


A case report: biventricular takotsubo cardiomyopathy with sequential ventricular recovery due to pulmonary hypertension

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Background

Biventricular Takotsubo cardiomyopathy (BTC) is estimated to occur in 25–42% of those with Takotsubo cardiomyopathy (TC). Little is known about which subset of patients are predisposed to having concomitant right ventricular (RV) involvement, or the pattern of recovery in BTC.

Case summary

We describe a 69-year-old woman who presented with dyspnoea and was subsequently diagnosed with BTC. We propose that this was triggered by an exacerbation of chronic obstructive pulmonary disease on a background of multiple predisposing factors including recent bereavement, previous excessive alcohol use, status as a current smoker, and anxiety. During her admission, she required non-invasive ventilation and inotropic support to manage her type two respiratory failure and acute heart failure. Serial echocardiograms during the admission allowed us to capture and present the sequential recovery of ventricular systolic function, with the left ventricular (LV) recovery preceding the right ventricle.

Discussion

Our patient fulfils the International Takotsubo Diagnostic criteria of transient LV dysfunction, emotional and physical triggers, electrocardiogram abnormalities, raised troponin and brain natriuretic peptide and no occlusive coronary artery disease. We hypothesize that pulmonary hypertension-related strain on the right ventricle due to lung disease, may have led to the observed delay in the recovery of RV function, despite the full recovery of LV function.

Keywords

Takotsubo cardiomyopathy • Echocardiogram • Sequential recovery • Pulmonary hypertension • Heart failure • Graves disease • Case report

Learning points

- Biventricular Takotsubo cardiomyopathy (TC) is a rare entity and may have a worse outcome than classical TC. Having a background of co-existing lung pathology may have increased our patient's likelihood of right ventricular (RV) involvement, and the subsequent delayed RV recovery.
- Predisposing factors to this case of TC include female gender, recent bereavement, anxiety and stress, chronic obstructive pulmonary disease, previous alcohol excess, current smoking, and later diagnosed thyrotoxicosis.

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Introduction

Takotsubo cardiomyopathy (TC) is an uncommon condition, with the following features: transient left ventricular (LV) dysfunction, emotional and/or physical triggers, electrocardiogram (ECG) abnormalities, raised troponin and brain natriuretic peptide and no occlusive coronary artery disease.¹ The presenting symptoms of TC often mimic acute coronary syndrome (ACS). It is estimated that 2–3% of those presenting as ACS actually have TC.^{1,2} Although TC usually affects the left ventricle, biventricular TC (BTC) is known to occur, and it is suggested that these patients are more haemodynamically unstable and have a poorer prognosis.³

As far as we know, the sequential recovery of BTC has not previously been reported. Here, we have shown a case where the right ventricular (RV) systolic function recovers after LV function that may be determined by the underlying long-term strain due to chronic obstructive pulmonary disease (COPD)-related pulmonary arterial hypertension (PAH).

Timeline

Day of presentation (admission)	Presented to hospital with dyspnoea and chest pain. Electrocardiogram (ECG)—ST elevation with Q waves in V1–V4. Point of care echocardiogram—biventricular systolic impairment. Working diagnosis of biventricular Takotsubo cardiomyopathy (BTC) proposed, with differential diagnosis of old ST-elevation myocardial infarction. Treated with non-invasive ventilation (NIV) for type 2 respiratory failure.
Day 2	Persistent hypotension requiring inotropic support. Troponin continuing to rise. ECG—new right bundle branch block with T-wave inversion. Formal echocardiogram—confirmation of biventricular systolic impairment with preservation of basal function.
Day 6	Echocardiogram revealed complete recovery of left ventricular systolic function. Right ventricular systolic function remained abnormal with mid and apical dyskinesia of the free wall. Further ECG changes—new atrial fibrillation with persistent ST elevation in V1–V4 with biphasic T waves.
Day 8	Echocardiogram—complete recovery of biventricular systolic function. ECG changes persist. Invasive coronary angiogram—non-obstructive coronary artery disease hence Takotsubo cardiomyopathy (TC) diagnosis confirmed.
Day 15	Second episode of type 2 respiratory failure, possibly due to aspiration following a choking episode at breakfast. Repeat bedside echocardiogram—no evidence of recurrence of TC. Good response to less than 24 h of NIV.
Day 31	Discharged following inpatient rehabilitation.

