 DOI: 10.18231/2348-7240.2017.0002

Takotsubo Cardiomyopathy: A reversible cardiomyopathy Camouflage of Acute coronary syndrome

NS Neki[1,*], Neeraj Joshi[2], Gurminder Singh Multani[3], Gagandeep Singh Shergill[4], Rubal Sharma[5]

[1]Professor, [2,3,4]Junior Resident, [5]Intern, Dept. of Internal Medicine, Govt. Medical College & Guru Nanak Dev Hospital, Amritsar, Punjab

***Corresponding Author:**
Email: drneki123@gmail.com

Abstract

Takotsubo cardiomyopathy (TCM) is an uncommon form of acute cardiomyopathy showing left ventricular apical ballooning. Its clinical characteristics resemble those of a myocardial infarct, while its imaging characteristics are critical on correctly characterizing and diagnosing the disease. It is a reversible cardiomyopathy, a rare variant that presents within a different patient profile and with its own hemodynamic considerations. Its recognition is important for prognostic, evaluation and treatment considerations.

Keywords: Takotsubo cardiomyopathy, Apical ballooning

Introduction

The term "takotsubo" is taken from the Japanese name for an octopus trap, whose shape is similar to the systolic apical ballooning appearance of the LV .In the most common and typical form of this disorder ,mid and apical segments of the LV are depressed and there is hyperkinesis of the basal walls.

First described in Japan in 1990 by Sato et al,[(1)] Takotsubo Cardiomyopathy (TCM) is an acute cardiac condition that involves left ventricular apical ballooning and mimics acute myocardial infarction (MI). It is also known as 'transient left ventricular (LV) apical ballooning syndrome,' 'takotsubo-like left ventricular dysfunction,' 'ampulla cardiomyopathy,' 'stress-induced cardiomyopathy,' and 'broken heart syndrome.'

TCM patients present with symptoms of chest pain, electrocardiograph (ECG) ST-segment elevation, and cardiac markers consistent with an acute coronary syndrome (ACS). However, angiography finds no significant coronary stenosis, and the LV apex is found to balloon, which usually resolves in week.

Epidemiology

Stress cardiomyopathy was first described in 1990 in Japan and has since been increasingly recognized around the world. Stress cardiomyopathy occurs in approximately 1 to 2 percent of patients presenting with troponin-positive suspected acute coronary syndrome (ACS) or suspected ST-elevation myocardial infarction.[(2)] A prevalence of 1.2 percent was reported from a registry of 3265 patients with troponin-positive ACS.[(3)]

Stress cardiomyopathy is much more common in women than men and occurs predominantly in older adults. In the International Takotsubo Registry (a consortium of 26 centers in Europe and the United States) of 1750 patients with stress cardiomyopathy, 89.9 percent were women and mean age was 66.4 years.[(4)]

History and pathogenesis

The pathogenesis of this disorder is not well understood. Animal models and ventricular biopsies suggest that this acute cardiomyopathy may result from

a. intense sympathetic stimulation with heterogeneity of myocardial autonomic innervations
b. diffuse myocardial spasm
c. direct catecholamine toxicity
d. genetic predisposition.

Although TCM was named in the early 1990s, the idea of a stress-induced physical disorder or death has been in the literature for decades. In 1942 Walter B. Cannon[(5)] wrote a remarkable article detailing numerous accounts of so-called "Voodoo death" reported by educated and independent observers. The cases of Voodoo death occurred among many different aboriginal tribes throughout the world. The cases involved people who were "hexed" or condemned to death by medicine men or Voodoo priests. In all cases the condemned person and all his/her family and associated believed there was no escaping the death that was sure to ensue. In most of these cases poison was ruled out or unlikely as the cause of death, and Cannon postulated that intense fear could so over-activate the sympathetic and sympatho-adrenal systems that death ensued.[(5)]

Cebelin and Hirsch[(6)] reported in 1980 the post-mortem analysis of myocardium from 15 victims who died from physical assault but whose autopsies revealed no internal injuries sufficient to cause death. Many of these patient's (73%) hearts showed myofibrillar degeneration and "contraction band" necrosis. Cebelin and Hirschpostulated that the cause of death could have been a catecholamine mediated "stress cardiomyopathy."

