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CASE REPORT
Heart failure

Takotsubo syndrome following radiofrequency ablation of atrial fibrillation in a patient with coronary artery anomaly: a case report

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Background Takotsubo syndrome (TTS) is an acute heart failure syndrome usually induced by emotional or physical stress. The prevalence of TTS seems to be higher than previously anticipated. Radiofrequency catheter ablation could be a rare trigger of TTS. The pathophysiology is not fully understood. Sympathetic stimulation plays an important role on the development of TTS.

Case summary A 62-year-old woman was referred for RFCA because of drug-refractory symptomatic paroxysmal atrial fibrillation. No other chronic diseases were stated except for a hypertension history. Three hours after the AF ablation, the patient complained of chest pain. New electrocardiographic abnormalities were presented including progressive T-wave inversion and significant QT prolongation. Multimodality imaging, including echocardiography, coronary angiography, left ventriculography, and computed tomography was conducted in establishing the TTS diagnosis. The congenital coronary artery anomaly was confirmed at the same time. Both transthoracic echocardiography and left ventriculography showed typical TTS changes. Elevation of the brain natriuretic peptide and Troponin I was observed during the acute phase. Angiotensin-converting enzyme inhibitor and β-blocker were administrated during hospitalization and after discharge. Two weeks later, echocardiography and cardiovascular magnetic resonance revealed a total recovery of left ventricular function and apex kinesis.

Discussion Sometimes, it is hard to distinguish TTS from acute coronary syndrome because of similar manifestations. Multimodality imaging is helpful to confirm the diagnosis. Radiofrequency catheter ablation could be a rare trigger of TTS, and its incidence may increase in patients with coronary artery anomaly. Coronary spasm and increased cardiac sympathetic activity induced by the ablation might be the mechanism involved.

Keywords Case report • Takotsubo syndrome • Atrial fibrillation • Radiofrequency catheter ablation

ESC Curriculum 2.2 Echocardiography • 6.1 Symptoms and signs of heart failure • 6.5 Cardiomyopathy • 5.3 Atrial fibrillation

Learning points

- Radiofrequency catheter ablation could be a trigger of Takotsubo syndrome.
- Coronary spasm and increased cardiac sympathetic activity induced by the ablation might be the mechanism involved.

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Introduction

Takotsubo syndrome (TTS) is an acute and usually reversible heart failure syndrome that typically is present with acute chest pain of cardiac origin, breathlessness, and palpitations in the absence of significant coronary artery disease on angiography.[1] Since initial reported in Japan in 1990, more and more TTS cases have been diagnosed in different clinical settings. With growing awareness of TTS, sympathetic activation seems to be central to its pathophysiological mechanism. A high level of catecholamine might precipitate direct myocardial injury, plaque rupture, multi-vessel epicardial spasm, microcirculatory dysfunction, and an increased cardiac workload that contributes to an acute situation of supply–demand mismatch followed by post-ischaemic stunning.[2,3]

Timeline

60 days before admission	Diagnosed as paroxysmal atrial fibrillation (PAF).
1 day before the procedure	The initial left ventricular eject fraction (LVEF) was 58%. Physical examination and biomarkers were unremarkable.
The day of procedure	3 h after the procedure, the patient complained of mild retrosternal and back pain. The Electrocardiogram (ECG) showed flat T-wave in all the leads. Transthoracic echocardiography (TTE) excluded pericardial effusion.
1 day after the procedure	The T-waves inversed in all the leads on ECG.
2 days after the procedure	ECG monitor revealed progressive T-wave inversion in pre-cordial leads, along with significant QT prolongation peaked to 678 ms. TTE revealed a new left ventricular apex akinesis with a reduction of LVEF to 50%. Troponin I level and NTpro-BNP level elevated significantly. Left ventriculography showed apical ballooning during systole. The coronary angiography and the coronary computed tomography angiography exclude concomitant CAD or possible coronary injury during the procedure. The patient was diagnosed with Takotsubo syndrome and treated with angiotensin-converting enzyme inhibitor and β-blocker.
5 days after the procedure	The patient was asymptotic and discharged with a dramatic improvement in LVEF.
20 days after the procedure	Deeper T-wave inversions on ECG. Total recovery of LV function on TTE. No myocardial scar on late gadolinium-enhanced cardiovascular magnetic resonance.
50 days after the procedure	Shallower T-wave inversions on ECG.
80 days after the procedure	The follow-up ECG showed normal T waves.

Case history

A 62-year-old female Chinese with drug-refractory symptomatic paroxysmal atrial fibrillation was referred for radiofrequency catheter ablation (RFCA). She had a history of hypertension for 2 years. Physical examination and biomarkers were unremarkable. Transthoracic echocardiography showed an initial left ventricular ejection fraction (LVEF) of 58%. With the patient under conscious sedation, complete isolations of all pulmonary veins, cavotricuspid isthmus, and superior vena cava were achieved without any complications.

