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Thyrotoxicosis presenting as exertional dyspnea and pulmonary hypertension: Case report and review of literature

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Abstract

Objectives: In this case study, we describe a 35-year-old woman with pulmonary hypertension that was secondary to thyrotoxicosis who presented with exertional dyspnea. In the approach to exertional dyspnea, detailed physical examination and laboratory findings helped to get the diagnosis.

Methods: Echocardiography showed right ventricular systolic pressure = 60 mmHg. A suppressed thyroid-stimulating hormone was seen in lab tests. The patient was treated with radioactive iodine.

Results: Palpitations and shortness of breath improved, and both her thyroid-stimulating hormone and T4 levels decreased. Echocardiography and the pulmonary pressure were normal after treatment.

Conclusions: Thyrotoxicosis is one of the etiologies of pulmonary hypertension, but the exact etiology and pathogenesis remain unknown. Some patients may have symptomatic pulmonary hypertension that can be resolved by hyperthyroidism treatment.

Keywords

Dyspnea, pulmonary hypertension, thyrotoxicosis

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Introduction

Pulmonary arterial hypertension (PAH) is defined based on the following hemodynamic criteria: a mean pulmonary artery pressure (PAP) of more than 25 mmHg at rest, pulmonary artery wedge pressure less than 15 mmHg, and pulmonary vascular resistance more than 3 Wood units.[1] There are various cardiovascular manifestations for hyperthyroidism, such as cardiomegaly, increased cardiac output, atrial fibrillation, and, in certain cases, congestive heart failure.[2,3] The relationship between hyperthyroidism and pulmonary hypertension was first specified in 1980.[4] In recent years, researchers have suggested that an association exists between hyperthyroidism and pulmonary hypertension.[5–8] There are some questions about the exact pathogenesis of PAH and the role of treatment in regulating the pulmonary vascular resistance in patients with thyrotoxicosis. A 35-year-old woman with hypothyroidism and pulmonary hypertension, who presented with exertional dyspnea (FC III), was studied. We demonstrated the reversibility of pulmonary hypertension and its symptoms following treatment with radioactive iodine.

Case report

The patient was a 35-year-old woman who had been suffering from exertional dyspnea in function class 3 (FC III) and palpitations for about 3 months, and she was hospitalized after a presumptive diagnosis of pulmonary embolism (PE). Echocardiography results were recorded at the time of admission: tricuspid regurgitation gradient (TRG) = 45 mmHg, right

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ventricular systolic pressure (RVSP) = 60 mmHg, and ejection fraction (EF) = 50%. The patient underwent a computed tomography angiography test, but there was no evidence of PE, so the patient was discharged. A week later, the patient returned with shortness of breath and heart palpitations. A lung perfusion scan was performed for further investigation, and the results were normal. Next, to investigate the cause of the shortness of breath and pulmonary hypertension, the patient was referred to the pulmonary hypertension clinic. In the initial physical examination, hand tremors, tachycardia, and sweating hands were observed. No evidence of Raynaud's disease, petechiae, purpura, or scleroderma was observed during the skin examination. In the initial assessment, thyroid-stimulating hormone (TSH), human immunodeficiency virus antibody (HIVAb), alanine aminotransferase (ALT), aspartate aminotransferase (AST), antinuclear antibody (ANA), and a complete blood count (CBC) were examined. The blood test results were AST = 25 U/L, ALT = 27 U/L, TSH = 0.007 µU/L, and HIVAb was negative. A thyroid physical examination was normal. Auscultation of the heart discovered a murmur II/VI in the left sternal border (LBS) that followed the regular rhythm. Moreover, there were no symptoms of sleep apnea in the patient's history. Graves' disease diagnosis was made. She was treated with 20 mg methimazole daily; after 3 weeks, there was no change in her symptoms, and the TSH was still low. The dose of methimazole was increased to 40 mg daily, but after 3 weeks, the patient was still complaining of shortness of breath, while the TSH and T4 values remained unchanged. Finally, the patient was treated with radioactive iodine. During the following 4 weeks, the patient's palpitations and shortness of breath improved, and both her TSH and T4 levels decreased (Table 1). To check the heart status and pulmonary hypertension, following the treatment of thyrotoxicosis, the patient underwent echocardiography, and the pulmonary pressure was normal (Table 1).

Table 1. Patient characterization before and after treatment.

	Before treatment	After treatment
TSH	0.007 µIU/mL	3.7 µIU/mL
Free T4	3.98 ng/dL	0.44 ng/dL
TRG	45 mmHg	25 mmHg
RVSP	60 mmHg	35 mmHg
IVC	22 mm	17 mm
RVD	29 mm	29 mm
TAPSE	21 mm	20 mm
Main PA diameter	27 mm	25 mm
Function class	3	1

TSH: thyroid-stimulating hormone; T4: thyroxine; TRG: tricuspid regurgitation gradient; RVSP: right ventricle systolic pressure; IVC: inferior vena cava; RVD: right ventricle diameter; PA: pulmonary artery; TAPSE: tricuspid annular plane systolic excursion.

