Case Reports of Severe Coronary Artery Spasm Associated with Three Different Endocrine Hyperfunction

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Disorders of the endocrine system including hormone hyperfunction and hypofunction have multiple effects on cardiovascular system. However, in clinical practice, there are many cases of delayed or overlooked diagnosis of underlying endocrine dysfunction in patients presenting chest pain or other cardiac symptoms. Herein, we report three cases of endocrine hyperfunction presenting as coronary spasm; Graves’ hyperthyroidism, pheochromocytoma, and primary hyperparathyroidism. Chest pains disappear after treatment for these endocrine diseases. Endocrine hyperfunctions such as the three cases described above should be considered as possible diagnosis in patients with complaint of chest pain. High index of suspicion are needed.

Keywords: Coronary artery spasm with hyperthyroidism; Pheochromocytoma; Hyperparathyroidism

INTRODUCTION

Disorders of the endocrine system including hormone hyperfunction and hypofunction have multiple effects on cardiovascular system. However, in clinical practice, there are many cases of delayed or overlooked diagnosis of underlying endocrine dysfunction in patients presenting chest pain or other cardiac symptoms. Some of these cases showed worsened clinical course. These patients had serious morbidity and mortality. Herein, we report three cases of endocrine hyperfunction presenting as severe coronary spasm. In addition, we performed relevant literature review.

CASE REPORTS

1. Case 1: Coronary artery spasm due to Graves’ hyperthyroidism and impending thyroid storm after coronary angiography

A 49-year-old female patient visited the emergency room (ER) with chief complaint of epigastric pain. Ten years ago, the patient was diagnosed with hyperthyroidism. She maintained antithyroid drug until 2 years ago. She stopped the medication herself. At arrival, her electrocardiogram (ECG) showed sinus tachycardia (120 bpm/min) with ST segment depression in precordial lead. Troponin I (TnI) and creatine kinase muscle-brain fraction (CK-MB) were elevated (TnI, 2.57 ng/mL [reference value, 0.16 ng/mL]; CK-MB, 20.88 ng/mL [reference value, 4.94 ng/mL]). Echocardiogram showed hypokinesia of the left ventricular (LV) apex and mild hypokinesia of mid posterior wall with normal LV systolic function. Non ST segment elevation myocardial infarction was suspected. However, there was no occlusive lesion with relatively normal coronary artery in coronary artery angiography (CAG). Laboratory results were: free T4 at 143.6 pmol/L (reference range, 11.5-22.7 pmol/L), TSH < 0.01 μU/mL (reference range, 0.55-4.78 μU/mL), anti-TPO antibody titer at 215 IU/mL (reference value, 34 IU/mL), and thyroid stimulating immunoglobulin at 26.19 IU/mL (reference value, 1.75 IU/mL). Thyroid ultrasound showed diffuse goiter with markedly increased vascularity (Fig. 1). After CAG, dyspnea and orthopnea were developed. Chest X-ray showed pulmonary edema with bilateral pleural effusion. The patient’s state was considered as impending thyroid storm precipitated by CAG. High
dose propylthiouracil and lugol solution were started to treat hyperthyroidism. Heart failure management with loop diuretics was done concurrently. Cardiac function and thyroid function of the patient were improved. Finally, the patient underwent total thyroidectomy. She has been free of symptoms.

2. Case 2: Recurrent coronary spasm due to pheochromocytoma with markedly delayed diagnosis
A 62-year-old male patient visited the ER with chief complaint of substernal chest pain. This was the third time he visited our ER with the same symptom for the past 10 years. In his two previous visits, blood pressures were high. ECGs revealed ST segment elevation on S1-3. However, 1st CAG of the patient showed normal coronary artery. In his 2nd CAG, coronary spasm (variant angina) was confirmed using ergonovine provocation. But at the present visit, the patient still felt chest pain despite of treatment with anti-spasm medications. EKG showed sinus tachycardia with ST segment depression and markedly elevated cardiac enzyme, with TnI at 7.25

Fig. 1. (A, B) Thyroid ultrasound of the patient. Thyroid ultrasound showed diffuse goiter with markedly increased vascularity.

Fig. 2. (A) Contrast enhanced computed tomography of abdomen (circle) and (B, C) tumor scan (I-123 MIBG, circle). This shows a 4.6-cm sized right adrenal mass with strong enhancement and central necrosis. MIBG accumulation was seen in marginal area of the tumor. MIBG, metaiodobenzylguanidine.
ng/mL (reference value, 0.16 ng/mL) and CK-MB at 29.81 ng/mL (reference value, 4.94 ng/mL). Echocardiogram showed severe hypokinesia of inferoposterolateral wall with mild LV systolic dysfunction (ejection fraction = 47%) and concentric LV hypertrophy. Third CAG was performed due to markedly elevated cardiac enzyme and newly developed wall motional abnormality. However, CAG showed only non-significant stenosis. On the other hand, chest pain of the patient was episodic and accompanied with high blood pressure, palpitation and headache. Therefore, hormonal studies and adrenal imaging were performed. Biochemical study showed elevated plasma metanephrine at 1.47 nmol/L (reference value, 0.50 nmol/L) and normetanephrine at 6.00 nmol/L (reference value, 0.90 nmol/L). Abdomininal computed tomography (CT) showed 4.6-cm sized strong enhanced adrenal mass in right adrenal gland that was compatible with pheochromocytoma (Fig. 2). The patient is going to have an adrenalectomy after alpha blocker treatment.

