**Novel Insights from Clinical Experience** 

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# Transient Left Ventricular Systolic Dysfunction with Thrombus and Subsequent Cardioembolic Stroke in Short-Term Overt Hypothyroidism

Jeong Hoon Yang<sup>a</sup> Hye Won Jang<sup>b</sup> Sung-Ji Park<sup>a, c</sup> Seung Woo Park<sup>a, c</sup>

Divisions of <sup>a</sup>Cardiology and <sup>b</sup>Endocrinology and Metabolism, Department of Internal Medicine, and <sup>c</sup>Cardiovascular Imaging Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

# **Established Facts**

- Recently, cases of takotsubo cardiomyopathy in thyrotoxicosis have been reported.
- Rarely, a ventricular thrombus develops in cases with transient left ventricular systolic dysfunction and the ventricular thrombus is associated with cerebrovascular accidents.

# **Novel Insights**

- This is the first reported case in the medical literature of transient left ventricular systolic dysfunction with thrombus and subsequent cardioembolic stroke in a patient with short-term overt hypothyroidism.
- Acute hypothyroidism during thyroxine withdrawal for radioactive iodine therapy must be considered in the differential diagnosis of transient left ventricular systolic dysfunction.

# Key Words

Thrombus · Stroke · Hypothyroidism

#### Abstract

A 57-year-old woman was referred for cardiomegaly on a chest X-ray taken during thyroxine withdrawal for radioiodine therapy after total thyroidectomy. Baseline transthoracic echocardiography showed left ventricular (LV) wall motion abnormalities and an LV apical mural thrombus. Coronary angiography revealed normal epicardial coronary arteries. Despite anticoagulation treatment, the patient de-

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Accessible online at: www.karger.com/crd veloped abrupt aphasia, agraphia and acalculia. The distal branch of the inferior segmental branch on the left middle cerebral artery was not well visualized on magnetic resonance angiography. Three days later, the patient had made a near full neurological recovery. After 4 weeks of anticoagulation therapy, the apical mural thrombus and wall motion abnormalities resolved. This is the first reported case in the medical literature of transient LV systolic dysfunction with thrombus and subsequent cardioembolic stroke in a patient with short-term overt hypothyroidism.

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Sung-Ji Park, MD, PhD Division of Cardiology, Cardiovascular Imaging Center, Samsung Medical Center Sungkyunkwan University School of Medicine 50 Irwon-dong, Gangnam-gu, Seoul 135-710 (Korea) Tel. +82 23 410 3419, E-Mail tyche.park@gmail.com

#### Introduction

Hypothyroidism is known to cause a decrease in ventricular pressure and contractility, unloading of the heart and cardiomyocyte atrophy [1]. However, the clinical presentation of short-term overt hypothyroidism is not obvious, and cardiovascular changes produced by cardiac unloading may be difficult to differentiate from alterations due to heart failure [2–4]. To date, the impact of acute hypothyroidism on cardiac function has been investigated in only a few inconclusive studies [5]. Here, we present a rare case of cardioembolic stroke in a patient with transient left ventricle (LV) systolic dysfunction with apical mural thrombus and overt hypothyroidism after total thyroidectomy.

#### **Case Report**

A 57-year-old woman presented with a history of papillary thyroid carcinoma that had been treated with total thyroidectomy 11 weeks prior to presentation to our department. After the thyroidectomy, the patient underwent radioactive iodine (RAI) therapy after a 4-week thyroxine withdrawal period. The blood laboratory tests at the time of RAI therapy showed that the thyroid-stimulating hormone level was markedly elevated to 81.08 mU/l (normal range 0.3–6.5), and free thyroxine was significantly reduced to 0.01 ng/dl (normal range 0.64–1.72). The patient was treated with thyroid hormone replacement immediately after RAI therapy and then referred to our department due to cardiomegaly that was noted on chest X-ray without any chest symptoms (fig. 1a).

