

Severe right heart failure in two patients with thyrotoxicosis

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Congestive heart failure is a recognised complication of uncontrolled thyrotoxicosis but isolated right heart failure is rarely seen in association with thyrotoxicosis. Two cases of right heart failure associated with thyrotoxicosis are presented. In a 45-year-old man with right heart failure, investigations for all common secondary causes of right heart failure were negative. The only concurrent disease identified was thyrotoxicosis. The right heart failure subsided after treatment of the thyrotoxicosis. In a 36-year-old woman, the right heart failure had two underlying causes, thyrotoxicosis and an atrial septal defect. Treatment of thyrotoxicosis alone resulted in improvement of pulmonary hypertension and right heart failure. Thyrotoxicosis should be considered as a possible cause of pulmonary hypertension or isolated right heart failure.

Introduction

Right heart failure (RHF) is often accompanied by severe left heart failure. Isolated RHF occurs only occasionally and its common causes are pulmonary hypertension (PH), tricuspid stenosis or regurgitation, and constrictive pericarditis. Rarely, thyrotoxicosis can present as isolated RHF or PH, which are reversible on achieving a euthyroid state. The potential mechanisms are discussed.

Case 1

A previously healthy 45-year-old man presented to the Caritas Medical Centre in July 2004 with diarrhoea and vomiting for 2 weeks. He also reported weight loss of 9 kg over the past 2 months. On physical examination, he had tachycardia, bilateral ankle oedema, and a raised jugular venous pressure. There was no goitre or exophthalmos. A chest X-ray showed cardiomegaly. Electrocardiography showed atrial fibrillation (AF) at a rate of 100/min. The thyroid stimulating hormone (TSH) level was suppressed to <0.03 mIU/L (reference range, 0.5-4.7 mIU/L) and free thyroxine (T_4) was raised to 46.2 pmol/L (reference range, 9.1-23.8 pmol/L). Both anti-thyroglobulin and anti-microsomal antibodies were $<1/100$ (reference level, both $<1/100$ titre). A transthoracic echocardiogram revealed a dilated right ventricle of 3.4 cm (reference range, 0.7-2.3 cm) with severe tricuspid regurgitation (TR). The right ventricular systolic pressure (RVSP) was 26 mm Hg (reference level, <25 mm Hg). The right ventricular function was markedly impaired but the left ventricular function was satisfactory with an ejection fraction of 53% (reference range, 55-75%) [Fig 1]. Further investigations for the isolated RHF including a transoesophageal echocardiogram (TEE) showed no structural heart defects. A thoracic computed tomography scan excluded pulmonary embolism. He was negative for antinuclear antibodies.

Key words
Heart failure; Heart septal defects, atrial;
Hypertension, pulmonary; Thyrotoxicosis

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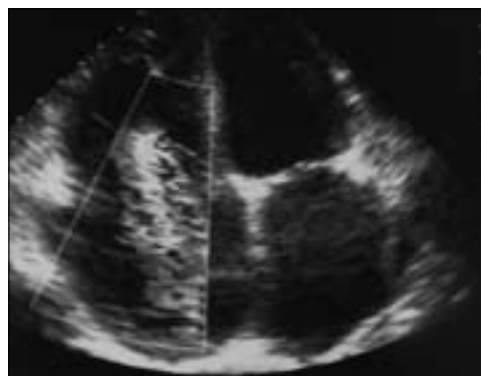


FIG 1. Transthoracic echocardiogram of case 1 showing a dilated right ventricle with severe tricuspid regurgitation



FIG 2. Chest X-ray of case 2 on admission showing significant cardiomegaly with pulmonary congestion

