ISOLATED RIGHT-SIDED HEART FAILURE IN A PATIENT WITH HYPERTHYROIDISM

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SUMMARY – Hyperthyroidism has many characteristic manifestations of various organ systems. Cardiovascular effects are frequent in these patients. A less known complication of hyperthyroidism is reversible right-sided heart failure and pulmonary hypertension. In the patient presented, the symptoms of atrial fibrillation and right-sided heart failure were the first manifestations of hyperthyroidism. Doppler echocardiography confirmed pulmonary hypertension. Other secondary reasons for pulmonary hypertension were excluded. Graves' disease was the only reasonable choice. The treatment of hyperthyroidism resulted in conversion in sinus rhythm, withdrawal of symptoms and signs of right-sided heart failure, and normalization of pulmonary artery pressure.

Key words: *Pulmonary hypertension; Thyroid hormones; Graves' disease; Echocardiography*

Introduction

An excess of thyroid hormones in hyperthyroidism affects cardiovascular system in many ways. It leads to a decrease of vascular resistance, tachycardia at rest, and increase of left ventricle ejection fraction and blood volume. This results in an increased cardiac output[1].

The most common clinical manifestations of hyperthyroidism include sinus tachycardia, atrial fibrillation, and in rare occasions heart failure[1]. There are a few case reports of isolated right-sided heart failure and pulmonary hypertension in patients with hyperthyroidism[2,3].

We describe a female patient with atrial fibrillation and right-sided heart failure as the first manifestations of thyroid dysfunction.

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Case Report

A 36-year-old Caucasian female was hospitalized because of fatigue, shortage of breath, palpitations and swollen legs. Palpitations and shortage of breath had started eight months before admission to the hospital, and leg swelling appeared two months earlier and increased gradually.

She denied loss of weight, any hair or skin changes, diarrhea, cough or hemoptysis. She also denied previous diseases and other risk factors of atherosclerosis. She had one regular pregnancy. Two months before hospitalization amenorrhea appeared. The patient denied exposure to chemicals, tobacco, alcohol or illicit drugs, and she did not use appetite suppressors.

On examination the patient was pale, respiratory rate was 25/min and temperature 37 °C. The jugular veins were distended. There was a moderate and diffuse enlargement of the thyroid gland without palpable nodules. Physical examination revealed tachycardia with irregular heart rhythm, heart rate was 124/min; a grade 2/6 systolic murmur along the left sternal border; blood pressure was 130/80 mm Hg. Hepatomegaly, abdominal distension, and bilateral leg edema

