Transient ST-Segment Elevation due to Iatrogenic Hyperthyroidism in a Patient with Normal Coronary Arteries

Çetin Mustafa¹, Uçar Özgül², Güven Çetin Zehra² and Çiçekçioğlu Hülya²

Abstract

A 53-year-old man presented with angina pectoris and ST-segment elevation in V₁-V₄ leads. Electrocardiogram changes and chest pain were completely resolved with nitroglycerine infusion. Coronary angiogram revealed normal epicardial vessels. These findings suggest that the acute myocardial ischemia was secondary to coronary vasospasm. From his medical history we learned that he was taking L-thyroxine and the dose had been increased two months previously. He was found to be in thyrotoxic state at admission. L-thyroxine treatment was withheld and diltiazem was given. He had no further symptoms. In conclusion we think that acute myocardial ischemia was likely secondary to L-thyroxine-induced coronary spasm.

Key words: coronary vasospasm, thyrotoxicosis, angina pectoris

(Intern Med 50: 1595-1597, 2011)

(DOI: 10.2169/internalmedicine.50.5099)

Introduction

Cardiac manifestations of thyrotoxicosis have been reported to be atrial fibrillation, angina pectoris, myocardial infarction and heart failure (1). Thyrotoxicosis is rarely associated with acute myocardial ischemia (angina pectoris or myocardial infarction) without significant coronary artery disease. Endogenous thyrotoxicosis causes acute myocardial ischemia in most cases, however there are several reports of cases due to iatrogenic thyrotoxicosis (2-5).

Coronary vasospasm is defined as a transient abnormal contraction of an epicardial coronary artery that results in myocardial ischemia. Patients who suffer from chest pain, in particular relatively young patients and those who smoke, should be considered in terms of coronary vasospasm (6). The prevalence of coronary vasospasm is higher in the Japanese population than in the Western population; this is likely due to genetic as well as environmental factors (7).

We describe a 53-year-old man with normal coronary arteries, who had transient ST-segment elevation in anterior precordial leads due to iatrogenic hyperthyroidism, which

was likely secondary to L-thyroxine-induced coronary spasm.

Case Report

A 53-year-old Caucasian man presented to the emergency service with squeezing chest pain which started 20 minutes earlier; it had awoken him in the early morning from sleep. The pain radiated from the chest to the back. Blood pressure was 130/70 mmHg, pulse rate was 98 bpm with a regular rhythm and physical examination revealed normal findings. The electrocardiogram (ECG) revealed ST segment elevation in leads V₁-V₄ and ST segment depression in leads DII, DIII, aV_F (Fig. 1). He had no diabetes mellitus, smoking habit, hypertension, hyperlipidemia or alcohol addiction. Routine biochemical findings on admission were as follows: blood urea nitrogen: 22 mg/dL (N:10-50 mg/dL), creatinine: 0.9 mg/dL (N: 0.7-1.3 mg/dL), AST: 23 IU/L (N:15-37 IU/L), ALT: 32 IU/L (N: 30-65 IU/L), sodium: 138 mEq/L (N: 135-147 mEq/L), potassium: 4.3 mEq/L (N: 3.5-5.5 mEq/L), chloride: 100 mEq/L (N: 95-105 mEq/L), calcium: 9.2 mEq/mL (N: 8.5-10.2 mEq/mL). The patient was admitted to the

¹Department of Cardiology, Atatürk Chest Disease and Chest Surgery Education and Research Hospital, Sanatoryum caddesi, Turkey and ²Department of Cardiology, Ankara Numune Education and Research Hospital, Talatpaşa Bulvarı, Turkey

Received for publication January 2, 2011; Accepted for publication March 7, 2011

Correspondence to Dr. Mustafa Çetin, mdmustafacetin@yahoo.com

Figure 1. ECG revealing ST-segment elevation in leads V₁ through V₄ at admission.

Figure 2. ECG revealing complete resolution of ST-segment elevation after intravenous administration of nitroglycerine.

Figure 3. Coronary angiography showing normal epicardial coronary arteries.

coronary care unit and intravenous nitroglycerine was started. Angina pectoris and ECG findings were completely resolved following intravenous administration of nitroglycerine (Fig. 2). As we considered that this clinical situation was probably due to coronary vasospasm, oral nitrate and diltiazem treatment were administered. No symptoms or ECG changes occurred and cardiac enzymes and troponin levels were not elevated during the follow-up. Transthoracic echocardiogram revealed no segmentary wall motion abnormality. To exclude an obstructive coronary lesion we performed angiography, which revealed normal epicardial coronary arteries (Fig. 3). While investigating the mechanism of coronary vasospasm we learned from his medical history that in 2006, he was diagnosed as having Hashimoto's thyroiditis and was receiving daily 100 mcg L-thyroxine therapy. Two months previously the daily dose of L-thyroxine was increased to 300 mcg when TSH level was found to be 61 $\mu\text{IU/mL}$ (N: 0.4-5.0 $\mu\text{IU/mL}$). At admission to coronary care unit, free T₃ was 4.5 pg/mL (N: 2.5-3.9), free T₄ was 2.5 ng/dL (N: 0.61-1.48) and TSH was 0.03 $\mu\text{IU/mL}$. L-thyroxine treatment was withheld until thyroid function tests (TFT) returned to normal. In this time period diltiazem was given at a daily dose of 120 mg. After normalization of TFT, low-dose L-thyroxine was restarted and diltiazem was discontinued.

Discussion

Chest pain due to thyrotoxicosis differs from typical angina pectoris by occurring at rest, recent onset and rapid progression of symptoms and dramatic relief of symptoms in the euthyroid state (8). The possible causes of acute myocardial ischemia in thyrotoxic patients with normal coronary arteries is unclear, but several mechanisms have been proposed such as temporary major coronary artery occlusion, small vessel disease and increased myocardial oxygen demand (5).

