European Journal of Case Reports in Internal Medicine

Takotsubo Cardiomyopathy Due to Combined Use of Phentermine and Lisdexamfetamine

Tara Burleigh, Birgit Khandalavala
Department of Family Medicine, University of Nebraska Medical Center, Omaha, NE, USA

Doi: 10.12890/2020_001595 - European Journal of Case Reports in Internal Medicine - © EFIM 2020

Received: 24/02/2020
Accepted: 11/03/2020
Published: 04/05/2020

How to cite this article: Burleigh T, Khandalavala B. Takotsubo cardiomyopathy due to combined use of phentermine and lisdexamfetamine. *EJCRIM* 2020;**7**: doi:10.12890/2020_001595.

Conflicts of Interests: The Authors declare that there are no competing interests.

ABSTRACT

Objectives: This is the first case report of iatrogenic Takotsubo syndrome (TS) due to a combination of lisdexamfetamine and phentermine.
Background: TS is characterized by transient acute ballooning of the left ventricular wall. Typically, it occurs in extremely stressed post-menopausal women, however a few iatrogenic causes have been described recently.
Results: A 55-year old woman prescribed lisdexamfetamine and phentermine, presented with acute substernal chest pain. Acute coronary syndrome was excluded. The echocardiogram was diagnostic of TS, and she recovered spontaneously, with supportive care.
Conclusion: Caution with the use of sympathomimetic medications in post-menopausal women appears warranted.

LEARNING POINTS

- This is the first case report in the published English literature of medication-induced Takotsubo cardiomyopathy due to combination use of lisdexamfetamine and phentermine.
- This provides new information about iatrogenic causes of Takotsubo cardiomyopathy.
- Caution is indicated in the use of such medications, particularly in post-menopausal women, who are at higher risk.

KEYWORDS

Phentermine, Takotsubo disease, lisdexamfetamine, sympathetic overstimulation

INTRODUCTION

Takotsubo cardiomyopathy (TC) or 'broken-heart syndrome' is a transient disease of the myocardium with ballooning of the left ventricular wall during the acute phase [1,2]. The bulging abnormality on imaging resembles an ancient Japanese vessel (tako-tsubo) used to trap octopuses. TC is also referred to as apical ballooning syndrome or stress-induced cardiomyopathy [1]. The condition is increasingly being recognized, and is thought to occur as a result of overstimulation of the sympathetic nervous system leading to temporary cardiac distention of the left ventricle [1]. Mostly women under conditions of extreme emotional or physical stress [3] appear to be impacted. Stimulant medications are often implicated due to sympathetic overstimulation [4]. The classic presentation mimics acute coronary syndrome and includes chest pain, shortness of breath with ST-segment elevation and elevation of serum creatine kinase [1]. Coronary angiography is required to distinguish between TC and ischaemic disease [1]. Clinical management is predominantly supportive, with outcomes and prognosis largely favourable [5]. We describe an atypical case of TC in a hospitalized 55-year-old woman, with no apparent emotional or physical triggers, who was previously prescribed an oral combination of lisdexamfetamine and phentermine daily by an external provider, apparently for binge-eating disorder and obesity.

European Journal
of Case Reports in
Internal Medicine

CASE DESCRIPTION

A 55-year-old woman presented with unprovoked substernal chest pressure radiating to the jaw, with onset 2 hours prior to arrival in the emergency department. She had been resting before this with no emotional or physical stress reported. Associated symptoms included diaphoresis, nausea and dyspnoea. Her medical history was significant for essential hypertension and obesity (BMI 45 kg/m^2). Her vital signs at the time of presentation were blood pressure 130/85 mmHg, pulse 92, respiration rate 18 bpm, body mass index (BMI) 57.13 kg/m^2, and peripheral capillary oxygen saturation (SpO_2) 96%. She was afebrile. She had been prescribed 40 mg lisdexamfetamine for the previous 1 year and 37.5 mg phentermine was added a month prior to her presentation by her prescribing psychiatrist. Both medications were prescribed apparently for the treatment of binge-eating disorder and appetite suppression.

Initial troponin was elevated to 2.02 ng/ml and peaked at 5.75 ng/ml and the electrocardiogram demonstrated an anterolateral infarct (*Fig. 1*). The patient was treated promptly with sublingual nitroglycerin and her chest pain subsided. Immediate coronary angiography did not demonstrate the presence of significant coronary atherosclerotic disease. Transthoracic echocardiography estimated a left ventricular ejection fraction of 40% and demonstrated akinesis of the apex, apical septal, apical inferior and apical lateral walls with hyperdynamic basal segments, consistent with TC (*Fig. 2*).

The patient was treated with lisinopril and carvedilol. The stimulant medications were discontinued, and the patient was discharged on hospital day 3, with complete resolution of her symptoms. An echocardiogram one month later exhibited normalization of left ventricular systolic function.

