Takotsubo Cardiomyopathy presenting as ST-elevation myocardial infarction: wide triggering spectrum and specific echocardiographical pattern in a consecutive case series report

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Abstract

We report a series of six consecutive cases of Takotsubo Cardiomyopathy (TCM) presenting as ST-elevation acute myocardial infarction and consequently addressed to the emergency coronary angiography, inside a time-frame of one year (2015). This series underlines the wide possible triggering spectrum and clinical severity of TCM and recognizes echocardiography as an essential imaging technique in the diagnosis due to its widespread availability and feasibility in the acute care setting.

Keywords: Takotsubo cardiomyopathy, wall motion abnormalities, echocardiography

Introduction

An association between emotional or physical stressful triggers and cardiovascular adverse events has been described for many years.

Transient left ventricular (LV) apical ballooning is a cardiac syndrome characterized by LV dysfunction accompanied by echocardiographic, electrocardiographic, and biologic features mimicking an acute myocardial infarction [1], usually preceded by emotional or physical stressors. It was first described in Japan and it was named Takotsubo cardiomyopathy (TCM) because of the resemblance between the left ventricular appearance in systole and the shape of a pot with a round bottom and a narrow neck (Takotsubo = Japanese octopus trap) [2,3]. This syndrome is characterized by acute LV dysfunction with regional wall motion abnormalities (WMA) extended beyond a single

coronary vascular bed, absence of significant obstructive coronary obstructive disease, and rapid improvement of LV function within a few days or weeks [4].

TCM has been recognized as an important consideration in the differential diagnosis of acute coronary syndromes [5]. The difference with anterior myocardial infarction accounts for the extent of LV dysfunction, far beyond left anterior descending artery (LAD) territory [4]. The prevalence of this pathology is estimated to be 2% of patients undergoing coronary angiography for acute coronary syndromes [6,7].

In the specific settings of acute interventional management of ST-elevation myocardial infarction (STEMI), TCM recognition represents a rare but important finding since these patients have the potential to completely recover if they are properly supported to overcome the acute phase [8]. Therefore, we report the consecutive cases of TCM encountered during one year of STEMI interventional management in a high-experienced center.

During the year 2015 we performed emergency coronarography in 258 patients with STEMI within the first 12 hours of onset and we diagnosed TCM in 6 patients (2.3%). We used a modified version of Mayo Clinic Criteria for Diagnosis of TCM [9], including also the patients who developed TCM in the setting of neurological disorders [10].

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Case 1

A 57 year old male patient, with epilepsy, was admitted with an anterior STEMI complicated with cardiogenic shock. Chest pain was preceded by two seizures. Initial ECG showed minimal ST elevation in the precordial leads. Echocardiographic findings consisted of circumferential mid-ventricular akinesia and apical dyskinesia, a Wall Motion Abnormality Scoring Index (WMSI) of 2.35 and a severely depressed LV ejection fraction (EF) of 20% (fig 1a,b). Troponin levels were only slightly elevated, disproportionate to the large WMA. Coronarography revealed normal coronary arteries. Intra-aortic balloon pumping (IABP) was required during the first 3 days. In the 15th day, echo control revealed significantly improved EF (45%) with apical hypokinesia. He was discharged the 16th day. One month later his EF was normal without wall motion abnormalities (fig 1c,d). We interpreted the case as TCM induced by seizures.

Case 2

A 73 year old female patient presented to the emergency room with rest chest pain associated with dyspnea. The patient had a severe psychological impact several days before hospitalization. On admission, she had stable blood pressure levels but signs of acute left ventricular failure were present. Initial evaluation revealed, ST-elevation in DI, aVL on ECG, slightly increased Troponin

levels, akinesia in the apical segments with WMSI of 1.85 and EF of 35%. Coronary arteries were normal. A follow-up echocardiogram performed in the 5th day of hospitalization, revealed marked improvement in WMA with only mild apical hypokinesia and normal EF. This case was regarded as a TCM with a psycho-emotional trigger.