Case presentation

A 69-year-old lady presented to our hospital with a few days' history of intermittent episodes of breathlessness, and reduced exercise tolerance to a few yards. On the morning of her admission, she described a brief episode of chest pain, which her family had thought was a panic attack.

She had a background history of alcoholic liver disease with cirrhosis (Child-Pugh score A), portal hypertensive gastropathy, hiatus hernia, healed duodenal ulcer, and chronic anxiety. She was a current smoker of over 30 pack years and had been abstinent from alcohol for 3 years.

On arrival, our patient was alert and oriented. Her observations showed a pulse rate of 127bpm, blood pressure (BP) of 166/78 mmHg, respiratory rate of 34, oxygen saturation of 86% on 5 L oxygen, and temperature of 36.3°C. Auscultation of her chest revealed bilateral wheeze, with normal heart sounds. She had cold peripheries with a prolonged capillary refill time and no peripheral oedema.

Her first arterial blood gas (ABG) revealed acute decompensated type two respiratory failure (T2RF) (Table 1). Given her background, she was treated initially as an infective exacerbation of likely underlying, undiagnosed COPD, and was started on antibiotics, nebulizers, and steroids.

Within a couple of hours, she became increasingly agitated and subsequently less responsive. A repeat ABG revealed worsening T2RF (Table 1) and non-invasive ventilation (NIV) in the form of bi-level positive airway pressure was commenced.

Chest X-ray revealed hyperinflation with upper lobe diversion (Figure 1A), and her ECG showed ST elevation in the anterior leads (Figure 1B). Blood tests revealed an elevated white cell count, troponin, brain natriuretic peptide, and D-dimer (Table 2). She was reviewed by intensive care, and the working diagnosis was ST-elevation myocardial infarction with LV failure resulting in T2RF. ACS treatment with aspirin, clopidogrel, and fondaparinux was commenced, and urgent cardiology opinion was requested.

Upon cardiology review, a bedside echocardiogram showed severe LV systolic dysfunction, with dyskinesia of the mid and apical septal and lateral walls, with preservation of basal function. The mid and apical segments of the RV free wall were dyskinetic with preservation of basal function. A possible diagnosis of BTC was proposed. However, based on the presence of Q waves across the chest leads on the ECG, and the fact that BTC is a diagnosis of exclusion, the differential diagnosis was that of a prior infarct with persistent ST elevation.

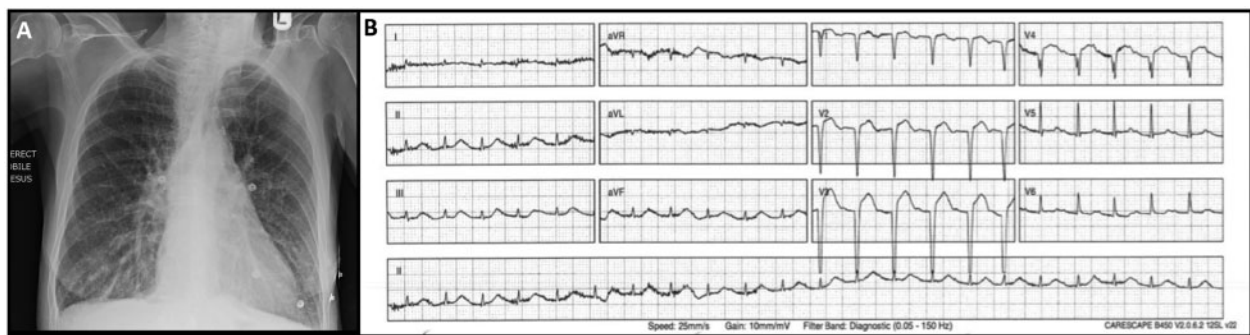
A computed tomography pulmonary angiogram (CTPA) ruled out pulmonary embolism, and the patient was responding well to NIV, with a repeat ABG 3 hours after initiating NIV showing resolution of acidosis and hypercapnia, but persistent hypoxaemia (Table 1).