There have been reports of familial cases, raising the possibility of a genetic predisposition. Small studies of patients with stress cardiomyopathy have found genetic heterogeneity and suggest a possible polygenic basis.[7]

Clinical presentation

The most common presenting symptom is acute substernal chest pain, but some patients present with dyspnea or syncope. In the International Takotsubo Registry study, the most common symptoms were chest pain, dyspnea, and syncope (75.9, 46.9, and 7.7 percent, respectively).[4]

Some patients develop symptoms and signs of heart failure, tachyarrhythmias (including ventricular tachycardia and ventricular fibrillation), bradyarrhythmias, sudden cardiac arrest, or significant mitral regurgitation.[8] Approximately 10 percent of patients with stress cardiomyopathy develop symptoms and signs of cardiogenic shock (such as hypotension, abnormal mental status, cold extremities, oliguria, or respiratory distress).[4]

Left ventricular outflow tract obstruction, induced by left ventricular basal hyperkinesis produces a late peaking systolic murmur, similar to that heard in patients with hypertrophic cardiomyopathy and can contribute to the development of shock and cause severe mitral regurgitation.[9] Symptoms and signs of transient ischemic attack or stroke may develop (likely due to embolization from apical thrombus).

Investigation modalities

Electrocardiogram: Electrocardiographic abnormalities are common in patients with stress cardiomyopathy.ST segment elevation is frequent (e.g., in 43.7 percent of patients in the International Takotsubo Registry study.[4] ST segment elevation occurs most commonly in the anterior precordial leads and often is similar to that seen with an acute ST-elevation MI.ST depression is a less common finding (e.g., occurring in 7.7 percent[4] among patients with stress cardiomyopathy. Other findings include QT interval prolongation, T wave inversion, abnormal Q waves, and non-specific abnormalities.

Cardiac biomarkers: Serum cardiac troponin levels are elevated in most patients with stress cardiomyopathy (e.g., median initial troponin 7.7 times the upper limit of normal with interquartile range 2.2 to 24 in the International Takotsubo Registry study,[4] while creatine kinase levels are generally normal or mildly elevated (e.g., median creatine kinase 0.85 times the upper limit of normal with interquartile range of 0.52 to 1.48). The normal to mild elevation in creatine kinase contrasts with the substantial (approximately 10 percent) risk of severe hemodynamic compromise.

Natriuretic peptides: Levels of brain natriuretic peptide (BNP) or N-terminal pro-BNP are elevated in most patients with stress cardiomyopathy.[4,10] As an example, BNP levels were elevated in 82.9 percent of patients with stress cardiomyopathy in the International Takotsubo Registry study, with median level 6.12 times the upper limit of normal (interquartile range 2.12 to 15.70). BNP levels in a matched cohort of patients with stress cardiomyopathy exceeded those seen in matched cohort of patients with acute coronary syndrome (median 5.89 versus 2.91 times the upper limit of normal).

Identification of wall motion abnormalities: LV dysfunction is identified by echocardiography or left ventriculography, which reveals regional wall motion abnormalities (hypokinesis, akinesis, or dyskinesis) in one of the characteristic patterns.

Apical type: In the typical form of this disorder, there is systolic apical ballooning of the LV reflecting depressed mid and apical segments, and there is often hyperkinesis of the basal walls. This type was present in 81.7 percent of patients in the International Takotsubo Registry study.[4]

Less common (atypical) variants:

Mid-ventricular type: In the second most common type, ventricular hypokinesis is restricted to the mid-ventricle with relative sparing of the apex.[11] This type was present in 14.6 percent of patients in the International Takotsubo Registry study.

Basal type: Hypokinesis of the base with sparing of the mid-ventricle and apex (reverse or inverted Takotsubo). This type was present in 2.2 percent of patients in the International Takotsubo Registry study.

Focal type: A rare focal variant is characterized by dysfunction of an isolated segment (most commonly the anterolateral segment) of the LV.[4] This type was present in 1.5 percent of patients in the International Takotsubo Registry study.

Global type: Rarely, patients have global hypokinesis.[12]

Cardiovascular magnetic resonance: Cardiovascular magnetic resonance (CMR) imaging may be helpful in the diagnosis and evaluation of stress cardiomyopathy, particularly when the echocardiogram is technically suboptimal and/or there is coexistent coronary artery disease. CMR may assist in the differential diagnosis, delineate the full extent of ventricular abnormalities, and identify associated complications.

The following are key CMR features of stress cardiomyopathy:

Late gadolinium enhancement (LGE) on CMR imaging is generally absent in stress cardiomyopathy in contrast to MI in which intense (i.e., >5 standard deviations above the mean signal intensity of remote myocardium) subendocardial or transmural LGE is seen.[13] LGE is also useful in differentiating stress cardiomyopathy from myocarditis, which is characterized by patchy late gadolinium enhancement. However, when a low threshold for LGE is used (e.g., three standard deviations above the mean signal

intensity of remote myocardium), LGE is occasionally detected in stress cardiomyopathy.[12]

Diagnosis

The clinical presentation of stress cardiomyopathy is similar to that of acute coronary syndrome (with or without ST elevation). These conditions are differentiated by angiography, which demonstrates critical disease in the coronary artery supplying the dysfunctional ventricular territory in patients with acute coronary syndrome; such critical coronary artery disease or evidence of acute plaque rupture is lacking in patients with stress cardiomyopathy. While some patients with stress cardiomyopathy have concurrent significant coronary artery disease, the extent and location of such disease does not match the territory of the observed wall motion abnormalities.