Three hours after the procedure, she complained of retrosternal and back pain related to breathing and body position change. New electrocardiogram (ECG) showed a flat T wave in all the leads. In the next 3 days, ECG monitor revealed progressive T-wave inversion in pre-cordial leads, along with significant QT interval prolongation peaked to 678 ms (*Figure 1A* and Supplementary material online, *Video S5*). Transthoracic echocardiography excluded pericardial effusion. However, it revealed a new left ventricular apex akinesis with a reduction of LVEF to 50% (*Figure 1B*). Coronary anatomy was evaluated using multiple angiographic views and coronary computed tomography angiography (CCTA). Obstructive atherosclerotic plaques were excluded. Left ventriculography showed apical ballooning during systole, which is consistent with typical TTS (*Figure 1C* and Supplementary material online, *Video S1*). Troponin I level peaked to 2.21 ng/mL (normal $<$0.04 ng/mL), N-terminal pro-B type natriuretic peptide (NT pro-BNP) elevated to 1601 pg/mL (normal $<$300 pg/mL), other laboratory tests were unremarkable.

In the coronary angiography (11 h after the RFCA), we saw a single coronary artery anomaly, with smooth blood flow, originating from the right coronary sinus of Valsalva, and continues its course as a left circumflex artery (LCX) (*Figure 2A* and Supplementary material online, *Videos S2–S4*). In the ascending aorta angiography, the left coronary artery was absent (*Figure 2B* and Supplementary material online, *Video S4*). To find the 'disappeared' left anterior descending artery (LAD), CCTA was performed. Coronary computed tomography angiography found a single coronary artery arising from the right sinus of Valsalva and almost immediately giving off a narrow LAD with an intramural coronary course which travels down the anterior interventricular sulcus (*Figure 2C* and *D* and Supplementary material online, *Video S3*). The most probable reason for missing it on the coronary angiography is that the tip of the catheter is deep enough to pass by the origin of the proper LAD.

Supportive therapy was given in the acute phase. Angiotensin-converting enzyme inhibitor and β-blocker were

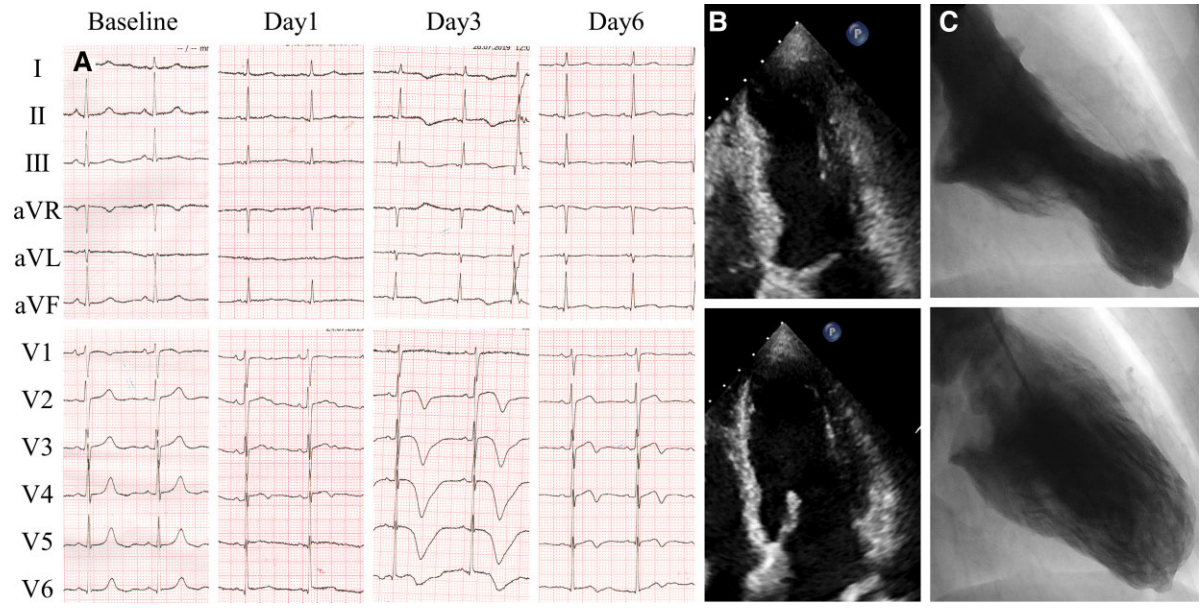

Figure 1 The electrocardiogram change during a 6-day hospitalization (*A*); transthoracic echocardiography (*B*) and left ventriculography (*C*) revealed a new left ventricular apex akinesis and apical ballooning during systole.