Her troponin increased to 2000 ng/L, and in view of the patient's complex background and acute illness, she was managed in our intensive care department. She was deemed too unstable to undergo invasive coronary angiography.

On her second day in hospital, she became hypotensive with a BP of around 90/60 mmHg. Repeat ECG showed resolution of Q waves, and a new right bundle branch block with deep T-wave inversion. Her troponin had further risen to 3000 ng/L. Repeat bedside

Table 1 Arterial blood gas results (A) on admission, (B) following optimal medical therapy with nebulizers and controlled oxygen therapy, and (C) after 3 hours of NIV

	(A) Admission	(B) After optimal medical therapy	(C) After 3 h of NIV
pH	7.218	7.085	7.358
pCO ₂ (kPa)	8.62	11.5	5.46
pO ₂ (kPa)	31.46	7.43	8.50
Bicarbonate (mmol/L)	25.8	25.9	23.0
Base excess (mmol/L)	-2.75	-4.0	-2.5
Lactate (mmol/L)	4.1	3.3	3.1
SO ₂ (%)	100	74.1	91.6
Oxygen therapy	15L non-rebreathe mask	6L nasal cannula	NIV

**Figure 1** Admission investigations. Chest X-ray (A): hyperinflated lung fields with upper lobe diversion and parenchymal infiltrate in the right lower zone. Electrocardiogram (B): sinus tachycardia with borderline 1st degree heart block. Q waves present across the chest leads with marked ST elevation in chest-leads V1–V4.

echocardiogram (Videos 1 and 2) remained consistent with BTC (Figure 2). The systolic pulmonary pressure (SPAP) was elevated at 47–52 mmHg, estimated from the moderate tricuspid regurgitation. Metaraminol and subsequently dobutamine and noradrenaline were commenced for BP support. Our local tertiary centre advised switching these to a levosimendan infusion for 24 hours, and intra-aortic balloon pump support was felt unnecessary. Our patient haemodynamically stabilised with improved BP and urine output.

Over Days 4 and 5, following the cessation of levosimendan, our patient still required low dose inotropic support.

On Day 6, our patient developed rate-controlled atrial fibrillation (AF) with ST elevation in V1–V4 with biphasic T waves, although, she remained free of chest pain (Figure 2H). In spite of her new AF, repeat echocardiogram (Video 3 and Supplementary Video S1) revealed complete recovery of the LV systolic function with no evidence of regional wall motion abnormality. Her right ventricle continued to show basal wall preservation of function and mid to apical RV dilatation and dyskinesia, and SPAP of 54 mmHg. Troponin level had further fallen to 329 ng/L. Supportive management continued.

Over the next 48 hours, after clinical improvement, inotropic support was weaned. On Day 8, repeat echocardiography showed that in addition to the prior recovery of her LV function, her RV function had also fully recovered (Figure 2E and F, Supplementary Video S2).

Table 2 Blood test results on admission

Blood test	Result	Normal range
Hb (g/L)	106	110–150
MCV (fL)	86.3	80–101
WCC (10 ⁹ /L)	18.7	3.7–11.1
Neutrophils (10 ⁹ /L)	14.0	1.7–7.5
Platelets (10 ⁹ /L)	297	150–450
CRP (mg/L)	3.5	0–6
Urea (mmol/L)	7.6	2.5–7.8
Creatinine (μmol/L)	45	49–90
eGFR (mL/min)	>90	>90
ALT (IU/L)	25	1–34
ALP (IU/L)	123	30–130
GGT (IU/L)	51	0–37
Troponin I (ng/L)	732.5	2.3–11.7
BNP (pg/mL)	367	0–100
D-dimer (ng/mL)	1762	0–230

Our patient had a normocytic anaemia, raised white cell count which was predominantly a neutrophilia, unremarkable C-reactive protein, normal renal function, and mildly deranged liver function. She had an elevated troponin, BNP, and D-dimer. Other clotting parameters were normal.

