Case Report

Takotsubo in Acute and Chronic Coronary Artery Disease

Mina Girgis, MD, and Zion Sasson, MD

Division of Cardiology, Mount Sinai Hospital, Toronto, Ontario, Canada

ABSTRACT

Cardiomyopathy of Takotsubo syndrome (TS) is typically triggered by an emotional stress in postmenopausal women. Coexistent coronary artery disease presents diagnostic dilemmas in patients with TS, as seen in the 2 cases presented. In the first case, acute coronary syndrome acts as a physical trigger for TS when a middle-aged man presents with an inferior myocardial infarct, and in the second case, coronary artery disease is a bystander when an elderly woman develops TS after a fall and facial trauma. The novel teaching point is that acute non–left anterior descending acute coronary syndrome could trigger TS.

RÉSUMÉ

La cardiomyopathie du syndrome de Takotsubo (ST) est généralement déclenchée par un stress émotionnel chez les femmes en post-ménopause. Comme nous l'avons observé dans les 2 cas présentés, la coronaropathie coexistante pose des dilemmes en matière de diagnostic chez les patients atteints du ST. Dans le premier cas, le syndrome coronarien aigu agit comme un déclencheur physique du ST lorsqu'un homme d'un certain âge subit un infarctus de la région inférieure du myocarde, et dans le second cas, la coronaropathie constitue un « spectateur » lorsqu'une femme âgée subit un ST après une chute et un traumatisme facial. La nouvelle leçon à retenir est que le syndrome coronarien aigu qui ne provient pas de l'artère interventriculaire antérieure pourrait déclencher le ST.

Takotsubo syndrome (TS), first described in 1983, is typically a transient cardiomyopathy after an emotional, and occasionally physical, trigger.[1] It is not uncommon for TS to occur in patients with coronary artery disease (CAD), as recognized by the current diagnostic criteria.[1] When the 2 conditions overlap, elucidating the etiology of cardiac dysfunction becomes challenging, especially in the presence of disease upstream from dysfunctional myocardial segments. We present 2 cases with such diagnostic overlap.

Case 1

A 63-year-old man, being treated with ramipril for hypertension, presented to the hospital with retrosternal chest discomfort radiating to his right hand, nausea, vomiting, and diaphoresis. Symptoms occurred at rest without a precipitating physical or emotional event. Blood pressure was 184/107 mm Hg (right arm, seated), and pulse was regular at 82 beats/min. There was an S4 on auscultation. Cardiopulmonary examination results were otherwise unremarkable.

Electrocardiogram (ECG) showed sinus rhythm with inferior ST elevations and pathological Q waves (Fig. 1A). Emergency coronary angiography showed severe multivessel disease, with an acute occlusion of the posterior descending artery, which was stented, 70% stenosis in the mid-right coronary artery, and 90% stenosis in the ostial posterolateral branch, which were also stented. On the left, there were 40% to 50% stenotic lesions in the mid and distal left anterior descending (LAD) arteries, and first and second diagonal arteries, as well as chronic total occlusion lesions in the mid-circumflex and second obtuse marginal arteries. Left ventriculography showed mid-to-apical left ventricular akinesis, with basal constrictors moving best (Videos 1-5 ▣, view videos online).

On echocardiography, left ventricular ejection fraction was 40%, with circumferential akinesis of the mid-to-apical segments; right ventricle and valves were normal. Pulmonary pressure was 46 mm Hg (assuming a right atrial pressure of 3 mm Hg). There was also a decrease in the global longitudinal strain with a marked decrease in the apical segments (Fig. 1C and D).

Over the next 24 hours, cardiac monitoring revealed newly diffuse deep T-wave inversions, prolongation of the corrected QT interval, and intermittent nonsustained polymorphic ventricular arrhythmia, without electrolyte disturbance. The patient was asymptomatic with a decreasing high-sensitivity troponin T from a peak of 761 ng/L (normal < 14 ng/L). Urgent repeat angiography showed patent stents with otherwise unchanged coronary lesions and a persistent apical ballooning.

Novel Teaching Points

1. Acute non-LAD ACS could trigger TS.
2. Significant LAD coronary disease could coexist as a bystander in TS.
3. InterTAK score is a guide to be interpreted within the overall clinical context and not as an exclusive diagnostic tool.

During follow-up 3 weeks post-discharge, the patient was asymptomatic, and echocardiography showed complete resolution of the apical dysfunction and recovery of left ventricular ejection fraction.

