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Unstable Angina with Normal Coronary Angiography in Hyperthyroidism: A Case Report

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Hyperthyroidism is associated with an increase in myocardial oxygen consumption that, due to an imbalance of oxygen demand and supply, can cause angina. However, subclinical hyperthyroidism rarely presents as chest pain in the resting state. Herein, we present a case of subclinical hyperthyroidism involving a 58-year-old male who complained of frequent chest tightness and typical electrocardiographic changes while in a resting state. Coronary angiography showed no significant lesion. Laboratory data showed that the patient suffered from hyperthyroidism, for which he was successfully treated with anti-thyroid agents. We are reminded that typical chest pain might be the first symptom of hyperthyroidism.

Key Words: angina pectoris, unstable angina, hyperthyroidism
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Typical chest pain with a normal major epicardial coronary artery, which is sometimes encountered in clinical practice, is caused by such physical disorders as cardiomyopathy, aortic valve disease (stenosis and regurgitation), mitral valve prolapse, ventricular hypertrophy, pulmonary hypertension, pulmonary embolism, aortic dissection, coronary small vessel disease, syndrome X, and coronary spasm. Herein, we present the case of a patient whose coronary angiography was normal but who complained of frequent typical chest pain at rest that was later found to be caused by hyperthyroidism.

Case Presentation

A 58-year-old man visited our cardiovascular clinic complaining of frequent chest tightness at rest. He described his chest discomfort as being an oppressive, non-radiating sensation located over the anterior chest wall. It came and went in a crescendo–decrescendo-like pattern and persisted for around 10 minutes. It occurred with dyspnea, diaphoresis, and palpitation while resting, especially in the early morning. He said he had experienced a noticeable increase in frequency. A baseline electrocardiogram (EKG), done in the absence of symptoms, was normal. As the frequency of his discomfort had increased and because he was suspected of having unstable angina, the patient was admitted to our hospital. Early one morning while he was in the hospital, the patient experienced the same chest tightness. It came with ST-segment depression and T-wave inversion (Figure 1). Cardiac enzymes were not elevated. Aspirin, β-blocker, and heparin were prescribed.

Further inquiry into his medical history found only weight loss and poor exercise tolerance. He was not found to have hand tremors, heat intolerance, or a bad temper, nor did he have a history of hypertension, diabetes, smoking, or coronary artery disease.

The patient had a blood pressure of 138/80 mmHg and a regular pulse of 88/min. A grade II systolic murmur was heard over the left lower sternal border. He had no signs of an enlarged thyroid gland, exophthalmos, pretibial myxedema, or lid lag.

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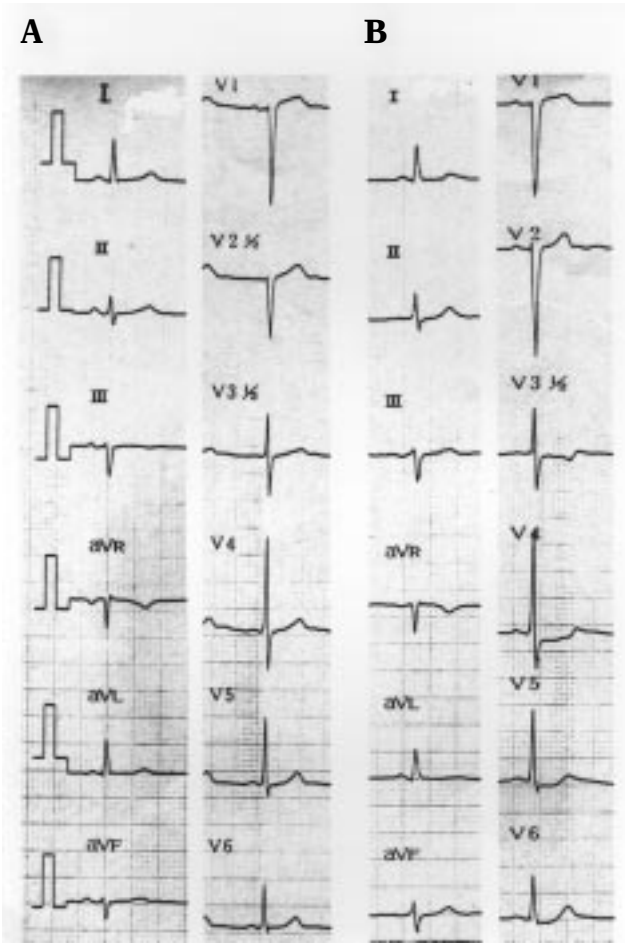

Figure 1. *Electrocardiography showing ST-T changes over V3–V6: (A) at rest; (B) during chest tightness.*

