Broken Heart Syndrome

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Abstract

Takotsubo Cardiomyopathy (TC) is also known as Stress Induced Cardiomyopathy or Broken Heart Syndrome. Typically there is transient systolic dysfunction of the apical or the mid segments of the left ventricle that occurs in the presence of acute emotional stress. Some atypical variants have been described. Hyperadrenergic state associated with emotional stress is cited as the probable etiology. It mimics Acute Myocardial Infarction with concomitant rise in cardiac biomarkers, ECG, 2D-Echocardiography abnormalities comprising of left ventricular dysfunction with regional wall motion abnormality, no significant Coronary Artery Disease on angiography.

It is a variant of dilated cardiomyopathy. Medical management of TC is similar to dilated cardiomyopathy. This syndrome has characteristic reversible left ventricular systolic dysfunction. Our article aims to increase the awareness of this syndrome amongst practitioners for its early recognition and correct management. Also there is a marked rise in number of studies regarding Takotsubo cardiomyopathy after 2008.

Precipitating Factors

Death of loved one, receiving bad news or any extreme emotional swing, car accident, unexpected financial loss, intense fear, acute exacerbation of bronchial asthma, domestic violence, acute intracranial events, intracranial bleeding (SAH, ICH), head trauma, ischemic stroke, acute medical illness including sepsis, surgical procedures, overproduction of endogenous catecholamines (pheochromocytoma), administration of exogenous catecholaminergic agents (inhaled β-agonist, methylxanthines, epinephrine/amphetamines, cocaine), Drugs like Duloxetine, Venlafaxine, Levothyroxine are some of the precipitating factors.

Clinical Presentation

A typical presentation of Takotsubo cardiomyopathy is sudden onset chest pain, shortness of breath, features of congestive heart failure with ECG changes mimicking acute anterior wall STEMI. Other symptoms include palpitations, giddiness, cough etc.

Only 20% of TC are known to present with heart failure. Not
much work done with regard to haemodynamic instability in patients with this type of cardiomyopathy. Park et al reported an incidence of 28% of Takotsubo-type LV dysfunction in patients admitted to the intensive care unit for non-cardiac physical illness.

**Etiopathogenesis**

The etiology of TC is not fully understood. It is studied that there are multiple factors like some amount of vasospasm, failure of microvasculature and abnormal response to catecholamines released in response to stress. Studies over past 20 years have shown that older women are more vulnerable because of reduced levels of estrogen after menopause (90%). The average ages at onset are between 58 to 75 years. Only 3% cases are seen under age 50. Because of these factors, the path to TC is not fully understood, but research has shown that it is a response to a stressful event, such as physical or emotional stress.

Microvascular Dysfunction: This is one of the most acceptable theories behind broken heart. It is believed that the defect occurring in the coronaries is at such a small level which can not be picked up by coronary angiography. It can be a microvascular vasospasm or multiple simultaneous spasms of coronary arteries which cause enough loss of blood flow to cause transient stunning of the myocardium. But further research showed that the suspected microvasculature and the affected myocardial area was not correlating each other. Another hypothesis is that of microvascular ischemia in the absence of obstructive epicardial CAD. Multiple reports have documented abnormal myocardial perfusion in the LV apical and midventricular segments that correspond with the regional distribution of the LV wall motion abnormality. But, cardiac magnetic resonance imaging could not document myocardial necrosis in the presence of mild elevation of Troponin levels in Takotsubo cardiomyopathy. 17

Wraparound LAD: This anatomical variant of coronary artery which supplies the major portion of left ventricle was initially considered as one of the reasons behind Takotsubo Cardiomyopathy. But further research showed no significant correlation between normal coronaries and wraparound LAD. According to Hoyt J et al, 97 patients with LV apical ballooning were studied retrospectively for coronary anatomy and presence of coronary artery disease (CAD) by coronary angiography and compared to a matched control group with anterior ST-elevation MI. Patients with transient apical ballooning failed to have higher frequency of wraparound LAD. This theory also fails to explain the variants of TC where sparing of apex can also be seen.

Catecholamine mediated direct myocardial injury: In one study, catecholamine levels and their metabolites were found to be 2- to 3-fold higher in TC patients compared with those presenting with acute MI with similar clinical findings. Contraction band necrosis and mononuclear inflammatory infiltrates are seen in some endomyocardial biopsies of TC which again co-relates with catecholamine-mediated cardiotoxicity. These findings probably reflect consequences of high intracellular concentrations of Ca2+, and it has been proposed that Ca2+ overload in myocardial cells produces the ventricular dysfunction in catecholamine cardiotoxicity. High local concentrations of norepinephrine demonstrated in basal LV segments might evoke hyperkinesis, which increases mechanical wall stress at the apex and its ballooning. This theory also explains the rise in end-diastolic pressure and BNP levels. So, this heart condition seem to be the result of combination of myocardial necrosis and decreased β-adrenoceptor responsiveness with high local catecholamine concentrations that cause both the abnormalities. Additionally, reversible intracellular accumulation of glycogen and extracellular accumulation of matrix proteins are observed, which goes in favor of metabolic myocardial injury. Kloner et al demonstrated that a pathological changes in myocardium are not same as stunned myocardium of ischemia/infarction.

