Swiss Archives of Neurology, Psychiatry and Psychotherapy

Case report | Published 19 June 2019 | doi:10.4414/sanp.2019.03022
Cite this as: Swiss Arch Neurol Psychiatr Psychother. 2019;170:w03022

Takotsubo cardiomyopathy in the context of major neurocognitive disorder and multiple risk factors

Loss of main support person leading to significant stress and broken heart syndrome

Johnson a,b Jeremy C.S., Byrne a,b Gerard J.A.

[a] Older Persons' Mental Health Service, Royal Brisbane & Women's Hospital
[b] Discipline of Psychiatry, School of Clinical Medicine, Unviersity of Queensland

Summary

Objective: To present a case of takotsubo cardiomyopathy (TTC) in the context of major neurocognitive disorder and identify important considerations for psychiatrists.

Conclusions: Patients with neurocognitive disorders who are treated with antidepressants may be at increased risk of TTC. Treatment of anxiety and depression in patients with previous TTC should be monitored closely, and antidepressants less likely to cause hyponatraemia are recommended.

Keywords: takotsubo cardiomyopathy, broken heart syndrome, neurocognitive disorder, dementia, anxiety, antidepressants

Introduction

Takotsubo cardiomyopathy (TTC) is an acute and reversible weakening of the cardiac muscle, resulting in ballooning of the ventricles ("takotsubo" is the Japanese term for "octopus trap", referring to the appearance of the left ventricle). It usually presents with chest pain and dyspnoea [1], is most commonly seen in postmenopausal women following significant stress and has a 30-day mortality rate of about 5%. TTC is also known as "broken heart syndrome" or "stress induced cardiomyopathy" because stressful events, such as the loss of a loved one, often act as precipitants. TTC was historically hypothesised to be caused by elevated serum catecholamines such as norepinephrine (noradrenaline) [2, 3]. More recently, persuasive arguments have been advanced for a pathological mechanism related to sympathetic hyperactivation [4, 5]. This is consistent with findings that chronic anxiety, associated with increased bursts of sympathetic activity due to mental and physical stress [6], and the predisposing factor of early life trauma [7], increase the risk of TTC. Thus, psychiatrists may be involved in the care of these patients and should be aware of the risk of TTC following significant stress, anxiety and relapse of psychiatric illness.

The cardiac symptoms of TTC have been elucidated [1], whereas precipitating events have not yet been systematically evaluated. Nonetheless, a meta-analysis [1] identified that in 74% of cases, TTC was preceded by a significant stressor. Psychological stressors include loss of a family member, marital conflict and work-related stressors, but also events such as the loss of a pet [8]. Cases have been reported in which relapsing psychiatric illnesses were the precipitating stressors (e.g., bipolar and major depressive disorders) [9] as well as catatonia [10, 11]. There have also been reports of TTC associated with dementia [9, 12–16], including one case of vascular dementia [13], although not as the precipitating stressor. Here we report a case of TTC where a major neurocognitive disorder (possible vascular subtype) increased vulnerability to stress following the loss of a main support person, in the context of multiple risk factors.

Case report

Ms Sato, a 79-year-old Caucasian woman, was referred to the community Older Persons' Mental Health Service with concerns of worsening panic attacks. She had recently moved into a nursing home where she was being managed with escalating doses of oxazepam. She had been transferred to the nursing home directly from the rehabilitation unit following an admission for takotsubo cardiomyopathy (TTC). Her medical history included hypertension, aortic stenosis, atrial fibrillation and ovarian cancer. Her psychiatric history included anxiety following aortic valve replacement 3 years earlier. Desvenlafaxine had been trialled by her general practitioner (GP), but owing to adverse effects it was ceased after 3 days and her anxiety was managed with diazepam. She was being treated by her GP at the nursing home with mirtazapine 45 mg at night and oxazepam 7.5 mg four times a day. Her other medications were amlodipine, olmesartan, amiodarone and rivaroxaban.

