Dobutamine stress echo-induced apical ballooning (Takotsubo) syndrome

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Aims We report a case of dobutamine stress echocardiography (DSE) resulting in transient apical ballooning syndrome to highlight this rare condition as a potential complication of DSE.

Background Takotsubo cardiomyopathy, or transient apical ballooning syndrome, is a recently described form of left ventricular (LV) dysfunction induced by stress. Clinically it can mimic acute coronary syndrome in its presentation. It is characterized by an atypical distribution of LV dysynergy with apical ballooning and compensatory basal hyperkinesis. Coronary angiography is normal. It has preponderance in females. Although the aetiology of Takotsubo syndrome remains obscure catecholamine release appears to be the principal trigger.

Results We report a case of dobutamine-induced transient LV apical ballooning in a woman without coronary disease, during a dobutamine stress echocardiogram. There was evidence of ventricular recovery by 72 h.

To our knowledge, only three other case reports describe dobutamine-induced Takotsubo cardiomyopathy.

Conclusion Dobutamine stress echocardiography is a widely performed diagnostic test, however, it can rarely result in presumed catecholamine-induced transient apical ballooning syndrome.

KEYWORDS
Dobutamine stress echo; Apical ballooning; Takotsubo cardiomyopathy; Broken heart syndrome; Catecholamine-induced transient cardiomyopathy

Introduction

Takotsubo cardiomyopathy, also known as transient LV apical ballooning syndrome, was originally described in Japan in 1991, due to the resemblance of the LV ventriculogram to the appearance of a particular octopus pot.\(^1\)\(^2\) It has since been described in a number of ethnic groups.\(^3\)\(^4\)

In a systematic review of this condition, it is estimated to account for ~2% of all acute myocardial infarction presentations.\(^4\) It is most commonly triggered by significant emotional, physical, or mental stress, accounting for 30–50% of all cases, although it has been described to occur with underlying medical disorders such as phaeochromocytoma, subarachnoid haemorrhage, exacerbation of bronchial asthma, Guillain-Barré syndrome, non-cardiac surgery, sepsis, and critical illness experienced by patients in intensive care units.\(^5\)\(^6\)

Dobutamine stress echocardiography (DSE) is a commonly performed diagnostic non-invasive test to assess the stress-induced regional wall abnormalities indicative of ischaemia, and also to assess viability and contractile reserve in specific situations. Three case reports exist demonstrating the potential of DSE to induce apical ballooning syndrome, although the exact mechanism remains poorly understood.

Herein, we describe a case of Takotsubo cardiomyopathy caused by DSE, and postulate that it occurred as a result of apical hyper-responsiveness to adrenergic stimulation.

Case

A 61-year-old lady was referred for assessment of exertional shortness of breath. She had a prior history of hypertension and a 40-pack year smoking habit. There was a family history of premature vascular disease. Her baseline electrocardiogram (ECG) showed hypertensive change, with inferolateral repolarization abnormalities, and on that basis, a dobutamine stress echocardiogram was performed (Figures 1–4).

A standard dobutamine/atropine protocol was used with 10 mcg/kg/min dose increments at 3 min intervals. Her resting echocardiogram and blood pressure were normal. At 70% of her age-predicted heart rate, on 40 \(\mu\)g/min infusion of dobutamine, she developed typical cardiac chest

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pain, with associated inferolateral ST elevation, hyperacute anterolateral T-waves, and ventricular bigeminy. On review of the DSE images, it was apparent that there was severe akinesis of the apical, anteroseptal, and apicolateral segments at peak dobutamine infusion (Figures 5 and 6). No evidence of a mid-cavity obstruction gradient was demonstrated. She was immediately transferred to the cardiac catheterization laboratory and underwent coronary angiography. Her epicardial vessels were normal and a mid-left anterior descending coronary artery segment of bridging was noted. Left ventriculography revealed hyperdynamic basal myocardial segments with near-cavity obliteration, distal anterior, inferior, lateral, and apical akinesis, and the LV end diastolic pressure was 22 mmHg (Figures 7–9).

She was transferred to the coronary care unit, where she was commenced on beta-blockade, and anti-coagulated. Troponin I peaked at 4.8 ng/dL (0.01–0.04) and creatinine kinase peaked at 243 mg/dL (21–232). Her in-hospital course was complicated by atrial fibrillation with rapid ventricular response rates, requiring chemical cardioversion with amiodarone, and by mild left ventricular (LV) failure, requiring intravenous diuresis. Repeat echocardiography at 72 h showed near-normal LV function with mild residual apical and anteroseptal hypokinesia.

Repeat cardiac catheterization before discharge on day five, revealed markedly improved LV function, with an estimated ejection fraction of 50–55%, and mild residual anteroapical hypokinesia.
She has been symptom free since discharge and repeat echocardiogram at 8 weeks, revealed complete recovery of LV function.

