

A Broken Heart Coexisting with Obstructive Coronary Artery Disease: Double Trouble

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Abstract

Background: Takotsubo is a syndrome characterized by transient regional systolic dysfunction of the left ventricle (LV). The most common clinical presentation mimics acute myocardial infarction without angiographic evidence of obstructive coronary artery disease or acute plaque rupture.¹⁻³ The diagnosis and management became a challenge when it presented as atypical symptoms and significant obstructive coronary artery. Thus, this case report highlights the diagnosis and management of Takotsubo Cardiomyopathy with obstructive coronary artery disease.

Case illustration: A 71-year-old woman came to the emergency room with a chief complaint of dyspnea from one week ago which worsened in the last three days. The initial electrocardiogram showed slight ST-elevation, and thorax Rontgen showed the congestion and elongation of the aorta. Increased high-sensitive Cardiac Troponin T and The NT-Pro BNP levels were present, along with apical ballooning of the LV and reduced RV function. Physiological stress was found to be the death of her husband one week ago. Although the left ventriculography of this patient was classically depicted as the octopus trap, we did find obstructive coronary artery disease in the left anterior descending artery.

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Introduction

AcTakotsubo cardiomyopathy (TCMP), broken heart syndrome, or apical ballooning syndrome is a prototypical acute heart failure syndrome characterized by transiently impaired left ventricular systolic function. In the acute phase, symptoms and signs of TCMP are virtually indistinguishable from those of acute coronary syndrome (ACS).^{4,5} The unique feature of TCMP is the occurrence of a preceding emotional or stressful physical event in approximately two-thirds of patients.^{3,5,6} According to the Mayo Clinic Diagnostic Criteria, diagnosis of TCMP required an angiogram without signs of obstructive coronary artery disease (CAD).⁷ In the footnote of the revised version, it is stated that a patient with obstructive coronary atherosclerosis may also develop TCMP. However, this is rare in our experience and the published literature, perhaps because such cases are misdiagnosed as acute coronary syndrome.³

The widely accepted mechanism for TCMP is catecholamine surge due to acute emotional or physical stress and effected the Left ventricle with regional and density differences of beta-adrenergic receptors.^{8,9} The beta2-adrenergic receptor is mainly expressed in the

apical segment of LV. In contrast, the beta1-receptor is expressed mainly in the basal segment of LV. Both epinephrine and norepinephrine have positive inotropic effects through Gs-coupling protein. The rise in levels of epinephrine trigger beta2-adrenoceptors to switch from Gs to Gi coupling, which is associated with a negative inotropic response of the left ventricular apex.⁸ The excessive catecholamine release was from the adrenal medulla and locally from the sympathetic nerve. These catecholamine surges lead, through a different mechanism, to myocardial damage. The myocardial damage, in turn, becomes a substrate of transient apical ballooning.¹⁰ This mechanism protects the left ventricular myocardium from the catecholamine storm, thus limiting the degree of myocardial injury in the acute phase of TCMP.⁸

The prevalence of Takotsubo cardiomyopathy is 2% of all patients with clinical presentation of acute coronary syndrome. The low prevalence of TCM was thought to be caused by unawareness of the disease entity aside from the rarity in occurrence.⁵ Among the Takotsubo patients, 85 to 90% of the patients are women aged 65-70 years.^{6,7} Therefore, Takotsubo cardiomyopathy should be suspected in postmenopausal women patients with symptoms of

