

A life-threatening reverse Takotsubo syndrome in a young breastfeeding woman: a case report

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Background

Takotsubo syndrome (TTS) is characterized by transient left ventricular (LV) dysfunction and is usually triggered by emotional, physical, or combined stress. This syndrome has been increasingly recognized, although it remains a challenging and often misdiagnosed disorder.

Case summary

A 36-year-old breastfeeding woman was admitted with sudden dyspnoea and oppressive chest pain. On admission, she was lethargic, hypotensive, and tachycardic. The electrocardiogram showed rapid atrial fibrillation and diffuse ST-segment depression. The transthoracic echocardiogram (TTE) revealed severe LV systolic dysfunction, with midventricular and basal akinesis, compensatory apical hyperkinesia, and without intraventricular gradient. Emergent coronary angiogram showed normal coronary arteries. A presumptive diagnosis of reverse TTS with cardiogenic shock (CS) was made. The patient was transferred to the intensive care unit after intubation and inotropic and vasopressor support was initiated. During hospitalization, rapid clinical improvement was observed. In 3 days, the patient was weaned from haemodynamic support and extubated. Furthermore, β -blocker and angiotensin receptor blocker were initiated and tolerated. Cabergoline was also administered to inhibit lactation. The presumptive diagnosis was further strengthened by cardiac magnetic resonance and all triggering factors were excluded. At hospital discharge she was asymptomatic and the follow-up TTE was normal, which confirmed the diagnosis of reverse TTS.

Discussion

We present a case of a young woman, 8 months after delivery, which developed a life-threatening reverse TTS without triggering factor identified. Reverse TTS is a rare variant of TTS with different clinical features and is more likely to be complicated by pulmonary oedema and CS.

Keywords

Case report • Reverse Takotsubo syndrome • Cardiogenic shock • Breastfeeding

Learning points

- Reverse Takotsubo syndrome (TTS) is a rare variant of TTS with different clinical features, including younger age, lower brain natriuretic peptide values, less impaired ejection fraction, and more frequent ST-segment depression.
- Reverse TTS is more likely to be complicated by pulmonary oedema and cardiogenic shock.
- Breastfeeding remains controversial in patients with heart failure.

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Introduction

Takotsubo syndrome (TTS), also known as ‘broken-heart syndrome’ or ‘stress cardiomyopathy’ was first described in 1983 in a 64-year-old Japanese female.^{1,2} Through the years, this syndrome has been increasingly recognized, although it remains a challenging and often misdiagnosed disorder.³ Takotsubo syndrome is characterized by transient left ventricular (LV) dysfunction and is usually, but not obligatory, triggered by emotional, physical, or combined stress.²

Although the exact pathophysiological mechanisms are incompletely understood, current evidence suggests that acute release of catecholamines from the sympathetic nerves, the adrenal medulla, or drug therapy could be central to its pathogenesis.^{2,4,5}

Based on the distribution of regional wall motion abnormalities this syndrome can be divided into typical variant (apical ballooning), which occurs in ~80% of cases,⁶ and atypical variants.

The atypical variants are uncommon and include the midventricular, reverse, isolated right ventricular, focal wall motion patterns, and global form variants.²

Nowadays, TTS represents ~2% of suspected cases of acute coronary syndrome.⁷ The proportion of reverse TTS varies in published literature. In an extensive study, which analysed 1750 patients from the International Takotsubo Registry, only 2.2% had reverse TTS.⁸

We report a case of 36-year-old woman with life-threatening reverse TTS.