The diagnosis of TCM remains controversial. The diagnostic criteria most widely accepted were published by the Mayo Clinic[14] in 2004. In 2008, a new criterion was added to them: a normal epicardial coronary artery. Mayo clinic diagnostic criteria:

1. Suspicion of AMI based on precordial pain and ST elevation observed on the acute-phase ECG.
2. Transient hypokinesia or akinesia of the middle and apical regions of the LV and functional hyperkinesia of the basal region, observed on ventriculography or echocardiography.
3. Normal coronary arteries confirmed by arteriography (luminal narrowing of less than 50% in all the coronary arteries) in the first 24 h after the onset of symptoms.
4. Absence of recent significant head injury, intracranial hemorrhage, suspicion of pheochromocytoma, myocarditis, or hypertrophic cardio myopathy.

Treatment

Patients should be treated as having ACS unless proved otherwise. Aspirin and heparin should be initiated, and a cardiologist be consulted. The diagnosis of TCM will be made if PCI is the initial treatment. Although thrombolysis will not benefit these patients, it should not be withheld if PCI is not available and the patient otherwise meets criteria.

Treatment of TCM during the acute phase is mainly symptomatic treatment. Hemodynamically stable patients are often treated with diuretics, angiotensin-converting enzyme (ACE) inhibitors and β-blockers. To reduce the risk of thromboembolism, patients with loss of motion of the LV apex should be treated with anticoagulant therapy until the contractility of the apex is improved unless there is a definite contraindication.

Intra-aortic balloon pump equipment is required for hemodynamically unstable patients in addition to cardiopulmonary circulatory support and continuous veno-venous hemofiltration.[15] There is controversy on the use of cardiac stimulants because of increased circulating catecholamines.[16] However, cardiac stimulants are used in 20%-40% of patients with TCM. Levosimendan may be beneficial because of its inotropic action and vasodilator effect.[17]

For patients with severe LV outflow tract obstruction with hemodynamic compromise, treatment with a β-blocker or α-adrenoceptor agonist such as phenylephrine and volume expansion should be considered. Calcium channel blockers can be used to decrease LV outflow tract pressure gradient. It is of utmost importance to avoid treatment with nitrites or inotropic drugs in these cases.[18] For patients with suspected vasospasm, the use of calcium channel blockers such as verapamil or diltiazem is suggested.

There is no consensus regarding long-term management of TCM, although it is reasonable to treat patients with β-blockers and ACE inhibitors during the ventricular recovery period. However, no data support the continuous use of these drugs for the prevention of TCM recurrence or improvement of survival rate. After LV function normalizes, physicians may consider discontinuation of these drugs.

Prognosis

Patients with TCM usually have a good prognosis, and almost perfect recovery is observed in 96% of the cases.[19] Mortality rate in hospital vary at one to two percent. TCM was formerly thought to follow a relatively benign course. However, Sharkey et al[20] described that approximately 5% of TCM patients experienced cardiac arrest. While their long-term survival rate is the same as that in healthy subjects, patients with TCM have a greater risk of death at the time of initial onset.[19]

Conclusion

Stress cardiomyopathy is a syndrome characterized by transient regional left ventricular dysfunction in the absence of significant coronary artery disease. Postulated pathogenic mechanisms include catecholamine excess, microvascular dysfunction, and multivessel coronary artery spasm. A lot of attention has been focused on TCM recently and this entity has been characterized as a transient LV dysfunction with rapid recovery generally induced by a stressful emotional or physical event.

The diagnosis of stress cardiomyopathy should be suspected in adults who present with a suspected acute coronary syndrome (with symptoms such as chest pain or dyspnea in combination with electrocardiographic changes and/or cardiac troponin elevation), particularly when the clinical manifestations and electrocardiographic abnormalities are out of proportion to the degree of elevation in cardiac biomarkers. A physical or emotional trigger is often but not always present.

Diagnostic criteria include presence of transient regional wall motion abnormalities (typically not in a single coronary distribution), absence of angiographic evidence of obstructive coronary disease or acute plaque rupture, presence of new electrocardiographic abnormalities or modest troponin elevation, and absence of pheochromocytoma or myocarditis.

In patients who present with a clinical picture consistent with acute coronary syndrome (ACS, such as ST elevation myocardial infarction, non-ST elevation myocardial infarction, or unstable angina), clinical suspicion of possible stress cardiomyopathy should not alter evaluation and management of these ACS conditions. The significant majority of these cases are due to occlusion of a coronary artery and revascularization therapy should not be delayed.