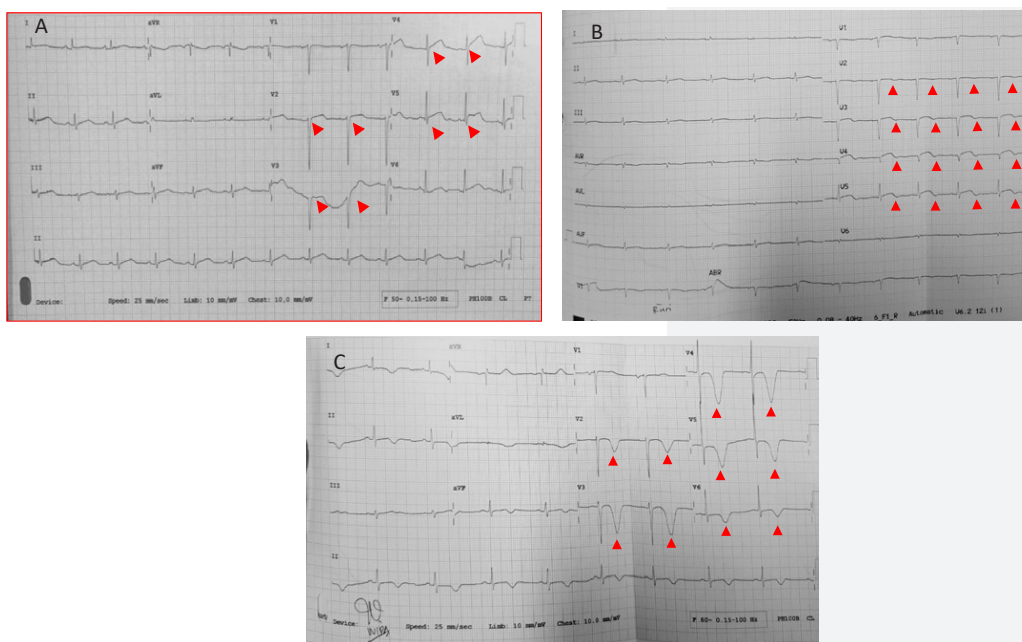


Figure 1. A. ECG at admission with slight ST elevation (red arrow); B. ECG at day 3 hospitalization with biphasic T wave (red arrow); C. ECG at week three follow-up with deep T wave inversion. (red arrow).

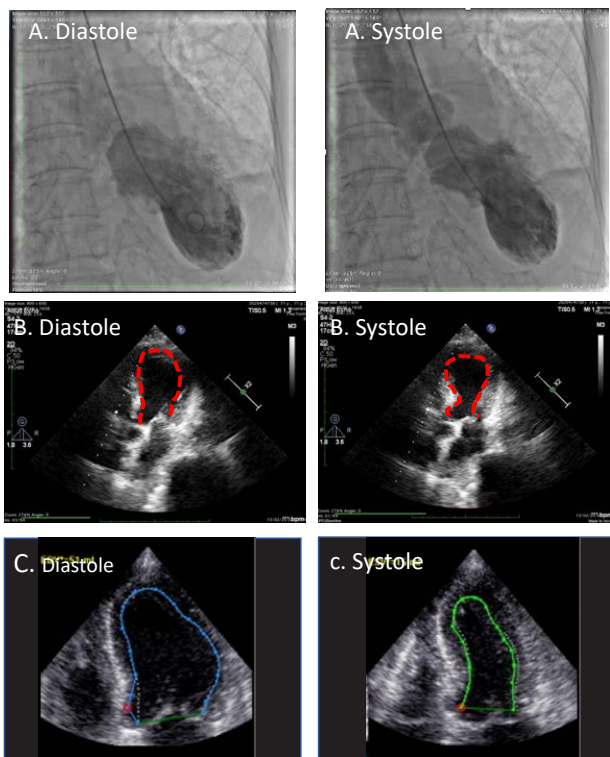


Figure 2. Left ventricular angiography and echocardiography during diastole and systole. A. Ventriculography at admission showing apical ballooning. B. Echocardiography at admission with a 4-chamber view during diastole and systole showing apical ballooning and reduced LVEF 33%. C. Echocardiography at week three follow up with 4-chamber view during diastole and systole showing apical ballooning and reduced LVEF 71%.

chest pain and/or dyspnoea with the combination of electrocardiographic changes and/or cardiac troponin elevation.⁸ Differentiating Takotsubo cardiomyopathy from true acute coronary syndrome is paramount due to the difference in treatment and potential harm of using any antiplatelet and catecholamine-based medications in Takotsubo cardiomyopathy.⁹ In this case, we will report and highlight the diagnostic and management challenges of TCMP with obstructive coronary artery disease and less common presentation.

