

# A case report: ‘happy heart’ syndrome in a patient treated with atomoxetine for attention deficit hyperactivity disorder

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## Background

Takotsubo syndrome (TS) is an acute cardiac disease entity with a clinical presentation resembling that of an acute coronary syndrome. Numerous physical stress factors including pheochromocytoma, epinephrine, and norepinephrine administration, and even physiological exercise have been reported to induce TS. Takotsubo syndrome induced by medications causing elevation of plasma norepinephrine as serotonin-norepinephrine reuptake inhibitor or selective norepinephrine reuptake inhibitor (atomoxetine) has been reported.

## Case summary

We report on the case of a 49-year-old woman who was on atomoxetine treatment for attention deficit hyperactivity disorder, developed TS in association with sexual intercourse.

## Discussion

The TS pattern in this patient was the type of mid-apical ballooning with apical tip-sparing at presentation. Two days later, TS evolved to mid-ventricular pattern. Takotsubo syndrome resolved completely 1 month after the index presentation.

## Keywords

Case report • Atomoxetine • Takotsubo syndrome • Happy Heart

## Learning points

- A woman treated with a selective norepinephrine reuptake inhibitor (atomoxetine) developed Takotsubo syndrome (TS) during sexual intercourse.
- Initial left ventricular mid-apical ballooning pattern with apical tip-sparing evolved to mid-ventricular TS, which recovered completely 1 month after index presentation.

## Introduction

Takotsubo syndrome (TS) is an acute cardiac disease entity with a clinical presentation resembling that of an acute coronary syndrome.<sup>1–3</sup> The disease is characterized by a transient left ventricular wall motion

abnormality with regional distribution resulting in a conspicuous ballooning of the left ventricle during systole.<sup>4</sup> It affects predominantly women and is often preceded by emotional or physical stress.<sup>1,3,4</sup> Countless physical stress factors including pheochromocytoma,<sup>5</sup> epinephrine,<sup>6</sup> and norepinephrine<sup>7</sup> administration, and even physiological exercise have been reported as a trigger factor for TS.<sup>1,3</sup> Takotsubo syndrome induced by exogenously administered norepinephrine or medications causing elevation of plasma norepinephrine as serotonin-norepinephrine reuptake inhibitor or selective norepinephrine reuptake inhibitor (S-NRI) (atomoxetine) has been reported.<sup>7</sup> To our knowledge, only two cases of atomoxetine-triggered TS have been described.<sup>7</sup> Herein, we report on the case of a 49-year-old woman who was on atomoxetine treatment for attention deficit hyperactivity disorder (ADHD) and developed TS in association with sexual intercourse.

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## Timeline

| Symptoms  | Clinical examination   | Laboratory findings  | Initial treatment   | Clinical investigation   | Final treatment   | Follow-up and outcome   |
|---|--|--|---|--|---|---|
| <b>Day 1</b>  |  |  |   | <b>Day 2–3</b>   |   |   |
| Chest pain, dyspnoea, and dizziness in association with sexual intercourse in a woman treated with atomoxetine for attention deficit hyperactivity disorder | Blood pressure 120/94 mmHg<br>Electrocardiogram with no remarkable changes | Troponin 710 ng/L<br>Echocardiography showed mid-apical ballooning with apical tip-sparing, good basal contraction, and markedly depressed left ventricular ejection fraction (30–35%) | Atomoxetine discontinued and treatment with acetylsalicylic acid, beta-blocker, and angiotensin-converting enzyme inhibitor was initiated | Invasive coronary angiography revealed normal coronary arteries<br>New echocardiography showed findings typical for mid-ventricular takotsubo syndrome | Acetylsalicylic acid, beta-blocker, and angiotensin-converting enzyme inhibitor | Patient clinically recovered<br>Cardiac magnetic resonance imaging showed complete resolution of the left ventricular wall motion abnormality; there was no late gadolinium enhancement |

