Post-Operative Takotsubo Cardiomyopathy: Case Report and Review of Literature: How Much we Know

Abstract
Takotsubo cardiomyopathy (TTC), also called transient apical ballooning of the left ventricle, is a recently described and often under-diagnosed entity. The syndrome is observed predominantly in the postmenopausal women with signs very mimicking acute myocardial infarction. In most of the case reports emotional or physical stress factors have been identified as a trigger and perioperative stress has been suggested as the trigger in some cases. Outcome is favourable with the right treatment, though recurrences are possible. Here in this review, discussing 65 years old gentleman undergoing hepatico-jejunostomy developed immediate post-operative cardiovascular collapse leading to cardiac arrest and subsequently revived after adequate resuscitation. Immediate 2D echocardiography done on the same day demonstrated ejection fraction (EF) only 20% with hypokinesia and apical bulging with LV systolic dysfunction preserving left ventricular narrow base mid-segments and apical balloon in gand on subsequent supportive treatment, EF improved to 60% suggesting as case of stress induced cardiomyopathy i.e. Takotsubo cardiomyopathy. The aetio-pathogenesis, diagnosis, prevention and management of this syndrome is elaborately described in terms of literature evidence.

Abbreviations: MOJ: Medcrave Online Journal; ECG: Electrocardiogram; EF: Ejection Fraction; IV: Intravenous; CVP: Central Venous Catheter; CPR: Cardiopulmonary Resuscitation; IABP: Intra-Aortic Balloon Pumping

Introduction
Takotsubo syndrome, also known as ampulla cardiomyopathy, broken heart syndrome, idiopathic apical ballooning syndrome, and stress induced myocardial stunning, has been first described by Japanese authors in 1996 and subsequently specified in 2001; it derives from the resemblance between the ancient octopus and tsubo as pot, hence the name. Initially as mostly cases from Japan was reported, a genetic component was suspected, although now lots of cases being reported from non-asian populations in the united states and Europe. It is common among post-menopausal women precipitated by sudden emotional or physical stress [3,4]. These patients usually have a benign or unremarkable past medical history and the degree of symptom severity and presentation varies [3]. There is marked gender discrepancy in TTC and female in the postmenopausal period with mean age 58 to 77 years are commonly affected [5]. It is also proposed that in the post-menopausal period, due to reduced estrogen levels, there is altered endothelial function in response to exposure to sudden, unexpected emotional or physical stress. Cases being reported in younger age group of patients, a noteworthy case of 31 year old healthy women during caesarean section [6] and 31 year old premenausal women during breast surgery [7].

