

## CASE REPORT

# A variant form of Takotsubo syndrome secondary to Sumatriptan: A case report

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## Abstract

Takotsubo syndrome (TS), also known as stress-induced cardiomyopathy or broken heart syndrome, is an acute reversible left ventricular systolic dysfunction that mimics an acute coronary syndrome. It has various types and mechanism of pathogenesis is not very well defined. It is more common in postmenopausal women and is associated with emotional or physical stress. We report a case of type III takotsubo syndrome in a postmenopausal woman after taking sumatriptan for migraine headache.

## Keywords

Takotsubo syndrome, Stress-induced cardiomyopathy, Sumatriptan, Triptan, Migraine headache

## 1 Introduction

Takotsubo syndrome (TS) is an acute reversible left ventricular (LV) systolic dysfunction. It usually mimics an acute coronary syndrome presenting with chest pain or dyspnea, electrocardiographic abnormalities and elevated cardiac biomarkers <sup>[1]</sup>. It is characterized by an abnormal LV segmental contractility without any evidence of obstructive coronary artery disease <sup>[2]</sup>. Takotsubo syndrome is also known as stress induced cardiomyopathy, apical ballooning syndrome or “Broken heart syndrome”.

It is more common in women, particularly post-menopausal and a trigger in the form of physical or psychological stress can be detected in a classical presentation <sup>[1]</sup>. Several triggers have been described in literature inducing TS. We describe a rare case of variant form of TS in a woman after taking sumatriptan for her migraine headache.

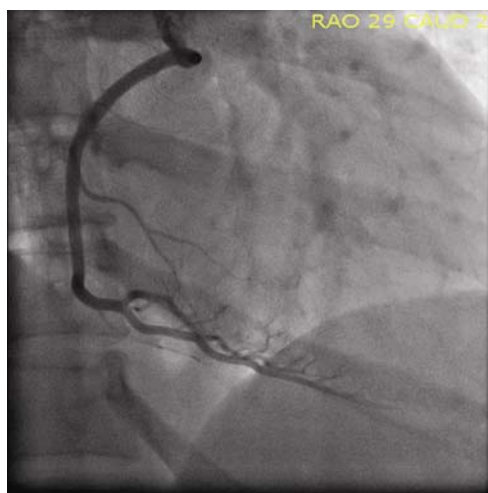
## 2 Case report

A 51 year-old caucasian female was transferred to our facility for management of non-ST elevation myocardial infarction. She presented to the referring emergency department with sudden onset of substernal chest pain. Her past medical history was significant for chronic obstructive pulmonary disease, hypothyroidism, tobacco use, migraine headaches, depression and a remote history of deep venous thrombosis. She was taking topiramate, levothyroxine, temezapam, aspirin, bupropion and as needed sumatriptan. Her last use of sumatriptan was two years ago. She reported use of sumatriptan as an

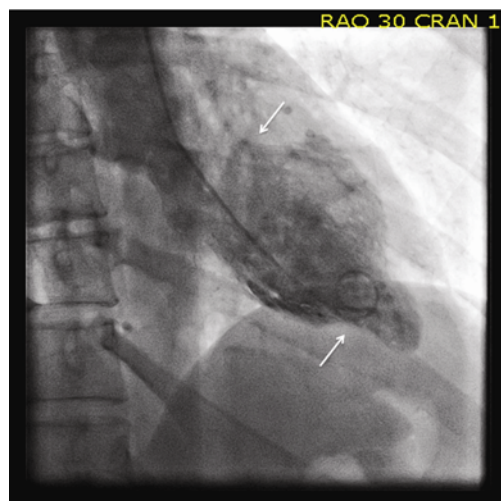
abortive therapy for her severe migraine headache. Thirty minutes after taking sumatriptan she developed sudden substernal chest pain and presented to the emergency department. Her initial workup showed stable hemodynamics and T-wave inversions in anterolateral leads on electrocardiogram. Initial cardiac enzymes, Troponin I, were normal but subsequent Troponin I became elevated to 0.44 (normal < 0.30 ng/mL) and she was transferred to our facility for further management. She was given an oral aspirin 325 mg, clopidogrel 300 mg and one dose of subcutaneous injection of enoxaparin 1 mg /kg body weight by the sending facility. She was also treated with intravenous morphine and topical nitroglycerin paste for her chest pain. On presentation to our hospital she was chest pain free, headache had subsided, hemodynamically stable and her cardiac exam was within normal limits. Her repeat electrocardiogram showed persistent T wave inversions in leads V1-3 and avL. In addition to dual antiplatelet therapy she was also started on beta-blockers, atorvastatin and an echocardiogram was performed. Her echocardiogram showed hypokinesia of mid to apical LV walls and an ejection fraction of 20%-25%. Next morning, she was taken to cardiac catheterization laboratory for evaluation of her coronary arteries and severe LV systolic dysfunction. Her coronary angiograms showed normal coronary arteries (see Figure 1 and 2). The left ventriculogram showed severely hypokinetic mid-ventricular walls, normal contracting base and hyper-contractile apex consistent with type III takotsubo cardiomyopathy (see Figure 3).



**Figure 1.** Coronary angiogram showing normal left coronary artery circulation.



**Figure 2.** Coronary angiogram showing normal right coronary circulation.



**Figure 3.** Left ventriculogram showing mid-ventricular ballooning and basal and apical hypercontractility consistent with type III takotsubo morphology (arrows).

The patient had no post procedural complications. Next day, she was discharged from the hospital on aspirin, carvedilol, lisinopril and her sumatriptan was stopped. She followed up at our office after 8 weeks and a repeat echocardiogram showed improvement of LV systolic contractility and an ejection fraction of 45%-50% without any wall motion abnormalities. It was concluded that sumatriptan induced her chest pain and initial symptoms leading to TS.

