Hyperthyroidism Presenting with Severe Pulmonary Hypertension: A Case Report and Literature Review

Han-Luen Huang¹,⁴, Lin-Chyun Chen², Wen-Chin Ko¹,³

Hyperthyroidism affects the cardiovascular system in many ways including increased heart rate, cardiac arrhythmias, impaired diastolic function and increased systolic blood pressure. We report a case of severe pulmonary hypertension and right heart failure with no identifiable cause other than hyperthyroidism. After recognition and treatment of hyperthyroidism, the patient had prompt hemodynamic and symptomatic recovery.

Key words: pulmonary artery hypertension, hyperthyroidism, autoimmune thyroid disease, right-sided heart failure

Introduction

Primary pulmonary hypertension is an irreversible disease and has a grim prognosis. It is important to exclude all other possible causes before making this diagnosis. However, most recent reviews and texts do not list thyrotoxicosis or hyperthyroidism as one of the causes of pulmonary hypertension¹⁻⁴. Few cases of pulmonary hypertension due to hyperthyroidism have been reported in the literature. Here we report a female patient with hyperthyroidism who presented with severe pulmonary hypertension which resolved after successful treatment of hyperthyroidism.

Case Report

A 53-year-old female received regular follow up checks for her diabetes mellitus and hypertension in our out-patient department. Four months before admission, she developed dyspnea on exertion. Echocardiogram at that time revealed normal chamber size with normal left ventricular (LV) function, and insignificant pericardial effusion. There was trivial tricuspid regurgitation with a pressure gradient of 28 mmHg. Estimated right ventricular systolic pressure was 38 mmHg. No intracardiac shunt was detected. Two weeks before admission, she developed progressive right-sided heart failure with lower leg edema, jugular vein engorgement and weight gain. There were also progressions of dyspnea on exertion and orthopnea despite diuretic therapy. Otherwise, her blood pressure had a tendency to be higher and her pulse pressure to be wider over the last few months. A chest roentgenogram demonstrated a prominent pulmonary artery and dilated cardiac chamber size as compared with film taken half a
year earlier. (Fig. 1) Repeated echocardiograms showed enlarged left and right atrium chamber size and normal left ventricular systolic function with a minimal amount of pericardial effusion. However, there was mild to moderate tricuspid regurgitation with a pressure gradient of 54 mmHg. Estimated right ventricular systolic pressure was 69 mmHg.

On admission, her blood pressure was 198/92 mmHg. An electrocardiogram revealed sinus tachycardia with a rate of 120 bpm. (Fig. 2) Thoracic computed tomography failed to show definite pulmonary parenchymal lesion but a small amount of pleural effusion and ascites. The probability of pulmonary embolism was interpreted as low after 99mTc-MAA perfusion lung scintigraphy.

Severe pulmonary hypertension and high cardiac output were proven by pulmonary artery catheterization technique (systolic pulmonary artery pressure: 89 mmHg, mean pulmonary artery pressure: 44 mmHg, cardiac output: 7.21 L/min, cardiac index: 4.48 L/min/m$^2$; blood pressure 142/70 mmHg) after entering the intensive care unit. Her arterial blood gas analysis showed a pH of 7.43, PCO$_2$ 40.1 mmHg, PO$_2$ 146 mmHg, bicarbonate 26.8 mmol/L under oxygen 6 L/min. The presence of mild exophthalmos led to the examination of thyroid function. The report was consistent with hyperthyroidism, with serum triiodothyronine (T3) of 257 ng/dl (normal range 80-200 ng/dl) and serum tetraiodothyronine (T4) of 20.9 ng/dl (normal range 4.5-12.5 ng/dl), free T4 of 5.37 ng/dl (normal range 0.56-1.8 ng/dl), thyroid stimulating hormone (TSH) of 0.01 uIU/ml (normal

![Fig. 1](image-url)  Enlarged cardiac chamber size and prominent pulmonary artery shadow on admission
range 0.25-4 uIU/ml). Titers of antithyroglobulin was 39.1% (normal range 0-15%), anti-peroxidase was 68.1 U/ml (normal range 0-100 U/ml). The diagnosis of Grave’s disease was made according to the above findings.