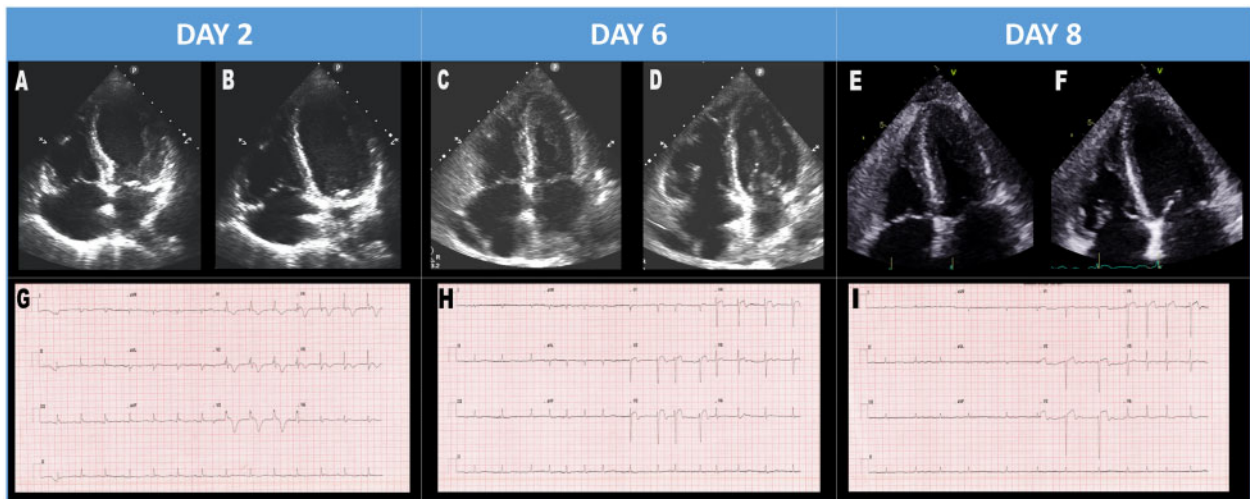


Figure 2 Transthoracic echocardiography images and corresponding ECGs on Days 2, 6, and 8 of admission. Apical four-chamber views showing (A) systolic and (B) diastolic frames demonstrating mid and apical wall dyskinesia with preserved basal contractility in both LV and RV free wall, on Day 2 of admission. ECG showed new right bundle branch block with deep T-wave inversion (G). Day 6 echocardiography images show resolution of LV systolic function with persisting RV free wall mid-apical dilatation and dyskinesia in (C) systole and (D) diastole. Corresponding ECG (H) shows new atrial fibrillation with ST elevation and biphasic T waves across the chest leads. On Day 8, echocardiography images revealed fully resolved biventricular systolic function (E) systolic and (F) diastolic frame. ECG changes persist (I).

