HYPERTHYROIDISM - AN UNDER INVESTIGATED & TREATABLE CAUSE OF PULMONARY HYPERTENSION: PRESENTATION OF 6-PATIENT SERIES AND REVIEW OF THE LITERATURE

Tolstoy R.1, Senthil Kumar2, Rajendiran G.1 and *Gauri Shankar J.1

1Department of Medicine, PSG Institute of Medical Sciences and Research, Peelamedu, Coimbatore -641004.
2Department of Endocrinology, PSG Institute of Medical Sciences and Research, Peelamedu, Coimbatore -641004
*Author for Correspondence

ABSTRACT
Pulmonary hypertension (PH) is a life-threatening condition and carries a grave prognosis if untreated. Therefore it should be thoroughly investigated to rule out possible secondary causes of PH Prognosis as secondary PH depend on its etiology. Currently evidences are mounting about the increasing association between hyperthyroidism and PH. Here we are presenting 6 cases of secondary PH associated with hyperthyroidism, wherein the treatment of hyperthyroidism in 4 of them led to the resolution/improvement of PH. Thyrotoxicosis should be considered as an important treatable etiology for the PH.

Key Words: Pulmonary Hypertension, Hyperthyroidism

INTRODUCTION
Thirty years ago, adults diagnosed with PH could expect to live less than 3 years (D’Alonzo et al., 1991). The overall prevalence of PH in the current general population is unknown, owing to the heterogeneity of the disease. Cardio-pulmonary disorders are the most common causes of secondary PH. Though the association between thyroid disorders and PH is becoming more evident, it still remains an uninvestigated entity in the PH work up. Thyroid disorders are kept under ‘others’ column in the ‘Venice clinical classification of pulmonary hypertension’ (2003) and are grouped under metabolic causes in the ‘Dana point classification of pulmonary hypertension’ (2008/9) along with rarer diseases like Gauchers and Glycogen storage disorders (Simonneau et al., 2009). Current reports show that thyrotoxicosis has been a major cause of worsening of PH. The association between thyrotoxicosis and PH has been further proven with improvement of PH after restoration of euthyroid state (Karnath et al., 2006; Neto et al., 2005; Nakchbandi et al., 1999; Mercè et al., 2005; Yari et al., 2005; Thurnheer et al., 1997; Virani et al., 2003; Wassem et al., 2006). In our hospital we have seen 6 patients who had PH and hyperthyroidism. Of these, following restoration of euthyroid status, PH was completely resolved in 3 patients and improved in 1 patient. Two patients were lost to follow up. Until now only few cases of reversible PH associated with hyperthyroidism have been reported worldwide (Ferris et al., 2001). This is the first report from India on the association between PH and thyrotoxicosis and the improvement of PH following the treatment of thyrotoxicosis.

CASES
Patient 1: This 50 year lady was admitted with dyspnoea on exertion. Her vitals were stable. Cardiovascular and respiratory system examination were normal. ECG showed persistent juvenile pattern. Echocardiogram revealed pulmonary artery hypertension with right ventricular dysfunction. Thyroid function tests revealed hyperthyroidism. She was commenced on antithyroid medications, betablockers, statins and aspirin. Though her compliance was initially not good, she later became euthyroid and asymptomatic with medications. Her subsequent echocardiogram revealed normal right ventricular function and no PH.
Case Report

Patient 2: This 55 year lady came to master-health check-up with dyspnoea on exertion, palpitation, leg swelling and weight loss. She had goiter, pedal edema and elevated JVP. Respiratory system examination was normal. ECG showed sinus tachycardia. Echocardiogram revealed moderate PH with mild right ventricular dysfunction and hyperdynamic state. TFT revealed hyperthyroidism. She was initiated with antithyroid medications and betablockers. She became euthyroid with medications and become symptom free. Her subsequent echocardiogram revealed normal right ventricular function and no PH.

Patient 3: This 65 year gentleman was admitted with dyspnea, paroxysmal palpitations and giddiness. ECG revealed paroxysmal atrial fibrillation. Echocardiogram revealed moderate PH (RVSP 57mmhg) and hyperdynamic state. TFT revealed hyperthyroidism. He was initiated with antithyroid medications and betablockers. He later became euthyroid and asymptomatic with medications. His subsequent echocardiogram revealed resolution of PH.