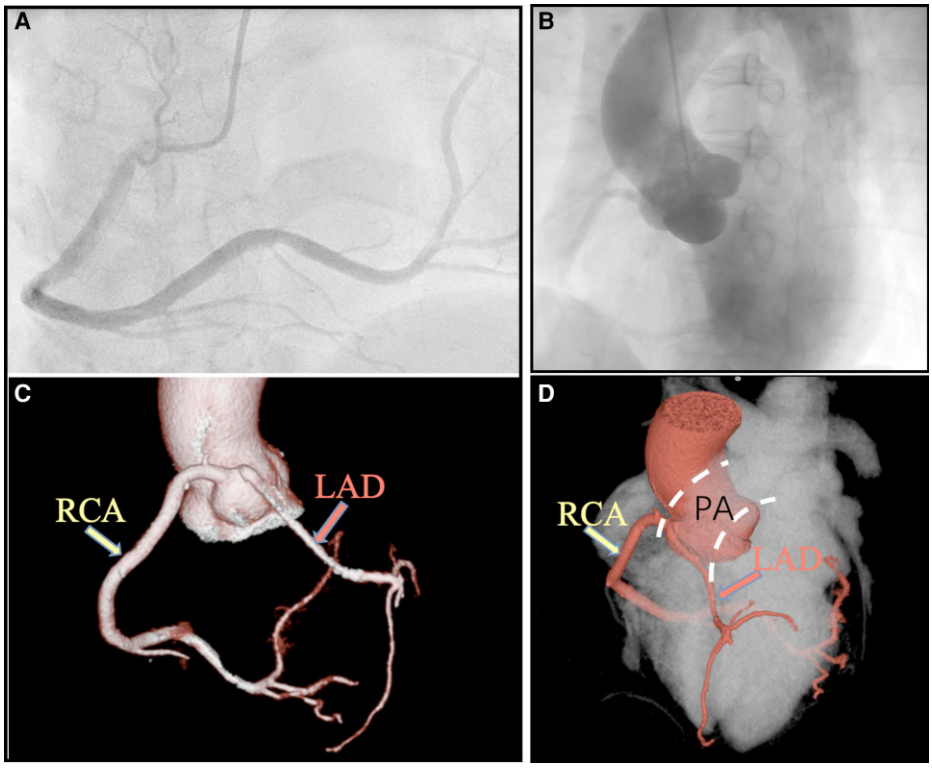

Figure 2 Coronary angiography (*A*) and the ascending aorta angiography (*B*) showed a huge right coronary artery, the left anterior descending artery and left circumflex artery were absent; coronary computed tomography angiography showed a huge right coronary artery (arrow) and a little left anterior descending artery (arrow), which was originated from the right coronary sinus (*C*, *D*); The interarterial left anterior descending artery arises from the right coronary artery and courses between the aorta and pulmonary artery and then travels down the anterior interventricular sulcus.