患有甲狀腺毒症並出現嚴重右心衰竭的兩名病人

充血性心衰竭是一種已知的不受控甲狀腺毒症的併發症，至於右心衰竭與甲狀腺毒症有關的個案卻很罕見。本文報告兩宗同類病例。一名出現右心衰竭的45歲男性，所有有關右心衰竭的繼發病因均屬陰性，唯一同時出現的是甲狀腺毒症。而病人經甲狀腺毒症治療後，右心衰竭的症狀亦隨之消失。另一名36歲女性同樣出現右心衰竭，其甲狀腺毒症及心房中隔缺損可能是病因。病人經甲狀腺毒症治療後，肺動脈高壓及右心衰竭的情況均有改善。甲狀腺毒症可被視為肺動脈高壓及個別性右心衰竭的可能病因。

His heart failure symptoms were controlled with frusemide. Carbimazole and propranolol were initiated. His heart rate reverted to sinus rhythm 1 week later and he became euthyroid after treatment with carbimazole for 1 month.

A follow-up transthoracic echocardiogram 5 months later showed only mild TR with a mildly dilated right ventricle of 2.6 cm. The RVSP was 21.6 mm Hg. He declined radioactive iodine treatment, and carbimazole was continued for 18 months. Throughout a 2-year follow-up after stopping carbimazole, he remained euthyroid and had no relapse of RHF or AF.

Case 2

A 34-year-old healthy housewife was admitted to the Caritas Medical Centre in July 2004 with progressive dyspnoea and ankle swelling for 2 weeks. On admission, her blood pressure was 140/80 mm Hg and she had an irregular pulse of 140 beats/min. She was in heart failure with a grade 3/6 pan-systolic murmur at the lower left sternal border. She had a small, diffuse goitre but no ophthalmopathy.

A chest X-ray showed gross cardiomegaly with pulmonary congestion (Fig 2). An electrocardiogram revealed AF at a rate of 166/min. Her TSH was suppressed to <0.03 mIU/L and free T₄ 74.6 pmol/L. Her anti-microsomal antibody was 1/400 and anti-thyroglobulin antibody 1/100. A transthoracic echocardiogram showed a grossly dilated right ventricle of 3.1 cm with moderate TR. There was significant PH with a RVSP of more than 69 mm Hg. The left ventricle ejection fraction was 54%.

She was diagnosed with acute pulmonary oedema and given non-invasive ventilatory support. She was treated with frusemide, angiotensin-converting enzyme inhibitor and digoxin. Propylthiouracil 150 mg thrice daily was commenced. Investigations for secondary causes of PH including autoimmune markers were negative. A thoracic computed tomographic scan showed no evidence of

pulmonary embolism.

She was euthyroid at 6 weeks after starting propylthiouracil, and a follow-up transthoracic echocardiogram revealed that her right ventricle was still dilated with moderate TR. The RVSP had decreased to 59 mm Hg. There was a suspicious flow over the atrial septum. A TEE confirmed a secundum atrial septal defect (ASD) of 1.7 cm in diameter with left-to-right flow. The option of closing the ASD after controlling the thyrotoxicosis was offered but she had poor compliance with drug treatment and follow-up assessment. She declined radioactive iodine treatment or thyroidectomy. She still required propylthiouracil treatment and was in AF after 3 years.

Discussion

Perry and Graves first described the effects of thyrotoxicosis on the cardiovascular system nearly 200 years ago. Excess thyroid hormone has a direct inotropic and chronotropic action on the heart. It also increases the total blood volume and decreases the total systemic vascular resistance. All these factors contribute to the increase in cardiac output.^{1,2} Although both systolic contraction and diastolic relaxation of the heart are enhanced, a subset of patients with thyrotoxicosis present with paradoxical left ventricular failure.³ Forfar et al⁴ showed that hyperthyroid patients fail to demonstrate the expected rise in left ventricular ejection fraction with exercise, a state that can be reversed after antithyroid treatment.

Predominant or isolated RHF is rarely associated with thyrotoxicosis. To our knowledge, only 16 cases⁵⁻⁷ of reversible isolated RHF and PH associated with thyrotoxicosis have been reported. The most striking feature of all the reported cases was normalisation of cardiovascular findings after controlling the thyrotoxicosis.