## Case presentation

A 49-year-old woman presented with acute chest pain. The past history was not remarkable apart from being treated with thyroxine 125 µg o.d. for hypothyroidism, pregabalin 150 mg b.i.d. for chronic neurogenic back pain, and atomoxetine 60 and 18 mg daily for ADHD. In association with sexual intercourse, she developed acute chest pain associated with mild dyspnoea and some dizziness. The chest pain disappeared after sublingual nitroglycerine on admission to the hospital. The patient developed transient hypotension and bradycardia after nitroglycerine, which stabilized after atropine injection. The electrocardiogram (*Figure 1*) revealed no remarkable changes. Laboratory results showed modest elevation of troponin T (maximum 710 ng/L), C-reactive protein <5 mg/L, and normal cholesterol levels. Echocardiography 1 day after admission revealed a-/hypokinesia in the mid-apical regions with good contraction of the apical tip segment (apical tip-sparing) and the basal segments with marked reduction of left ventricular ejection fraction, 30–35% ([Supplementary material online, Video S1](#), echocardiography). Atomoxetine was discontinued and treatment with acetylsalicylic acid, beta blocker, and angiotensin-converting enzyme inhibitor was initiated. Invasive coronary angiography 1 day after admission showed normal coronary arteries (*Figure 2A and B*; [Supplementary material online, Video S2](#), left coronary artery). A new echocardiography 3 days after admission showed a-/hypokinesia in the middle segments of the left ventricle circumferentially, with good contractions in both the basal and apical segments resulting in a pattern consistent with mid-ventricular TS ([Supplementary material online, Video S3](#), contrast echocardiography). Left ventricular systolic function recovered completely within 1 month from admission as demonstrated by cardiac magnetic resonance imaging, which did not show late gadolinium enhancement

([Supplementary material online, Video S4](#), cardiac magnetic resonance imaging).

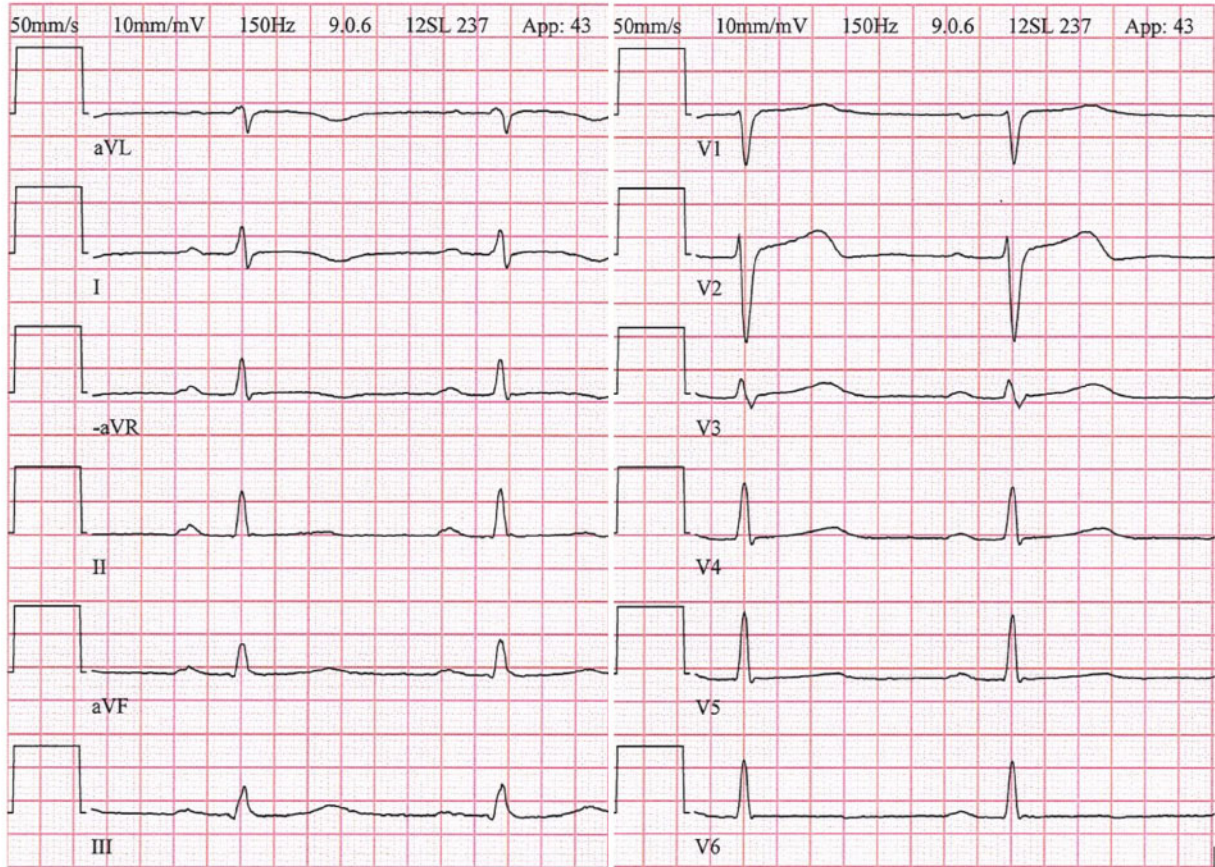
## Discussion

We present a case of a woman treated with atomoxetine for ADHD who developed TS following sexual intercourse ('happy heart' syndrome). The TS had a mid-apical pattern with apical tip-sparing ([Supplementary material online, Video S1](#), echocardiography), which evolved to typical mid-ventricular TS pattern 2 days later ([Supplementary material online, Video S3](#), contrast echocardiography). Of 1750 TS patients, Ghadri *et al.*<sup>8</sup> identified a total of 485 TS patients with a definite emotional trigger factor. Of these, 20 TS patients (4.1%) presented with pleasant preceding events. The mid-ventricular TS pattern was more prevalent among the 'happy hearts' than among the 'broken hearts'. Our patient had also mainly mid-ventricular involvement.