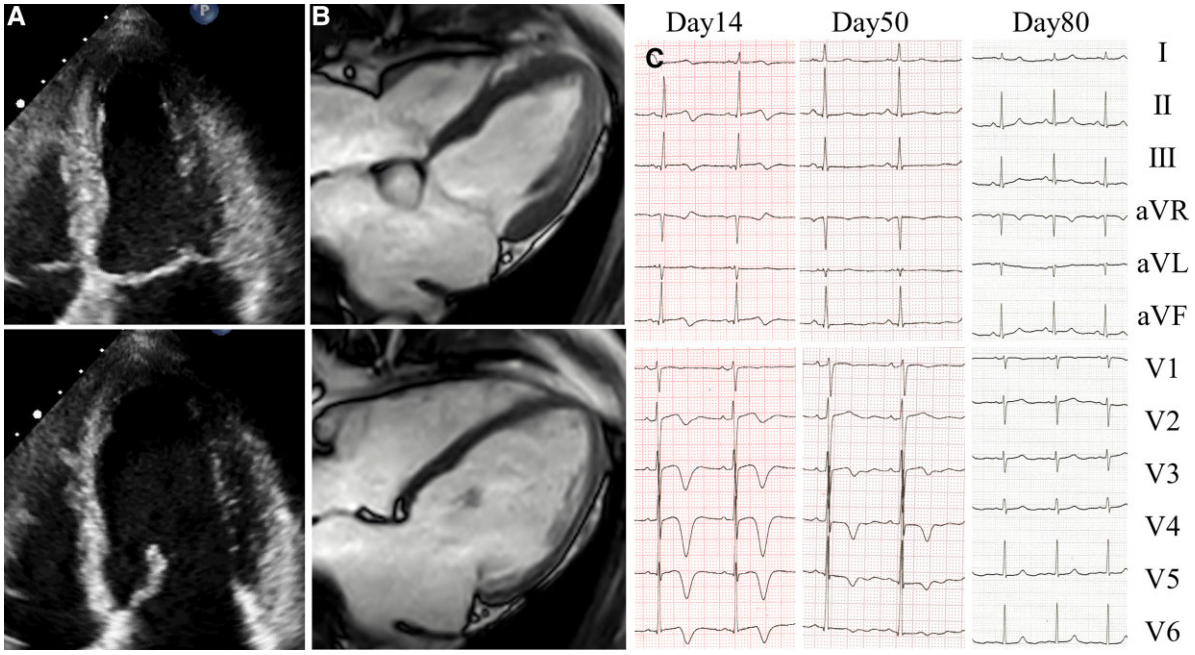

Figure 3 The echocardiography (*A*) and cardiovascular magnetic resonance (*B*) 2 weeks later after discharge; the follow-up electrocardiographic showed deeper T-wave inversions last up to months (*C*).

administrated before coronary angiography and continued after discharge. During a 6-day hospitalization, the patient's symptoms gradually relieved and hemodynamically stable, accompanied with a dramatic improvement of LVEF and ECG abnormalities (*Figure 1A*). Two weeks after discharge, echocardiography (*Figure 3A* and Supplementary material online, *Video S6*) and cardiovascular magnetic resonance revealed a total recovery of LV function, without myocardial scar on late gadolinium-enhanced cardiovascular magnetic resonance (*Figure 3B*), resulting in the diagnosis of TTS. T-wave changes of the patient were consistent with the classic ECG manifestations of TTS: initial T-wave inversion during Days 1–3; transient improvement in T-wave inversions during Days 2–6; and deeper T-wave inversions that can last up to months (*Figure 3C*).

Discussion

Takotsubo syndrome is typically characterized by reversible left ventricular dysfunction following emotional or physical stress.[1] Medicine or invasive procedures can induce the syndrome. Given that emotional and other medical stresses and the intake of sympathomimetic drugs were ruled out during her detailed history and routine examination, RFCA may be regarded as a trigger of TTS in this patient. Few cases of TTS after RFCA have been reported.[4,5] However, to our knowledge, this is the first report of the TTS followed RFCA in a patient with a single right coronary artery (RCA). Diagnosis of TTS is often challenging due to the wide spectrum of clinical presentations. Multimodality imaging, including echocardiography, left ventriculography, magnetic resonance imaging, computed tomography, and nuclear imaging, is helpful to establish the diagnosis.[6] Several diagnostic criteria for TTS have already been proposed. To improve the diagnostic accuracy, the international expert consensus document on Takotsubo proposed new diagnostic criteria.[3] For this case, the diagnosis became confused due to the coronary artery anomaly found in coronary angiography and left ventriculography. However, the diagnostic procedure fits well in with the consensus document recommendations for diagnosis.[3] The application of multimodality imaging played an important role for the confirmation of the diagnosis.

So far, the pathophysiology mechanism of TTS is complex. Stimulation of the sympathetic nervous system is known to play a critical role in the pathogenesis of TTS.[7] However, the patient in this case does not have a prior history of stress-related psychological conditions. The mechanism of this case can be hypothesized to enhanced adrenergic tone/sympathetic dominance with vagal denervation due to RFCA which can damage autonomic nerves. An increase in the heart rate and a decrease in heart rate variability observed in our patient following ablation support the transient parasympathetic nervous withdrawal.[8] The cardiac ganglionated plexus (GP), containing autonomic nervous, is generally located at the cavoatrial junctions, and on the left atrial wall in the vicinity of the venoatrial junctions and the pulmonary veins. Owing to the locations are common target sites of cardiac ablation procedures, stimulation of GP in ablation is not uncommon. Few cases have reported that TTS occurred in catheter ablation of cardiac arrhythmias.[9–11]

Coronary artery spasm is one of the pathophysiology mechanisms of TTS.[2] Transient coronary spasm is common in cases of RFCA. Direct thermal injury and autonomic nerve activity imbalance are the proposed mechanisms.[12] In the present patient with an abnormal coronary course, the ablation of tissue carrying a coronary artery branch may cause coronary spasm. Besides, increased cardiac

sympathetic activity can induce coronary microvascular constriction in the context of endothelial dysfunction,[2] and anomalous coronary arteries are more frequently affected by spontaneous spasm.[13] Therefore, tests of endothelial dysfunction could be necessary for this patient to evaluate the tendency to recur spontaneously.

In conclusion, we report a case of TTS following RFCA of atrial fibrillation in a patient with a single RCA. Coronary spasm induced by the ablation and the removal of the normal vagal inhibition to adrenergic stimuli due to ablation of atrial GP might have contributed to the pathophysiological process.

Lead author biography

Dr Xiaoxia Liu is an electrophysiologist, who specializes in the intervention for tachyarrhythmia. She received an MD degree from Harbin Medical University, Harbin, China in 2017. Her research interests are mainly focused on atrial fibrillation.

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 authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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