Discussion

Hyperthyroidism may increase mortality and morbidity secondary to cardiovascular disease.[9] Pulmonary hypertension is one of the important complications of hyperthyroidism, increasing the risk of heart failure in 6%–16% of patients with thyrotoxicosis.[10,11] There is no clear data concerning the prevalence and incidence of pulmonary hypertension in such patients. Certain studies, however, have indicated that the prevalence of pulmonary hypertension in patients with hyperthyroidism ranges from 41% to 65%.[12,13] One of the largest studies, by Marvisi et al.,[14] was conducted on 114 patients with hyperthyroidism that showed mild pulmonary hypertension in 43% of patients. In one study, most of the patients with pulmonary hypertension due to hyperthyroidism were asymptomatic.[15] Conversely, some studies have found that the prevalence of thyroid disease is significantly higher in patients with severe pulmonary hypertension. In a large observational study, Li et al. evaluated thyroid disease in 356 patients with severe pulmonary hypertension and compared them with a matched control group. Most patients had mild thyroid disease.[16] Among those with PH, 85 patients (24%) had thyroid Disease vs 17control patients (15%). In another study, they found that the prevalence of hyperthyroidism among the 41 patients with PAH was 22.5%.[17]

The exact pathogenesis of pulmonary hypertension observed in patients with hypertension remains unclear, yet various mechanisms have been proposed. These mechanisms include endothelial injury secondary to high cardiac output.[9–18] Given the fact that PH may also develop in patients with normal cardiac output indicates that the association between hyperthyroidism and PH is autoimmune, causing endothelial damage or dysfunction.[19] Several interesting hypotheses have been proposed that link PAH and thyroid disease with autoimmunity. For example, Sahin et al.[20] found that autoimmune thyroid diseases, such as Graves' disease and Hashimoto's disease, are more frequently associated with PAH than multinodular goiter. Hyperthyroidism-induced vasospasm is another hypothesis.[12] There is also another, not firmly supported, hypothesis that an increased metabolism of intrinsic pulmonary vasodilators and changes in molecular regulators of vascular remodeling likely explain this association and may lead to PAH.[16,21] These results indicated that another pathogenic mechanism, in addition to increased cardiac output, has a role in pulmonary hypertension caused by hyperthyroidism.

Unlike these hypotheses, certain limited studies reject the presence of an autoimmune pathogenic link between hyperthyroidism and pulmonary hypertension.[22] We presented a case of hyperthyroidism with pulmonary hypertension in a 35-year-old woman, who was referred to our PH clinic with progressive dyspnea (FC III), without evidence of PE. Based on previous studies,[14–22] pulmonary hypertension, secondary to hyperthyroidism, is a very common disease, but most of these patients were asymptomatic.[15] Many previous studies have shown the important role of treatment in normalizing PAP.[19,23,24] But we have some different options for treatment of thyrotoxicosis such as surgery, medical therapy, and radioactive iodine. There are limited data comparing the efficacy

of these treatment methods in reducing pulmonary pressure. Some studies have evaluated the role of methimazole, compared with surgery, in the regulation of pulmonary vascular resistance in patients with hyperthyroidism and PAH. These studies have shown that methimazole has a direct vasodilator effect on the pulmonary vascular system. The methimazole group had a more rapid drop in PAP after 15 days, while the normalization of PAP in the surgery group lagged behind in the normalization of thyroid hormones.[14] This phenomenon is due to the efficacy of methimazole on the inhibition of *N*-Nitro-L-arginine methyl ester (L-NAME), indicating an increase in the production of nitric oxide.[23] Another study was conducted in 1997 by Thurnheer et al. on four cases of hyperthyroidism with a mean PAP of 40 ± 11 mmHg. After treatment with radioactive iodine, PAP was reduced to a mean of 25 ± 6 mmHg, which matched the 25 mmHg in our patient, 1 month after treatment with radioactive iodine.[25] There is no head-to-head examination between methimazole and radioactive iodine, comparing their efficacy in reducing pulmonary hypertension.

Conclusion

Pulmonary hypertension, which is found in cases secondary to hyperthyroidism, is a common complication. Such patients may have asymptomatic mild pulmonary hypertension. The increase in PAP usually reverses after treatment of thyroid disease; therefore, some patients may have symptomatic pulmonary hypertension that can be resolved by treatment with radioactive iodine.

Limitations

As we know, performing right heart catheterization is the gold standard for diagnosis of pulmonary hypertension. But in this case report, because of some ethical problems, we could not perform right heart catheterization for documentation of pulmonary hypertension and rule out other reasons of pulmonary hypertension.

Declaration of conflicting interests

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Ethical approval

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Informed consent

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