Case 3

A 80 year old female presented in the emergency ward after a syncopal episode. She had a recent history of interstitial pneumonia. Initial ECG showed ST-elevation in the DI and aVL leads and troponin levels were elevated. Echocardiography revealed a LV with severe hypokinesia in the apical segments (WMSI=1.25) with preserved EF. Emergency coronary angiography revealed normal coronary arteries. During the second day of hospitalization she developed three episodes of "torsade de pointes" on the background of a QT-segment elongation, requiring electric conversion. ECG and echocardiogram aspects entirely normalized until the 10th day of hospitalization. The patient met the criteria for TCM though the triggering factor was not entirely clear (possible stress induced by physical illness: pneumonia).

Case 4

A 55 year old female, developed a clinical picture of STEMI complicated with cardiogenic shock in the sec-

Fig 1. Echocardiography in a patient with TCM induced by seizures: a) Apical four chambers echocardiograms recorded during acute phase in diastole and, b) in systole, revealing apical ballooning; c) Echocardiograms recorded after one month, in diastole and, d) in systole, showing complete recovery. Arrowheads highlight wall motion direction.

ond day after a neurosurgical intervention for a cerebral aneurysm, with consecutive subarachnoid hemorrhage (SAH). Blood pressures of 80 mmHg were maintained under inotrop infusion. Echocardiography revealed large akinesia involving all mid ventricular segments, apical

diskinesia and EF of 20 %. Moreover, WMA involved also the right ventricle with a severely decreased tricuspid annular plane systolic excursion (TAPSE). Coronarography showed normal coronary arteries. After 24 hours she died due to hemodynamic instability. The suspicion

Fig 2. TCM triggered by emotional stress induced by severe epistaxis (acute phase): a) Color Tissue-Doppler imaging recordings in diastole and, b) in systole; 2D echocardiograms are depicted in panels c) during diastole and d) systole. Arrowheads underlie wall motion direction

Fig 3. Longitudinal strain (LS) imaging in a patient with TCM triggered by epistaxis. Acute phase: a) End-diastolic LS in A4Ch view; b) Peak instantaneous LS during systole in A4Ch view, showing basal left ventricular systolic shortening (red = negative LS) and apical systolic lengthening (blue = positive LS); c) Bull's Eye plotting of the peak systolic strain from PLAX, A4Ch and A2Ch views. At 6-months follow-up showing complete recovery: d) End-diastolic LS in A4Ch view; e) Peak instantaneous LS in A4Ch view, revealing homogeneous shortening (red) consecutive to complete recovery of myocardial kinetics; f) Bull's Eye plotting of peak systolic strain from PLAX, A4Ch and A2Ch views. PLAX = parasternal long axis view, A4Ch= Apical four chambers view, A2Ch=Apical two Chambers view.

of TCM induced by SAH (by Mayo Clinic criteria) [10] was raised, though the criteria of LV function improvement was not met. According to the Japanese Guidelines for diagnosis of TCM proposed in 2007, this patient would have been diagnosed as “cerebrovascular disease with Takotsubo-like myocardial dysfunction” [11,12].

Case 5

An 80 year old female was admitted with anterior STEMI suspicion. Clinical picture of STEMI developed after an episode of epistaxis which triggered a great emotional impact. Ultrasound examination revealed a LV apical ballooning pattern both on color Tissue-Doppler imaging (fig 2a,b) and 2D echo-mode (fig 2c,d), with EF of 40%.

Two-dimensional longitudinal strain was performed (fig 3a,b,c). A severely decreased global longitudinal strain was measured during the acute phase of TCM. Longitudinal strain detected altered LV mechanics also at the base of the heart. No coronary artery lesions were found. Echocardiographic control a week later revealed LV wall motion normalization with a normal global longitudinal strain (fig 3d,e,f).

Case 6

A 74 year old female patient presented with severe chest pain and dyspnea triggered by a nightmare with severe emotional discomfort. ECG revealed ST-segment elevation in V1-V2 and deep large T waves in V3-V6 leads. An emergency coronary angiography was performed, with normal coronary arteries. Echocardiography revealed apical hypokinesia with a WMSI of 1.25 and preserved global LV ejection fraction. Control echocardiography performed in the 3rd day of hospitalization showed complete LV recovery. The case was interpreted as emotionally induced TCM.

Discussions

TCM is a rather rare pathology though its prevalence may be underestimated either by under-recognition of the less severe TCM cases or by non-inclusion of the patients who die acutely [13]. Moreover, the criteria we used, addressed only to cases of STEMI with normal coronary artery disease. However, latest recent papers also recognize a “TCM component” in cases of myocardial infarction with significant coronary lesions [13]. Therefore, considering the aforementioned data, in daily practice, TCM prevalence might be much greater than currently presented in the literature (1.7-2.2%) [1] or observed in our center (2.3%).