Upon review, it was immediately evident that Ms Sato was suffering from cognitive impairment. She scored 57/100 on the Addenbrooke's Cognitive Examination – Revised (ACE-R) and had significant deficits in memory, fluency, language and visuospatial function. Consistent with

Correspondence:
Jeremy C.S. Johnson , Psychiatric Registrar, Royal Brisbane & Women's Hospital, Butterfield St, Herston QLD, AUS-4029 Brisbane,
jcsjohnson[at]yahoo.com

the geriatrician assessment (see below), a diagnosis of major neurocognitive disorder possible vascular subtype was made, based on cerebrovascular risk factors and deficits in complex attention and executive function, although no brain imaging had been completed. Despite her poor performance on the ACE-R, she engaged well at interview and provided a reasonable history that was bolstered with collateral. There was no evidence of delirium.

Ms Sato's childhood was spent living rurally with her parents and one older sister. Her father worked on a farm and her mother was a homemaker. She was home schooled. Her father abused alcohol, resulting in physical and emotional abuse towards Ms Sato, her mother and her sister. Ms Sato and her sister continued living in their childhood home after the death of their parents. From the age of 60 years onwards, Ms Sato acted as a carer for her sister, who had suffered a stroke. Prior to that Ms Sato had worked at a supermarket for 42 years. She had no financial concerns and reported that they had been "frugal".

One month prior to Ms Sato developing TTC, her sister deteriorated physically and was placed in the nursing home. Collateral history from her GP and neighbour revealed that Ms Sato's functioning had soon declined. Previously, with support from her sister, she had been managing the shopping, cooking and cleaning. She had regularly worked in the garden and enjoyed daily walks. Both the GP and the neighbour had known of the cognitive deficits but reported a co-dependency with her sister that masked her significant cognitive impairment. Ms Sato's inability to cope independently after the placement of her sister in the nursing home resulted in gradually worsening anxiety. Escitalopram 10mg was initiated by the GP.

During one of her walks Ms Sato had a fall and was found to have chest pain and dyspnoea with an electrocardiogram (ECG) demonstrating ST elevation in the inferolateral leads. Urgent coronary angiography did not demonstrate significant occlusion, whereas ventriculography showed significant apical hypokinesis and basal hyperkinesis, diagnostic of TTC. She was also found to be hyponatraemic (serum sodium 118 mmol/l), which normalised with fluid restriction and cessation of escitalopram started 5 days earlier. She spent 2 weeks on the cardiology ward and 1 month in rehabilitation, at which time a diagnosis of dementia was made following serial cognitive testing (MMSE, MoCA, and ACE-R). The geriatrician determined that Ms Sato was unsafe to be discharged home and she was admitted to the nursing home where her sister lived.

Although reunited with her sister, Ms Sato had lost her independence. She could no longer take her usual walks, nor spend time in the garden, and had been separated from her dog. This difficult adjustment precipitated panic attacks. Ms Sato reported she had always been a worrier, but that she was confident she would improve upon adjusting to her new lifestyle. With mindfulness-based cognitive behaviour therapy we were able to cease the oxazepam and Ms Sato's symptoms improved. Her mirtazapine dose was maintained at 45 mg per day. On last review she was no longer experiencing panic attacks and had not had any relapse of her cardiac symptoms.

Discussion

We have reported a case of TTC following the loss of a co-dependent supportive relationship occurring against the background of a major neurocognitive disorder, in the context of multiple risk factors. The loss of Ms Sato's main support person did not immediately lead to significant stress and TTC; rather it occurred 1 month later following anxiety caused by an inability to function independently. This report adds to the literature describing TTC in patients with dementia [9, 12–16]. Previous case reports have identified dementia as contributing to psychological stress, or that there were no identifiable stressors; thus further research is required to elucidate the relationship between dementia and TTC. This case is consistent with research suggesting that chronic anxiety and adverse childhood events increase the risk of developing TTC [4–7].

Selective serotonin reuptake inhibitors (SSRIs) have been implicated in TTC [17–19] and Ms Sato had recently commenced escitalopram. A retrospective study found SSRIs to be more strongly associated with TTC than other antidepressants [19]. They suggested a mechanism of increased norepinephrine (noradrenaline) reuptake inhibition, although this is more consistent with serotonin-noradrenaline reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs), which are also associated with TTC [19–21]. A post-marketing review [21] found 21 cases of TTC associated with SNRIs compared with 5 with SSRIs. The authors reported that SNRIs are associated with greater risk than SSRIs, such that SNRI product information requires warnings regarding TTC [21].

