Unexpected outcome(positive or negative) including adverse drug reactions

Takotsubo cardiomyopathy as a source of cardioembolic cerebral infarction

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Summary

Takotsubo cardiomyopathy is a stress-related cardiomyopathy that mimics acute myocardial infarction. However, it is frequently without obstructive coronary artery disease and is mainly seen in postmenopausal women after an emotional or physiological event. In rare cases, it favours the formation of intracardiac mural thrombus and subsequent cardioembolic events. We report a rare case where a patient developed a cerebral infarction as a cardioembolic sequela of takotsubo cardiomyopathy following the death of her beloved dog. The patient was successfully managed with anticoagulation where a repeat echocardiogram 4 months later showed resolution of the apical thrombus along with recovery of systolic function and left ventricle regional wall abnormalities. This case serves to increase awareness about the rare cardioembolic complications of takotsubo cardiomyopathy and emphasise the need for serial echocardiographic examinations and anticoagulation.

BACKGROUND

Takotsubo cardiomyopathy (TC), or 'apical ballooning syndrome', is an acute cardiomyopathy first described by Dote *et al*¹ in 1991 for its 'octopus trap' like morphology and transient left ventricular ballooning. It mimics an acute myocardial infarction with sudden onset of chest pain, ECG abnormalities and relatively minor increases in cardiac enzymes, but is characterised by the absence of obstructive coronary artery disease^{2–9} (figure 1). Seen to be more common in postmenopausal women, TC is often preceded by emotional or physiological stress which results in transient apical and mid-ventricular wall-motion abnormalities of the left ventricle (LV).^{2–9} There have been a large number of cases where TC was discovered after a cerebral infarction and the stroke was assumed to be the physiological and emotional trigger.^{9–10} In our case, we report a patient where the cerebral infarct was the rare cardioembolic sequela of TC.

CASE PRESENTATION

A 65-year-old postmenopausal woman with medical history of hypertension, hyperlipidaemia and tobacco abuse presented to the stroke service with sudden onset of right homonymous hemianopia. She had recently experienced two episodes of shortness of breath and chest pain following the

unexpected death of her beloved dog 5 days preceding the stroke. The patient denied additional focal neurological deficits or cardiopulmonary symptoms. On admission, the patient's physical examination was unremarkable other than the right visual field loss corresponding to a National Institute of Health Stroke Scale score of 2. Her blood pressure was 150/90 mm Hg, heart rate was 87 beats/min and temperature was 98.4°F.

INVESTIGATIONS

Patient's CT scan and MRI of the brain showed hypo-attenuation of her left occipital lobe suggestive of acute left posterior cerebral artery infarct with no evidence of haemorrhage (figure 2). Routine laboratory studies were unremarkable except for the elevated troponin I of 0.09 ng/ml. The 12-lead ECG showed normal sinus rhythm with QT-prolongation and T wave inversions in the anterolateral leads I, aVL and V2–V6 (figure 3). Transthoracic echocardiography (TTE) performed after hospital admission revealed an apical thrombus measuring 2.1 cm × 1.4 cm, apical akinesis and mildly reduced left ventricle systolic function with an ejection fraction of 40–50% (figure 4). No intracardiac shunt was observed after administration of agitated saline. Coronary angiography showed normal arteries with no significant obstructive lesions.

Identifying Patients with Takotsubo Cardiomyopathy	
1.	Transient akinesis or dyskinesis of the left ventricular apical and mid-ventricular segments with regional wall-motion abnormalities extending beyond a single epicardial vascular distribution
2.	Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture
3.	New electrocardiographic abnormalities (either ST-segment elevation or T-wave inversion)
4.	Absence of recent significant head trauma, intracranial bleeding, pheochromocytoma, obstructive epicardial coronary artery disease, myocarditis, hypertrophic cardiomyopathy

Figure 1 Proposed by Bybee *et al*³ from the Mayo Clinic in 2004.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis includes other causes of cerebral infarction such as hypercoagulability, intracardiac shunt, intrapulmonary shunt or atrial fibrillation. Aforementioned diagnoses were ruled out by a comprehensive work-up. Most importantly, patient's cerebral infarction may have occurred earlier and thus triggered the TC. However, the clear presentation of cardiac symptoms and temporal sequence of events support that the cerebral infarction was the cardioembolic sequela of her stress cardiomyopathy. Other diagnoses also include viral myocarditis and pulmonary embolism which are low in differential given the patient's history and presentation.