Temporary coronary artery occlusion may be caused by in-situ coronary thrombosis or thromboembolism with spontaneous lysis of clot or vasospasm. Thromboembolism usually occurs in thyrotoxic patients with accompanying atrial fibrillation or congestive heart failure. The abnormalities of the coagulation system have been reported in patients with thyrotoxicosis. Erem et al reported increased levels of plasma fibrinogen and several coagulation factors, von Willebrand factor, antithrombin, and PAI-1 and decreased levels of t-PA in patients with overt hyperthyroidism (9). In addition, two other experimental studies showed an impaired fibrinolytic activity in hyperthyroid patients (10, 11). Therefore, based on these studies, thyrotoxic patients are prone to thrombosis.

Coronary vasospasm related to thyrotoxicosis most often

occurs at rest, particularly from midnight to early morning, and is usually not induced by exercise in the daytime. The prognosis of vasospasm induced by hyperthyroidism is good. These patients are expected to have no more angina once they become euthyroid. The possible mechanisms for coronary vasospasm were reported to be an imbalance of autonomic cardiac innervation (12), increased levels of thromboxane A2 and decreased levels of prostacyclin in the coronary circulation (13). In-vitro studies indicated that vasoconstrictive agents such as catecholamines and 5-hydroxytryptamine have augmented effects on vascular smooth muscle in the thyrotoxic state (14). Also thyrotoxicosis is a hyperadrenergic state due to increased adrenergic receptor sensitivity and an increased number of receptors, thus stimulation of adrenergic receptors on coronary arteries may provoke coronary vasospasm (15). In the present patient, the prompt relief of angina and ST-segment elevation after intravenous nitroglycerin administration and the presence of normal coronary arteries in cardiac catheterization suggest that the acute myocardial ischemia was secondary to coronary vasospasm.

In the present patient, the clinical course highly favored coronary vasospasm so that provocation test was not considered and medical treatment was started. The role of provocation test in the diagnosis of coronary vasospasm is controversial (16). Patients with a high clinical suspicion of coronary vasospasm can be started on medical treatment without provocation test. In patients with some clinical suspicion, non-invasive tests such as ergonovine stress echocardiography can be used. An invasive provocation test can be considered in the case of symptoms refractory to medical treatment.

In conclusion, we think that the rapid, uncontrolled dose increase of L-thyroxine and the abrupt rise in thyroid hormone levels were responsible for the acute myocardial ischemia in the present patient. Physicians must pay attention to thyroid replacement therapy by starting treatment with low doses and adjusting doses gradually at six- or eight-week intervals.

The authors state that they have no Conflict of Interest (COI).

References

1. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. *N Engl J Med* **344**: 501-509, 2001.
2. Gowda RM, Khan IA, Soodini G, Vasavada BC, Sacchi TJ. Acute myocardial infarction with normal coronary arteries associated with iatrogenic hyperthyroidism. *Int J Cardiol* **90**: 327-329, 2003.
3. Bergeron GA, Goldsmith R, Schiller NB. Myocardial infarction, severe reversible ischemia, and shock following excess thyroid administration in a woman with normal coronary arteries. *Arch Intern Med* **148**: 1450-1453, 1988.
4. Locker GJ, Kotzmann H, Frey B, et al. Factitious hyperthyroidism causing acute myocardial infarction. *Thyroid* **5**: 465-467, 1995.
5. Kohno A, Hara Y. Severe myocardial ischemia following hormone replacement in two cases of hypothyroidism with normal coronary arteriogram. *Endocr J* **48**: 565-572, 2001.
6. Kawano H, Ogawa H. Endothelial function and coronary spastic angina. *Intern Med* **44**: 91-99, 2005.
7. Yasue H, Kugiyama K. Coronary spasm: clinical features and pathogenesis. *Intern Med* **36**: 760-765, 1997.
8. Somerville W, Levine SA. Angina pectoris and thyrotoxicosis. *Br Heart J* **12**: 245-257, 1950.
9. Erem C, Ersoz HO, Karti SS, et al. Blood coagulation and fibrinolysis in patients with hyperthyroidism. *J Endocrinol Invest* **25**: 345-350, 2002.
10. Morishita E, Hashimoto T, Asakura H, et al. Increased plasma levels of free tissue factor pathway inhibitor in patients with Graves' disease. *Thromb and Haemost* **79**: 919-923, 1998.
11. Chadarevian R, Bruckert E, Giral P, Turpin G. Relationship between thyroid hormones and fibrinogen levels. *Blood Coagul Fibrinolysis* **10**: 481-486, 1999.
12. Yasue H, Touyama M, Shimamoto M, Kato H, Tanaka S, Akiyama F. Role of autonomic nervous system in the pathogenesis of Prinzmetal's variant form of angina. *Circulation* **50**: 534, 1974.
13. Moliterno D, DeBold CR, Robertson RM. Case report: coronary vasospasm-relation to the hyperthyroid state. *Am J Med Sci* **304**: 38-42, 1992.
14. Shepherd JT, Vanhoutte PM. Mechanisms responsible for coronary vasospasm. *J Am Coll Cardiol* **8**: 50A-54A, 1986.
15. Hammond HK, White FC, Buxton IL, Saltzstein P, Brunton LL, Longhurst JC. Increased myocardial beta-receptors and adrenergic responses in hyperthyroid pigs. *Am J Physiol* **252**: H283-H290, 1987.
16. Adlam D, Azeem T, Ali T, Gershlick A. Is there a role for provocation testing to diagnose coronary artery spasm? *Int J Cardiol* **102**: 1-7, 2005.