Timeline

Time	Events
1st day of hospitalization	Presented with dyspnoea, palpitations and oppressive chest pain Patient was intubated and haemodynamic support was initiated Echocardiogram: severe left ventricular (LV) systolic dysfunction; midventricular and basal ballooning Coronary angiogram: normal coronary arteries Admitted on intensive care unit with cardiogenic shock probably induced by reverse Takotsubo syndrome
4th day of hospitalization	Transferred to the Cardiology ward extubated and without haemodynamic support Cabergoline was administered to inhibit lactation
5th day of hospitalization	β-blocker and angiotensin receptor blocker were initiated

Continued

Continued

Time	Events
6th day of hospitalization	Cardiac magnetic resonance (cMR): no late gadolinium enhancement (LGE)
10th day of hospitalization	Echocardiogram: normal LV function, without segmental kinetic changes
6 months after hospital discharge	Echocardiogram: normal LV function, without segmental kinetic changes
1 year after hospital discharge	cMR: no LGE

Case presentation

A 36-year-old woman, 8 months after delivery and still breastfeeding, with no other relevant medical history and no regular medication, was admitted to the emergency department with sudden dyspnoea, palpitations, and oppressive chest pain radiating to her left shoulder for more than 1 h.

In the previous weeks she was asymptomatic, without fever or infectious symptoms. She denied recent emotional or traumatic events. She also denied regular or recent medication. There was no relevant family history, regarding cardiovascular diseases or autoimmune disorders.

On admission, the patient was lethargic, diaphoretic, hypotensive (systolic heart pressure of 60 mmHg), and tachycardic (rate of 145 b.p.m.). The physical exam revealed apical systolic murmur of 2/6 in the Levine scale and pulmonary crackles. The remaining physical examination was unremarkable.

The 12-lead electrocardiogram revealed an atrial fibrillation with rapid ventricular response, left anterior hemiblock, poor anteroseptal R-wave progression, diffuse ST-segment depression, and normal QTc (Figure 1). Considering the haemodynamic instability, she underwent a successful electrical cardioversion. However, there was not a significant clinical improvement with reversal to sinus rhythm.

The transthoracic echocardiogram (TTE) revealed normal cardiac chambers, normal right ventricular function, severe LV systolic dysfunction with midventricular and basal akinesis as well as compensatory apical hyperkinesis. Besides that, it also showed moderate mitral regurgitation, low cardiac output (3 L/min), and excluded intraventricular gradient (Video 1).

Due to haemodynamical impairment, the patient was intubated and inotropic support with dobutamine combined with dopamine was initiated due to systolic heart pressure lower than 90 mmHg.

Admission laboratory findings showed a haemoglobin of 15 g/dL [normal range (NR): 11.9–15.9 g/dL], normal white cell blood count, normal renal function, negative C-reactive protein, elevated myocardial necrosis markers (troponin I level of 9.6 ng/mL, NR: <0.045 ng/mL, which peaked in 24 h to 12 ng/mL) and slightly elevated N-terminal brain natriuretic peptide (250 pg/mL, NR: <125 pg/mL). In addition, these also showed type 2 respiratory failure, metabolic and respiratory acidosis (pO₂ 55 mmHg, NR: 75–100 mmHg; pCo₂ 48 mmHg,

