Reversible Pulmonary Hypertension and Isolated Right-sided Heart Failure Associated with Hyperthyroidism

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Hyperthyroidism may present with signs and symptoms related to dysfunction of a variety of organs. Cardiovascular pathology in hyperthyroidism is common. A few case reports describe isolated right heart failure, tricuspid regurgitation, and pulmonary hypertension as the prominent cardiovascular manifestations of hyperthyroidism. Although most textbooks do not mention hyperthyroidism as a cause of pulmonary hypertension and isolated right heart failure, the literature suggests that some hyperthyroid patients may develop reversible pulmonary hypertension and isolated right heart failure. We report a case of hyperthyroidism presenting with signs and symptoms of isolated right heart failure, tricuspid regurgitation, and pulmonary hypertension, which resolved with treatment of hyperthyroidism.

KEY WORDS: hyperthyroidism; cardiovascular pathology; heart failure; tricuspid regurgitation; pulmonary hypertension.
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CASE

A 56-year-old previously healthy woman presented with a 3-month history of weight loss (25 lb), dyspnea at rest, weakness, intermittent palpitations, nervousness, and heat intolerance. She denied any hair or skin changes, anorexia, diarrhea, cough, or hemoptysis. She worked as a clerk. She denied exposure to chemicals, tobacco, alcohol, or illicit drugs. Her examination revealed a blood pressure of 100/60 mmHg and decreased oxygen saturation (89% on room air). There was a diffuse, nontender goiter without palpable nodules. Jugular venous distention, a pansystolic murmur at the left sternal border, hepatomegaly, abdominal distention, and bilateral leg edema were also noted. On EKG, she had atrial fibrillation with a rate of 110/minute. Laboratory evaluation revealed a white blood count of 13,800/μL with normal differential, hemoglobin (Hgb) 9 g/dL, hematocrit 30%, platelet count 157,000/μL, normal electrolytes, bilirubin 1.9 mg/dL, alkaline phosphatase 187 U/L, aspartic transaminase 170 U/L, alanine transaminase 177 U/L, TSH 0.0 IU/mL, and free T_4 9.8 ng/dL. Sedimentation rate, rheumatoid factor, antinuclear antibodies, and rapid protein reagents were all normal. Chest roentgenogram revealed a prominent left pulmonary artery and possible pruning of the vessels. Abdominal ultrasound revealed mild ascites and mildly enlarged liver. Spiral computed tomography of the chest revealed no evidence of pulmonary embolus. The patient was diagnosed with hyperthyroidism. Iodine^{131} uptake was low, which was consistent with thyroiditis. However, the uptake was performed after the contrast computed tomography of the chest, which might have interfered with the iodine uptake. (The free iodine load of contrast media interferes with iodine uptake in the thyroid compromising diagnostic thyroid uptake for about 2 months after administration of contrast media.)[1]

The heart rate was controlled with intravenous diltiazem, and the patient was anticoagulated. The patient was not given any specific treatment for hyperthyroidism and was discharged on metoprolol and warfarin to be followed up in the outpatient clinic.

Upon further outpatient follow-up, the patient continued to be hyperthyroid. Thyroid-stimulating immunoglobulins were present and a repeat iodine^{131} uptake was high. Findings were consistent with Graves' disease.

Because of atrial fibrillation and signs and symptoms suggestive of cardiac dysfunction, an echocardiogram was performed. This revealed right atrial and ventricular dilatation, right ventricular systolic dysfunction, severe pulmonic and tricuspid regurgitation, and an elevated pulmonary artery systolic pressure of 75 mmHg. There was no left ventricular systolic or diastolic dysfunction. Left ventricular ejection fraction was normal at 60%. No structural heart valve abnormalities were noted. Pulmonary function and sleep studies were normal. Other causes of pulmonary hypertension, such as alcohol abuse, HIV infection, and vitamin deficiency were ruled out.

The patient was treated with methimazole and in a few weeks became euthyroid in sinus rhythm. At that time liver function tests normalized and a repeat echocardiogram revealed a normal size and function of the right ventricle and only mild tricuspid regurgitation. Pulmonary artery systolic pressure improved to 45 mmHg.

Anemia improved to a Hgb of 11 g/dL.