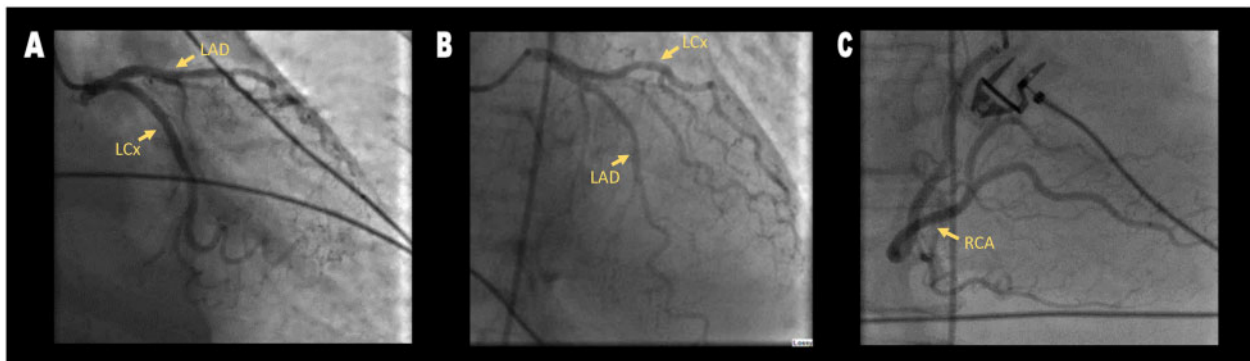


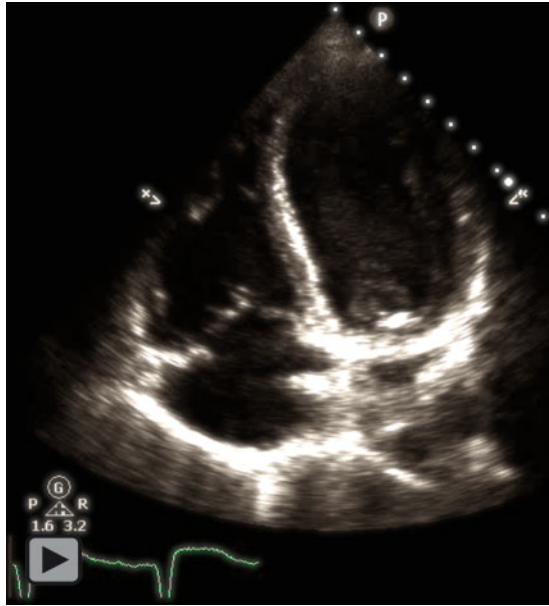
Figure 3 Invasive coronary angiography images showing non obstructive coronary artery disease. (A and B) Left anterior descending (LAD) and left circumflex (LCx) arteries and (C) right coronary artery (RCA).

The previously documented SPAP remained >56 mmHg, which was interpreted as her baseline due to her COPD. Invasive coronary angiography confirmed no obstructive coronary artery disease (Figure 3), thus we could confirm that our patient had indeed suffered from BTC, as up until this point, we had been unable to rule out myocardial infarction. Her ECGs continued to show persistent anterior ST elevation with biphasic T-wave changes.

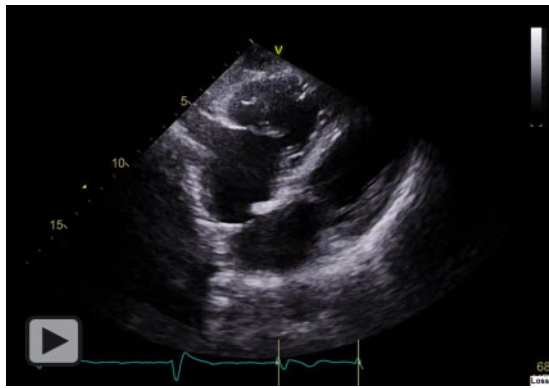
Our patient continued to improve and was stepped down to the coronary care unit and was engaging well with inpatient rehabilitation. Unfortunately, on the morning of Day 15, she developed another episode of T2RF, possibly due to aspiration following a choking episode on breakfast. Focused echocardiography ruled out the recurrence of TC, and she responded swiftly to NIV, requiring less than 24 hours.

She was transferred to the respiratory ward for ongoing management of her airway disease and discharged 2 weeks later.

Co-incidentally, her thyroid function tests (TFT) on Day 6 showed raised T4 and undetectable thyroid-stimulating hormone level (Supplementary material online, Table S1). After confirmation with repeated blood tests, the diagnosis of thyrotoxicosis was made. The endocrine review and subsequent thyroid-receptor antibody levels suggested autoimmune thyroiditis or Graves' disease. At a later stage, carbimazole treatment was commenced and beta-blocker continued with regular endocrine follow-up. Our patient had a brief admission in September 2020 with mild shortness of breath. Repeat echocardiography showed normal biventricular systolic function, normal LV diastolic function and filling pressures and an SPAP of 40 mmHg.



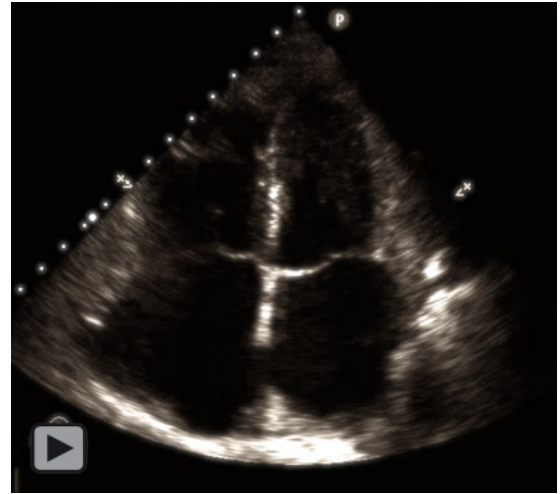
Video 1 Initial transthoracic echocardiography. Apical four-chamber view showing dyskinetic mid and apical segments of both LV and RV free wall and preserved basal wall kinesis in keeping with the echo diagnosis of biventricular Takotsubo cardiomyopathy.