The patient had been hypertensive for 10 years. There was no history of diabetes, smoking or dyslipidemia and no family history of early coronary artery disease. On initial presentation, the blood pressure was 87/65 mm Hg and the pulse rate was 96 beats/ min with a regular heart beat. The physical examination revealed no abnormal findings. Myocardial specific enzymes, creatine kinase-MB and troponin I were normal. The N-terminal fragment of proB-type natriuretic peptide was markedly elevated to 8,103 pg/ml (normal range 0–222 pg/ml). The patient's resting electrocardiogram revealed a sinus rhythm and negative T waves in the precordial leads (fig. 1b). Baseline transthoracic echocardiography (TTE) showed akinesia of the apical and mid segments, normal wall thickness, and an LV ejection fraction of 30–35%. TTE revealed an LV apical mass with an echodensity compatible with an apical mural thrombus (fig. 1c–e).

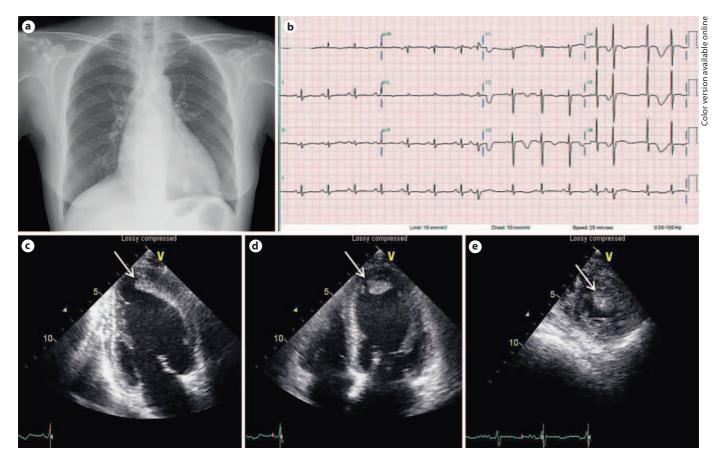
The patient was treated with a low-dose  $\beta$ -blocker, an angiotensin-converting enzyme inhibitor and intravenous heparin followed by oral anticoagulation with warfarin. She underwent coronary angiography to rule out coronary artery disease, which revealed normal epicardial coronary arteries. The following day, a cardiac magnetic resonance (MR) examination was performed to better characterize the myocardium. There was no delayed contrast enhancement or perfusion defect observed on the cardiac MR imaging (MRI), and a mobile thrombus at the LV apex was detected. Three hours after the cardiac MRI, the patient developed abrupt aphasia, agraphia and acalculia despite anticoagulation treatment. MRI of the brain demonstrated a perfusion delay in the inferior division of the left middle cerebral artery territory and acute infarction in the right cerebellar hemisphere. On MR angiography, the distal branch of the inferior segmental branch of the left middle cerebral artery was not well visualized. The day after the patient's acute ischemic stroke, TTE revealed a slight decrease in the apical thrombus, improvement of LV contractility, and an increase in thrombus mobility (fig. 2). Three days later, the patient had made a near full neurological recovery and was discharged on day 17. The follow-up TTE performed after 4 weeks of anticoagulation therapy showed complete resolution of the apical thrombus of the LV and a marked improvement in the regional contractility of the LV apical and mid segments (fig. 3).

## Discussion

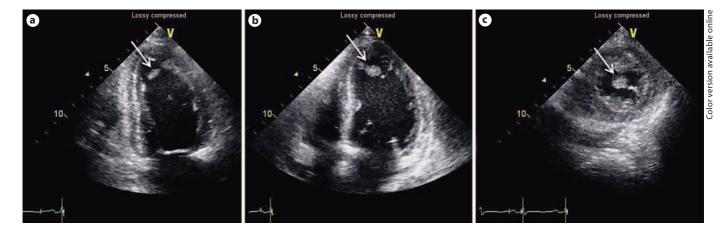
The cardiovascular system is the most important target organ of the thyroid hormone, which has a variety of effects on cardiac function as well as on peripheral vascular tone [4]. Many of the clinical manifestations of hyperthyroidism are caused by alteration of cardiovascular hemodynamics due to thyroid hormone excess. Hemodynamic effects of hypothyroidism are opposite to those of hyperthyroidism [3]. Severe thyrotoxicosis can result in significant LV systolic dysfunction and a low cardiac output state, and postulated mechanisms underlying this process include long-standing tachycardia and direct toxic effects of thyroid hormones on the myocardium [6]. However, the clinical presentation of overt hypothyroidism is not obvious and most patients have few symptoms and signs, such as bradycardia, narrow pulse pressure, some degree of exercise impairment, and abnormal ECG findings including QT interval lengthening and flattening or inversion of the T wave, which reflects a prolonged cardiac action potential [2]. Acute hypothyroidism can occur after thyroxine withdrawal in patients who have undergone total thyroidectomy for thyroid cancer; however, studies of the association between acute hypothyroidism and cardiac function are very rare [7, 8]. Furthermore, there are no published reports of reversible, transient LV systolic dysfunction or a demonstrable change in cardiac size in short-term overt hypothyroidism. Interestingly, our patient, who had acute hypothyroidism, exhibited severely depressed LV systolic function and negative T waves in the precordial leads on electrocardiography. Recently, cases of takotsubo cardiomyopathy in thyrotoxicosis have been reported [9, 10]. However, the association between hypothyroidism and takotsubo cardiomyopathy has not been

