Improvement in Pulmonary Hypertension and Closure of a Patent Foramen Ovale with Treatment of Hyperthyroidism in a Patient with Graves' Disease

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Abstract: Pulmonary hypertension and recurrence of a previously closed patent foramen ovale seen in Graves' disease patients could be reversed with treatment of hyperthyroidism. We are reporting the case of a 41 year old woman, who presented with features of Graves' disease and pulmonary hypertension which, in turn, led to a right to left shunt through a patent foramen ovale. After 8 weeks of treatment for hyperthyroidism, her pulmonary artery pressure decreased and patent foramen ovale was not noticeable. This is the first reported case of PFO closure with reduction of pulmonary artery pressure associated with treatment of hyperthyroidism to our knowledge.

Keywords: Graves' disease, pulmonary hypertension, patent foramen ovale, closure of patent foramen ovale, treatment for hyperthyroidism.

INTRODUCTION

Pulmonary hypertension (PH) is a chronic and progressive condition that can lead to right heart failure and death. It is defined as mean pulmonary artery pressure (mPAP) greater than or equal to 25mm of Hg measured with right heart catheterization. Pulmonary capillary wedge pressure can be less than or equal to 15mm of Hg in pre-capillary pulmonary hypertension or more than 15 mm of Hg in post-capillary pulmonary hypertension. Echocardiography is used for screening for PH with tricuspid regurgitation peak velocity and systolic artery pressure as main parameters. PH can present as persistent dyspnea on exertion, chest pain, palpitation, and/or fatigue [1].

According to the 5th World Symposium on Pulmonary Hypertension held at Nice, France in 2013, pulmonary hypertension is classified into 5 groups [2]

1. Pulmonary arterial hypertension (with idiopathic and familial subtypes)
2. PH due to left heart disease
3. PH due to lung diseases and/or hypoxia
4. Chronic thromboembolic pulmonary hypertension
5. PH with unclear multifactorial mechanism

In PH with unclear multifactorial mechanism (Group 5) comes the subgroup of PH due to metabolic disorders. This includes autoimmune thyroid diseases which can be hypo/hyperthyroidism [1] or euthyroid lymphocytic thyroiditis. Approximately 50% of PH patients have underlying autoimmune thyroid diseases [3]. Thus PH is an underappreciated, but frequently encountered finding in hyperthyroid patients. Pulmonary hypertension may also occur in non-autoimmune hyperthyroidism.

Isolated right heart failure, tricuspid regurgitation and pulmonary hypertension can be the prominent cardiovascular manifestations of hyperthyroidism [4]. Pulmonary hypertension may be one of the causes of exertional dyspnea often reported by hyperthyroid patients [1]. The various mechanisms postulated by which the hyperthyroid state causes pulmonary hypertension are high cardiac output [5], autoimmune induced pulmonary vascular endothelial injury, and increased pulmonary vascular resistance caused by increased metabolism of certain pulmonary vasodilator substances [4]. Also thyroid hormone is permissive and drives angio-proliferation [5]. Contributing causes to exertional dyspnea in hyperthyroidism are: hyperthyroidism itself, autoimmune mechanisms and obstructive sleep apnea [4] associated with an enlarged thyroid gland resulting in tracheal compression. Two case reports have demonstrated the reversibility of pulmonary hypertension with the antithyroid drugs methimazole, carbimazole and propylthiouracil [6]. These drugs suppress autoimmunity, as well as lower the serum levels of thyroid hormones; therefore, it is

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E-ISSN: 2310-9874/14

not clear what fraction of the benefit is from the former and what is from the latter.

Patent Foramen Ovale (PFO) is present in 10-34% of live human births and often closes spontaneously in the first few years of life. Persistent PFO is associated with increased risk for ischemic stroke, transient ischemic attack and paradoxical peripheral coronary embolism. However, surgical closures to reduce these risks are not routinely recommended as they are unproven [7]. In the presence of elevated right atrial pressure, which can be caused by pulmonary hypertension, pulmonary regurgitation or tricuspid regurgitation, a right to left shunt through PFO may occur in atrial systole [8]. Closure of PFO causes an improvement in the degree of hypoxemia in patients with obstructive sleep apnea [9]; but the impact of PFO closure on PH and systemic hypertension needs to be investigated.

A search of available databases did not disclose any previous reports of closure of PFO associated with treatment of hyperthyroidism.

CASE REPORT AND METHODS

This is a case report of a patient in whom, we observed a reduction in pulmonary artery pressure and the resolution of an atrial, systolic right to left shunt in conjunction with PFO closure, concomitantly with treatment of hyperthyroidism. The patient is a 41 year old Swedish woman who presented to our emergency department with complaints of dyspnea at rest, palpitations, tremor and photophobia shortly after deplaning from a transatlantic flight. She had no known personal or family history of thyroid disorders. She had no history of skin changes, vomiting, headache, diarrhoea, cough, hemoptysis, exposure to chemicals, tobacco, alcohol or illicit drugs. Her menstrual cycles were regular and normal.