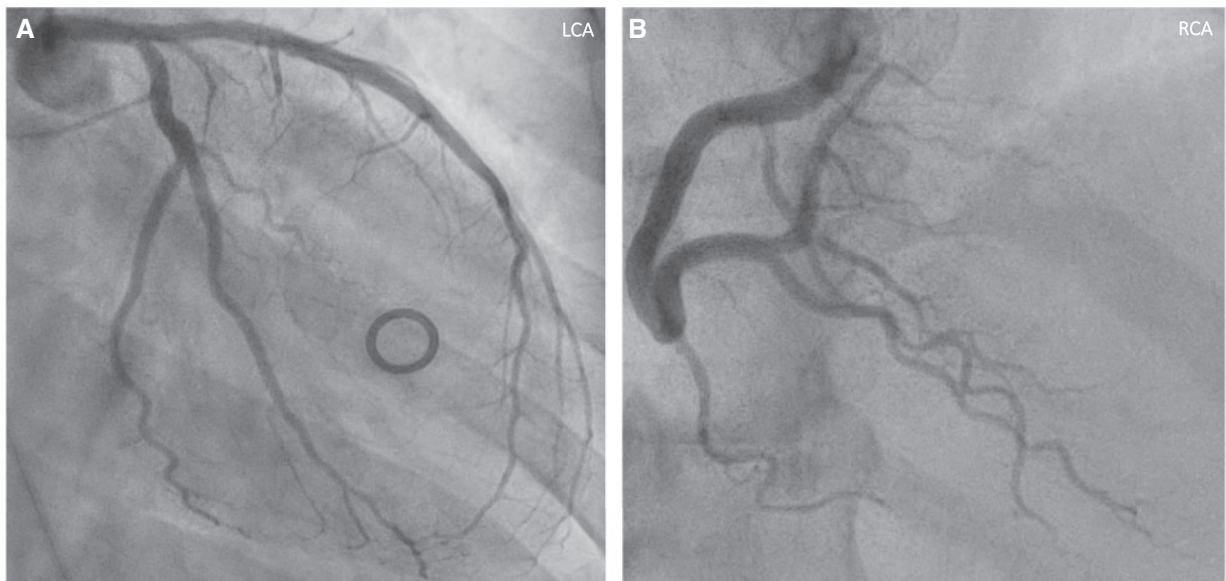
Atomoxetine, a S-NRI used for the treatment of ADHD,<sup>9</sup> has been reported to trigger TS.<sup>7</sup> To our knowledge, two cases of documented atomoxetine-triggered TS have been reported (*Table 1*). Both cases<sup>10,11</sup> developed apical TS pattern after increasing the dose of atomoxetine. In our case, atomoxetine dose was not increased before the index presentation, but further physical stress could have triggered TS.

## Conclusion

A case of 'happy heart' syndrome triggered by a lovely physical activity in a woman who was treated with atomoxetine for ADHD is described. The TS pattern was of mid-apical ballooning with apical



**Figure 1** The 12 leads electrocardiogram shows sinus rhythm. No remarkable changes are seen.



**Figure 2** Left coronary artery in (A) and right coronary artery in (B) showed no signs of obstructive coronary artery disease.

**Table 1** Clinical features on admission, in-hospital complications and outcome in the three known patients with atomoxetine-induced TS

| Authors          | Year | Age, years | Gender | S-NRI, trigger factor           | Reasons for S-NRI administration  | Presenting symptoms, manifestations | TS localization/time (where available)                         | Complications   | Recovery/time |
|------------------|------|------------|--------|---------------------------------|---|-------------------------------------|--|---|---------------|
| Yamaguchi et al. | 2014 | 11         | Male   | Atomoxetine                     | Dose increased for ADHD   | Loss of consciousness, bradycardia  | Apical   | Long QT time (829 ms), need of pacemaker 4 days later | Yes/2 weeks   |
| Naguy et al.     | 2016 | 26         | Female | Atomoxetine                     | Dose increased to 40 mg b.i.d. for ADHD; the patient continued fluoxetine treatment | Chest pain and dyspnoea             | Apical   | No  | Yes/5 weeks   |
| Current case     | 2019 | 49         | Female | Atomoxetine, sexual intercourse | ADHD  | Chest pain, dyspnoea and dizziness  | Mid-apical (apical tip sparing), Day 1; mid-ventricular, Day 3 | No  | Yes/4 weeks   |

ADHD, attention-deficit hyperactivity disorder; S-NRI, selective norepinephrine reuptake inhibitor; TS, takotsubo syndrome.

tip-sparing at presentation, which evolved to mid-ventricular pattern 2 days later and recovered completely 1 month after admission.