### 3 Discussion

Japanese authors first described Takotsubo syndrome in 1990s<sup>[3]</sup>. The true prevalence of TS is unclear and there are no clear risk factors associated with TS<sup>[2]</sup>. The diagnostic criteria remain controversial and multiple criteria have been presented in literature<sup>[4-8]</sup>. Bybee et al published the Mayo clinic criteria in 2004, which have been modified recently by Prasad et al, and is the most commonly used criteria to diagnose TS<sup>[5, 7]</sup> (see Table 1).

**Table 1.** Diagnostic criteria of Takotsubo Syndrome

| Mayo Clinic criteria                                                                                                                                                           | Prasad criteria                                                                                                                                                                                                                     |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Suspicion of AMI based on precordial pain and ST elevation observed on the acute-phase ECG                                                                                     | Transient hypokinesia, akinesia, or dyskinesia of the middle segments of the LV, with or without alterations at the apex. Regional abnormalities of wall motility extend in the area of distribution of a single epicardial vessel. |
| Transient hypokinesia or akinesia of the middle and apical regions of the LV and functional hyperkinesia of the basal region, observed on ventriculography or echocardiography | Absence of an obstructed coronary artery or angiographic evidence of acute rupture of a plaque                                                                                                                                      |
| Normal coronary arteries confirmed by arteriography (luminal narrowing of less than 50% in all the coronary arteries) in the first 24 hours after the onset of symptoms        | New ECG abnormalities (ST elevation and/or T-wave inversion) or elevation of cardiac troponin.                                                                                                                                      |
| Absence of recent significant head injury, intracranial hemorrhage, suspicion of pheochromocytoma, myocarditis, or hypertrophic cardiomyopathy                                 | Absence of:<br>Recent head injury<br>Intracranial hemorrhage<br>Pheochromocytoma<br>Myocarditis<br>Hypertrophic cardiomyopathy                                                                                                      |

The LV adopts a shape of a pot, thus receiving its name takotsubo syndrome (in Japanese takotsubo means an octopus trap). Typically, LV appears with a narrow base and globular apex but atypical forms and variants of takotsubo syndrome have been described and can comprise up to one third of the total presentations <sup>[2, 9]</sup> (see Table 2).

**Table 2.** Types of Takotsubo Syndrome

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|                                                          |
|----------------------------------------------------------|
| Type I. Takotsubo cardiomyopathy with apical ballooning. |
| Type II. Midventricular ballooning.                      |
| Type III. Cardiomyopathy with apical hypercontractility. |
| Type IV. Basal ballooning.                               |
| Type V. Involvement of other segments.                   |

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The exact mechanism and pathogenesis of this disorder is unknown. The histological inflammatory changes in TS differ from coagulation necrosis as seen in myocardial infarction from coronary artery occlusion <sup>[1]</sup>. Multiple pathological mechanisms responsible for TS have been proposed. A few concepts are discussed below.

Multivessel epicardial coronary artery spasm resulting in reversible regional myocardial stunning <sup>[10]</sup> has been proposed but this hypothesis does not explain the histological changes observed in TS <sup>[11]</sup>. Another hypothesis is coronary microvascular dysfunction <sup>[12]</sup>. Impaired microvascular function and myocardial metabolic disturbances have been found in patients with TS on basis of thallium-201 and 18 F-fluorodeoxyglucose myocardial scans <sup>[13]</sup>.

Increased catecholamine release from stress giving cardiotoxicity is another possibility <sup>[14, 15]</sup>. Catecholamine produce vasoconstriction and direct myocyte damage from increase calcium release, which activates cAMP, causing myocyte damage and free radical release <sup>[10, 16]</sup>. The myocardial histological changes in TS are similar to those seen in catecholamine cardiotoxicity in animals and humans <sup>[17, 18]</sup>. Sympathetic nervous mechanisms causing release of catecholamine and giving myocardial stunning may also play a part in catecholamine-induced cardiotoxicity <sup>[1, 19]</sup>. Low estrogen states increase the risk of microvascular dysfunction in high catecholamine conditions placing perimenopausal and postmenopausal women on higher risk to develop TS <sup>[2, 20]</sup>.

Sumatriptan has a similar mechanism of action and adverse-effect profile as other triptans (e.g. zolmitriptan, frovatriptan) <sup>[21]</sup>. It is a 5HT<sub>1B/1D</sub> receptor agonist that has been approved for treatment of acute migraine headache. Cases of transient ischemia, myocardial infarction and arrhythmias have been described with use of 5HT<sub>1</sub> receptor agonist <sup>[22-24]</sup>. 5HT<sub>1B</sub> receptor is known to cause coronary artery spasm and its expression has been demonstrated on coronary artery smooth muscle cell <sup>[25, 26]</sup>. Theoretically, because sumatriptan can induce coronary vasospasm, it is quite possible that this vasospasm in setting of neurogenic insult like acute migraine headache can cause LV dysfunction leading to TS.

To our knowledge triptan induced TS has been reported once in literature <sup>[27]</sup>. Our case is unique because of variant form of TS with sumatriptan use for acute migraine headache in a postmenopausal woman. Migraine headache has been described as a risk factor for TS in a case report <sup>[28]</sup>, however our patient had similar episode in the past without complications. Therefore, we believe that migraine headache and use of sumatriptan in postmenopausal state caused her LV dysfunction leading to TS.

## 4 Conclusion

Takotsubo syndrome or cardiomyopathy is a novel form of heart failure that mimics acute coronary syndrome. Precipitating and pathological mechanisms are complex and not very well understood. Our case highlights medications acting on sympathetic system along with physical stress as a risk factor in developing TS in postmenopausal women.

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