artery stenosis. Left ventriculography showed apical akinesis and ballooning (Figure 1), suggesting the diagnosis of TTC. Conservative treatment with beta-blocker was provided, after which the patient did not complain of any chest pain throughout the rest of her hospital stay. One month after discharge, she was seen in the outpatient clinic, and follow-up echocardiography revealed complete resolution of her left ventricular apical ballooning.

Case 2

A 92-year-old woman presented to the ED with a complaint of chest pain. She had a history of cardiomegaly and complete atrioventricular block, and had received dual-chamber pacemaker implantation in October, 2003. Upon admission to the ED, physical exam showed rapid breathing pattern at a rate of 22/minute. The electrocardiogram showed pacemaker rhythm, no ST elevation. Laboratory study revealed elevated troponin I level with a value of 48.67 ng/dl, creatinine kinase (CK) of 473 U/L and creatine kinase-myocardial band (CK-MB) of 153 U/L. Cardiac catheterization showed patent left coronary artery and 50% stenosis over the proximal right coronary artery (Figure 2). Left ventriculography showed apical ballooning with an ejection fraction of 45%, compatible with TTC. After transfer to the ordinary ward, conservative treatment was provided, and her chest tightness subsided thereafter.

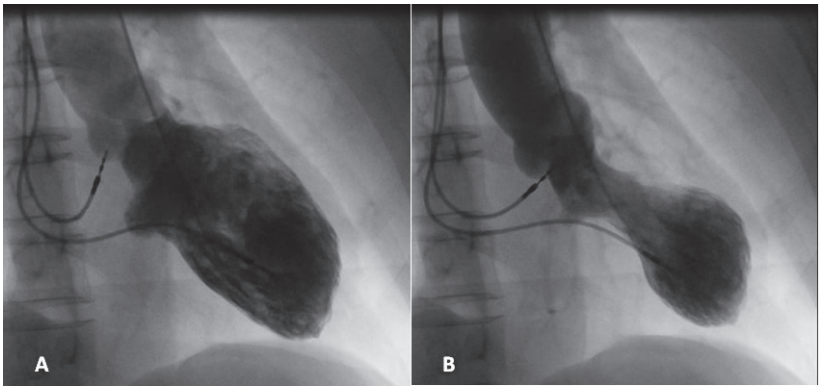

Figure 1. (A) End-diastolic phase; (B) End-systolic phase. Left ventriculogram during systole shows apical ballooning akinesis with basal segment hyperkinesis.

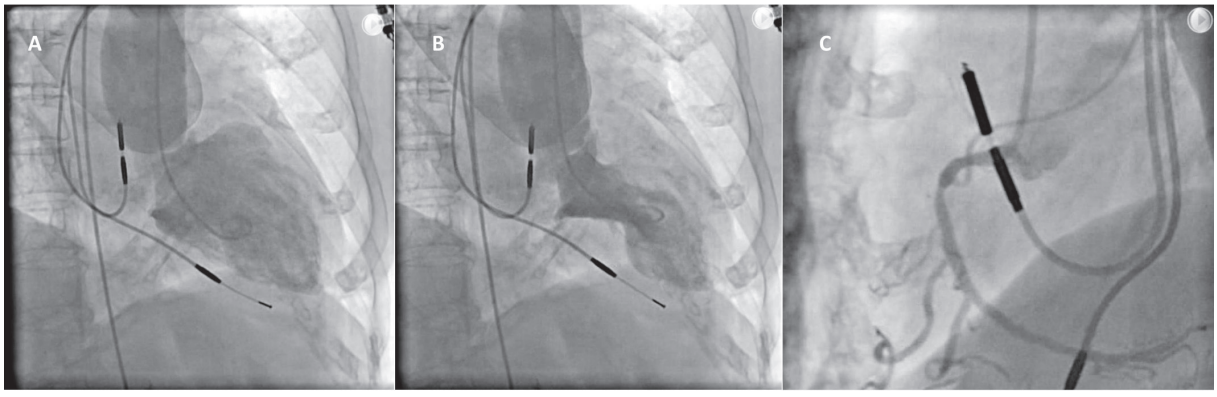

Figure 2. (A) End-diastolic phase; (B) End-systolic phase. (C) Coronary angiography shows patent right coronary artery with insignificant stenosis.