## Lead author biography



Dr Petros Athanassopoulos BSc, MD, PhD, is a Consultant Cardiologist at the Karolinska University Hospital in Stockholm, Sweden. Dr Athanassopoulos has an international clinical- and research-background in Vascular Medicine, Heart Failure (HF) and Heart Transplantation. He received his

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## 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 author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** none declared.

## References

- Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, Cammann VL, Crea F, Galiuto L, Desmet W, Yoshida T, Manfredini R, Eitel I, Kosuge M, Nef HM, Deshmukh A, Lerman A, Bossone E, Citro R, Ueyama T, Corrado D, Kurisu S, Ruschitzka F, Winchester D, Lyon AR, Omerovic E, Bax JJ, Meimoun P, Tarantini G, Rihal C, Y.-Hassan S, Migliore F, Horowitz JD, Shimokawa H, Lüscher TF, Templin C. International Expert Consensus Document on Takotsubo Syndrome (Part I): clinical characteristics, diagnostic criteria, and pathophysiology. *Eur Heart J* 2018;**39**:2032–2046.
- Y-Hassan S, Tornvall P. Epidemiology, pathogenesis, and management of takotsubo syndrome. *Clin Auton Res* 2018;**28**:53–65.
- Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, Cammann VL, Crea F, Galiuto L, Desmet W, Yoshida T, Manfredini R, Eitel I, Kosuge M, Nef HM, Deshmukh A, Lerman A, Bossone E, Citro R, Ueyama T, Corrado D, Kurisu S, Ruschitzka F, Winchester D, Lyon AR, Omerovic E, Bax JJ, Meimoun P, Tarantini G, Rihal C, Y.-Hassan S, Migliore F, Horowitz JD, Shimokawa H, Lüscher TF, Templin C. International Expert Consensus Document on Takotsubo Syndrome (Part II): diagnostic workup, outcome, and management. *Eur Heart J* 2018;**39**:2047–2062.
- Y-Hassan S, De Palma R. Contemporary review on the pathogenesis of takotsubo syndrome: the heart shedding tears: Norepinephrine churn and foam at the cardiac sympathetic nerve terminals. *Int J Cardiol* 2017;**228**:528–536.
- Y-Hassan S. Clinical features and outcome of pheochromocytoma-induced takotsubo syndrome: analysis of 80 published cases. *Am J Cardiol* 2016;**117**:1836–1844.

6. Y-Hassan S. Clinical features and outcome of epinephrine-induced takotsubo syndrome: analysis of 33 published cases. *Cardiovasc Revasc Med* 2016;**17**: 450–455.
7. Y-Hassan S. Serotonin norepinephrine re-uptake inhibitor (SNRI)-, selective norepinephrine reuptake inhibitor (S-NRI)-, and exogenously administered norepinephrine-induced takotsubo syndrome: Analysis of published cases. *Int J Cardiol* 2017;**231**:228–233.
8. Ghadri JR, Sarcon A, Diekmann J, Bataiosu DR, Cammann VL, Jurisic S, Napp LC, Jaguszewski M, Scherff F, Brugger P, Jäncke L, Seifert B, Bax JJ, Ruschitzka F, Lüscher TF, Templin C. Happy heart syndrome: role of positive emotional stress in takotsubo syndrome. *Eur Heart J* 2016;**37**:2823–2829.
9. Garnock-Jones KP, Keating GM. Atomoxetine: a review of its use in attention-deficit hyperactivity disorder in children and adolescents. *Paediatr Drugs* 2009;**11**:203–226.
10. Yamaguchi H, Nagumo K, Nakashima T, Kinugawa Y, Kumaki S. Life-threatening QT prolongation in a boy with attention-deficit/hyperactivity disorder on atomoxetine. *Eur J Pediatr* 2014;**173**:1631–1634.
11. Naguy A, Al-Mutairi H, Al-Tajali A. Atomoxetine-related Takotsubo Cardiomyopathy. *J Psychiatr Pract* 2016;**22**:232–233.