Approximately one third of patients are seen without preceding stressful event. In Europe, it is found more frequently in winter season.

**Diagnosis**

Cardiac Biomarkers: CPK-MB and Troponin-T are raised in mild to moderate levels on admission. Not all the biomarkers are raised in all cases. Pattern of rise in BNP level in this cardiomyopathy is observed quite similar to AMI.

ECG: In most of the cases, ECG shows ST segment elevation in anterior leads mimicking anterior wall AMI.

2D Echocardiography: shows the pathognomonic wall motion abnormalities, in which the base of the left ventricle is contracting normally or is hyperkinetic while rest of the left ventricle is akinetic or dyskinetic (Figures 2 and 3).

Pheochromocytoma is an important differential diagnosis from isolated TC which shows the same type of change in myocardium on echocardiography. But marked rise in peripheral
serum catecholamine levels in pheochromocytoma is the differentiating factor.

Focal myocarditis which may show the regional wall motion abnormality on echocardiography, but ECG shows diffuse ST segment elevation which is not confined to particular coronary territory. Also there may be long history of fever. The studies based on non-invasive versus invasive techniques for diagnosis of myocarditis show the endomyocardial biopsy is the only standard method.

A set of diagnostic criteria were proposed in 2004 for diagnosis of Takotsubo Cardiomyopathy by researchers at the Mayo Clinic, which have been modified recently:

1. Transient hypokinesis, akinesis, or dyskinesis in the left ventricular mid segments with or without apical involvement; regional wall motion abnormalities that extend beyond a single epicardial vascular distribution; and frequently, but not always, a stressful trigger.
2. Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture (Figure 4).
3. New ECG abnormalities (ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin.
4. Absence of pheochromocytoma and/or myocarditis.

Cardiac MRI: It is considered as the best non-invasive technique to pick up the TC (Figure 5). There will be an absence of late enhancement on delayed contrast sequences, which differentiates Takotsubo Cardiomyopathy from anterior STEMI. TC typically does not present late enhancement on CMRI, which demonstrates the absence of myocardial ischaemia. Large number of small pericardial effusions are picked up on CMRI which may be missed on echocardiography.2

**Variants of Takotsubo**

Inverted Takotsubo: It has been shown that left ventricular dysfunction in this syndrome includes not only the classic apical ballooning, but also in different angiographic coronary territories. Suppression of basal contraction and apical sparing has also seen in TC. It is labeled as “Inverted Takotsubo”.7 Kurowski et al found that 40% of patients with transient ventricular dysfunction had this atypical pattern.9

Isolated RV Takotsubo: Though isolated LV apical ballooning is common, there is only one case report is documented regarding isolated right ventricular apical ballooning of non-ischaemic pathology.1

Biventricular Takotsubo: Biventricular TC has been documented in many cases in recent years. When they were studied further, it was found that approximately 25% - 40% patients having additional right ventricular involvement.13,14 Biventricular involvement showed increased haemodynamic instability and increased risk of complications. Elseber and Prasad et al studied 6 out of 8 patients with RV involvement in Takotsubo Cardiomyopathy.5 (63%) required mechanical ventilation, 3(13%) required Intra-aortic balloon pump and one patient received CPR.

**Treatment and Prognosis**

Mainstay of treatment for systolic dysfunction is ACE inhibitors, Beta-blockers and Diuretics. These agents help in reducing the workload of heart while LV systolic...
function improves. Inotropic agents are not recommended because of high catecholamines state. Beta blockers play an important role in long term prevention of recurrence. Relaxation therapy and stress management also help in its prevention.

Despite the grave clinical presentation in some of the patients, most of them survive the initial acute event, with a very low rate of in-hospital mortality or complications. The long term prognosis is excellent. It typically improves within the first few days and normalizes within first few months.

**Conclusion (Questions Go Unanswered)**

The exact etiopathology of Takotsubo Cardiomyopathy is still not clear. All studies are retrospective in population who suffered. There is no tool available for prediction of the disease. Hence, the question arises, ‘who will suffer from Broken Heart?’

The data available shows that stress cardiomyopathy is followed by acute events. There is no study available regarding population who are exposed to chronic stress. Will they suffer from Takotsubo Cardiomyopathy?

Very limited studies are available regarding its complications. Members of Angina Pectoris-Myocardial Infarction (AP-MI) registered a retrospective study in Japan under the heading TLVABS (transient LV apical ballooning syndrome) in which 88 patients were studied, out of which 15% had cardiogenic shock and 8% required aggressive management and AIBP. But nobody described a right ventricular involvement in it. As RV involvement and haemodynamic instability have come to attention, this study has become less useful. Till now the incidence and clinical significance of LV thrombus in Takotsubo has not been well established. Sharkey et al. found one in 22 patients study. Very few case reports are available regarding the rare complications of Takotsubo cardiomyopathy e.g. acute mitral regurgitation, refractory hypotension and recurrent TC. There is no definite period of time mentioned by any study for recovery of LV systolic dysfunction.

The limitations for the studies can only be explained because of its reversibility and unique nature of cardiomyopathy. But many more studies are required in regard with Takotsubo Cardiomyopathy for early detection; which will aid in accurate management and reduce the hospital stay.

**References**