The thyroid gland was not palpable on physical examination. She had not consumed aspartame over the past few months. Antinuclear antibodies were negative and complements were within normal range. There was no history of Raynaud’s phenomenon. These findings made the diagnosis of connective tissue disease unlikely. This patient was on furosemide, propylthiouracil and propranolol therapy. Three months later, after initial antithyroid therapy, her thyroid function returned to a euthyroid state with T3 of 84.2 ng/dl and T4 of 5.6 ng/dl, TSH of 1.17 uIU/ml. Four months after therapy, echocardiography was performed again and it showed normalization in the sizes of the left and right atrium with trivial tricuspid regurgitation. The right ventricular systolic pressure was decreased to 39 mmHg. (Table 1) Chest roentgenogram 18 months later showed a decrease in cardiac chamber size. There was significant improvement of her dyspnea and leg edema.

**Discussion**

The normal pulmonary artery pressure in adults range from 18 to 30 mmHg for the systolic

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**Table 1** Serial echocardiographic parameters

<table>
<thead>
<tr>
<th></th>
<th>4 month before admission</th>
<th>On admission</th>
<th>3 months after antithyroid treatment</th>
</tr>
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<tbody>
<tr>
<td>LVEDD (mm)</td>
<td>42</td>
<td>43</td>
<td>44</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>28</td>
<td>28</td>
<td>26</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>60</td>
<td>65</td>
<td>73</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>36</td>
<td>38</td>
<td>31</td>
</tr>
<tr>
<td>MR severity</td>
<td>trivial</td>
<td>trivial</td>
<td>trivial</td>
</tr>
<tr>
<td>TR severity</td>
<td>trivial</td>
<td>moderate</td>
<td>mild</td>
</tr>
<tr>
<td>Estimated RVSP (mmHg)</td>
<td>38</td>
<td>69</td>
<td>39</td>
</tr>
</tbody>
</table>

LVEDD: left ventricular end diastolic diameter. LVESD: left ventricular end systolic diameter. LVEF: left ventricular ejection fraction. LAD: left atrial diameter. MR: mitral regurgitation. TR: tricuspid regurgitation. RVSP: right ventricular systolic pressure.

![Fig. 2 EKG showing sinus tachycardia after admission. There is no evidence of right ventricular hypertrophy. This indicates pulmonary hypertension is not chronic](image-url)
pressure and between 4 to 12 mmHg for the diastolic. Pulmonary hypertension is defined as systolic pulmonary artery pressure exceeding 30 mmHg or mean pulmonary artery pressure exceeding 25 mmHg at rest. When systolic pulmonary artery pressure exceeds 35 mmHg or the mean pulmonary artery pressure exceeds 30 mmHg during exercise, pulmonary hypertension is also indicated(6). Common symptoms of pulmonary hypertension are dyspnea on exertion, fatigue, syncope, exertional chest pain and palpitations(7).

Traditionally, pulmonary hypertension can be divided into primary and secondary types. Secondary pulmonary hypertension is the diagnosis given to patients with pulmonary hypertension caused by known etiology such as collagen vascular disease, congenital systemic-to-pulmonary shunts, left-sided valvular heart disease, and chronic obstructive pulmonary disease. Primary pulmonary hypertension is diagnosed as pulmonary hypertension with uncertain etiology. The World Health Organization (WHO) in 1998 created a diagnostic classification of pulmonary hypertension for clinical use. This classification is comprehensive but the hemodynamic differences are not obvious. Chatterjee et al. in 2002 proposed a hemodynamic-oriented classification of pulmonary hypertension. They divided pulmonary hypertension into four groups: pre-capillary, post-capillary, mixed and selective or nonselective increase in pulmonary blood flow(8). Patients with a high cardiac output state such as thyrotoxicosis or chronic anemia, belong to the increase in pulmonary blood flow group. There is also a mild increase in pulmonary vascular resistance (PVR) in this group. In our patient, hemodynamic data was consistent with high cardiac output and mild increase in PVR (cardiac output: 7.21 l/min, cardiac index: 4.48 l/min/m², PVR: 211 dyns/cm⁵).

Several studies have shown associations between autoimmune thyroid disease and pulmonary hypertension. Approximately 30-49% of previously diagnosed primary pulmonary hypertension patients were concomitant with autoimmune thyroid disease(9,10). Anti-thyroid agent, methimazole, and to a lesser degree, propylthiouracil, were found to have an immunosuppressive effect on such patients. After methimazole therapy to euthyroid status, pulmonary hypertension could be reversed(11,14,20). Primary pulmonary hypertension and hyperthyroidism both tend to affect young females. Since primary pulmonary hypertension carries a grave prognosis and therapeutic options are limited, hyperthyroidism should be ruled out before the diagnosis is confirmed(12,13). Without recognition and proper treatment, hyperthyroidism may progress into right side heart failure. If medical treatment of hyperthyroidism is given and achieves a euthyroid state, pulmonary artery pressure could be lowered(14). So current evaluation of thyroid function should be recommended in cases of unexplained pulmonary hypertension.