Patient 4: This 64 year lady presented with dyspnea and palpitations. She had pedal edema and goiter. Echocardiogram showed severe PAH. TFT revealed hyperthyroidism. She was treated with antithyroid medications and later with RAI. She became hypothyroid and is now on thyroxine supplements. She is asymptomatic now with a decrease in PH.

Patient 5 and 6: were both evaluated for dyspnea and detected to have PH and hyperthyroidism. No other cause for PH was present. They were lost in the follow up and are included in this series for enhancing the association between PH and hyperthyroidism.

DISCUSSION

Pulmonary hypertension is defined as mean pulmonary arterial pressure ≥ 25 mm Hg at rest or ≥ 30 mm Hg with exercise (Yari et al., 2005). Though can be asymptomatic, the typical symptoms include exertional dyspnea, fatigue, angina, and syncope. Dyspnoea is the commonest symptom and also the presenting complaint in all our patients. Hyperthyroidism also causes dyspnea due to increased oxygen consumption and carbon dioxide production (Zwillich et al., 1978). Lung compliance and respiratory muscle strength are decreased but improve with restoration of the euthyroid state (Stein et al., 1961 and Mier et al., 1989).

In our study all the 6 patients were detected to have PH on presentation and subsequently diagnosed with hyperthyroidism. They were tested negative for HIV infection, ILD, myocardial disease, collagen vascular disease, liver disease and COPD as a cause of PH. They were treated with antithyroid medications and followed up regularly with TFT and echocardiogram. Upon restoration of euthyroid state, all became asymptomatic and had normal RVSP except Patient 4 who still had raised but improved PAH.

An association between thyrotoxicosis and increased pulmonary artery pressure has been reported (Velasco et al., 1992), who each reported a single patient with elevated mean PH during hyperthyroidism, resolving after antithyroid therapy. Thurnheer et al., (1997) studied four patients with thyrotoxicosis and found an elevated mean pulmonary artery pressure of 40 ± 11 mm Hg, which decreased to 25 ± 6 mm Hg after achievement of a euthyroid state (Thurnheer et al., 1997). Nakchbandi et al., (1999) proved a similar case with pulmonary artery catheterization (Nakchbandi et al., 1999). Yari et al., (2005) described 3 men with PH and thyrotoxicosis, PH resolving after antithyroid therapy (Yari et al., 2005). All the above cases strongly suggest a cause and effect relationship between thyrotoxicosis and PH.

Possible mechanism of PH in a patient with hyperthyroidism include high cardiac output, endothelial dysfunction, Increased metabolism of endogenous pulmonary vasodilators like nitric oxide (Oden et al., 2005), alterations in the growth and development of pulmonary vascular cells resulting in changes in...
Case Report

vascular dynamics, decreased cholinergic output in hyperthyroid state could result in elevation pulmonary artery pressure (Arroliga et al., 2000) and decreased surfactant production and function (Oden et al., 2005). An association between mutations in the bone morphogenetic protein receptor and the presence of thyroid disease in patients with PH has been observed (Roberts et al., 2005). It has also been suggested that PH and hyperthyroidism may represent the different manifestation of an autoimmune disorder. Chu et al., reported 49% of the 63 patients with PH have concomitant Auto immune thyroid disorder (Chu et al., 2002). Yanai-Landau et al., (1995) reported 30% of 40 patients with PH had antithyroglobulin antibodies (Landau et al., 1995).

Evidence of PH secondary to hypothyroidism also increasing (Kashyap et al., 2001; Curnock et al., 1999).

Conclusion

In summary, the association between hyperthyroidism and PH is increasingly evident and further strengthened by the fact that PH improves following the treatment of hyperthyroidism. Screening for thyroid disorder therefore should be made mandatory for all unexplained PH. Hyperthyroidism is a worthy treatable cause of pulmonary hypertension which has grave prognosis otherwise.

REFERENCES


Case Report