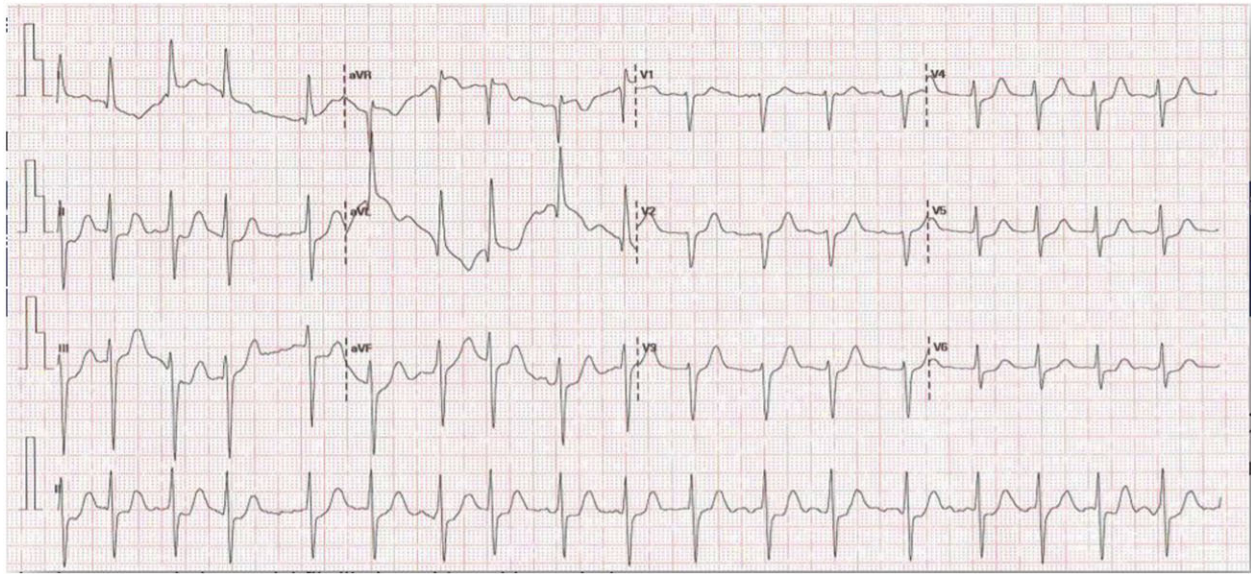
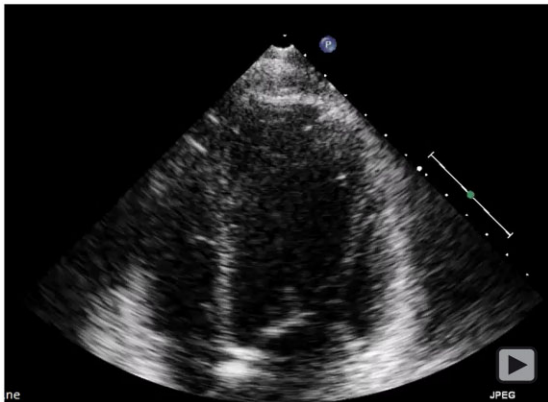
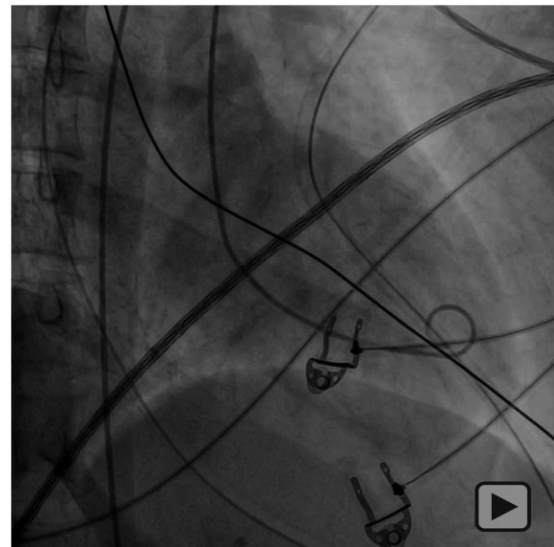


Figure 1 Admission electrocardiogram.



Video 1 Admission transthoracic echocardiogram which revealed a severe left ventricular systolic dysfunction, with midventricular and basal akinesis and compensatory apical hyperkinesis.



Video 2 Coronary angiogram which revealed normal coronary arteries.

NR: 35–46 mmHg; HCO₃⁻: 19.7 mmol/L, NR: 21–26 mmol/L; pH 7.2, NR: 7.37–7.45), and hyperlactatemia (3 mmol/L, NR: 0.5–2 mmol/L).

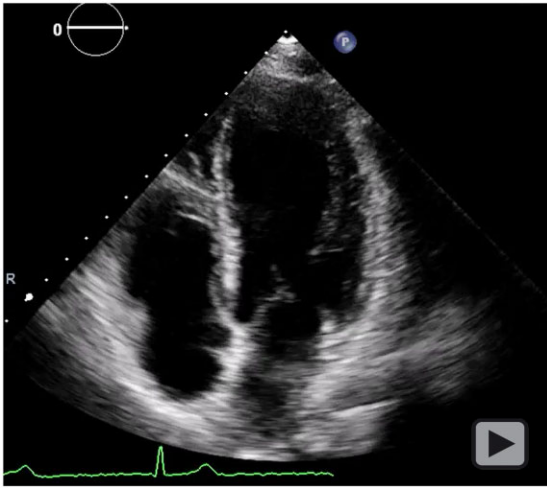
Considering the deterioration of the patient's condition, an emergent coronary angiogram and a ventriculography were performed. These revealed normal coronary arteries ([Video 2 and 3](#)) and the same segmental kinetic changes shown on TTE ([Supplementary material online, Video S1](#)).