Case Report
A 65 year old gentleman suffering from Cholangiocarcinoma was admitted for hepatico-jejunostomy. In his past medical history, suffering from diabetes mellitus since 8 years and was controlled on Insulin. No other significant past medical history was elicited. On physical examination, patient was icteric (total bilirubin 7mg/dl, direct bilirubin 4.5) with normal liver enzymes. Preoperative blood pressure 130/80 mm Hg and heart rate, without heart murmurs and lungs were clear. Electrocardiogram (ECG) and chest X-ray revealed no pathological findings. Pre-operative 2-D echocardiography shows normal valvular structures with ejection fraction (EF) 62% and exercise ECG shows no inducible ischemia. Rest of the preoperative tests were within normal limit. In the operating suite, non-invasive monitors were applied including pulse oxymeter (SpO2), non-invasive blood pressure, 5 lead ECG and peripheral nerve stimulator. Intravenous (IV) and radial arterial catheter were placed under local anesthesia. After adequate pre-oxygenation, patient was induced with midazolam 2mg, fentanyl 100 µgm, propofol 100 mg and tracheal intubation completed with Atracurium 30 mg. Post induction, right sided internal jugular venous triple lumen central venous catheter (CVP) was inserted and epidural catheter was placed at lumber 3-4 interspace with loss of resistance technique in lateral position. General anesthesia was maintained with oxygen: air (1:1) mixture and Isoflurane with continuous epidural infusion of bupivacaine 0.1% and fentanyl 4 µgm/ml @ 8 ml/hour. The surgical procedure proceeded without hemodynamic instability. At the end of the procedure, the patient was extubated in the operative table and vital parameters were normal. Total duration of surgery was 3.5 hours and blood loss was adequately replaced with whole blood and fresh frozen plasma under the guidance of CVP.
Post-operatively patient was monitored in the intensive care unit (ICU) with all the monitoring attached. Patient was awake and co-operative and complained of pain. After 2 hours of shifting to ICU, all the hemodynamic parameters were normal and patient developed sudden cardiac arrest in asystole with return of spontaneous circulation after 8 minutes of cardiopulmonary resuscitation (CPR). The ECG showed diffuse T-wave inversion. The patient was intubated and developed cardiogenic shock requiring treatment with vasoactive drugs (nor-adrenaline and dobutamine). A myocardial infarction was suspected. Immediate blood result for troponin T was elevated to 0.1 mg/L (normal value <0.03 mg/L), which elevated to 0.7 mg/L only 12 hours after cardiac arrest. Urgent cardiological evaluation sought and 2-D echocardiography done on the same day demonstrated EF only 20% with hypokinesia and apical bulging with LV systolic dysfunction preserving left ventricular narrow base mid-segments and apical ballooning suggesting TTC. Initial Vasoactive drugs continued with ventilatory support and subsequent ACE inhibitor, diuretics improves LV dysfunction. The echocardiography repeated on 4th postoperative day revealed improved EF 60%. Despite appropriate treatment, the patient developed sepsis from 5th postoperative day with elevated total leucocyte count, fever, liver function tests, and related complications of surgical intervention of biliary tract leading to portal sepsis (hypotension, raised leucocytes, ABG status & lactate confirming sepsis) and so it was not possible to safely evaluate the coronary angiography and ventriculography. Patient died of multiple organ failure on 10th postoperative day.

**Discussion**

TTC is a special form of transient cardiomyopathy that is precipitated by a stress situation. TTC a type of non-coronary ischaemic cardiomyopathy, with apical ballooning of left ventricle with narrow segment a rare but stress induced cardiomyopathy possible post-operative complications following major surgery. Immediate post-operative features mimic myocardial infarction in which there is sudden reversible weakening of the myocardium with development of systolic dysfunction leading to acute heart failure. Almost all studies on TTC are small and observational and the aetiology still not clear from any of the case reports described. This disease is potentially life threatening. A completely reversible rare syndrome after severe emotional stress or extended surgery has also been described. It can occur in any of the stressful surgical situations from Electroconvulsive therapy unit [8] to the liver transplant surgery [9]. The trigger for this syndrome remains uncertain. Analysing the various reports of TTC after surgical situations from Electroconvulsive therapy unit [8], initial Vasoactive drugs continued with ventilatory support and subsequent ACE inhibitor, diuretics improves LV dysfunction. The echocardiography repeated on 4th postoperative day revealed improved EF 60%. Despite appropriate treatment, the patient developed sepsis from 5th postoperative day with elevated total leucocyte count, fever, liver function tests, and related complications of surgical intervention of biliary tract leading to portal sepsis (hypotension, raised leucocytes, ABG status & lactate confirming sepsis) and so it was not possible to safely evaluate the coronary angiography and ventriculography. Patient died of multiple organ failure on 10th postoperative day.

The relationship between stress induced catecholamine release and myocardial dysfunction was noticed by Wittstein et al. [11] and they measured the catecholamine plasma levels in women presenting with transient LV apical ballooning syndrome and they discovered that the levels were markedly higher than in women presenting with an acute myocardial infarction [11]. Many authors also report an abnormal fatty acid metabolism with impaired glucose metabolism, transient abnormal catecholamine response or coronary microvascular dysfunction [3]. The mechanisms of coronary vasospasm that leads to temporary direct myocardial injury are cyclic AMP mediated calcium imbalance, free radicals or contraction band necrosis due to elevated catecholamine [11].

