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CASE REPORT
Coronary intervention

Triptan-induced takotsubo syndrome: a case report

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Background Takotsubo syndrome (TS) is a clinical condition mimicking acute coronary syndrome characterized by reversible acute systolic dysfunction. TS is typically associated with a catecholaminergic surge resulting from physical or emotional stress while some pharmacologic agents may act as a trigger.

Case summary Here, we report a case of TS secondary to rizatriptan, used for treatment of acute migraine. A 67-year-old woman with a history of dyslipidemia, type II diabetes, and migraine was admitted with chest heaviness shortly after taking rizatriptan for migraine. Deepening T wave inversion was seen in multiple territories on electrocardiogram and hs-troponin T was elevated. Cardiac imaging including echocardiogram coronary angiography and cardiac magnetic resonance imaging was consistent with a diagnosis of TS.

Discussion In this case, there was no emotional trigger for TS described. Given the compelling temporal correlation between the onset of typical chest pain and medication use, a diagnosis of TS secondary to rizatriptan was made.

Keywords Triptans • Takotsubo • Cardiomyopathy • Cardiac MRI • Case report

ESC Curriculum 2.1 Imaging modalities • 2.2 Echocardiography • 2.3 Cardiac magnetic resonance • 3.2 Acute coronary syndrome

Learning points

- Certain medications, including triptan medications used as first line of treatment for migraines are now being recognised as possible alternative triggers for this Takotsubo syndrome.
- A thorough medication history is essential for appropriately investigating and diagnosis of typical chest pain associated with elevated cardiac enzymes.

Introduction

Takotsubo syndrome (TS), a clinical syndrome characterised by reversible acute systolic dysfunction, accounts for a significant number of admissions for chest pain with elevated troponins each year.[1] Traditionally, TS has been linked to emotional and physical stressors, however, potential alternative triggers for TS, such as certain medications, are now becoming more recognised. Identifying the underlying cause of this condition is important for timely diagnosis and management. This case demonstrates the importance of thorough history taking for identifying the underlying trigger for TS.

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Timeline

Time	Event
Day 0	The patient took 10 mg rizatriptan for migraine and experienced chest heaviness. She presented to the emergency room and was admitted to hospital. She commenced treatment for possible acute coronary syndrome based on dynamic electrocardiogram changes and raised serum troponin levels.
Day 1	Coronary angiogram demonstrated mild diffuse coronary artery disease.
Day 2	Echocardiogram showed regional akinesis with apical ballooning consistent with Takotsubo Syndrome
Day 3	Cardiac magnetic resonance imaging showed inflammation/oedema in the mid to apical left ventricular segments without late gadolinium enhancement, consistent with Takotsubo Syndrome. Patient commences bisoprolol and perindopril.
Day 5	Patient discharged from hospital.
7 weeks after admission	Patient reviewed in outpatient clinic. Complete recovery noted.
3 Months After Admission	Follow Up Echocardiography Showing Complete Resolution Of Regional Wall Motion Abnormalities And Normalisation Of Left Ventricular Ejection Fraction.

Case presentation

A 67-year-old woman was admitted to hospital with central chest heaviness radiating to her left shoulder accompanied by shortness of breath but no nausea or diaphoresis. Prior to developing chest heaviness, she noticed the onset of migraine and took 10 mg of rizatriptan orally. Her symptoms began shortly after taking this medication. She noted that in the past, she had experienced chest heaviness, albeit less severe, after taking rizatriptan. Additional past medical history included dyslipidaemia, type II diabetes mellitus and hiatus hernia. She was otherwise fit and well at baseline, living independently and engaging in regular light exercise involving walking several blocks. At the time of presentation, her blood pressure was 142/86 mmHg, heart rate 73 b.p.m., and SpO2 98%. A cardiorespiratory examination was normal.

The initial electrocardiogram (ECG) showed normal sinus rhythm with occasional ventricular ectopic beats, normal ST segments, and T waves (*Figure 1A*). Her full blood count revealed a normal white cell count of 10.68 × 109/L (normal range 4.0 to 11.0 × 109/L) but a slightly elevated neutrophil count of 7.98 × 109/L (normal 1.9 to 7.5 × 109/L) which normalised within 12 h. Her high sensitivity troponin T was initially 135 ng/L (normal <15 ng/L), increasing to 179 ng/L at 4 h and 188 ng/L at 9 h. Her chest X-ray demonstrated a normal cardiothoracic ratio with no other abnormalities. The InterTAK Diagnostic Score was 65 (73.7% probability of TS).