Case Presentation

We present the case of 71 years old woman with acute heart failure whose dyspnoea started one week before admission and progressively worsened. Upon

presentation in our emergency, she could not walk more than three meters without experiencing debilitating dyspnoea and sleeping in a sitting position. The onset of acute dyspnoea coincides with the passing of her husband. The patient denied having any chest discomfort or chest pain symptoms. Her risk factors were menopause and hypertension, for which amlodipine of 5 mg once daily had been consumed routinely for the past two years. At admission, Her vital signs were stable except for blood pressure which was 184/100 mmHg. Her physical findings were unremarkable with good peripheral perfusion except rales limited to the basal of both lungs, which was consistent with left heart congestion. The electrocardiogram showed sinus rhythm, and rS pattern in the V2-4, with slight ST elevation II, aVF, and V4-V6. (Image c1A; white arrow).

Findings on the laboratory test were within normal limits except for the elevation of high-sensitive Troponin-T (Hs-troponin T) and NT-Pro BNP. The level of Hs-troponin T was 56 ng/mL (normal <14 ng/mL) and increased to 66 ng/mL in the third hour. The level of NT-Pro-BNP was 8895 ng/mL (normal < 125 ng/mL). Chest emergent echocardiography revealed reduced left ventricle ejection fraction (LVEF 33%), reduced right ventricular systolic function (TAPSE 1.3 cm) with apical ballooning of the left ventricle, akinetic of the apical left ventricular segment, and normal-kinetic of the mid basal segment. The presence of congestion and bilateral pleural were confirmed with chest X-ray and Lung ultrasound findings. The patient was stratified as TCMP high risk and cardiogenic shock SCAI classification stage B. High-risk stratification warranted an emergent coronary angiography to further diagnosis confirmation and management strategy.

Emergent coronary angiography and left ventriculography were performed. The left ventriculography findings were consistent with echo findings, left ventricular apical ballooning. (Image 3; upper image); The coronary angiography, after administration of 300 mcg of intracoronary nitroglycerin, revealed the left main artery (LM), the left circumflex artery (LCx), and the dominant right coronary artery (RCA) and were at worse with minor irregularities only. However, the left anterior descending artery (LAD) had diffuse stenosis along with 70-80% stenosis along the ostial to the proximal part and 90% stenosis at the mid part with no visible thrombus. Ad



Figure 3. Angiography Coroner A. LAO Caudal projection showed LAD only reaching di apical. (not wrapped around LAD) 2. LAD with diffuse disease from ostial to mid part causing stenosis 70-90%; C. Post PCI with 2 DES stents at LAO cranial projection. .

hoc PCI was performed and two contiguous drug-eluting stents were successfully deployed from the LM to the mid-LAD with good final angiographic results and TIMI 3 flow.

The congestion and bilateral pleural effusion were treated with intravenous nitrate and diuretics. Dual antiplatelets and statin were administered before PCI and continued thereafter. Once the congestion and bilateral effusion had resolved, the disease-modifying pharmacological therapy for heart failure, such as Renin Angiotensin Aldosterone System (RAAS) inhibitor and beta-blocker was initiated and up-titrated. At discharge, the patient was prescribed dual antiplatelet (aspirin 80 mg od and clopidogrel 75 mg od), RAAS blocker (ramipril 10mg daily, spironolactone 25 mg daily), Beta-blocker (bisoprolol 1,25 mg once daily) as recommended in heart failure guidelines.¹¹ At week three during follow-up, She was able to return and carry on her usual activities without symptoms of dyspnoea. The electrocardiography findings showed markedly deep T wave inversion in the precordial lead V2-V5 with prolonged QTc (538 mSec) (Image 1C). The echocardiography findings revealed global normal-kinetic with LVEF 7I% and TAPSE 1.9 cm, with resolved apical ballooning compared to the in-hospital echocardiography.

