Vasospastic Angina in Thyrotoxicosis—Case Reports

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Abstract

We encountered 2 patients with thyrotoxicosis accompanied at its onset by progressive angina. The ST segment was elevated in one patient and depressed in the other patient during the spontaneous attacks. Coronary arteriographic findings were normal during control, and spasm was induced by ergonovine. No patients had chest pain even without antianginal medication after successful treatment of thyrotoxicosis. The coronary artery may become sensitive to spasm during thyroid hormone excess even in cases without significant coronary artery disease and previous chest pain.

Introduction

The cardinal effects of thyroid hormone on the cardiovascular system consist of increases in heart rate and stroke volume. However, thyrotoxicosis may also be complicated by atrial fibrillation, heart failure, atrioventricular block, angina pectoris, and myocardial infarction. Ischemic heart diseases such as angina pectoris and myocardial infarction have been reported to occur even in thyrotoxic patients without preexisting coronary lesions, but the evidence of coronary spasm as a pathogenesis of myocardial ischemia in patients with hyperthyroidism has been demonstrated previously in only 2 patients. Coronary spasm, abnormal microcirculation, and thromboembolism are among the possible causes of myocardial ischemia in thyrotoxic patients with normal coronary arteries. We confirmed spasm as an etiologic factor for myocardial ischemia in the 2 cases of thyrotoxicosis with normal coronary arteries described here.

Case Reports

Patient 1, a fifty-seven-year-old male, noted excess sweating and easy fatiguability in August, 1984. Two weeks later, he felt anterior chest pain of two to three minutes' duration early...
in the morning, and as it increased in frequency to two to four times a week, he visited a community hospital. He reported a weight loss of 4 kg during the previous two months. On admission, the blood pressure was 128/68 mmHg and the heart rate was regular at 108/min. Diffuse goiter and tremor were noted, but ocular symptoms were absent. Thyroid hormones were elevated with T₃ and T₄ being 309 ng/dl and 15.1 µg/dl, respectively. Diffuse radioisotope uptake was observed in the thyroid glands by scintigraphy. An elevated ST segment was observed during a chest pain attack in CM₃ by Holter ECG. The symptom was relieved by the administration of propranolol (80 mg/day), nifedipine (40 mg/day), and methimazole (30 mg /day), and the patient was discharged. He was readmitted to Mie University Hospital for coronary angiography on November 15. The thyroid hormone level was normal on admission. Coronary risk factors included hypertension of twelve-years' duration and smoking of one pack/day for thirty-four years. After medication was suspended, coronary arteriography was performed, and complete occlusion of the left anterior descending coronary artery and 90% narrowing of the right coronary artery and the left circumflex artery were observed (Fig. 1) following an injection of intravenous ergonovine (0.4 mg), accompanied by an elevation of the ST segment in V₃-V₆ and chest pain. No significant coronary artery lesions were observed after
the administration of intracoronary nitroglycerin. After normalization of the thyroid function, spontaneous episodes of chest pain subsided without antianginal medication and were not induced even during treadmill exercise.

Patient 2, a forty-four-year-old female, felt progressive chest pain of two to three minutes' duration on exertion early in the morning since March, 1984. She was admitted to a local hospital with a diagnosis of unstable angina. A depression of the ST segment was observed in leads II, III, aVF, and V5-V6 during the anginal attack, as well as during treadmill exercise (Fig. 2). She had lost 10 kg of body weight during the previous three months. Elevation of thyroid hormone levels (T3 360 ng/dl, T4 15.6 μg/dl) and enlargement of the thyroid glands

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Fig. 2. Electrocardiographic findings in case 2. Treadmill exercise test demonstrated chest pain and ST-segment depression in leads II, III, aVF, and V5-V6.
were noted. The patient became asymptomatic following the administration of methimazole (30 mg/day), nifedipine (80 mg/day), propranolol (60 mg/day), and long-acting isosorbide dinitrate (160 mg/day) and was discharged. On readmission for coronary angiography in January, 1985, the blood pressure was 110/80 mmHg, heart rate was regular at 80/min, and diffuse goiter was observed. A thyroid scintigram showed diffuse uptake. The thyroid function was normal, and no coronary risk factor was present. The chest pain disappeared with normalization of thyroid function and was not observed during treadmill exercise. Coronary angiography performed without medication showed 90% spastic narrowing of the left anterior descending artery (Fig. 3) with chest-oppressive sensation following injection of ergonovine (0.4 mg), but no ST-T changes on ECG were noted. No coronary artery lesions were observed after the administration of intracoronary nitroglycerin. The patient was free from chest pain on only methimazole after normalization of the thyroid function.
Ischemic Heart Disease in Thyrotoxicosis