Additionally, a thoracic computed tomography (CT) showed diffuse bilateral ground-glass opacification suggestive of acute decompensated heart failure (HF). Both pulmonary embolism and acute aortic syndrome were excluded.

In summary, the patient was initially transferred to the intensive care unit with cardiogenic shock (CS) probably induced by reverse TTS. In 3 days, she was progressively weaned from haemodynamic support, extubated, and transferred to the Cardiology ward.

During the hospitalization, considering the initial differential diagnosis of peripartum cardiomyopathy and the need to initiate HF therapy was administered cabergoline 0.25 mg twice a day for 2 days.

Moreover, after haemodynamic stabilization, low doses of β -blocker and angiotensin receptor blocker (ARB) were initiated and tolerated.



Video 3 Coronary angiogram which revealed normal coronary arteries.

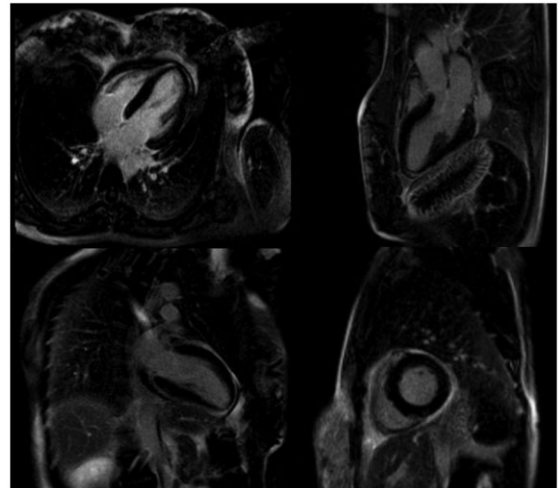


Figure 2 Cardiac magnetic resonance showed no late gadolinium enhancement.

On the sixth day of hospitalization, the presumptive diagnosis was further strengthened by a cardiac magnetic resonance (cMR), which showed improvement of the LV function with residual basal and

midventricular hypokinesia, light oedema, and no late gadolinium enhancement (LGE) on the affected segments ([Figures 2 and 3](#)).