Hyperthyroidism can manifest clinically as tachycardia, hypertension, wide pulse pressure, LV heave and, eventually, high cardiac output heart failure(15,16). Thyroid hormones may directly affect sino-atrial node firing which can then cause resting sinus tachycardia. It is the most common cardiovascular manifestation of hyperthyroidism(17). Thyroid hormones can directly increase arterial smooth muscle relaxation to reduce systemic vascular resistance and cause a lower diastolic arterial pressure(18). Activated renin-angiotensin-aldosterone system and up-regulated erythropoietin secretion in hyperthyroidism patients result in increased total blood volume and cardiac preload. Tachycardia and increased cardiac preload synergistically cause a high cardiac output state in hyperthyroidism in response to the peripheral metabolic demand promoted by thyroid hormones. On the other hand, tachycardia would lessen the
diastolic filling period and lead to more dependence of atrial kick. Over time, muscle degeneration can lead to atrial fibrillation and explains why this is commonly seen in patients with hyperthyroidism\(^\text{19}\). A recent study about phospholamban, the inhibitor of cardiac sarcoplasmic reticulum Ca\(^{2+}\)ATPase, may explain why an excess of thyroid hormones would increase cardiac contractility. An animal model showed decreased phospholamban mRNA levels in rabbit hearts with hyperthyroidism\(^\text{20}\).

Both cardiac and secondary pulmonary disease will cause pulmonary and right ventricular hypertension. In a prospective study, mild pulmonary hypertension was found in 43% of 114 patients with hyperthyroidism and pulmonary artery pressure went from 34.3 \(\pm\) 3.2 mmHg to 29.2 \(\pm\) 3.3 mmHg after treatment with methimazole\(^\text{21}\).

In patients with unexplained right side heart failure, pulmonary hypertension or isolated tricuspid regurgitation, hyperthyroidism should be taken into differential diagnosis\(^\text{22,23}\).

The etiology of the strong relationship between autoimmune thyroid disease and pulmonary hypertension remains unclear. One possible explanation is that increased total blood volume contributes to increased pulmonary blood flow and pulmonary vascular resistance\(^\text{8}\). Another possibility is the direct effect of thyroid hormones on the pulmonary vasculature. This theory is supported by the reversible change of pulmonary hypertension seen after the successful treatment of hyperthyroidism\(^\text{14}\). The mechanisms include an increase in metabolism of intrinsic pulmonary vasodilating substances and a decrease in vasoconstrictor metabolism\(^\text{24}\). Besides the effect of an excess of thyroid hormones, systemic auto antibodies may also play a role in pulmonary vascular endothelium injury and lead to pulmonary hypertension.

In summary, hyperthyroidism may result in pulmonary hypertension. Pulmonary hypertension can be reversed after correction of hyperthyroidism. Thus, hyperthyroidism should be excluded in patients with unexplained pulmonary hypertension.

**References**

肺動脈高血壓與甲狀腺機能亢進：病例報告

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肺動脈高血壓定義為休息狀態下肺動脈收縮壓超過30毫米汞柱，平均肺動脈壓超過25毫米汞柱；或在運動狀態下肺動脈收縮壓超過35毫米汞柱，平均肺動脈壓超過30毫米汞柱。原發性肺動脈高血壓定義為無任何次發性原因之肺動脈高血壓。根據文獻記載，約有30-49%原先被診斷為原發性肺動脈高血壓的病患合併有自體免疫性甲狀腺疾病。如果未經發覺及適當的治療，日後將會惡化成右心衰竭；若給與適當的治療，肺動脈高血壓將可獲得改善。這裡，我們報導一位53歲重度肺動脈高血壓的病患合併有自體免疫性甲狀腺疾病。在經過確認及治療甲狀腺機能亢進後，右心衰竭症狀消失，肺動脈高血壓也獲得改善。

關鍵詞：肺動脈高血壓，甲狀腺機能亢進，自體免疫甲狀腺疾病，右心衰竭

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