Prognosis of TCM is generally favorable, but a small subset has potentially life-threatening complications [12]. In a very large study, including all TCM patients from US hospitals during 2008-2009, in-hospital mortality was 4.2% whereas cardiogenic shock was present in 4.7% of cases [14].

Regarding the triggering factors, a preceding acute medical condition induced TCM in 43% of cases and emotional factors in the remaining cases [2]. Our case series illustrates the very heterogeneous nature of the clinical presentations, triggering factors and outcomes severity in TCM. The two patients with TCM induced by neurological causes (epilepsy and SAH) had a very severe course: both patients had extensive WMA, both developed cardiogenic shock and the patient with SAH died during the first 48 hours of onset. The severe outcomes of neurogenic TCM have been already demonstrated in previous papers. In the study of Stollberger et al [15], patients with TCM induced by seizures had a more serious course when compared to other TCM patients. Seizure-associated TCM manifests frequently as sudden hemodynamic deterioration which could result in death. Catecholamine release due to seizures might be more excessive and last longer, compared with other emotional or physical triggers of TCM [15]. Additionally, patients with SAH and TCM are known to have a very severe outcome, with a mortality of 36.6% in series of Kent et al [16].

Echocardiography is the essential imaging technique in the diagnosis of TCM and in its differentiation from acute myocardial infarction and include both classical techniques (as WMA evaluation by 2D-echo mode) and advanced techniques (as myocardial deformation imaging - longitudinal and radial strain). In the TCM patients, WMA extended beyond one coronary bed (e.g. LAD territory). Due to technical reasons we performed advanced myocardial deformation techniques only in a single patient. Due to its higher sensitivity in detecting subtle abnormalities when compared to the more traditional parameters like EF or WMSI, longitudinal strain detected altered LV mechanics also at the base of the heart. There are studies that showed that myocardial impairment in TCM extends beyond the segments with classical WMA [4] and that longitudinal strain in some of the posterior, inferior, and lateral segments is significantly lower in TCM compared to STEMI [17]. Moreover, when compared to healthy individuals, in TCM patients, longitudinal strain is diminished in almost all segments and not only in the anterior ones [17].

It is known that right ventricular dysfunction is a marker of the severity of TCM and is associated with lower LV EF [18]. The most severe patient (TCM in-

duced by SAH) of our case series, also had right ventricular WMA.

Some interactions between TCM and medication used in STEMI patients are worth mentioning. There are reports on the TCM development in patients receiving drugs such as epinephrine, even after exposure to doses routinely used in clinical practice [19]. We may speculate that catecholamine treatment in patients with STEMI and cardiogenic shock could induce in some patients a superimposed TCM, with very deleterious effects. Conversely, catecholamine-type inotropes administration in TCM complicated by cardiogenic shock have the potential of further aggravating the clinical course. Therefore, in these patients mechanical assistance or non-catecholamine inotropes such as levosimendan should be favored [8].

The mechanisms underlying TCM are not entirely known but a catecholamine surge was suggested [5]. High levels of circulating epinephrine may trigger in ventricular cardiomyocyte a switch in intracellular signaling from Gs to Gi protein, via beta 2 adrenoceptor (AR) [20]. At normal values, epinephrine binds to beta 2 AR resulting in positive inotropic effects through a Gq protein signaling. At higher concentrations, epinephrine stimulates a negative inotropic effect on myocytes by Gi protein [20]. It was demonstrated that elevated catecholamine levels decrease the viability of myocytes through cyclic AMP-mediated calcium overload [12].

Conclusion

This case series highlights the wide spectrum of possible triggering factors and clinical severities of TCM that are encountered by the interventional cardiologist in the real-life STEMI management. It also underlines the echocardiography as an essential imaging technique in the TCM diagnosis due to its widespread availability and feasibility in the acute care setting. Furthermore, some of the cases presented are an illustration of the fact that rapid diagnosis of TCM complicated by cardiogenic shock sets in motion specific treatment strategies (preferential use of intra-aortic balloon pumping over inotropic drugs).

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