DISCUSSION

Adverse cardiovascular effects of hyperthyroidism are well documented in the literature. High output biventricular heart failure with normal or decreased systemic and pulmonary vascular resistance is the expected cardiovascular complication of hyperthyroidism.[2–4]

Isolated right heart failure, variable degrees of tricuspid regurgitation, pulmonary hypertension, or different combina-

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tions of the three in patients with thyrotoxicosis have been infrequently reported.[5–22] Possible mechanisms of these cardiac abnormalities include increased blood volume[12,17,23,24] or increased right ventricular load because of increased cardiac output and venous return.[24] The thin-walled structure of the right ventricle, as opposed to the left ventricle, may render the right ventricle more susceptible to volume overload. High cardiac output-induced or autoimmune-induced pulmonary vascular endothelial injury may lead to pulmonary hypertension.[12,25,26] Increased pulmonary vascular resistance could also result from increased metabolism of certain pulmonary vasodilating substances.[26] These cardiac abnormalities in the reported cases were characterized by the reversibility of the pathology and the benign clinical course once thyrotoxicosis was treated and patients became euthyroid.[5–22] However, one report described a case of pulmonary hypertension and thyrotoxicosis that was complicated with further arrhythmias and asystole because of worsened thyrotoxicosis by amiodarone given for atrial fibrillation.[5] Atrial fibrillation was documented in only 2 of 14 reported cases of thyrotoxicosis and isolated right heart failure. Both of these cases had pulmonary hypertension and tricuspid regurgitation that resolved or improved after treatment of hyperthyroidism (Table 1).[5–22]

In the present case, thyrotoxicosis was associated with pulmonary hypertension, right ventricular failure, and severe tricuspid regurgitation, which resolved when the patient became euthyroid. Secondary causes of pulmonary hypertension, such as left ventricular failure, pulmonary embolus, chronic obstructive pulmonary disease, obstructive sleep apnea, alcohol abuse, HIV, vitamin deficiency, and vasculitides were ruled out. Our case is consistent with other reported cases, though it was at the extreme end of the spectrum regarding the severity of pulmonary hypertension (Table 1). This may illustrate that even severe pulmonary hypertension can be reversed when the underlying cause is corrected.

There has been at least one report of a thyrotoxic patient presenting with isolated right ventricular failure with normal pulmonary vascular resistance measured by right heart catheterization.[17] Right ventricular failure and tricuspid regurgitation might be directly related to thyrotoxicosis independently from pulmonary hypertension. Most of these cases of thyrotoxicosis and right ventricular failure and pulmonary hypertension were diagnosed as Graves' disease, indicating a possible autoimmune mechanism for this association.[27]

A prospective echocardiographic study of 39 hyperthyroid patients and 39 matched controls revealed that the mean pulmonary artery pressure in the hyperthyroid patients was significantly greater than in controls (38 vs 27 mmHg). Moderate to severe tricuspid regurgitation was significantly more common in the hyperthyroid group (7 vs 1). Most of the hyperthyroid patients did not have documented atrial fibrillation. These abnormalities resolved in most patients after 14 months of follow-up. This study and others suggest that isolated right-sided heart failure and pulmonary hypertension are more common than once thought. If an echocardiogram is done routinely on patients with hyperthyroidism, more of these cardiovascular abnormalities may be identified.[28]

Table 1. Characteristics of the current case and other reported cases (data taken from various studies[5–22])

Type of cardiac abnormality	Current case	Other reported cases
Atrial fibrillation	Yes	Documented in 2 of 14 cases
Pulmonary hypertension (method of evaluation)	Yes (by echocardiography only)	13 of 14 cases (8 cases by echocardiography only and 5 by echocardiography and right heart catheterization)
Systolic pulmonary artery pressure elevation	75 mmHg	33–71 mmHg
Tricuspid regurgitation	Yes (severe)	14 of 14 cases 8 cases of severe TR
Right ventricular dysfunction/ dilatation	Yes	14 of 14 cases

CONCLUSION

In the setting of hyperthyroidism, pulmonary hypertension and right ventricular dysfunction may be underdiagnosed. The symptoms are likely to be considered as part of the hyperthyroid syndrome. Because the cardiovascular findings resolve when the patient becomes euthyroid, patients who had these findings might not be evaluated for them.[5–22] It is important to consider hyperthyroidism in patients presenting with pulmonary hypertension or unexplained right heart failure. Furthermore, thyroid function evaluation should be included in the work up of primary pulmonary hypertension. Because amiodarone may trigger hyperthyroidism in patients with multinodular goiter or worsen coexisting thyrotoxicosis owing to its iodine content, it should not be used for rhythm or rate control of atrial fibrillation without ruling out hyperthyroidism or susceptibility to such condition.[5]

It remains unclear why only a subgroup of patients with thyrotoxicosis is prone to have isolated right heart failure with or without pulmonary hypertension.

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