TREATMENT

The patient was initially treated with aspirin which was changed to anticoagulant therapy with warfarin and an enoxaparin bridge once her thrombus was identified.

OUTCOME AND FOLLOW-UP

She did not suffer any additional neurological deficits or cardiovascular events during her hospitalisation and was discharged 5 days later after significant improvement in her right homonymous hemianopia. A repeat TTE performed 4 months following discharge showed resolution of the apical thrombus, recovery of systolic function and resolution of left ventricle regional wall abnormalities.

DISCUSSION

The pathophysiology of TC is still debated, but is believed to be related to catecholamine-induced endothelial dysfunction and cardiomyocyte injury. Plasma catecholamine levels are higher at presentation in patients with TC than in those with ST-elevation myocardial infarction.¹¹ Myocytes in the LV apex are thought to be particularly sensitive to excessive levels of catecholamines due to higher density of β -adrenoceptors.¹² Surges of catecholamines may induce cardiac myocyte injury via cyclic AMP-mediated calcium overload or indirectly due to catecholamine-induced endothelial dysfunction and associated damage to underlying myocytes.¹³

Although the likelihood of developing complications with TC appears to be low, it is important to note that the formation of LV thrombus is reported in 5–8% of total cases.^{14 15} In one study, thromboembolism was found to be the second most frequent cardiovascular complication following TC.¹⁶ Despite the fact that the left ventricular dysfunction in TC is a transient phenomenon, it favours the formation of intracardiac mural thrombus through catecholamine-induced platelet activation and low blood flow from wall motion abnormalities in the apical region.¹⁷ A systematic review by de Gregorio¹⁵ in 2009 reported that cardioembolic events were demonstrated in 33% (25% presented as stroke) of TC patients with apical thrombus. These patients received anticoagulant drugs and disappear-

Figure 2 CT scan and MRI of head showing hypo-attenuation of the left occipital lobe.

Figure 3 The 12-lead ECG showing QT-prolongation and T wave inversions in the anterolateral leads I, a VL and V2–V6.

ance of thrombus was documented to occur in 100% of the cases within the range of 9–90 days.¹⁵ To the best of our knowledge there have been approximately seven cases reporting stroke as a clear cardioembolic sequela of TC.^{16–23} In our case, we conclude that the cerebral infarction was the sequela of left ventricular dysfunction with cardiac embolism. We feel that our case report is unique because it provides the clearest temporal sequence of events indicating that our patient's stress cardiomyopathy was the result of acute emotional stress that preceded the embolic stroke. In addition, the work-up is both complete and highly supportive of our conclusion and other causes of cerebral embolism such as atrial fibrillation, patent foramen ovale or hypercoagulable states were excluded.

Prognosis for TC is generally favourable in the absence of significant underlying comorbid conditions.² As seen in our case, early apical thrombus formation and cardioembolic events following TC emphasises the need for serial echocardiographic examinations and anticoagulation. In one study, TTE was recommended every 48 h for prompt detection of left ventricle thrombus, cardioembolic complications and therapeutic decisions.¹⁵ Due to the role of

catecholamines in the pathophysiology of TC, patients may benefit from lifelong therapy of β -blockers to prevent future recurrences. Although the role of anticoagulation therapy in TC has not yet been defined, patients may benefit from anticoagulation therapy irrespective of the presence of a thrombus until the wall motion abnormality resolves.

Learning points

- ▶ Takotsubo cardiomyopathy (TC) is a stress-related cardiomyopathy mainly seen in postmenopausal women after an emotional or physiological event.
- ▶ It mimics an acute myocardial infarction without evidence of obstructive coronary artery disease.
- ▶ The pathophysiology of TC is believed to be related to catecholamine-induced endothelial dysfunction and cardiomyocyte injury.
- ▶ TC favours the formation of intracardiac mural thrombus and may present with cardioembolic complications such as cerebral infarction.
- ▶ Cardioembolic complications emphasise the need for serial echocardiographic examinations and anticoagulation.

Competing interests None.

Patient consent Obtained.

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Figure 4 Echocardiogram with bubble study revealing apical thrombus measuring 2.1 cm×1.4 cm.

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