Case 2

A healthy 72-year-old woman presented to the hospital after a mechanical fall and facial trauma, without chest pain, palpitations, or loss of consciousness. Her blood pressure was 134/77 mm Hg (right arm, sitting) and pulse was regular at 85 beats/min. There was facial swelling and tenderness, and an S4 on auscultation. Cardiopulmonary examination results were otherwise unremarkable.

ECG showed anterior T-wave inversions, which on serial follow-up became deeper and more diffuse, and there was an increase in the corrected QT interval (Fig. 2). High-sensitivity troponin T was 42 ng/L, which normalized on repeat. Head computed tomography showed nondisplaced fractures without intracranial hemorrhage. Echocardiogram was significant for left ventricular ejection fraction of 51%, with mid-to-apical segmental akinesis (Videos 6-8, view videos online).

Urgent coronary angiography revealed proximal LAD chronic total occlusion, 30% proximal circumflex, and 40% distal right stenosis. The LAD collateralized from the co-dominant right and circumflex arteries. Left vetriculogram showed apical akinesis.

After appropriate monitoring, she was discharged to her home with low-dose aspirin and a statin. Follow-up echocardiogram 2 months later showed normalization of all of the left ventricular wall segments.

Discussion

Diagnosing TS in the setting of CAD is challenging. Our first case was in a middle-aged man with a clear inferior ST-elevation myocardial infarction. Nonetheless, he developed transient apical dysfunction without significant upstream LAD disease. At the other end of the spectrum, our second case seemed to be classic TS in a postmenopausal woman after she fell and incurred facial fractures. However, the presence of a chronically occluded LAD transiently put the diagnosis of TS into question.

Although it remains largely elusive, the pathophysiology of TS is now understood to involve a catecholaminergic surge from an acute stress, causing cardiac supply—demand
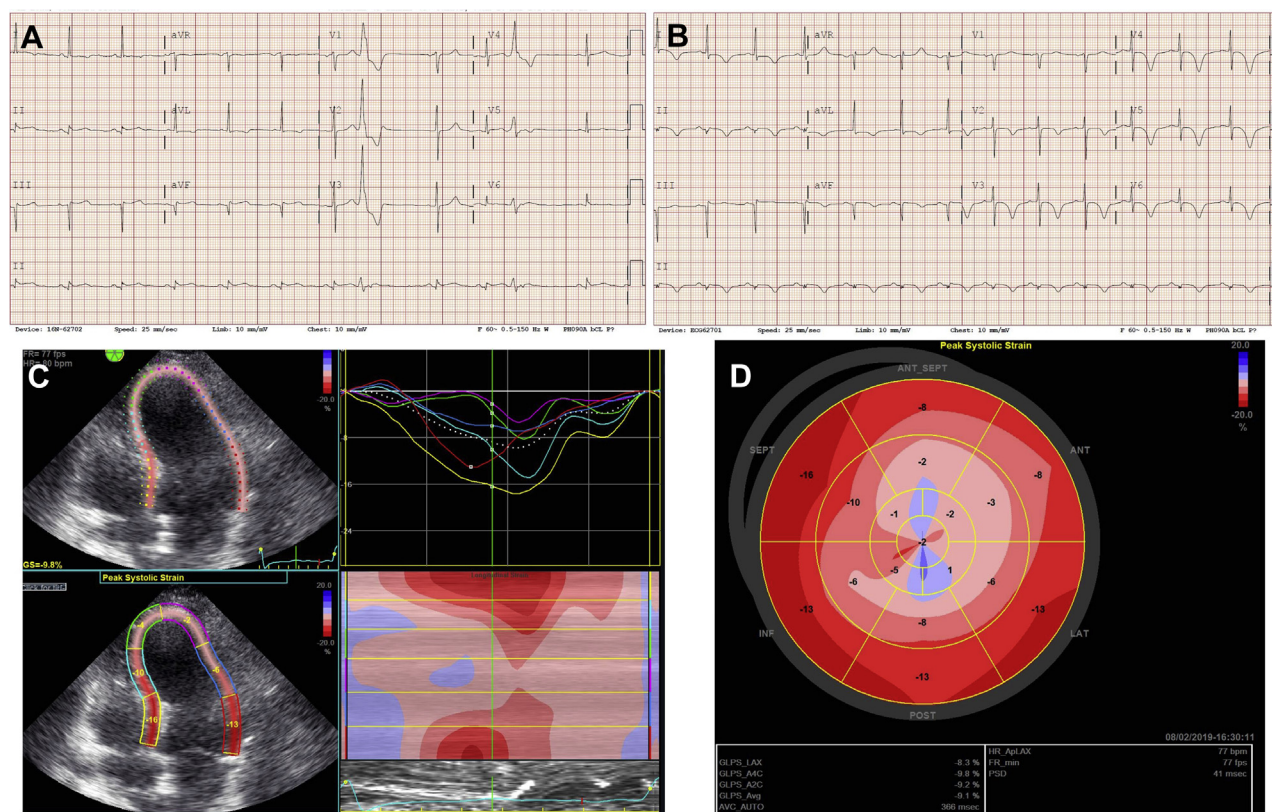