Discussion

TTC is a recently discovered transient left ventricular dysfunction. First described in Japan in 1990, it is also known as broken heart syndrome, apical ballooning syndrome or stress-induced cardiomyopathy. The term "takotsubo" is derived from the Japanese term for "octopus trap", since the left ventricular ballooning resembles the shape of an octopus trap. According to a systemic review, TTC accounts for approximately 2% of ST-segment elevation infarcts.[4]

The pathophysiology of TTC is poorly understood and several possible mechanisms have been postulated, including catecholamine-mediated toxicity, coronary artery spasm, autonomic imbalance and sex hormones.[5-7] Earlier literatures have reported takotsubo syndrome developing within hours after pacemaker implantation.[8] The mechanism hypothesized to be responsible for acute systolic dysfunction has included acute catecholamine release triggered by pacemaker implantation. Ventricular pacing has been shown to cause increased tissue norepinephrine level in animal models.[9] Previous study has also shown high plasma catecholamine levels in patients with pheochromocytoma can induce reversible cardiomyopathy.[10] Abraham et al. demonstrated that intravenous administration of catecholamines can cause stress cardiomyopathy, whereby the plasma catecholamine levels were markedly higher than in myocardial infarction.[5] Most patients with takotsubo cardiomyopathy who underwent myocardial biopsy have shown interstitial infiltrates of mononuclear lymphocytes, leukocytes, and macrophages; myocardial fibrosis; and contraction bands necrosis.[2,11] Interestingly, similar histological changes were found in catecholamine cardiotoxicity in both animals[12] and humans.[13] Catecholamine release can cause epicardial coronary spasm, microvascular coronary spasm and direct myocyte injury with contraction-band necrosis,[2] leading to myocardium damage and contractile abnormalities in multiple vascular territories.

To the best of our knowledge, this is the first report of TTC developing years after pacemaker implantation. Both patients are post-menopausal women who had received dual-chamber pacemaker implantation previously. Long term ventricular pacing has been shown to be associated with progressive myocardial dysfunction. Tse HF and Lau CP have reported long-term right ventricular apical pacing to be associated with myocardial perfusion defects, whereby the incidence increased with the duration of pacing. Their study revealed that 28 (65%) out of 43 patients with complete heart block, who were given dual-chamber rate-adaptive (DDDR) pacing had reduced local myocardium perfusion at the site of pacing as detected by Tl-201 scintigraphy, mainly over the apical region, further leading to impaired global left ventricular function. Of the 16 out of 28 patients with abnormal Tl-201 findings who underwent coronary angiography, only 3 (19%) had significant coronary artery disease. This study also found that patients with perfusion defects seemed to have had a longer duration of pacing than those without. It has been suggested that alteration of ventricular activation causes redistribution of mechanical load within the ventricular wall and may lead to reduction of the blood flow and myocardial wall thickness over the site of early activation.[14] Thus, we hypothesize that an abnormal ventricular activation sequence due to RV apical pacing may affect myocardial perfusion, causing functional ischemia and resulting in apical ventricular dysfunction, elevated cardiac enzymes, T wave inversion and ST elevation, as reflected in Takotsubo disease.

TTC is an acute cardiac disorder with a transient left ventricle wall motion abnormality. Although it has been noticed worldwide, the underlying pathophysiology and mechanism remain to be elucidated. We report two cases to alert physicians that pacemaker implantation may not only play a role in acute development of TTC, but can also be a predisposing factor for the development of TTC in the future.

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