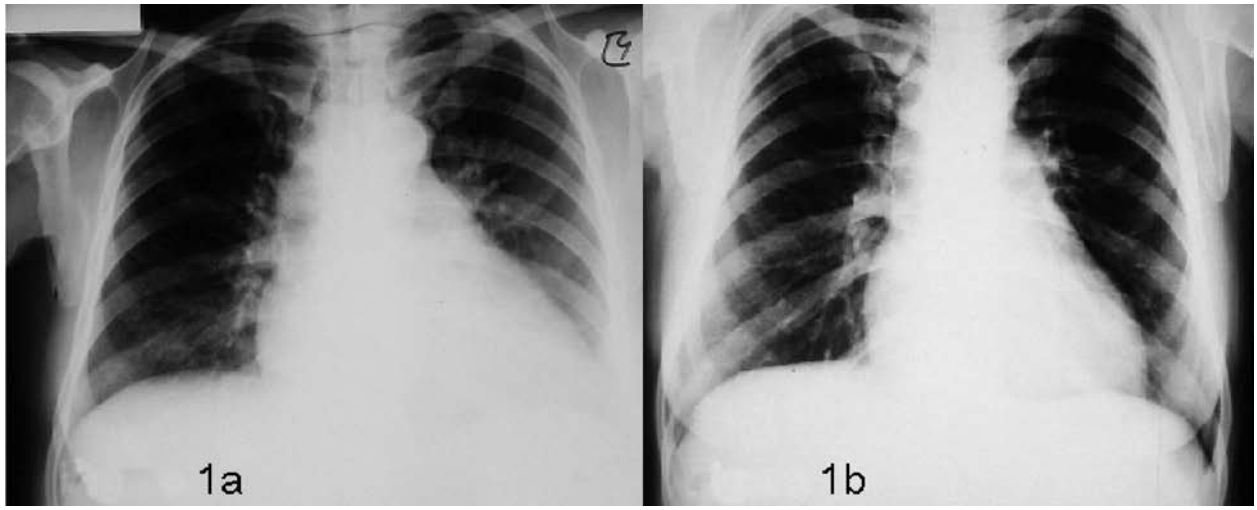

Fig. 1. (a) Chest roentgenogram showing cardiomegaly with prominent pulmonary arteries and left pleural effusion; (b) chest roentgenogram taken three months later showing normal heart without left pleural effusion.

were also noticed. There were no symptoms or signs of deep vein thrombosis or connective tissue diseases.

Electrocardiography showed atrial fibrillation with rapid ventricular response, heart rate was about 120/min, and one ventricular premature beat.

Laboratory tests were characteristic of Graves' disease: serum thyroid-stimulating hormone (TSH) level was undetectable (less than 0.01 mIU/L), total thyroxine (T4) concentration was 255 nmol/L (normal range, 50-150 nmol/L), free thyroxine (FT4) level was 39.2 pmol/L (normal range, 8.4-23.2 pmol/L), and free triiodothyronine (FT3) level was 10.9 pmol/L (normal range, 3.1-6.5 pmol/L). The antithyroglobulin antibody level was increased (764.2 IU/mL, normal range 0-80 IU/mL), and so was the antithyroperoxidase antibody level (320 IU/mL, normal range 0-130 U/mL). Increased levels of total bilirubin (41.2 μmol/L, normal range 0-21 μmol/L), direct bilirubin (18.8 μmol/L, normal range 0-3.4 μmol/L), alkaline phosphatase (132 IU/L, normal 30-120 IU/L) and uric acid (366 μmol/L, normal 154-357 μmol/L) were also detected. Sedimentation rate, antinuclear antibodies and rheumatoid factor were normal.

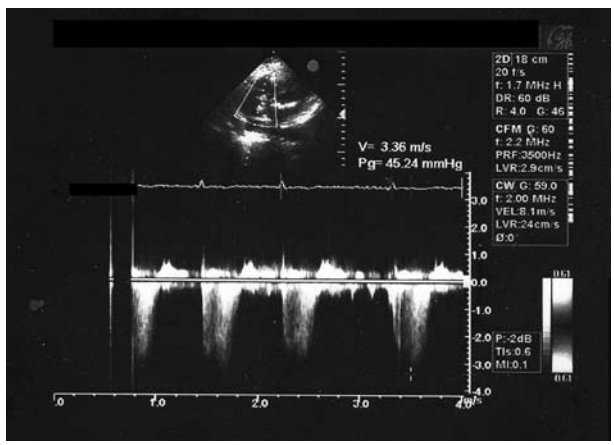

Fig. 2. Transthoracic echocardiogram revealing tricuspid regurgitation and elevated systolic pulmonary arterial pressure (55 mm Hg).

Chest roentgenogram showed cardiomegaly with prominent pulmonary arteries and left pleural effusion (Fig. 1a). The patient underwent a transthoracic echocardiogram, which revealed a dilated right atrium and a ventricle (3.5 cm) with moderate tricuspid valvular regurgitation and elevated systolic pulmonary arterial pressure of 55 mm Hg (Fig. 2). The left ventricle diameters were normal sized, with regular systolic function. Structural changes of the valves were not found, but a dilated left atrium and mild mitral regurgitation were detected.

Abdominal ultrasound revealed moderate hepatomegaly and mild ascites.

Spirometry showed normal pulmonary function. Spiral computed tomography of the chest revealed no evidence of pulmonary embolism or fibrosis. A ventilation-perfusion pulmonary scan was normal. Other possible reasons for pulmonary hypertension such as

HIV infection and sleep apnea syndrome were excluded.