Figure 1. Electrocardiogram (ECG) samples of patient 1. (**A**) Initial ECG at presentation. (**B**) Progression of the ECG 24 hours after the coronary angiogram. (**C**) Apical 4-chamber speckle-tracking strain analysis. (**D**) Bulls-eye of the speckle-tracking longitudinal strain analysis.
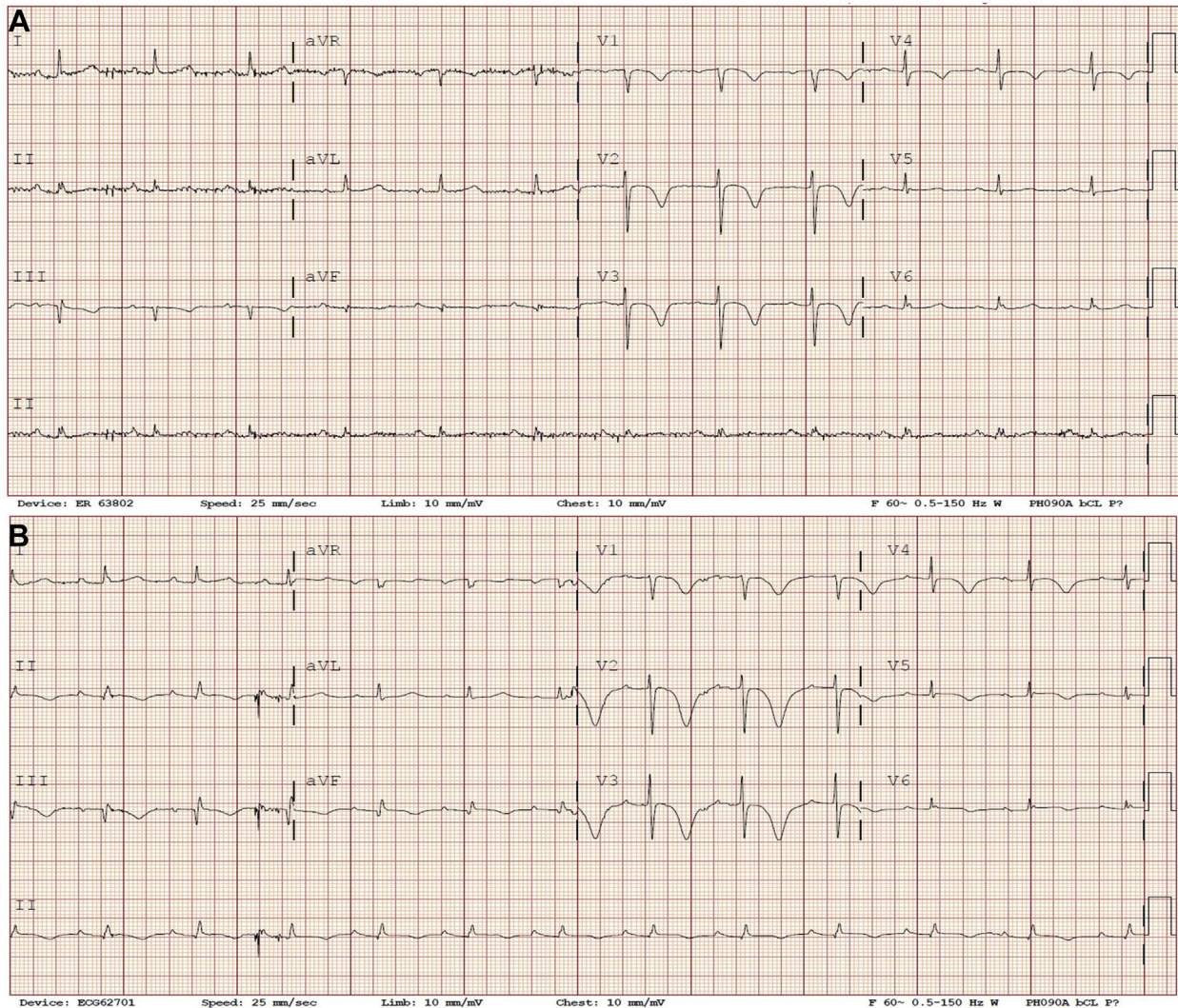
Figure 2. Electrocardiogram (ECG) and echocardiogram samples of patient 2. (**A**) Initial ECG at presentation. (**B**) Progression of the ECG in the next 24 hours.