A. On Examination

The patient appeared anxious and stated that she felt nervous. She was afebrile. Her apical heart rate was 110-156 bpm with regular rhythm. Her hair was soft with thin strands. She had bilateral chemosis, stare and exophthalmos. A pronounced thyroid bruit was present. Her hands were warm, moist and a moderate tremor was present on outstretching the hands. Tremors were present on extending the tongue and on her closed eyelids. Onycholysis was absent. A soft (grade1/6) systolic murmur was present, best heard at the left sternal border; no diastolic murmur was audible. Wide pulse pressure was noted (140/72 mm of Hg). Her deep tendon reflexes were brisk.

B. Laboratory Findings

Serum TSH by chemiluminescence was 0.013 mIU/L (Normal 0.4-5.5 mIU/L). Serum Total T4 by chemiluminescence was >30.0 mcg/dl (Normal 4.5-12.0 mcg/dl). T3RU by spectrophotometry was 53.89% (Normal 22.50-37.00 %). Total T3 by immunoassay was >800.0 ng/dl (Normal 60.0-181.0 ng/dl). Thyroid Stimulating Immunoglobulin (TSIG) by c AMP generating bioassay was 500% (Normal<140%). Transthoracic echocardiogram on admission showed severe tricuspid regurgitation, pulmonic regurgitation, a pulmonary artery (PA) pressure of 60mm of Hg and an atrial septal defect (ASD) of the secundum/PFO type with right to left atrial systolic shunt (See Figure **1**).

Other causes of PH like alcohol abuse, HIV infection, vitamin D deficiency, left ventricular failure, pulmonary embolus, COPD, obstructive sleep apnea, and vasculitides were ruled out.

Figure 1: Baseline Transthoracic Echocardiogram Showing PFO (arrow).

C. Treatment Given

She was started on methimazole 10mg daily, soon thereafter raised to 20mg daily when her full thyroid function tests became available. She was also given propranolol 10mg every 8 hours for systemic symptom relief.

D. Results after 8 Weeks of Treatment

After 8 weeks of treatment she was nearly asymptomatic. Serum TSH by chemiluminescence was

<0.012 mIU/L. Serum Total T4 by chemiluminescence was 12.4 mcg/dl. T3RU by spectrophotometry was 35.09%. Total T3 by immunoassay was 262.75 ng/dl. Repeat Transthoracic echocardiogram showed only minimal pulmonic and tricuspid regurgitation, reduction of the PA pressure to 39 mm of Hg and no evidence of PFO (See Figure **2**).

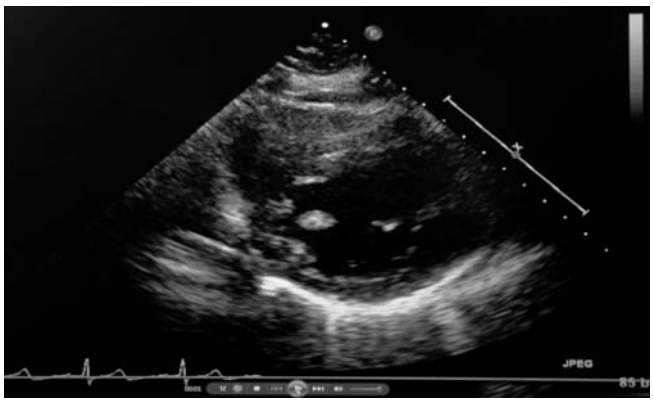

Figure 2: Post treatment Echocardiogram with Resolution of PFO.

CONCLUSION

Pulmonary hypertension is a frequently encountered, but underappreciated, reversible feature of hyperthyroidism, which has been reported in both Graves' disease and toxic multi-nodular goiter [3, 4]. It is unknown if it also occurs in iatrogenic hyperthyroidism. In this patient, who lacked additional predisposing factors, we suggest that her hyperthyroid Graves' disease resulted in PH, leading to an increase in right atrial pressure and the recurrence of a previously closed PFO with right to left shunt. With treatment of her hyperthyroidism there was a decrease in right sided pressures and the PFO again closed.

DISCUSSION

To our knowledge, this is the first reported case of PFO closure with amelioration of pulmonary hypertension associated with treatment of hyperthyroidism. Screening for pulmonary hypertension in hyperthyroid patients may be considered because a case study involving two patients has shown that early treatment with antithyroid drugs reversed their pulmonary hypertension [6] while delayed recognition and treatment of hyperthyroidism might lead to refractory pulmonary hypertension with partially irreversible structural change [10].

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Received on 15-08-2014 Accepted on 03-10-2014 Published on 28-11-2014

DOI: http://dx.doi.org/10.12970/2310-9874.2014.02.03.1