The diagnosis of Graves' disease was established on the basis of different clinical findings: thyroid hormones, positive immune markers, and diffuse goiter without ophthalmologic signs.

We started treatment with furosemide, propranolol, and propylthiouracil. Warfarin was added to therapy because of atrial fibrillation. She became euthyroid two months later, at the same time when conversion of the rhythm was detected. In the meantime, the levels of bilirubin, alkaline phosphatase, and uric acid were normalized. Three months later, chest roentgenogram showed normal heart without left pleural effusion (Fig. 1b). Repeated echocardiography showed normal pulmonary artery systolic pressure.

Discussion

Predominant or isolated right-sided heart failure is uncommon in hyperthyroidism. It can develop due to direct effects of hormone excess on the right ventricle myocardium leading to 'stunned myocardium', or due to afterload increase. The majority of reported cases had increased pulmonary pressure and the treatment of hyperthyroidism resulted in normalization of pulmonary artery pressure and resolution of right-sided heart failure[2,3]. The analysis of pulmonary artery pressure values showed the duration of increased pulmonary resistance, and not the pressure value, to be crucial for the occurrence of right-sided heart failure[4].

The first report on the possible relationship between hyperthyroidism and pulmonary hypertension was published in 1950[5]. This association was subsequently confirmed in other reports[2-4]. Studies mostly involved patients with recently diagnosed hyperthyroidism, with manifested or 'silent' pulmonary hypertension, and showed that the frequency of pulmonary hypertension was not only negligible but higher than expected, between 35% and 65%[6-9].

However, we can only speculate about the mechanisms that lead to pulmonary hypertension in patients with hyperthyroidism. It is assumed that the autoimmune mechanisms with subsequent endothelial damage, endothelial injury due to increased stroke volume, or increase in intrinsic pulmonary vasodilative substance metabolism could have an important role in its occurrence. The hypothesis which seems to be most likely is the one assuming that thyroid hormone excess raises the sensitivity to catecholamines with subsequent pulmonary vasoconstriction, reduces compliance of pulmonary artery, and increases vascular resistance. The aforementioned increase in metabolism of intrinsic pulmonary vasodilative substances (prostacyclins and nitro monoxide) and reduction of vasoconstrictive substance metabolism (serotonin, endothelin 1 and thromboxane) are important contributive factors to pulmonary hypertension development[7]. Today, the role is attributed to phospholamban, a small protein acting as a reversible inhibitor of Ca^{2+}ATPase activity in sarcoplasmic reticulum, whose concentration depends on phosphorylation status[7].

Contrary to primary pulmonary hypertension or secondary hypertension due to autoimmune vascular diseases, hyperthyroidism mediated pulmonary hypertension has a good prognosis, i.e. normalization of pulmonary artery blood pressure after appropriate treatment of hyperthyroidism. This was also the case in our patient.

This case report is interesting because the first manifestations of Graves' disease were cardiologic. It is another confirmation that, on differential diagnosis of right-sided heart failure with pulmonary hypertension, we should also consider hyperthyroidism.

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Sažetak

IZOLIRANO DESNOSTRANO SRČANO ZATAJENJE U BOLESNICE S HIPERTIREOZOM

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Hipertireoza dovodi do mnogo karakterističnih manifestacija na različitim organskim sustavima. Promjene na kardiovaskularnom sustavu često se susreću kod ovih bolesnika. Manje poznata komplikacija hipertireoze je reverzibilno zatajenje desnog srca i plućna hipertenzija. Prikazuje se bolesnica kod koje je prvi znak hipertireoze bila atrijska fibrilacija i zatajenje desnog srca. Doplerovim ehokardiografskim pregledom potvrđena je i plućna hipertenzija. Drugi mogući razlozi plućne hipertenzije su isključeni, tako da je Gravesova bolest ostala kao jedino moguće objašnjenje. Liječenje hipertireoze je rezultiralo konverzijom u sinusni ritam, povlačenjem simptoma desnostranog zatajenja srca i normalizacijom plućnog arterijskog tlaka.

Ključne riječi: *Plućna hipertenzija; Štitnjača, hormoni; Gravesova bolest; Ehokardiografija*