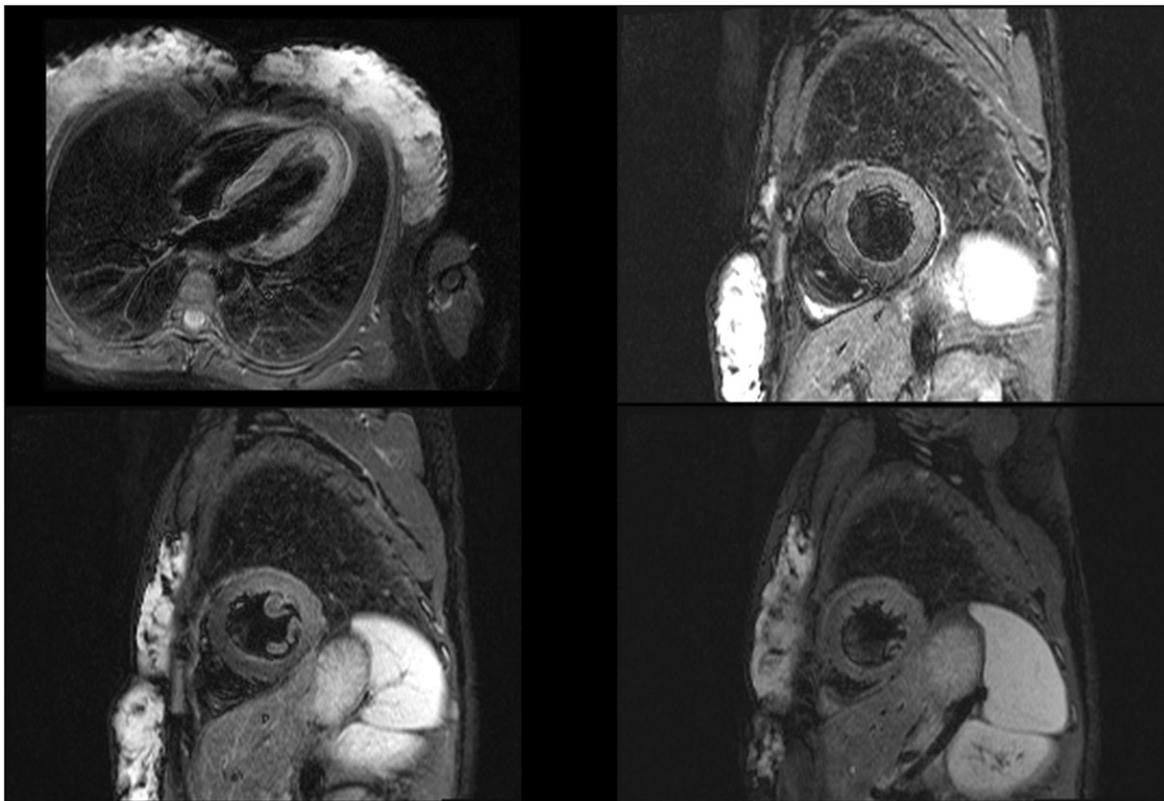


Figure 3 Cardiac magnetic resonance showed light oedema in basal and midventricular segments.

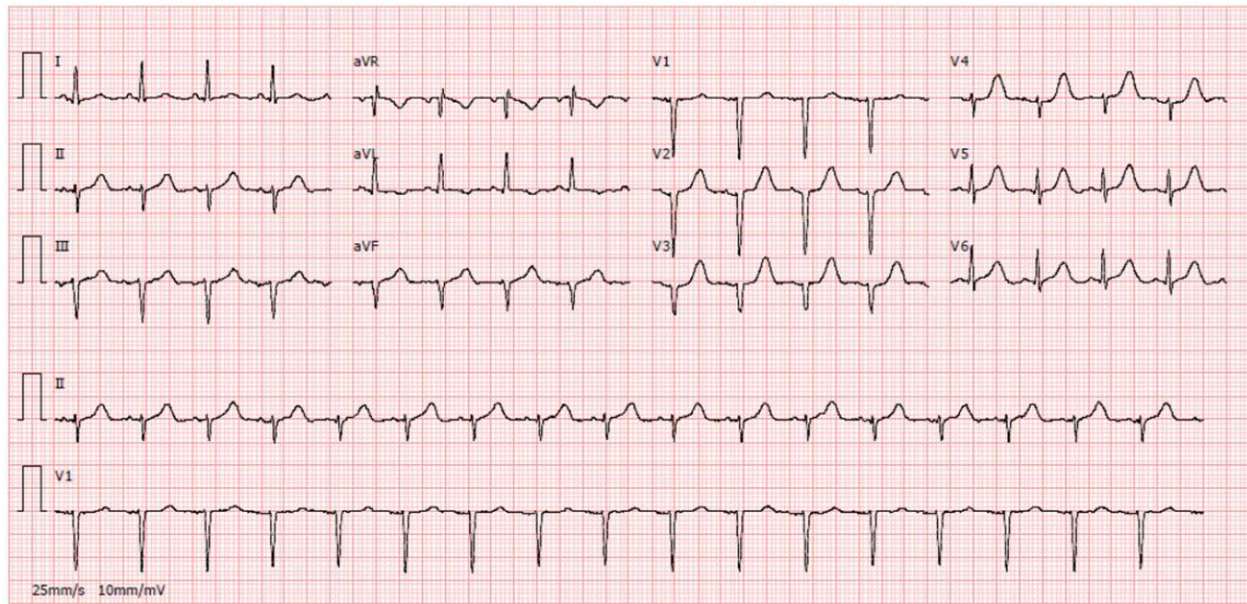


Figure 4 Electrocardiogram during hospitalization.

