Takotsubo Cardiomyopathy Associated with Primary Hyperthyroidism Secondary to Toxic Multinodular Goiter

Dale Murdoch, FRACP^{1,2} William O'Callaghan, MBBS³ Elham Reda, FRACP³
Selvanayagam Niranjana, FRACP^{3,4}

¹ Department of Cardiology, The Prince Charles Hospital, Brisbane, Australia

² School of Medicine, The University of Queensland, Brisbane, Australia

³ Department of Endocrinology, Gold Coast University Hospital, Gold Coast, Australia

⁴ School of Medicine, Griffith University, Gold Coast, Australia

Address for correspondence: Dale Murdoch, MBBS FRACP, The Prince Charles Hospital, Rode Road, Chermside, QLD 4032, Australia (e-mail: dale.murdoch@uq.edu.au).

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Abstract

Keywords

- ▶ takotsubo
- ▶ cardiomyopathy
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- ▶ toxic multinodular goiter

Takotsubo cardiomyopathy is increasingly recognized as a distinct clinical entity. An association with thyroid disease has been identified in several case reports, mostly in the context of Grave disease. We report the case of a 67-year-old woman presenting with takotsubo cardiomyopathy and thyrotoxicosis secondary to toxic multinodular goiter. Previously unreported, this suggests that this association is related to the direct effects of thyroid hormone, rather than an autoimmune mechanism. Thyroid disease should be considered in patients presenting with takotsubo cardiomyopathy.

A 67-year-old woman presented to the emergency department with sudden-onset severe respiratory distress. She reported associated palpitations but specifically denied chest pain or syncope. No psychosocial stressor was identified. Medical history included coronary artery disease (chronically occluded right coronary artery diagnosed at coronary angiography 3 years before), type-2 diabetes mellitus, dyslipidemia, hypertension, obesity, and former smoking. There was no history of thyroid disease or anemia.

The patient was treated for acute pulmonary edema of cardiac origin with oxygen and subsequently noninvasive ventilation, furosemide, aspirin, and enoxaparin and was transferred to the coronary care unit. Initial 12-lead electrocardiogram (ECG) taken at the time of admission showed sinus tachycardia without ST-segment elevation or other specific features of myocardial ischemia, and evolved over 12 hours with widespread precordial T-wave inversion. Troponin I was initially normal (0.03 µg/L) and became elevated at 12 hours (0.5 µg/L).

On further questioning, the patient specifically denied any preceding symptoms of hyperthyroidism. Thyroid examination found a nontender, asymmetric, and nodular goiter.

Primary hyperthyroidism was diagnosed, with a free T4 of 40 pmol/L (ref. 7.0–17) and thyroid stimulating hormone (TSH) of < 0.05 mU/L (ref. 0.3–4.5).

Initial echocardiogram demonstrated akinesis of the lateral, anterior, and septal apex and well-preserved basal function, with overall moderately impaired left ventricular systolic function (40–45%). The findings were highly suggestive of takotsubo cardiomyopathy, with regional wall motion abnormalities not matching a coronary artery anatomical distribution. Diagnostic coronary angiography revealed no change in coronary status from the study done 3 years before. Left ventriculogram was not performed because of the risk of dislodging potential apical thrombus and exacerbating hyperthyroidism with contrast media. The patient's clinical status improved with supportive care.

Antithyroid therapy was initiated and further investigation of thyroid disease was commenced. Thyroid peroxidase antibody, anti-thyroglobulin, and TSH-receptor antibodies were negative. A nuclear medicine thyroid scan showed marked asymmetrical enlargement of the right lobe and inhomogeneous tracer uptake consistent with multinodular goiter. A fine-needle aspiration of a large cold nodule was

performed under ultrasound guidance, and was also consistent with multinodular goiter, with no evidence of malignancy.

Repeat echocardiogram was performed 6 weeks after the initial presentation. Left-ventricular systolic function had completely normalized, without any regional wall-motion abnormalities and normal ejection fraction of 72%. The toxic multinodular goiter was treated with radioactive iodine and subsequent thyroid replacement therapy. The patient remained well in follow-up, without angina or dyspnea.

Takotsubo cardiomyopathy (TTC) is increasingly recognized as a distinct and underdiagnosed clinical entity that mimics acute coronary syndrome, mostly in postmenopausal females. It is characterized by the reversible apical ballooning of the left ventricle in the absence of significant coronary artery disease or vasospasm. The left ventriculogram appearance mimics the profile of its namesake, the round-bottomed and narrow-necked traditional Japanese octopus trap. Although classically linked to emotional stress as a trigger, in up to one-third of cases no identifiable precipitant can be found.

Hyperthyroidism has been linked to takotsubo cardiomyopathy in several case reports. In most cases, Grave disease is reported as the underlying etiology.^{1–5} One report describes Hashimoto thyroiditis⁶ and another describes iatrogenic thyroiditis following radioiodine therapy (iodine-131) in a patient with toxic multinodular goiter.⁷ Others have reported exogenous levothyroxine-induced takotsubo cardiomyopathy⁸ although it is arguable that this case was related to Grave disease and therefore it is unclear as to whether the true cause of the autoimmune disease or exogenous levothyroxine was the cause for the TTC.⁹

Our case documents an association between takotsubo cardiomyopathy and hyperthyroidism secondary to toxic multinodular goiter. This is the first time this association has been reported. This is important because it supports the argument that the association is related to the direct effects of thyroid hormone, rather than an autoimmune phenomenon as may be explained by antithyroid antibodies found in Grave disease. This is concordant with the report of exogenous thyroid hormone inducing TTC.

Wittstein et al¹⁰ reported markedly elevated catecholamine levels in patients with TTC. While the hyperthyroid state mimics adrenergic excess,⁵ plasma catecholamine levels are usually low-to-normal in patients with hyperthyroidism.¹¹ Therefore, TTC in these patients may be the result of

a common downstream mechanism in the myocardium not mediated by the β -adrenergic receptor.¹²

Although the exact mechanisms of takotsubo cardiomyopathy remain unknown, this association with hyperthyroidism brings us closer to unlocking the puzzle. In the meantime, one can argue that thyroid function testing is important in patients presenting with takotsubo cardiomyopathy, as it may identify an underlying, treatable disease.

Disclosure

No competing financial interests exist.

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