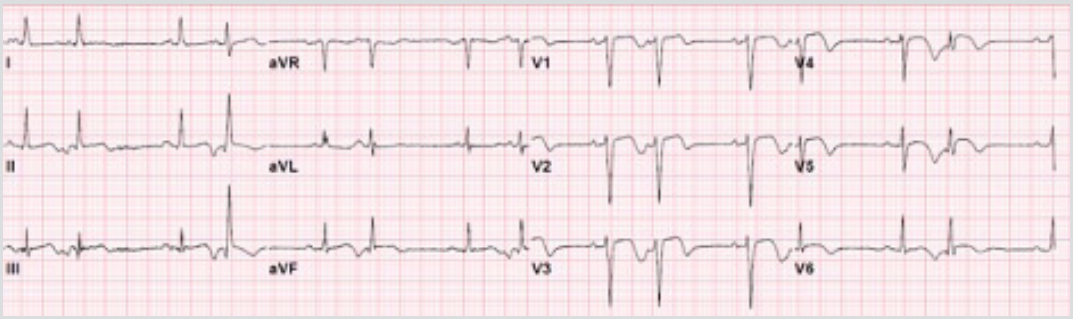

Figure 1. Echocardiogram (ECG) demonstrating myocardial ischaemia in the anterolateral distribution

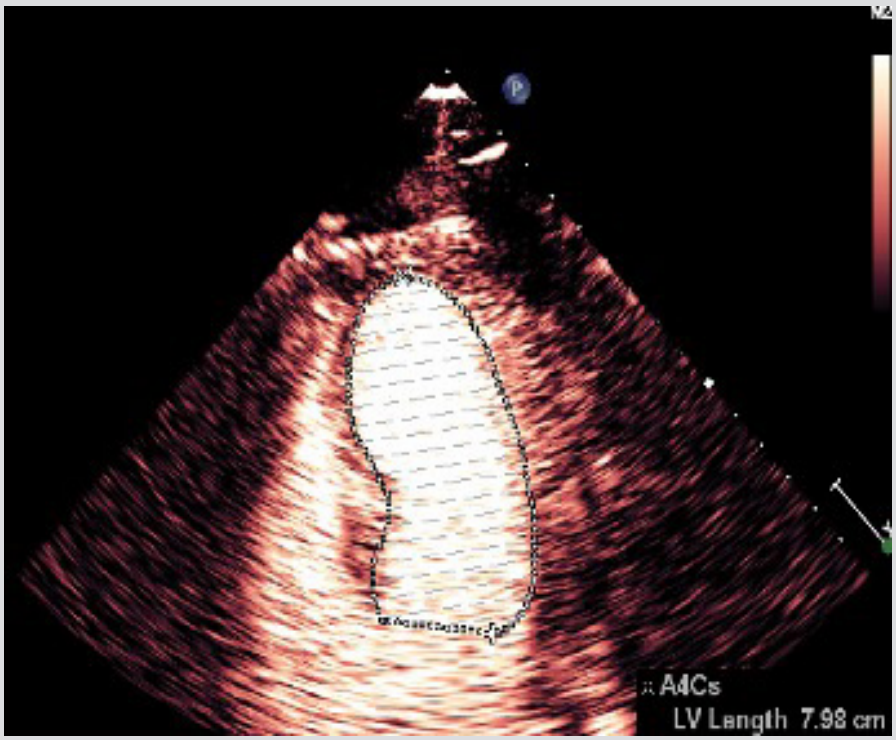

Figure 2. Transthoracic echocardiogram demonstrating apical ballooning of the left ventricle during systole, resembling the 'tako-tsubo' octopus trap

European Journal of Case Reports in Internal Medicine

DISCUSSION

This case report describes a case of iatrogenic Takotsubo cardiomyopathy induced by combination sympathomimetic medications. Takotsubo cardiomyopathy was first described in the 1990s [1], however, drug-induced disease is being increasingly reported [4, 6, 7]. While the precise aetiology of the condition is still unknown, it has been thought that overstimulation of the sympathetic nervous system causes increased contraction and ballooning of the ventricular myocardium [8]. In post-menopausal women, the reduced level of estrogen may increase vulnerability to sympathetic overstimulation [5]. Both phentermine and lisdexamfetamine are widely used sympathomimetic medications [6]. While isolated cases of monotherapy or combination stimulants causing TC are described in the literature [7, 9, 10], the combination of lisdexamfetamine and phentermine causing TC has not been previously reported in the published literature.

