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Editorial

Inverted Takotsubo cardiomyopathy: A rare entity often missed!

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Takotsubo cardiomyopathy (TTC) was first described in the Japanese population by Sato et al.[1] The name 'Tako Tsubo' came from the typical appearance of the left ventricle on ventriculogram resembling a fishing pot to trap octopus, which has a balloon-like bottom and a narrow neck. The condition is characterized by acute, reversible LV dysfunction in the absence of significant angiographic coronary stenosis, usually provoked by an episode of emotional or physical stress. It presents as acute coronary syndrome with chest pain, T-wave, and ST-segment changes on ECG, elevation of cardiac biomarkers, and left ventricular regional wall motion abnormalities. Sometimes, heart failure or hemodynamic instability may be present. There is a marked predilection for females.

Since the original description of this syndrome showing apical ballooning due to apical (with or without mid-ventricular segment) akinesis or hypokinesis with preserved or hypercontractile basal segments (the classic or apical type), three other patterns of LV involvement have been described. These are the inverted (reverse) type, the mid-ventricular type, and the localized type. In a study by Ramaraj et al.,[2] the relative frequencies of classic, inverted, and mid-cavitary types of TTC were found to be 67%, 23%, and 10%, respectively. In the inverted or reverse variant, basal and mid-ventricular segments are hypokinetic or akinetic with preserved contractility or hyperkinesis of apical segments. Although the clinical presentation, outcome, and management are mostly similar between the groups, patients with inverted TTC tend to be younger than those with other types of TTC. A triggering stress is usually present in patients with the classic variant, but almost always present in patients with the inverted variant. Moreover, there are other subtle differences between the inverted type and the other variants. Patients with the inverted variant of TTC tend to have lower prevalence of dyspnea, pulmonary edema, cardiogenic shock, T-wave inversion, and acute reversible mitral regurgitation.[3] Interestingly, it is observed that patients with inverted TTC have significantly higher levels of creatine kinase MB fraction (CK-MB) and troponins. The possible explanation is that the inverted TTC variant has greater extent of affected myocardium compared to the classic variant, where a smaller apical segment is involved, and the rise in cardiac markers, such as CK-MB and troponin, reflect the extent of the affected myocardium. Despite a greater mass of affected myocardium, patients with inverted TTC have a lower rise in N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and lower prevalence of heart failure. This may be explained by the anatomical location of the dysfunctional segment. Altered spatial relationship between mitral leaflets and subvalvular apparatus due to apical ballooning may cause acute mitral regurgitation, which may exacerbate heart failure in patients with classical variant of TTC. Systolic anterior motion (SAM) and dynamic left ventricular outflow obstruction occur in some patients with apical or mid-TTC. Increased wall stress due to dynamic outflow tract obstruction may also contribute to the higher levels of NT-proBNP in patients with classic or mid-TTC.[4]

The ventricular dysfunction in TTC usually resolves within weeks with a generally favorable prognosis. Ventricular arrhythmia may occur, particularly torsades de pointes associated with takotsubo-related QT prolongation. Rare complications are irreversible cardiogenic shock, LV rupture, embolization of LV thrombi, and complete heart block. Long-term prognosis is good. Recurrence is uncommon (2–5%) and may occur in a LV segment different from the one exhibiting the initial manifestation.

Activation of sympathetic and adrenomedullary hormonal systems due to emotional or physical stress resulting in 'adrenergic storm' has been suggested as the central mechanism for the occurrence of TTC. Plasma levels of catecholamines are found to be higher in TTC than that observed in patients with Killip class III myocardial infarction.[5] It is, however, not clear how these alterations result in myocardial stunning. One possible mechanism is stress-induced

increased sympathetic tone causing epicardial coronary artery spasm in patients without coronary artery disease. In an angiographic study of patients with TTC, 70% had coronary spasm in response to provocative maneuvers.[6] An alternative possibility is sympathetically mediated microcirculatory dysfunction (microvascular spasm) causing abnormal coronary flow in the absence of obstructive disease. A third possible mechanism of catecholamine-mediated myocardial stunning is direct myocyte injury. Cyclic AMP-mediated calcium overload, interference with cellular sodium and calcium transporters by oxygen-derived free radicals are some of the plausible mechanisms of myocyte injury.[7]

The inverted variant of TTC has been reported in situations such as following anti-depressant overdose, subarachnoid bleed, road traffic accident, anaphylactic shock,[8] and also in association with pheochromocytoma. In this issue, Sengupta SP et al. reported two cases of inverted TTC following attempted suicidal hanging. The type of TTC that occurs in suicidal hanging is not restricted to the inverted variant. The classic variant has also been previously described following attempted suicidal hanging.[9]

The observed preponderance of women with TTC suggests a biologic susceptibility to stress-related myocardial dysfunction, although the basis of this predisposition is unknown. The reason for the distribution of myocardial dysfunction in TTC is not yet well understood. Distribution, density, and sensibility of adrenergic receptors may play an important role. Areas with a higher density of adrenergic receptors may determine the areas of hypokinesis. Adrenoreceptor density is highest in the apex compared with the base in postmenopausal women, which explains the occurrence of the apical variant in older women.[10] Ramaraj et al. hypothesized that the presentation of inverted TTC at a young age might be due to the abundance of adrenoreceptors at the base compared to the apex at a younger age.[2] Possibly, the differences in the location or amount of adrenoreceptor with aging may affect different ballooning patterns of TTC. Both the patients in the case report were young. This may be the reason why they developed the inverted variant of TTC following the intense catecholamine surge that accompanies hanging.

The diagnosis of TTC should be suspected when the history taking reveals that cardiac symptoms are precipitated by intense emotional stress and no critical coronary disease is present. The left ventricular dysfunction is not limited to any single coronary artery territory and improves rapidly on serial echocardiography.

TTC accounts for about 1.2% of patients with troponin-positive acute coronary syndrome.[11] It has better short- and long-term prognosis than acute coronary syndrome. It is important for the clinician to be aware of the condition. Misdiagnosing TTC for myocardial infarction could have adverse consequences for the young patient, affecting his lifestyle, life insurance policy, and livelihood.

Conflicts of interest

The author has none to declare.

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