mismatch and culminating in a stunned myocardium, which in most cases recovers over a short period. Abnormal central nervous system interactions have been demonstrated in patients with TS, which could explain the exaggerated catecholamine release in response to stress.[2] Further, coronary spasm and microvascular dysfunction have been proposed as contributory factors in the cascade of TS by causing demand—supply mismatch.[1] Diabetes and the loss of estrogen's protective effects in postmenopausal women are associated with such endothelial dysfunction.

Atherosclerotic CAD also can be caused by similar risk factors. Therefore, the coexistence of both TS and CAD is not uncommon. Up to 15% of patients with TS have significant atherosclerotic plaques. In such patients, an aborted myocardial infarction seemed plausible as an explanation. Nevertheless, studies in patients with TS and LAD plaques failed to demonstrate plaque rupture, intracoronary thrombi, or dissection using intravascular ultrasound and optical coherence tomography, thereby questioning the broad applicability of the aborted myocardial infarction hypothesis.[3]

The International Takotsubo Registry formulated a score, the InterTAK Diagnostic Score, to help differentiate between a TS and a non—ST-elevation acute coronary syndrome (ACS) caused by plaque rupture. The score—based on history and ECG features—emphasizes the most common features of TS: female sex and an emotional trigger. A score ≥ 70 points favours a TS diagnosis and is confirmed by echocardiography. However, a score < 70 (as in both of our cases) would prompt an angiographic assessment to rule out acute plaque rupture.[4] Although cardiac magnetic resonance imaging could be helpful because subendocardial or transmural late gadolinium enhancement favours ACS, up to 40% of patients with TS who have no CAD could have late gadolinium enhancement.[4-6]

TS triggered by ACS is an intriguing phenomenon that is diagnosed in the presence of new myocardial segmental abnormalities that are not downstream of the acutely narrowed artery. A few published cases describe TS precipitated by ACS, where the culprit vessel arose predominantly from the left coronary tree.[7] To our knowledge, the only published case in which the trigger was an inferior infarct from the right

coronary artery was in a postmenopausal woman.[8] Our report expands on this literature with an example of apical TS triggered by an inferior ST-elevation myocardial infarction in a middle-aged man with a low InterTAK score.

Conclusion

TS and CAD, in their chronic and acute forms, can coexist. Although the clinical tools we have today assist in making the correct diagnosis, TS requires an integration of various diagnostic modalities, clinical context, follow-up, and, most important, a high degree of clinical suspicion. More studies are needed to bring us closer to the understanding of TS and its interaction with CAD.

Disclosures

The authors have no conflicts of interest to disclose.

References

1. Ghadri J-R, Wittstein IS, Prasad A, et al. International Expert Consensus Document on Takotsubo Syndrome (Part I): clinical characteristics, diagnostic criteria, and pathophysiology. Eur Heart J 2018;39:2032-46.

2. Templin C, Hänggi J, Klein C, et al. Altered limbic and autonomic processing supports brain-heart axis in Takotsubo syndrome. Eur Heart J 2019;40:1183-7.

3. Eitel I, Stiermaier T, Graf T, et al. Optical coherence tomography to evaluate plaque burden and morphology in patients with Takotsubo syndrome. J Am Heart Assoc 2016;5:e004474.

4. Ghadri J-R, Wittstein IS, Prasad A, et al. International Expert Consensus Document on Takotsubo Syndrome (Part II): diagnostic workup, outcome, and management. Eur Heart J 2018;39:2047-62.

5. Abbas A, Sonnex E, Pereira RS, Coulden RA. Cardiac magnetic resonance assessment of takotsubo cardiomyopathy. Clin Radiol 2016;71: e110-9.

6. Medina de Chazal H, Del Buono MG, Keyser-Marcus L, et al. Stress cardiomyopathy diagnosis and treatment. J Am Coll Cardiol 2018;72: 1955-71.

7. Y-Hassan S. Takotsubo syndrome triggered by acute coronary syndrome in a cohort of 20 patients: an often missed diagnosis. Int J Cardiol Res 2015;2:28-33.

8. Koeth O, Zeymer U, Schiele R, Zahn R. Inferior ST-elevation myocardial infarction associated with Takotsubo cardiomyopathy. Case Rep Med 2010;2010:1-4.

Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2019.06.003.