The mechanism for the association between thyrotoxicosis and PH is not clear. Animal studies^{8,9} have suggested that the right ventricle may be exposed to a significant haemodynamic stress accompanying the hyperthyroid state. An autoimmune process has often been proposed due to the marked female predominance, high frequency of autoimmune antibodies, and concomitant connective tissue diseases.¹⁰ Other suggested mechanisms include endothelial injury secondary to increased cardiac output, and increased metabolism of intrinsic pulmonary vasodilatory substances.⁸

The mechanism for the development of RHF in thyrotoxicosis is a combination of factors, namely, pressure overload from PH⁸ plus volume overload with the development of secondary TR² and possibly a direct 'toxic effect' of excess circulating thyroid

hormone causing a form of 'stunned myocardium' predominantly involving the right ventricle.¹¹

Cohen and Schattner⁵ reported two cases and reviewed six cases of RHF associated with thyrotoxicosis. All patients presented with signs of RHF, mostly ankle oedema. Nearly all patients had PH ranging from 27 to 60 mm Hg, measured using transthoracic echocardiograms and some with confirmatory right cardiac catheterizations. The pulmonary artery pressure (PAP) in these patients decreased following resolution of their thyrotoxicosis. The normalisation of PAP and resolution of all signs of RHF on treatment of the thyrotoxicosis support a causal association. Furthermore, Lozano and Sharma⁶ also reported one case and reviewed 11 cases of PH and RHF associated with thyrotoxicosis. When thyroid antibodies were measured in six cases, four were positive. Severe TR was present in seven (58%) of the 12 cases. Similarly, there was a drop in PAP after treatment of the thyrotoxicosis. A review of all the cases described by these two authors,^{5,6} shows that Graves' disease was documented in nine of the 16 cases and none had a toxic nodular goitre. This suggests an autoimmune mechanism for the association between thyrotoxicosis and PH or RHF. However, there is no firm evidence clarifying whether an autoimmune process and thyroid hormone excess or the latter alone cause the PH or RHF. Furthermore, AF was documented in eight of the 16 cases. Atrial fibrillation is the most common arrhythmia in patients with thyrotoxicosis, and contributes to left heart failure² but its role in the aetiology of RHF is not certain.

Our first patient had no pre-existing heart disease and thyrotoxicosis was his only concurrent

disease. His RHF resolved after successful treatment of his thyrotoxicosis, suggesting that it was the most likely cause of the RHF. In the second case, the patient had undiagnosed ASD, and while both the RHF and PH improved they did not resolve entirely after antithyroid therapy. Hence, it is likely that the thyrotoxicosis exacerbated the RHF in the presence of an underlying ASD.

Xenopoulos et al¹² presented a 47-year-old man with isolated RHF due to two rare underlying causes, thyrotoxicosis and a dysplastic tricuspid valve. Repair of the tricuspid valve and treatment of the thyrotoxicosis were both essential for successful treatment of his RHF. After the valve repair, reduction of his dose of propylthiouracil led to a recurrence of his thyrotoxicosis, which was associated with reappearance of florid RHF. In our second case, both the thyrotoxicosis and the ASD were contributing to the RHF and PH. Treatment of the thyrotoxicosis led to an improvement in the RHF and RVSP but significant PH persisted, indicating she was in need of cardiac catheterization and repair of the septal defect. Furthermore, definitive treatment of her thyrotoxicosis with radioactive iodine was preferable because of poor drug compliance and the severity of her heart failure.

Conclusion

In summary, we report two cases of reversible RHF associated with thyrotoxicosis. Thyrotoxicosis should be included in the differential diagnosis of secondary PH, isolated TR, or unexplained RHF. This is especially important because thyrotoxicosis is a treatable entity and the heart failure may be completely reversible.

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