Clinical management is generally supportive and similar to that of standard heart failure management, with angiotensin-converting enzyme inhibitors, beta-blockers and diuretics [5]. Imaging studies are critical to establish the presence of any coronary artery disease since the presentation and features of TC and acute coronary syndrome are often indistinguishable [5]. The exclusion of ischaemic cardiac arterial disease and diagnostic echocardiography often are adequate to establish the diagnosis [5]. In this case, discontinuation of the sympathomimetic medications resulted in complete remission. Occasionally, beta-blockers are continued long term to prevent recurrence, by reducing the effects of adrenaline and other stress hormones [5]. Since this condition is transient, long-term treatment is not required. The prognosis is generally favourable with 0–10% in-hospital mortality mostly related to non-cardiac death secondary to underlying medical illness [1].

The combination of phentermine and lisdexamfetamine is not approved by the Federal Drug Agency for binge-eating disorder or obesity. However, it is well known that many medications used by psychiatrists and other providers are 'off-label', with the intent of providing benefits to the patient [11, 12]. Determination of 'off-label' use is a careful clinical decision made by an informed patient and the prescribing physician [12]. Any off-label use has to wisely balance the possible benefits and potential harms [13].

The simultaneous use of phentermine and lisdexamfetamine has not been studied and is not currently being developed as combination therapy. There certainly could be potential risks when these drugs are taken together. Reports of serotonin syndrome and cardiac toxicity have been seen with the use of lisdexamfetamine and other medications, particularly the selective serotonin reuptake inhibitors. Since both are stimulants with increased common cardiovascular side effects, it is unlikely that this combination is being reviewed for widespread use or should be encouraged.

CONCLUSION

This case report highlights the risk of Takotsubo cardiomyopathy with the use of sympathomimetic drugs. Family practice providers should be aware of the distinction between the TC and acute coronary syndrome since the clinical presentation can be identical, yet the management and prognosis are significantly different. Caution with the use of sympathomimetic medications is imperative, particularly in women at risk. When clinicians are prescribing drugs with adrenergic effects, combinations of such drugs should preferably be avoided, or prescribed at the lowest effective dose for the shortest duration, with close monitoring, to prevent potential adverse cardiac side effects.

REFERENCES

1. Ono R, Falcão LM. Takotsubo cardiomyopathy systematic review: pathophysiologic process, clinical presentation and diagnostic approach to Takotsubo cardiomyopathy. *Int J Cardiol* 2016;**209**:196–205.
2. Sato H, Tateishi H, Uehida T. Takotsubo-like cardiomyopathy due to multi-vessel spasm. In: Kodama K, Haze K, Hon M, editors. Clinical Aspect of Myocardial Injury: From Ischemia To Heart Failure [in Japanese]. Tokyo: Kagakuhyouronsya Publishing Co; 1990: p. 56–64.
3. Yerasi C, Koifman E, Weissman G, Wang Z, Torguson R, Gai J, et al. Impact of triggering event in outcomes of stress-induced (Takotsubo) cardiomyopathy. *Eur Heart J Acute Cardiovasc Care* 2017;6(3):280–286.
4. Amariles P, Cifuentes L. Drugs as possible triggers of Takotsubo cardiomyopathy: a comprehensive literature search–update 2015. *Curr Clin Pharmacol* 2016;**11**(2):95–109.
5. Komamura K, Fukui M, Iwasaku T, Hirotani S, Masuyama T. Takotsubo cardiomyopathy: pathophysiology, diagnosis and treatment. *World J Cardiol* 2014;**6**(7):602–609.
6. Hendricks EJ, Rothman RB, Greenway FL. How physician obesity specialists use drugs to treat obesity. *Obesity* 2009;**17**(9):1730–1735.
7. Dziewierz A, Olszanecka A, Wilinski J, Rakowski T, Kleczynski P, Dubiel JS, et al. Inverted takotsubo cardiomyopathy in a patient with essential thrombocythemia exposed to anagrelide and phentermine. *Int J Cardiol* 2012;**160**(2):e31–32.
8. Kurisu S, Inoue I, Kawagoe T. Myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005;**352**(18):1923–1925; author reply 1923–1925.
9. Alsidawi S, Muth J, Wilkin J. Adderall induced inverted Takotsubo cardiomyopathy. *Catheter Cardiovasc Interv* 2011;**78**(6):910–913.
10. Kido K, Guglin M. Drug-induced takotsubo cardiomyopathy. *J Cardiovasc Pharmacol Ther* 2017;**22**(6):552–563.
11. Vijay A, Becker JE, Ross JS. Patterns and predictors of off-label prescription of psychiatric drugs. *PLoS One* 2018;**13**(7):e0198363.
12. Khanra S, Das B. Off-label psychotropics use: isn't it now an inevitable and a "norm" in psychiatry? *Indian J Psychol Med* 2018;**40**(4):390–391.
13. Wittich CM, Burkle CM, Lanier WL. Ten common questions (and their answers) about off-label drug use. *Mayo Clin Proc* 2012;**87**(10):982–990.