Angina pectoris in patients with thyrotoxicosis is characterized by (1) rest and exertional angina, (2) recent onset and rapid progression of angina, and (3) abrupt cessation of angina after successful treatment of thyrotoxicosis, as noted in our patients. Angina pectoris complicating thyrotoxicosis is not uncommon in the literature, and the incidence is reported by Bernstein et al to be 0.5-20% (usually 10-12%). Patients with thyrotoxicosis showing ischemic heart disease usually have significant coronary lesions and severe progressive symptoms, but myocardial ischemia develops even in few cases with less severe coronary artery disease as the myocardial oxygen consumption increases due to elevated thyroid hormone secretion.

There have been reports of thyrotoxic patients with normal coronary arteries exhibiting angina pectoris or myocardial infarction as in our patients. Yet, the involvement of coronary spasm in angina pectoris with normal coronary arteries was demonstrated in only 2 patients by Wei and Featherstone.

Coronary Spasm and Thyrotoxicosis

Although the mechanisms of myocardial ischemia in thyrotoxicosis have been unclear, there are some hypotheses of coronary events in cases without significant coronary arterial lesion as described previously. But coronary arterial spasm seems to be the most possible cause of documented myocardial ischemia during thyroid hormone excess. On the relation between thyroid hormone and coronary spasm, there are some recent experimental studies. Neurohumoral abnormalities are well known during thyrotoxicosis and may increase the sensitivity of coronary arterial spasm as described by Yasue. In an experimental study of the rat sympathetic system during thyroid hormone excess, an increase in β-receptors but a decrease in α-receptors, which cause vasoconstriction, were reported. Because atropine is known to have a possible mechanism suppressing coronary spasm, White et al observed inhibition of the parasympathetic nerves during thyrotoxicosis. From these experiments autonomic nerve function led to vasodilatation and appeared unlikely to be involved in the pathogenesis of coronary spasm during thyrotoxicosis. On the other hand, the experimental data indicate a decrease in the prostaglandin dehydrogenase activity. This enzyme degrades prostaglandin F, which is a potent vasoconstrictor, in thyroid hormone excess. But the clinical role of prostaglandin F on coronary artery spasm has been unknown. The possibility of the incidental occurrence of angina pectoris with thyrotoxicosis may be excluded from the absence of episodes in our 2 patients before the onset of thyrotoxicosis. Several reports of myocardial infarction occurring in thyrotoxicosis patients with normal coronary arteries also deny the coincidental occurrence of the two conditions. Although coronary spasm was not demonstrated in these studies, the involvement of coronary spasm in myocardial infarction in patients with normal coronary arteries appears probable. During coronary arteriography in our 2 patients, one showed clear coronary spasm accompanied by chest pain and an elevation of the ST segment, and the other showed no electrocardiographic change. In the latter patient, incomplete spasm during chest pain attacks or exercise and increased myocardial oxygen consumption during elevated thyroid hormone levels are considered to have resulted in depression of the ST segment.

A phenomenon of particular interest commonly observed in the patients of Wei and Featherstone, as well as ours, is that chest pain invariably disappeared after normalization of
thyroid hormone levels following successful treatment of thyrotoxicosis. Furthermore, according to Featherstone’s report, hypothyroidism was induced by ¹³¹I irradiation therapy, and chest pain recurred after the administration of levothyroxine sodium. These observations are strongly suggestive of the significance of thyroid hormones in triggering coronary spasm. Thyroid hormones may also have a direct action on the vascular smooth muscles to enhance their sensitivity to spasm, but this action also has yet to be clarified and needs further experimental study. During thyrotoxicosis, we must pay special attention to the possibility of coronary artery spasm in cases with chest pain and to the use of β-blockers, which may induce coronary spasm.

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References