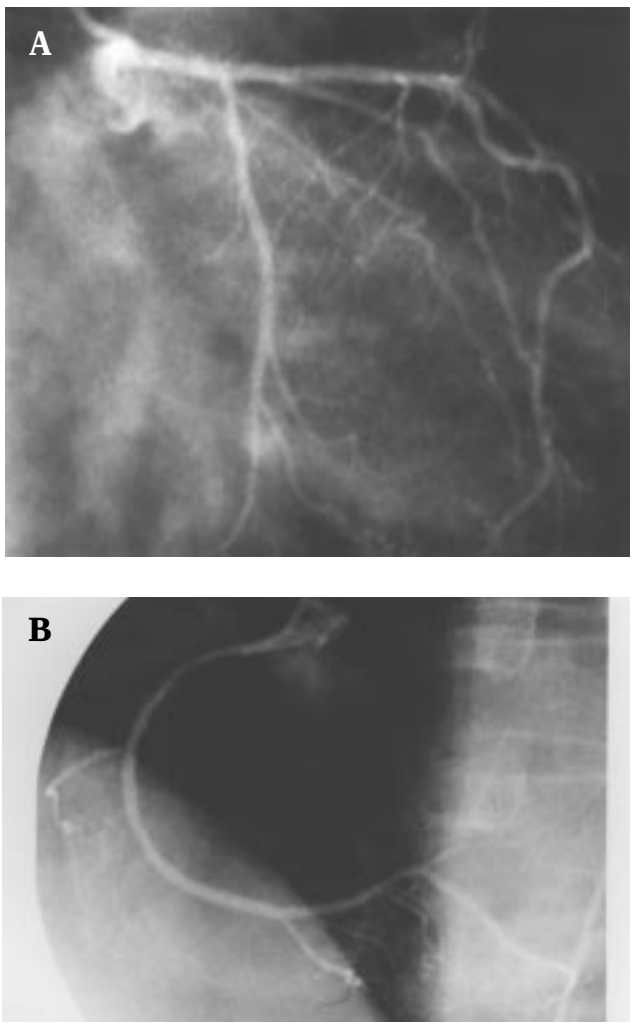

Figure 2. *Normal coronary angiography: (A) left right anterior oblique (RAO) view; (B) RAO and left anterior oblique (LAO) view.*

Routine laboratory tests showed that serum levels of lactate dehydrogenase (LDH), cholesterol, triglyceride, fasting sugar, creatine kinase (CK), and troponin-T were normal. Thyroid function tests revealed concentrations of thyroid stimulating hormone of less than 0.1 μU/mL (normal, 0.4–5 μU/mL), triiodothyronine of 531.4 ng/dL (normal, 80–200 ng/dL), and thyroxine of 23.6 μg/dL (normal, 4.5–11.5 μg/dL). Chest roentgenography showed only atherosclerosis of the aorta. Echocardiography showed left atrial and ventricular dilation, grade II aortic regurgitation, and septal hypertrophy.

Thallium-201 myocardial perfusion scan showed suspected right coronary artery (RCA) territory myoischemia. Selective coronary angiography was normal with systolic left ventricular function (Figure 2). No provoking test was performed.

The patient was treated with methimazole 15 mg three times daily (tid), isosorbide dinitrate 5 mg tid, and propranolol 60 mg tid at discharge. During cardiovascular clinic follow-up, he did not complain of any significant chest tightness and routine thyroid function tests were normal.

Discussion

Cardiovascular function, such as heart rate, cardiac output, and systemic vascular resistance, are related to thyroid function status. Changes in heart rate result from both an increase in sympathetic tone and a decrease in parasympathetic tone [1]. With the action of triiodothyronine on vascular smooth muscle cells [2], thyroid hormone can also dilate the resistant arterioles of the peripheral circulation, thereby decreasing systemic vascular resistance,

increasing heart rate and cardiac contractility, and directly increasing oxygen consumption. The increased heart rate, greater pulse pressure, and increased cardiac output in patients with hyperthyroidism resemble a state of increased adrenergic activity, despite normal or low serum concentrations of catecholamines [1].

Hyperthyroidism has been linked to many cardiovascular diseases such as atrial fibrillation [3], thromboembolism [4], congestive heart failure [5], acute pulmonary edema [6], atrioventricular block [7], pericarditis [8], stable angina [9], acute myocardial infarction [10,11], ventricular arrhythmia [12,13], and sudden death [14]. Angina pectoris has been reported to occur in 0.5–20% (usually 10–20%) of patients with active thyrotoxicosis [10]. Three possible mechanisms have been proposed to play a role in the pathogenesis of coronary occlusion with thyrotoxicosis [11]: significant underlying coronary atherosclerosis [9], coronary embolization, and direct damage to coronary arteries [15]. Differential diagnosis in hyperthyroidism patients with chest pain includes mitral valve prolapse, aortic valve disease, ventricular hypertrophy, pulmonary hypertension, cardiomyopathy, small-vessel disease [16], and coronary spasm [13,17].