A coronary angiogram showed mild diffuse coronary disease. Successive ECGs demonstrated gradual development of deepening T wave inversion in leads I, II, aVL, aVF, and V1–6 over the subsequent 48 h (*Figure 1B*). Echocardiogram on the day of admission showed severely reduced left ventricular ejection fraction (LVEF) of 34% with akinesis of the mid to apical left ventricle including the apex with preserved basal segment (see Supplementary material online, Videos Echo2Ch - Echo4Ch). Cardiac magnetic resonance imaging (CMR) performed 2 days later demonstrated evidence of myocardial oedema in the mid to apical left ventricle without late gadolinium enhancement (*Figure 2* and Supplementary material online, *Videos cMRI2Ch and cMRI4Ch*).

In the absence of obstructive coronary disease, the imaging features were consistent with TS. The patient was commenced on oral bisprolol 1.25 mg mane and perindopril 2 mg po mane were commenced. The patient remained well during her hospitalisation and her chest pain resolved. We advised the patient to discontinue use of rizatriptan and she was discharged from hospital with a plan for a repeat echocardiogram and cardiac rehabilitation. During follow up, bisprolol was stopped due to bradycardia and significant lethargy. Perindopril was later discontinued due to hypotension. At the clinic visit, seven weeks after admission, the patient remained well, with no cardiac symptoms to report. Follow-up transthoracic echocardiogram at 3 months showed complete resolution of the regional wall motion abnormalities and normalisation of her LVEF.

Discussion

TS (also known as stress cardiomyopathy or apical ballooning syndrome) is a transient syndrome of reduced left ventricular systolic function which can mimic acute coronary syndrome (ACS).[1] TS has been shown to be responsible for approximately 1–2% of hospital presentations in which troponin levels are raised. Although TS presents clinically similarly to ACS, there are important differences in their epidemiology, aetiology, and management. TS is more common among older women and patients with neurological or psychiatric history.[1]

Typical presenting symptoms of TS include acute chest pain, dyspnoea and syncope.[1] The most common ECG findings at presentation include ST segment elevation, ST depression, T wave inversion, and Qt prolongation.[1,2] Cardiac troponin levels are typically raised at the time of presentation. Interestingly, the mean rise in troponin has been shown in a previous study of a cohort of 910 patients to be greater in ACS than in TS, by a factor of 1.8 in patients with TS vs. 6 in ACS.[1] In this case, the troponin level increased by a factor of 1.33.

Echocardiogram is the mainstay of imaging for diagnosis of TS and there are five subtypes of TS distinguished by the regionality of wall motion abnormalities observed. The most common of these, which accounts for approximately 80% of cases, as was identified in this case, is apical type TS.[1] This regionality is typically associated with impaired LV function. CMR findings in TS typically include oedema of the hypokinetic region without gadolinium uptake.[3,4]

The intriguing aspect of this case is the apparent trigger for development of TS. The classical triggers of TS include emotional triggers such as anger, bereavement, conflict, or anxiety as well as physical triggers such as respiratory failure and neurological conditions including stroke, migraine, malignancy, and infection. Autonomic nervous system activation and a catecholamine surge, is thought to be important in development of TS, with a demonstrated rise in serum catecholamine concentrations in TS.[5]

Certain pharmacological agents have also been implicated in development of TS, including immune checkpoint inhibitors, dobutamine in the setting of cardiac stress testing, adrenaline, cocaine and other stimulants.[6–10] Prior case reports have described possible TS following use of sumatriptan and zolmitriptan.[11–13] Here, we have described a case of TS following rizatriptan use; the repeated development of symptoms in close temporal proximity to the use of this medication makes a compelling case for a causative association.

Triptans are a class of medications typically used as a first line treatment for acute migraine in adults. Although triptans generally have a