Discussion

The common findings for TCMP in the presented case are the following: 1) postmenopausal woman who had experienced a tragic loss of her husband as

emotional stress trigger,^{3, 5, 7, 12} 2) moderately elevated cardiac enzyme,^{3, 12} 3) mildly elevated ST elevation on EKG at presentation, dynamic changes EKG over three weeks,¹³ 4) return to normal left ventricular function within 4-8 weeks,^{1, 9, 14} and 5) acute heart failure as a complication of TCMP. Emotional stress, such as death or severe illness of a family member, etc., is a common trigger of TCMP in women, whereas physical stress, such as severe pain, noncardiac surgery, or noncardiac procedure, etc., is a more common trigger of TCMP in men.^{3, 5}

The most common acute ECG findings are ST segment elevation in the precordial leads and T wave inversions in most leads.¹² Evolving T waves deepen further to their first negative peak within three days, transiently turn shallow, then become significantly deeper on their second negative peak in 2–3 weeks. T wave changes may revert to normal after about 2–4 months.¹³ The dynamic changes at admission with slight ST elevation at the precordial lead V2-5 and marked deep T wave inversion with prolonged QTc interval in the corresponding precordial leads at 3 weeks follow up is consistent with the EKG dynamic changes of TCMP.

Cardiac troponin in most if not all TCMPs have a modest elevation that peaks within 24 hours.^{7, 15} The magnitude of increase in the cardiac troponin is less than that observed with a STEMI and disproportionately low for the extensive acute regional wall motion abnormalities.¹⁶

Dyspnoea as the initial presentation is not more common than acute chest pain. In the International Takotsubo Registry study, the incidence of dyspnoea

is much less at 46.9%, compared to 75.9% for chest pain.⁵ Emotional stress, such as death or severe illness of a family member, is a more common trigger of TCMP in women, whereas physical stress, such as severe pain or noncardiac surgery/ procedure, is a more common trigger of TCMP in men.^{3, 5} The clinical presentation of acute heart failure with bilateral pleural effusion was due to a complication of untreated TCMP. Medical help was not immediately sought when the symptom of dyspnoea had initially arisen. Acute heart failure presentation with high blood pressure could easily be misdiagnosis as vascular type acute heart failure due to uncontrolled hypertension.

The importance of emergent echocardiography, in the emergency room, is highlighted in this case as an important diagnostic tool. Misdiagnosis would have been reached without an echocardiogram. The emergent echocardiography and left ventriculography findings were consistent with apical ballooning. Another important finding was the reduction of RV systolic function (TAPSE 1.3 cm). Dysfunction of the left ventricle and right ventricle are thought to cause an increase in pulmonary vein pressure. This will cause leakage in the visceral pleural that ends up as pleural effusion.¹⁷ The presence of RV involvement has been associated with a higher prevalence of in-hospital major adverse cardiovascular events, including heart failure, cardiogenic shock, and in-hospital mortality.^{5, 18}

The presence of significant coronary artery disease does not preclude the diagnosis of TCMP. In our case, the LAD was not wrapped around the apex. Therefore could not be responsible for Apical ballooning during systole. A recent study from International Takotsubo Registry (InterTAK), the largest observational multicenter registry involving 26 centers in Europe and the United States with 1750 subjects, revealed that 234 subjects (23%) TCMP has an obstructive CAD and 52.1 % of TCMP with obstructive CAD presented with elevated cardiac enzyme and ST elevation.¹⁹ These findings show that the presence of obstructive CAD is not an exclusion of criteria unless the regional wall motion abnormality is limited to a single coronary territory.

There is no consensus regarding the management of obstructive CAD coexisting with TCMP. From the Inter-TAK registry, only 19% received an ad hoc PCI. However, the outcome of TCMP with obstructive CAD is much worse than TCMP without obstructive

CAD with a higher need for invasive and non-invasive ventilation, cardiogenic shock, and death. As compared to the match acute coronary syndrome cohort, the incidence of Cardiogenic shock, in hospitals and short-term mortality of TCMP with obstructive CAD is as high with no significant difference.¹⁹ Therefore it is reasonable to perform ad hoc PCI in TCMP with obstructive CAD as it was performed in our case, however, its possibility of reducing the invasive and non-invasive ventilation and preventing cardiogenic shock and death still needs further investigation.

In summary, the clinician should have a high index suspicion for takotsubo cardiomyopathy among post-menopausal women following acute emotional stress who present with acute heart failure and ECG changes suggestive of ischemia. An emergent echocardiogram adds great incremental diagnostic value. Emergent coronary angiography is important to exclude the presence of coexisting obstructive CAD. Revascularized obstructive CAD in TCMP is debatable, however, it is rational given the higher incidence of the need for mechanical ventilation, the incidence of cardiogenic shock, and in-hospital mortality.

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