There are many pathophysiologic hypotheses concerning angina and hyperthyroidism. One explanation involves the imbalance of oxygen supply and demand, which is caused by sympathetic system activation. Heart rate and contractility are enhanced by increased adrenergic sensitivity due to elevated density and affinity of β receptors [18] with a concomitant decrease in the number and affinity of α receptors [19], although plasma, urinary, and myocardial adrenaline concentrations and turnover levels are normal [20]. In addition, thyroid hormone may have a direct effect on the automaticity [21] and decreased cholinergic inhibition of the sinus node [22].

Somerville and Levine described the nature of angina pectoris coexisting with thyrotoxicosis: angina pain occurring at rest (angina pectoris decubitus), recent onset and rapid progression of symptoms, and abrupt cessation of angina with suppression of thyrotoxicosis [9]. In the same report, the authors noted a paucity of typical hyperthyroidism manifestations in these patients – less common weight loss, exophthalmos, tachycardia, or palpitation. In other reports [13,17], the diagnosis of hyperthyroidism was often delayed or only made in retrospect due to uncommon findings. Acute myocardial infarction has been reported to occur only rarely in thyrotoxicosis [11], but when it does, the infarction is more extensive than that in a patient in a euthyroid state [23].

Very few patients with thyrotoxicosis and ischemic heart disease have been reported to have normal coronary angiographic findings. The clinical manifestations of ischemic heart disease in thyrotoxicosis have been reported to be stable angina [17], acute coronary syndrome [24], and ventricular fibrillation [13]. Thromboembolism with recanalization [25] and coronary spasm [13,17] are two other possible mechanisms of temporary coronary artery occlusion, though thyrotoxicosis itself is not usually complicated with thromboembolism unless the thromboembolism occurs with atrial fibrillation, congestive heart failure, and abnormalities in platelets [26] or coagulopathy.

In our patient, as well as those reported by Wei et al [13] and Featherstone and Stewart [17], chest pain gradually decreased as thyroid function became normal. However, Featherstone and Stewart reported the recurrence of chest pain with the administration of levothyroxine for ^{131}I-irradiation-related hypothyroidism [17]. Locker et al also reported acute myocardial infarction occurring in a patient while levothyroxine was being titrated for hypothyroidism [27].

Our patient presented with typical resting chest pain and obvious EKG changes, the signs of unstable angina. It was therefore surprising to find that coronary angiography was normal. After reviewing the previous literature and reconsidering the possible causes, we came to the conclusion that temporary occlusion with embolism or spasm was the most plausible explanation. The patient did not suffer from atrial fibrillation, congestive heart failure, or coagulopathy, which might predispose him to thromboembolism. Instead of experiencing ST elevation in Prinzmental's angina, the patient had ST depression, which may have been caused by coronary spasm [28], depending on severity. However, without a provoking test, coronary spasm is mere speculation.

In conclusion, when angina pectoris occurs but coronary artery examination is normal, thyrotoxicosis should always be considered as a possibility and be excluded before certain treatments are used. Controlling the hyperthyroid state is important in treating angina pectoris in thyrotoxicosis, though a sudden increase in levothyroxine replacement should be avoided when treating patients with hyperthyroidism [27]. A β-adrenergic blocker could possibly induce spasm and should, therefore, be used cautiously. Further studies are needed to elucidate other possible mechanisms of angina-like endothelial dysfunction in cases of normal coronary artery findings in hyperthyroidism.

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甲狀腺機能亢進併正常冠狀動脈攝影的不穩定狹心症 — 病例報告

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藉由增加氧氣的需求，甲狀腺機能亢進造成氧氣供需不平衡而造成心狹痛的發作。然而甲狀腺機能亢進的病人很少一開始以休息時胸痛發作來表現。在此篇文章我們報告一位懷疑有甲狀腺機能亢進的 **58** 歲男性，其主訴休息時頻繁的胸痛且心電圖顯示典型狹心症的變化。然而其心導管檢查卻為正常。實驗室的檢查確定甲狀腺機能亢進的診斷。病人的胸痛在抗甲狀腺藥物的治療後消失。這個病例提醒我們典型的心狹痛可以是甲狀腺機能亢進的一開始表現。

關鍵詞：狹心症，不穩定型狹心症，甲狀腺機能亢進

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