Ms Sato was found to have hyponatraemia, which has also been associated with TTC in at least five case reports [22–26]. Three of these patients were being treated with antidepressants (SSRI, TCA, SNRI) [22, 23, 26], two of them in the context of psychogenic polydipsia [22, 23]. All of these cases had sodium levels similar to Ms Sato's (<120 mmol/l). The relationship between antidepressants and hyponatraemia is well known, but the mechanism by which hyponatraemia is linked to TTC is not clear, although sympathetic hyperexcitability is a possible explanation. Antidepressants have also been linked to recurrence of TTC [21]; thus, psychiatrists treating patients with anxiety and mood disorders following TTC should prescribe antidepressants judiciously.

Patients with neurocognitive disorders who are treated with antidepressants may be at increased risk of TTC. Treatment of anxiety and depression in patients with previous TTC should be monitored closely, and antidepressants less likely to cause hyponatraemia are recommended.

Written consent was obtained from Ms Sato and her substitute decision maker.

Disclosure statement

No financial support and no other potential conflict of interest relevant to this article was reported.

References

1 Singh K, Carson K, Usmani Z, Sawhney G, Shah R, Horowitz J. Systematic review and meta-analysis of incidence and correlates of recurrence of takotsubo cardiomyopathy. Int J Cardiol. 2014;174(3):696–701. doi: http://dx.doi.org/10.1016/j.ijcard.2014.04.221. PubMed.

2 Pavin D, Le Breton H, Daubert C. Human stress cardiomyopathy mimicking acute myocardial syndrome. Heart. 1997;78(5):509–11. doi: http://dx.doi.org/10.1136/hrt.78.5.509. PubMed.

3 Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med. 2005;352(6):539–48. doi: http://dx.doi.org/10.1056/NEJMoa043046. PubMed.

4 Y-Hassan S, Henareh L. Plasma catecholamine levels in patients with takotsubo syndrome: Implications for the pathogenesis of the disease. Int J Cardiol. 2015;181:35–8. doi: http://dx.doi.org/10.1016/j.ijcard.2014.11.149. PubMed.

5 Madias JE. Blood borne catecholamines and Takotsubo syndrome: An unsettled relationship. Int J Cardiol. 2015;186:198–9. doi: http://dx.doi.org/10.1016/j.ijcard.2015.03.299. PubMed.

6 Holwerda SW, Luehrs RE, Gremaud AL, Wooldridge NA, Stroud AK, Fiedorowicz JG, et al. Relative burst amplitude of muscle sympathetic nerve activity is an indicator of altered sympathetic outflow in chronic anxiety. J Neurophysiol. 2018;120(1):11–22. doi: http://dx.doi.org/10.1152/jn.00064.2018. PubMed.

7 Winzeler K, Voellmin A, Hug E, Kirmse U, Helmig S, Princip M, et al. Adverse childhood experiences and autonomic regulation in response to acute stress: the role of the sympathetic and parasympathetic nervous systems. Anxiety Stress Coping. 2017;30(2):145–54. doi: http://dx.doi.org/10.1080/10615806.2016.1238076. PubMed.

8 Nykamp D, Titak JA. Takotsubo cardiomyopathy, or broken-heart syndrome. Ann Pharmacother. 2010;44(3):590–3. doi: http://dx.doi.org/10.1345/aph.1M568. PubMed.

9 Corrigan FE, 3rd, Kimmel MC, Jayaram G. Four cases of takotsubo cardiomyopathy linked with exacerbations of psychiatric illness. Innov Clin Neurosci. 2011;8(7):50–3. PubMed.

10 Singh D, Williams O. Catatonia, major depression and Takotsubo cardiomyopathy in an elderly patient. Australas Psychiatry. 2013;21(2):181–2. doi: http://dx.doi.org/10.1177/1039856212469848. PubMed.

11 Peng TJ, Patchett ND, Bernard SA. Takotsubo Cardiomyopathy and Catatonia in the Setting of Benzodiazepine Withdrawal. Case Rep Cardiol. 2016;2016:. doi: http://dx.doi.org/10.1155/2016/8153487. PubMed.

12 Noguchi M, Yamaga K. A patient with possible dementia with Lewy bodies (DLB) who presented with Takotsubo cardiomyopathy. Psychiatry Clin Neurosci. 2010;64(2):213. doi: http://dx.doi.org/10.1111/j.1440-1819.2010.02068.x. PubMed.