Discussion

Takotsubo cardiomyopathy is a recently described clinical condition, originally described in 1991.1

Typically, it presents with symptoms and signs resembling an acute coronary syndrome, which can lead to inappropriate therapy, e.g. thrombolytic administration.7,8

It has preponderance in females (9:1). In most reported series, it commonly affects post-menopausal women, with an average age range of 62–75 years, although it has been reported in individuals aged 10–91 years.8

It commonly presents with chest pain (68%), although it may present with shortness of breath (20%), cardiogenic shock (4%), or ventricular arrhythmia (2%).5–7

Electrocardiogram typically shows ST elevation typical of acute myocardial infarction, deep global T-wave inversion, or prolongation of the QT interval; and the ECG changes can affect multiple territories. The ECG changes typically resolve over within months.7,8

It is associated with mild elevation in cardiac enzymes, disproportionately low given the extent of wall motion abnormality.7,8

Echocardiography shows a typical appearance of significant LV dysfunction, with preserved basal segment function, and moderate to severe dysfunction of the mid- and apical segments. The echocardiographic appearance improves rapidly over 3–5 days.
Cardiac magnetic resonance (CMR) does not show any evidence of myocardial necrosis, and endomyocardial biopsy tends to show a mononuclear infiltrate without any evidence of myocarditis or myocardial necrosis. Occasionally, contraction band necrosis can be observed, which is well described in catecholamine-induced myocyte injury.5,7,8

Angiography in the vast majority of described cases shows normal coronaries. Spontaneous or provoked multivessel epicardial vessel spasm has been described.5

The combination of apical and mid-ventricular wall motion abnormalities can cause intracavity LV gradient, which can cause haemodynamic instability, and result in systolic anterior motion of the anterior mitral leaflet, producing posteriorly directed mitral regurgitation.5

Recovery is usually rapid, although heart failure, cardiogenic shock, ventricular arrhythmia, mitral incompetence, LV outflow tract (LVOT) obstruction, and free wall rupture have all been described as a complication of this condition. In the published literature, it is associated with a 3.5% risk of recurrence. Right ventricular dysfunction has been described in up to one-third of cases. These patients are particularly prone to LV thrombus formation.7,8

In-hospital mortality has been estimated at 1.1%, with up to 20% experiencing heart failure. The commonest reported causes of mortality are cardiogenic shock and thromboembolism.8

Management is largely supportive, with fluid resuscitation (if no pulmonary congestion), beta-blockade, and occasionally afterload augmentation with phenylephrine in those with an LVOT gradient. Consideration should be given to therapeutic anti-coagulation to prevent thromboembolism. For those with haemodynamic instability, isotropes and intra-aortic balloon counterpulsation may be required.7,8

The exact mechanism of occurrence remains poorly understood, but several hypotheses exist.

Epicardial coronary spasm has been demonstrated in up to 11% of reported cases. Provoked spasm has been demonstrated in the catheterization laboratory, but its relevance remains unclear. Microvascular spasm and microvascular obstruction have been hypothesized, but the lack of subendocardial infarction on CMR undermines this theory.5,8

Catecholamine levels are significantly elevated in individuals with this condition, reflecting increased synthesis, reuptake, and removal metabolism of the adrenergic hormones.5 This may lead to catecholamine-induced cyclic adenylyl monophosphate calcium overload of the myocyte, resulting in direct myocyte injury.5 Catecholamines may also stimulate oxygen-free radical generation, which can cause local myocyte injury.5

Interestingly, it has been reported that the apical myocardium has an increased response to adrenergic stimulation, and may be vulnerable to surges in circulating catecholamine levels.5 Local release of catecholamines from adrenergic neurones in the myocardium seems unlikely as there is a higher norepinephrine content and concentration of sympathetic nerves at the base of the heart compared with the apex.9 A base-to-apex perfusion gradient may exist as occurs in individuals with coronary risk factors.10

Finally, sex differences may account for the condition occurring predominately in females, although it is worthwhile noting that higher circulating basal levels of catecholamines occur in men, and males produce a more marked elevation in catecholamines in response to stress.5 Despite this, it is well described that females appear more vulnerable to sympathetically mediated stunning, and postmenopausal alteration of endothelial function in response to decreased oestrogen levels has been associated advocated as a possible explanation.11

A recent paper postulated that the condition arises due to the hyperdynamic basal segments creating an intracavity gradient causing excess release or dehydration of catecholine, resulting in an isolated apical chamber that produces myocardial stunning without infarction.12-14 It is known that up to 20% of patients undergoing DSE develop a dynamic LV mid-cavity obstruction, and perhaps this reflects the potential mechanism of apical ballooning induced by DSE.13,14

In our case, no clear emotional or stress trigger could be identified. The only apparent initiation factor would appear to be dobutamine infusion. We postulate that increased apical responsiveness to adrenergic stimulation previously described, offers a potential mechanism as to how DSE could culminate in transient apical ballooning. In addition to overstimulation of the apical adrenergic receptors, dobutamine may also has worsened the hyperdynamic basal systolic function, creating an artificial LVOT gradient, and further stressing the myocardium, which was not demonstrated in our case. This mechanism, however, was demonstrated in a previous series where patients with Takotsubo cardiomyopathy underwent low-dose DSE following recovery, which provoked an LV mid-cavity gradient at peak dose.14

Conclusion

Dobutamine stress echocardiography is a widely performed test, and is largely safe, although induction of myocardial infarction is well recognized. Our report highlights the potential of DSE to induce transient apical ballooning, through a combination of adrenergic overstimulation and LV mid-cavity obstruction. All centres performing DSE should be aware of the potential complication of apical ballooning syndrome.

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