3. Case 3: A rare cause of coronary artery spasm: primary hyperparathyroidism

A 70-year-old female patient was referred to the endocrinology department because of incidentally detected hypercalcemia. The patient had complaint of intermittent episode of dizziness, chest discomfort, and muscle weakness. The admission ECG showed no abnormal findings except nonspecific T wave abnormality. During hospitalization, the patient had complaint of sudden chest pain. ECG showed transient ST segment elevation, but her cardiac enzyme showed normal range. Echocardiogram showed normal LV function with normal valvular function. Because the patient had multiple risk factors for coronary artery disease such as diabetes, hypertension, and dyslipidemia, CAG was performed. However, there was no significant occlusive lesion. Only moderate stenosis of coronary artery was observed. Laboratory tests results were: total calcium at 11.6 mg/dL (reference range, 8.4-10.2 mg/dL), phosphorus at 2.3 mg/dL (reference range, 2.5-4.5 mg/dL), parathyroid hormone at 284.22 pg/mL (reference range, 11-62 pg/mL), and glomerular filtration rate at approximately 44.4 mL/min/1.7. Neck ultrasonography showed about 2-cm sized well defined hypechoic mass below inferior pole of right thyroid gland. Technetium-methoxyisobutylisonitrile single photon emission CT/CT showed strong uptake of sestamibi (Fig. 3). Right parathyroidectomy was performed. Her serum calcium was normalized. The patient did not feel chest discomfort after parathyroidectomy.

DISCUSSION

Disorders of the endocrine system have multiple effects on cardiovascular system and may trigger cardiovascular risk factors. Hyperthyroid state is associated with enhanced sympatho-adrenal activity due to increased adrenergic receptor sensitivity and increased receptor numbers. Consequently, stimulation of sympathetic alpha-adrenergic receptors on coronary arteries leads to coronary vasospasm. In a retrospectively analysis of 325 patients diagnosis with coronary spasm in Korea, Choi et al. [1] reported 8 patients (4.69%) had hyperthyroidism, including 5 young female patients (age < 50 years old). On the other hand, there have been reported cases of thyroid crisis after CAG with contrast medium [2]. Therefore, under-diagnosed hyperthyroidism may lead to increased morbidity and mortality in patients after CAG. On the other hand, several endocrine abnormalities including hyperthyroidism can also induced stress cardiomyopathy (also defined as Takotsubo cardiomyopathy), characterized by transient LV dysfunction with chest symptoms, elevated cardiac enzymes, and electrocardiogram changes that resemble myocardial infarction [3,4]. Patho-

![Fig. 3](A, B) Parathyroid single photon emission computed tomography (99m technetium-methoxyisobutylisonitrile) showed focal increased uptake below inferior pole of the right thyroid gland (circle).
physiological mechanisms have been suggested to explain the unusual features of this syndrome, including multivessel epicardial spasm, coronary microvascular impairment, and microvascular spasm [5]. In our patient, initial presentation of chest pain was initiated by coronary spasm that may worsen to stress cardiomyopathy during hospitalization. Therefore, because many patients with acute coronary spasm need CAG, test of thyroid function is essential to reduce the procedural risk.

Pheochromocytoma can present with a multitude of symptoms mimicking other diseases. The pathogenesis of pheochromocytoma-related cardiac complications is thought to be cardiotoxic effect of catecholamine. Excess catecholamine action can lead to stress cardiomyopathy, ischemic heart disease, coronary spasm, myocardial stunning, and rarely cardiogenic shock [6,7]. However, pheochromocytoma remains a frequently overlooked diagnosis compared to hyperthyroidism.

It is well known that chronic hypercalcemia in primary hyperparathyroidism can cause hypertension, arrhythmias, ventricular hypertrophy, and calcifications of myocardium and cardiac valve. However, coronary spasm associated with hyperparathyroidism was rarely reported. One case study reported the occurrence of coronary spasm during spinal anesthesia in a patient with primary hyperparathyroidism [8]. Hypercalcemia is known as precipitating factor of intra-operative coronary spasm. Event in our patient, episode of acute chest pain with transient ST elevation, suggested that possibility of coronary artery spasm. However, unlike hyperthyroidism or pheochromocytoma, mechanism of coronary spasm in hyperparathyroidism is unclear. Further studies are needed to clarify the exact mechanism of coronary spasm.

In conclusion, normal endocrine function is essential to cardiovascular health. Disorders of the endocrine system have multiple effects on the cardiovascular system. Therefore, physicians must have awareness about the relationship between endocrine system and cardiovascular system. Furthermore, high index of suspicion and careful evaluation are needed. Endocrine hyperfunctions such as the three cases described above should be considered as possible diagnosis in patients with complaint of chest pain.

REFERENCES