13 De Gennaro L, Ruggiero M, Musci S, Tota F, De Laura D, Resta M, et al. Biventricular thrombosis in biventricular stress(takotsubo)-cardiomyopathy. J Thromb Thrombolysis. 2017;44(2):234–7. doi: http://dx.doi.org/10.1007/s11239-017-1510-4. PubMed.

14 Zuin M, Dal Santo P, Picariello C, Conte L, Zuliani G, D'Elia K, et al. Takotsubo cardiomyopathy in an elderly woman with Alzheimer's disease: a rare association. case report and mini-review of the literature. J Am Geriatr Soc. 2016;64(4):916–7. doi: http://dx.doi.org/10.1111/jgs.14071. PubMed.

15 Yanagawa Y, Mikasa M, Nishioka K, Hirano K. Dementia complicated with Takotsubo cardiomyopathy associated with unconsciousness induced by Wernicke's encephalopathy. BMJ Case Rep. 2013;2013:. doi: http://dx.doi.org/10.1136/bcr-2013-009473. PubMed.

16 Cerri AP, Teruzzi F, Gregorio M, Bellelli G, Annoni G. Takotsubo cardiomyopathy in an elderly patient with severe Alzheimer's disease: a case report. J Am Med Dir Assoc. 2012;13(3):207–9. doi: http://dx.doi.org/10.1016/j.jamda.2011.09.002. PubMed.

17 Verduin ML. Commentary on 2 cases of takotsubo cardiomyopathy involving psychotropic medication. J Psychiatr Pract. 2016;22(3):239–40. doi: http://dx.doi.org/10.1097/PRA.0000000000000153. PubMed.

18 Conrad SK, Catalano MC, Catalano G. The use of fluoxetine in a patient with takotsubo cardiomyopathy. J Psychiatr Pract. 2016;22(3):234–8. doi: http://dx.doi.org/10.1097/PRA.0000000000000151. PubMed.

19 Dias A, Franco E, Figueredo VM, Hebert K, Quevedo HC. Occurrence of Takotsubo cardiomyopathy and use of antidepressants. Int J Cardiol. 2014;174(2):433–6. doi: http://dx.doi.org/10.1016/j.ijcard.2014.04.028. PubMed.

20 Christoph M, Ebner B, Stolte D, Ibrahim K, Kolschmann S, Strasser RH, et al. Broken heart syndrome: Tako Tsubo cardiomyopathy associated with an overdose of the serotonin-norepinephrine reuptake inhibitor Venlafaxine. Eur Neuropsychopharmacol. 2010;20(8):594–7. doi: http://dx.doi.org/10.1016/j.euroneuro.2010.03.009. PubMed.

21 Woronow D, Suggs C, Levin RL, Diak IL, Kortepeter C. Takotsubo common pathways and SNRI medications. JACC Heart Fail. 2018;6(4):347–8. doi: http://dx.doi.org/10.1016/j.jchf.2017.12.011. PubMed.

22 Purdy A, Ren B. A broken heart: A rare complication of hyponatremia. J Med Cases. 2018;9(5):147–50. doi: http://dx.doi.org/10.14740/jmc3050e.

23 Cecconi A, Franco E, de Agustín JA, Vilchez JP, Palacios-Rubio J, Sánchez-Enrique C, et al. Hyponatremia-induced stress cardiomyopathy due to psychogenic polydipsia. Int J Cardiol. 2016;202:618–20. doi: http://dx.doi.org/10.1016/j.ijcard.2015.09.123. PubMed.

24 Santos M, Dias V, Meireles A, Gomes C, Luz A, Mendes D, et al. Hyponatremia--an unusual trigger of Takotsubo cardiomyopathy. Rev Port Cardiol. 2011;30(11):845–8. doi: http://dx.doi.org/10.1016/j.repc.2011.09.006. PubMed.

25 AbouEzzeddine O, Prasad A. Apical ballooning syndrome precipitated by hyponatremia. Int J Cardiol. 2010;145(1):e26–9. doi: http://dx.doi.org/10.1016/j.ijcard.2008.12.195. PubMed.

26 Worthley MI, Anderson TJ. Transient left ventricular apical ballooning syndrome following a hyponatraemic seizure. Int J Cardiol. 2007;115(3):e102–4. doi: http://dx.doi.org/10.1016/j.ijcard.2006.07.091. PubMed.