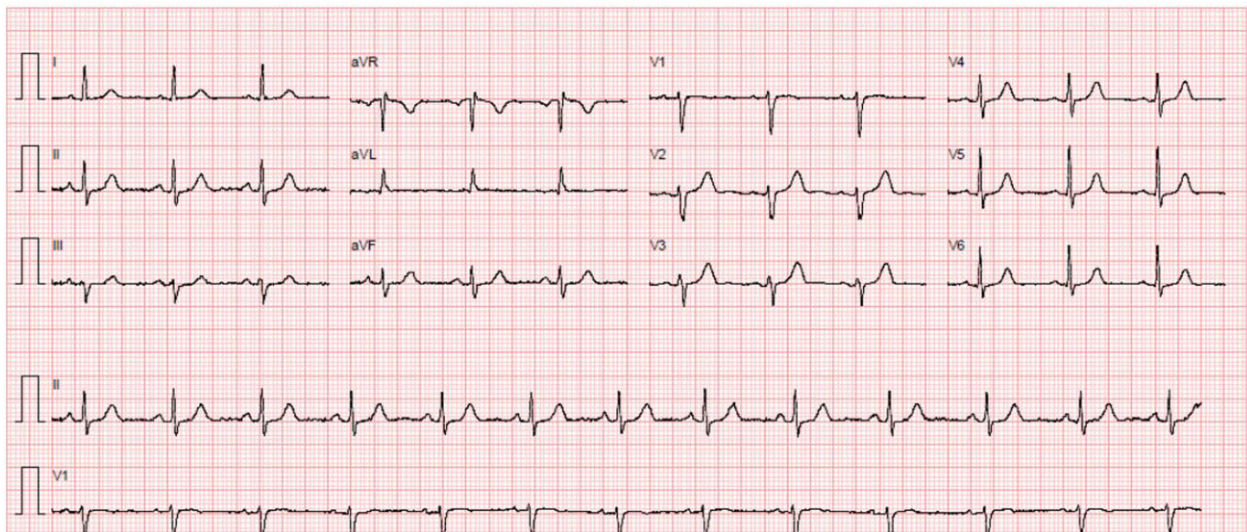


Figure 5 Follow-up electrocardiogram.

In order to try to identify the triggering factor, the patient was submitted to an extensive study.

She underwent a cranioencephalic and abdominal CT, which excluded cerebral anomalies and morphologic alterations in adrenal gland.

Furthermore, she had normal levels of urinary metanephrines (520 $\mu\text{g}/24\text{ h}$, NR: $<785\ \mu\text{g}/24\text{ h}$) which excluded pheochromocytoma, and normal levels of thyroid-stimulating hormone (0.883 $\mu\text{UI}/\text{mL}$,

NR: 0.55–4.78 $\mu\text{UI}/\text{mL}$), free thyroxine (1.2 ng/dL, NR: 0.89–1.76 ng/dL), and free triiodothyronine (3.4 pg/mL; NR: 2.3–4.2 pg/mL) which excluded postpartum thyroiditis.

In addition, the polymerase chain reaction for herpesvirus 6, parvovirus B9 deoxyribonucleic acid, and enterovirus ribonucleic acid were negative. The human immunodeficiency virus, hepatitis B and C virus, and respiratory virus serologies tests were negative and the results of the following immunoglobulin M were also negative:

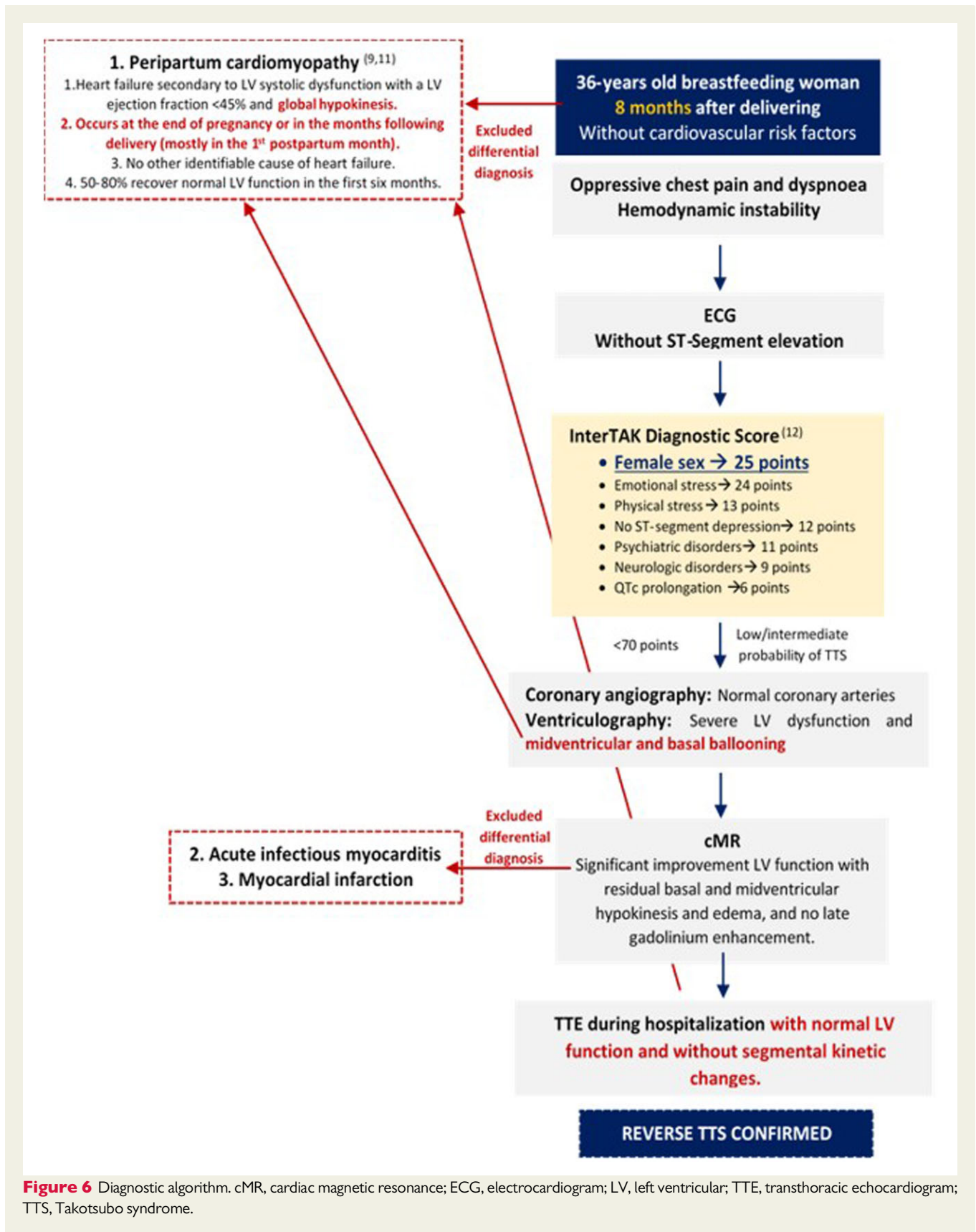


Figure 6 Diagnostic algorithm. cMR, cardiac magnetic resonance; ECG, electrocardiogram; LV, left ventricular; TTE, transthoracic echocardiogram; TTS, Takotsubo syndrome.

cytomegalovirus, herpes simplex virus, adenovirus, Epstein–Barr virus, and toxoplasmosis.

Moreover, a postpartum depression was excluded after a psychiatric evaluation.

During hospitalization, serial 12-lead electrocardiograms showed sinus rhythm, left anterior hemiblock, poor anteroseptal R-wave progression with QT interval prolongation, however, without T-wave inversion (Figure 4).

On the 10th day of hospitalization, the patient repeated the TTE and the LV function was normal, without segmental kinetic changes or valvulopathies (Supplementary material online, Video S2).

The patient was discharged with the final diagnosis of reverse TTS without triggering factor and medicated with β -blocker and ARB, in maximum tolerated doses.

She was evaluated in cardiology consultation 1 month, 6 months, and 1 year after hospital discharge. She remained asymptomatic and without rehospitalizations.