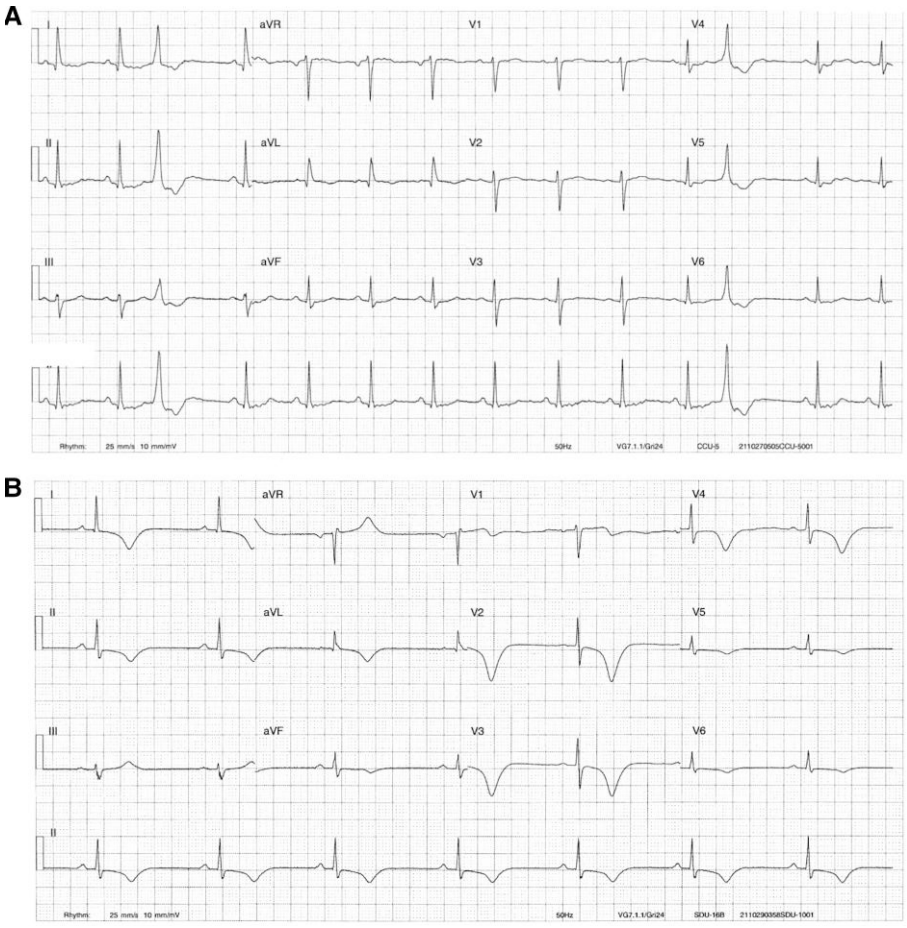

Figure 1 ECG recordings obtained at the time of initial assessment (*A*) and 48 h after initial assessment (*B*).

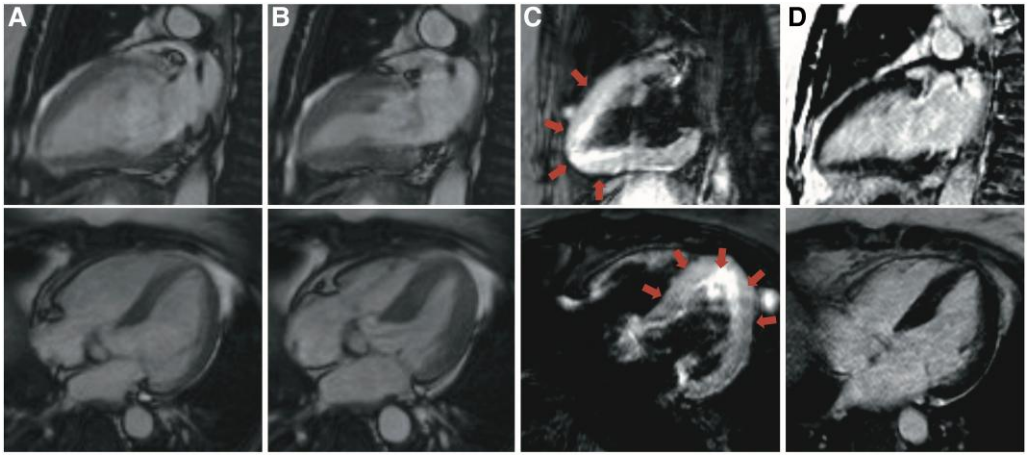

Figure 2 Cardiac magnetic resonance imaging showing snapshot of cine two-chamber (top row) and four-chamber views (bottom row) using steady-state free precession (SSFP) sequences timed at diastole (column *A*) and systole (column *B*). Column *C* shows the corresponding black blood T2-weighed spin echo triple inversion recovery (STIR) imaging with evidence of myocardial oedema of the mid to apical left ventricle (arrows) and the absence of abnormal late gadolinium enhancement on delayed T1 weighted Phase Sensitive Inversion Recovery sequences (Column *D*).

favourable adverse effect profile, they are contraindicated in patients with a history of ACS or known coronary artery disease, due to their vasoconstrictive effects on coronary arteries.[14] They cause vasoconstriction of cranial arteries by acting as selective serotonergic 5-HT-1B receptor agonists,[15] while activation of 5-HT-1D receptors augments the release of vasoactive peptides from trigeminal nerve terminals and inhibits nociceptive signalling.[15] Thus, coronary vasoconstriction and vasospasm represent a likely mechanism via which Triptan medications might precipitate development of TS. As mentioned, conditions such as migraine itself have been implicated as triggers for TS. This raises the question: is the development of TS in this case a direct result of the physiological effects of triptan medications or a result of the physiological aberration that occur in migraine itself? In this case, repeated development of chest pain after Triptan use, and the known vasoconstrictive effect of Triptans on coronary arteries implicates this class of medications as a causative agent.

This case highlights the possible serious adverse effects that may result from Triptan use. A greater awareness of this possible association should raise suspicion for TS in patients presenting with chest pain who have taken Triptan medications and may inform investigation of patients presenting with typical chest pain in whom a history of migraine is established.

Lead author biography

I am a basic trainee with the Royal Australasian College of Physicians. I have a PhD in cancer therapeutics and have an interest in cardio-oncology.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

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