Although takotsubo syndrome classically presents with chest pain, dyspnea, and ECG changes, these findings are not invariably present. Dyspnea may be a more common presentation in African American women [12]. Although most patients recover without complications after an episode of takotsubo cardiomyopathy, serious complications including congestive heart failure (occurring in as many as 44%–57% of patients) [13], pulmonary edema often requiring endotracheal intubation and mechanical ventilation, and cardiogenic shock (15%–45% of cases) requiring vasopressor or inotropic therapy [14] and even intra-aortic balloon pumping (IABP) [15] do occur. Our patient presents in cardiogenic shock in the immediate post-operative period. Other complications such as ventricular arrhythmias including torsade de pointes [16], syncope, cardiac arrest, apical thrombosis, and thromboembolism including stroke, dynamic intraventricular gradients, and obstruction (up to 25%) [17] with or without systolic anterior motion of the mitral valve, severe mitral regurgitation, ruptured ventricle, and death (1%–3% but as high as 21%) have been reported [14]. Elesber et al. [18] at the Mayo Clinic observed a recurrence rate of 11.4% over an average follow-up of 4.4 ± 4.6 years of 100 patients with takotsubo cardiomyopathy (2.9% per year over the first 4 years and 1.3% per year thereafter). Interestingly, only 2 of the 10 patients who experienced a recurrence had an identifiable precipitating event at that time.

Mayo Clinic diagnostic inclusion criteria of TTC [19,20]: all the 4 criteria are required for the diagnosis:

- a) Transient left ventricular hypokinesia, akinesis, or dyskinesia with or without apical involvement. The regional wall motion abnormalities typically extend beyond a single epicardial coronary distribution. It is frequently, but not always, a stressful trigger.
- b) Absence of obstructive coronary artery disease or angiographic evidence of acute plaque rupture.
- c) New electrocardiogram changes: ST-segment elevation and/or T-wave inversion or modest elevation of cardiac troponin levels.
- d) Absence of pheochromocytoma and myocarditis.

In our patient, all the criteria are fulfilled except coronary angiography which was not done due to technical reasons. Timely diagnosis and intervention with hemodynamic support leads to rapid reversal of LV dysfunction and increases the chance of survival [2]. There is no definite treatment for TTC, supportive
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Anaesthetic considerations

Perioperative stress and its effect on cardiovascular system well known. Stress response to Surgery begins during induction of general anaesthesia and lasts till 3-4 days post-surgery that results from activation of sympathetic nervous system that initiates a cascade of physiologic and metabolic events. Mortality following cardiac ailments is the most common cause of death after major surgical procedures[23]. In post-menopausal age group TTC is considered as one of the differential diagnosis in patients demonstrating myocardial dysfunction in the perioperative period. Anaesthetic management is not different from balanced anaesthetic technique with special interest to:

a. Beta blockers: to attenuate the transient LVOT obstruction,
b. Dihydropyridine calcium channel blockers are recommended in patients with coronary artery vasospasm,
c. Aspirin and Angiotensin converting enzyme inhibitors (ACEI) role is not clear. Long term use of ACEI before the onset of TTC protected against cardiogenic shock, sustained ventricular arrhythmias and death [21].
d. Calcium sensitizer Levosimendan is the best choice of inotropes when required [22].
e. If patient presents with acute decompensating heart failure in shock, management includes positive pressure ventilation, LV assist devices, IABP support. Dopamine and dobutamine can be used in hypotensive patients without substantial LVOT obstruction [17]. However, it is recommended that dobutamine be avoided in patients with severe systolic dysfunction or LVOT obstruction with hypotension and shock [10].
f. Phenylephrine, α-agonistic drug should be used with caution, and vigilant haemodynamic monitoring, tissue perfusion, and mentation should be monitored, because it might precipitate coronary vasospasm [17].
g. In presence of QT prolongation in ECG, selective antiarrhythmic medications should be given.

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