The follow-up TTE revealed normal LV function without kinetic segmental changes. Furthermore, the follow-up 12-lead electrocardiogram showed a sinus rhythm with normal QRS axis, normal R-wave progression, and QT interval (Figure 5). In addition, the patient repeated the cMR which confirmed the follow-up TTE findings and excluded oedema as well as LGE.

Discussion

We present a case of a young woman, 8 months after delivery, who was admitted to our emergency department with sudden CS of unknown cause.

The diagnostic approach is summarized in Figure 6.

In view of recent delivery, peripartum cardiomyopathy was considered. This disease is defined by 2019 position statement from HF Association of the European Society of Cardiology Study Group as HF secondary to LV systolic dysfunction and global hypokinesia, which occurs at the end of pregnancy or in the months following delivery, with no other identifiable cause.⁹ Although the current definition does not include the limit of postpartum months, it highlights the first month while previous definitions included up to 5 months after delivery.^{10,11} Additionally, our patient had midventricular and basal ballooning, instead of global hypokinesia. She also had a fast LV function recovery, not characteristic of peripartum cardiomyopathy.

Furthermore, in this singular case we decided to administer cabergoline to inhibit lactation, a dopamine receptor agonist on D2-receptors, with higher affinity for D2-receptors, longer half-life, and less adverse effects than bromocriptine.

Currently, many HF drugs are compatible with breastfeeding if used with caution, although lactation and breastfeeding remain controversial due to its high metabolic demands. The decision on whether to inhibit lactation should be shared and should always take into consideration both the health of the mother and of the infant. In our case, the infant was 8-month-old and had already started solid food, which made the decision easier.

For diagnosis we followed the InterTAK Diagnostic Criteria and at admission our patient scored 25 points.¹² This revealed a low probability for TTS, due to which an emergent coronary angiography was performed, that excluded coronary artery disease. In the subacute phase,

the patient underwent cMR, which strengthened the presumptive diagnosis of reverse TTS besides excluding the diagnosis of myocardial infarction and acute infectious myocarditis. On the 10th day of hospitalization, the TTE was normal, and the diagnosis was confirmed.

The transient nature of the electrocardiographic abnormalities (left anterior hemiblock, poor anteroseptal R-wave progression, and QT interval prolongation) also corroborated the diagnosis of TTS as reversibility is one of the cornerstones of this pathology.

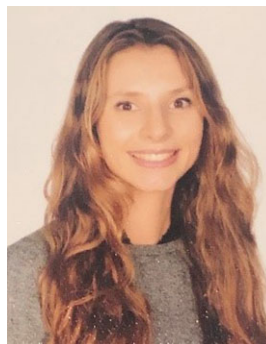
After an extensive study, no triggering factor was found.

Reverse TTS is a rare variant of TTS (2.2% of cases)⁸ and appears usually in patients with pheochromocytoma, subarachnoid haemorrhage, or epinephrine-induced TTS.¹² This variant has different clinical features, including younger age, lower brain natriuretic peptide values, less impaired ejection fraction, and more frequent ST-segment depression. Furthermore, it is more likely to be complicated by pulmonary oedema and CS. However, recurrence rates and follow-up outcomes are like typical TTS.⁷

We consider that InterTAK Diagnostic Criteria is less likely to identify this atypical variant because it includes non-ST-segment depression as an important criterion (1/7: 12 points). However, in this case, the absence of identifiable trigger and the normal QT interval at admission were also responsible for a lower admission score.

In summary, TTS remains a challenging diagnosis not as benign as initial thought. This case represents a rare variant, with atypical manifestations and a recent history of delivery as confounding factor.

Lead author biography



Carla Marques Pires (born on 1 April 1992) is a Cardiology resident at Braga Hospital, Portugal. She did her integrated master's in medicine in School of Health Sciences, University of Minho, Braga with a final score of 17 values (out of 20). In addition to her clinical activities, she is a researcher at the Clinical Academic Center of Braga Hospital and collaborates as a Lecturer in clinical practice classes of integrated master's in medicine in School of Health Sciences, University of Minho.

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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