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Cardioembolic Stroke in a Patient with Hypothyroidism

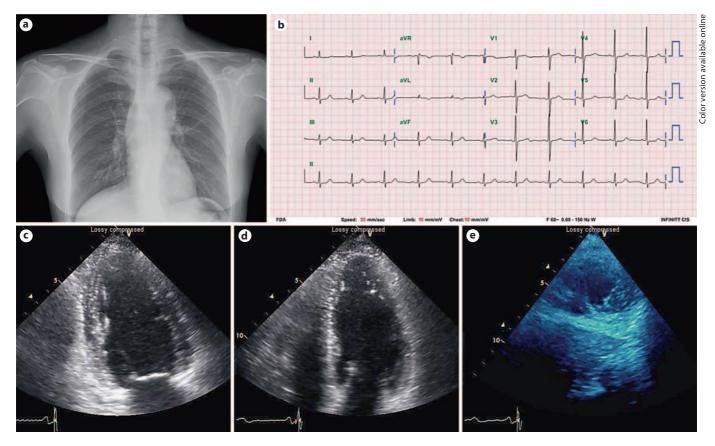


**Fig. 1. a** The patient's chest X-ray showed cardiomegaly at presentation. **b** The patient's electrocardiography showed negative T waves in the precordial leads. TTE showed an LV apical mass with an echodensity compatible with an apical mural thrombus (white arrow) in the 2-chamber apical view (**c**), 4-chamber apical view (**d**), and parasternal short axis view (**e**).



**Fig. 2.** TTE revealed a slight decrease in the apical thrombus but an increase in thrombus mobility (white arrow) in the 2-chamber apical view (**a**), 4-chamber apical view (**b**), and parasternal short axis view (**c**).

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**Fig. 3. a** The patient's chest X-ray showed a normal cardiac size after 4 weeks of anticoagulation therapy. **b** The patient's electrocardiography showed no abnormal findings. TTE showed the complete resolution of the apical thrombus of the LV in the 2-chamber apical view (**c**), 4-chamber apical view (**d**), and parasternal short axis view (**e**).

established. Rarely, a ventricular thrombus develops in cases with transient LV systolic dysfunction, such as takotsubo cardiomyopathy, and the ventricular thrombus is associated with cardioembolic adverse events, with cerebrovascular accidents in particular [11, 12]. A previous study reported that an LV thrombus was detected in 4 out of 53 patients with takotsubo cardiomyopathy [13]. In the current case, the patient had acute short-term hypothyroidism after total thyroidectomy and then presented with transient LV systolic dysfunction with an apical mural thrombus and subsequent cardioembolic stroke. The patient fully recovered after medical treatment that included thyroxine replacement, anticoagulation, a  $\beta$ -blocker and an angiotensin-converting enzyme inhibitor.

In conclusion, acute hypothyroidism during thyroxine withdrawal for RAI must be considered in the differ-

Cardioembolic Stroke in a Patient with Hypothyroidism ential diagnosis of transient LV systolic dysfunction. Physicians should be aware that ventricular thrombosis may develop during the earliest stages of the disease and that dislocation of emboli can occur during the recovery of LV wall motion. Appropriate medical management can result in dramatic improvement of the associated cardiovascular derangements.

### **Conflict of Interest**

The authors declare no financial or other conflicts of interest.

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Yang/Jang/Park/Park