Video 2 Initial transthoracic echocardiography. Subxiphoid transthoracic echocardiogram showing four-chamber view and dyskinetic mid and apical segments of both LV and RV free wall and preserved basal wall kinesis in keeping with the echo diagnosis of biventricular Takotsubo cardiomyopathy.

Discussion

Our case is a unique demonstration of the sequential recovery of BTC. We propose that the delay in recovery of RV function, may be due to increased RV afterload secondary to PAH due to pre-existing lung disease. Shao *et al.*,⁴ based on animal experiments, proposed the differential wall stress hypothesis, in the development of different phenotypes of TC. He suggested that the presentation of TC would depend on afterload related wall stress of myocytes. High afterload



Video 3 Day 6 transthoracic echocardiography. The apical four-chamber view showing the LV systolic function had fully recovered, but RV free wall mid and apical segments remained dyskinetic in keeping with sequential recovery of BTC.

conditions e.g. pulmonary embolism result in basal wall stress-related akinesis (atypical TC) with the preservation of the apex (McConnell's sign), whereas low afterload conditions would be responsible for the manifestation of typical TC.⁴ In our case of BTC we found typical biventricular apical ballooning with preservation of basal segmental function, which may be due to chronic pre-existing PAH affecting myocardial fibre stress differently to an acute increase in afterload.

Nevertheless, BTC can occur in those with no respiratory disease. In such cases, one might assume that the PAH is confounded by LV dysfunction, that can cause RV strain, as a plausible explanation of why the RV normalization follows LV improvement. In our patient, in spite of the full normalization of LV systolic function, the SPAP remained elevated and persisted after the full recovery of the RV function. This would be in keeping with our theory of this patient's COPD-related PAH and thus maladaptation in the RV myocytes during 'catecholamine insult' manifesting as BTC and protracted recovery.

Data on the recovery pattern of BTC is sparse and although there have been case reports describing asymmetrical wall motion abnormality between the left ventricle and right ventricle,^{5,6} we believe our report is the first that, based on a series of transthoracic echocardiograms during hospital stay, describes the *sequential* recovery of BTC.

In our patient, repeated TFTs confirmed hyperthyroidism, probably due to Graves' disease, and appropriate treatment was initiated with endocrine follow-up. There are a few cases of thyrotoxicosis-associated TC in the literature, suggesting thyroxine-related sensitization of the myocytes to catecholamines as the possible mechanism.⁷ However, in our patient, we saw a complete recovery of biventricular systolic function within 8 days of her admission, despite ongoing rising thyroxine levels (prior to initiation of carbimazole), thus the extent to which thyrotoxicosis contributed to TC in our patient is difficult to ascertain.

The exact aetiology of TC is unclear but there is evidence that patients with TC have higher levels of circulating catecholamines, which are released during emotional and physiological stress.^{2,8} Our patient had a number of known precipitants of TC, including a recent bereavement, anxiety, smoking history, and previous alcoholism.^{1,9} In addition, she was also found to be thyrotoxic due to a new diagnosis of Graves' disease.

Our patient's presentation carried previously reported high-risk features that have been associated with poor in-hospital outcome, i.e. tachycardia, persistent ST-segment elevation and RV involvement.¹⁰ The management of TC is largely supportive and is parallel to the management of acute heart failure and arrhythmia.¹⁰ Patients may need inotropic support to maintain BP, as was the case with our patient.

Lead author biography



Dr Megha Agarwal is a Cardiology Registrar, training in the Oxford Deanery. She has an interest in heart failure, academia and medical education.

Supplementary material

[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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