Wall motion abnormalities in patients with stress cardiomyopathy are typically detected by echocardiography or left ventriculography. The differential diagnosis of stress cardiomyopathy includes ACS, cocaine-related ACS, multivessel coronary artery spasm, myocarditis, and pheochromocytoma.

Financial support and sponsorship: Nil

Conflicts of interest: There are no conflicts of interest

References

1. Sato H, Tateishi H, Uchida T, et al. Takotsubo type cardiomyopathy due to multivessel spasm. In: Kodama K, Haze K, Hon M, editors. Clinical aspect of myocardial injury: from ischemia to heart failure. Kagaku Hyoronsha; Tokyo: 1990. pp. 56–64. [in Japanese]
2. Prasad A, Dangas G, Srinivasan M, Yu J, Mehran R, Stone G et al. Incidence and angiographic characteristics of patients with apical ballooning syndrome (takotsubo/stress cardiomyopathy) in the HORIZONS-AMI trial: an analysis from a multicenter, international study of ST-elevation myocardial infarction. Catheter Cardiovasc Interv 2014;83:343.
3. Kurowski V, Kaiser A, von Hof K, Killermann DP, Mayer B, Hartmann F, et al. Apical and midventricular transient left ventricular dysfunction syndrome (tako-tsubo cardiomyopathy): frequency, mechanisms, and prognosis. Chest 2007;132:809.
4. Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M, et al. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. N Engl J Med 2015;373:929.
5. Cannon WB. "Vodoo" death. American Anthropologist. 1942;44:169–181.
6. Cebelin MS, Hirsch CS. Human stress cardiomyopathy: myocardial lesions in victims of homicidal assaults without internal injuries. Hum Pathol. 1980;11:123–132.
7. Handy AD, Prasad A, Olson TM. Investigating genetic variation of adrenergic receptors in familial stress cardiomyopathy (apical ballooning syndrome). J Cardiol 2009;54:516.
8. Abe Y, Kondo M, Matsuoka R, Araki M, Dohyama K, Tanio H et al. Assessment of clinical features in transient left ventricular apical ballooning. J Am Coll Cardiol 2003;41:737.
9. Villareal RP, Achari A, Wilansky S, Wilson JM. Anteroapical stunning and left ventricular outflow tract obstruction. Mayo Clin Proc 2001;76:79.
10. Madhavan M, Borlaug BA, Lerman A, Stress hormone and circulating biomarker profile of apical ballooning syndrome (Takotsubo cardiomyopathy): insights into the clinical significance of B-type natriuretic peptide and troponin levels. Heart 2009;95:1436.
11. Eitel I, von Knobelsdorff-Brenkenhoff F, Bernhardt P, Carbone I, Muellerleile K, Aldrovandi A, et al. Clinical characteristics and cardiovascular magnetic resonance findings in stress (takotsubo) cardiomyopathy. JAMA 2011;306:277.
12. Win CM, Pathak A, Guglin M. Not takotsubo: a different form of stress-induced cardiomyopathy--a case series. Congest Heart Fail 2011;17:38.
13. Eitel I, Behrendt F, Schindler K, Kivelitz D, Gutberlet M, Schuler G, et al. Differential diagnosis of suspected apical ballooning syndrome using contrast-enhanced magnetic resonance imaging. Eur Heart J 2008;29:2651.
14. Bybee KA, Kara T, Prasad A, Lerman A, Barsness GW, Wright RS, et al. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. Ann Intern Med. 2004;141:858–865.
15. Patel HM, Kantharia BK, Morris DL, Yazdanfar S. Takotsubo syndrome in African-American women with atypical presentations: a single-center experience. Clin Cardiol. 2007;30:14–18.
16. Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. Circulation. 2005;111:472–479.
17. Padayachee L. Levosimendan: the inotrope of choice in cardiogenic shock secondary to takotsubo cardiomyopathy? Heart Lung Circ. 2007;16 Suppl 3:S65–S70.
18. Yoshioka T, Hashimoto A, Tsuchihashi K, Nagao K, Kyuma M, Ooiwa H, et al. Clinical implications of midventricular obstruction and intravenous propranolol use in transient left ventricular apical ballooning (Tako-tsubo cardiomyopathy) Am Heart J. 2008;155:526.e1–526.e7.
19. 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.
20. Sharkey SW, Windenburg DC, Lesser JR, Maron MS, Hauser RG, Lesser JN, et al. Natural history and expansive clinical profile of stress (tako-tsubo) cardiomyopathy. J Am Coll Cardiol. 2010;55:333–341.