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Case Report

Graves' disease presenting as right heart failure with severe pulmonary hypertension

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ABSTRACT

We report a patient who presented to our institution with clinical features of right sided heart failure and hyperthyroidism. Diagnosis of grave's disease induced reversible severe pulmonary hypertension leading to severe tricuspid regurgitation and right sided heart failure was made after all the common causes were ruled out using the biochemical and radiological investigations and review of literature. Graves' disease is a common cause hyperthyroidism, is an immune system disorder that results in the overproduction of thyroid hormones.

Keywords: Graves' disease, Hyperthyroidism, Heart failure, Tricuspid regurgitation, Pulmonary hypertension

INTRODUCTION

Grave's disease, named after Robert J. Graves, MD, circa 1830s, is an autoimmune disease characterized by hyperthyroidism due to circulating autoantibodies.[1] Thyroid - stimulating immunoglobulins bind to and activate thyrotropin receptors, causing the thyroid gland to grow and the thyroid follicles to increase synthesis of thyroid hormone.

Grave's disease accounts for 60-80% of cases of hyperthyroidism, with a female/male ratio of 5-10:1 and peak incidence between the ages of 40 and 602.

CASE REPORT

A 45-year-old man presented to our emergency department with progressive dyspnoea which progressed from NYHA grade II to NYHA grade IV over 1 month, bilateral pedal since 2 weeks, pain in right hypochondrium, abdominal fullness, nausea & vomiting since 2 weeks, 15 kg weight loss over 2 months inspite of normal appetite, heat intolerance, generalized weakness and easy fatigability since 1 month. His past medical history was unremarkable. Patient denies any addiction including alcohol. On admission general examination revealed pulse rate of 98/min regular waterhammer in character, blood pressure difference between the upper and lower limbs of 50 mmhg with higher values in lower limbs (positive Hill's sign), jugular venous pressure was 12 cm, in addition patient had pallor and icterus. Staring and frightened appearance of the eyes (Kocher sign fig. 1), lid retraction in primary gaze (Dalrymple sign figure 1), lid lag (retarded descent of the upper lid on down gaze Von Graefe sign figure 2), diffusely enlarged thyroid gland (goiter figure 3), Pistol shot sounds were heared over the femorals (traube's sign), Duroziez murmur, b/l pitting pedal oedema was present. On systemic examination Apex beat was hyperdynamic in character felt in 5 intercostal space displaced 3 cm lateral to midclavicular line, Left parasternal heave was present, Diastolic shock was present, Systolic thrill was present in mitral area & tricuspid area. Dull note present in second intercostals space. Auscultation revealed Soft S1 widey split S2 and loud P2 present in pulmonary area with Grade 5 pansystolic murmur in tricuspid area and Grade 4 pansystolic in mitral area. One finger breadth Tender

hepatomegaly present with liver span of 14 cm was present. Shifting dullness was present.

Laboratory evaluation revealed a hemoglobin (Hgb) 9.6 g/dL, white blood count of 11,400/µL with normal differential count, hematocrit 29.9%, platelet count 178,000/µL, normal serum creatinine & electrolytes, bilirubin 3.6 mg/dL, alkaline phosphatase 216.1 U/L, aspartic transaminase 35.0 U/L, alanine transaminase 34.3 U/L, TSH 0.012 IU/mL, free T3 14.2 pmol/L and free T_4 51.1 pmol/L. Ultrasound of neck revealed bulky thyroid gland with mildly increased vascularity and fine echotexture. Abdominal ultrasound revealed mild ascites and mildly enlarged liver. Spiral computed tomography of the chest revealed no evidence of pulmonary embolus. Auto-antibody screen revealed positive antimicrosomal, anti-thyroglobulin and TSH-receptor antibodies and negative antinuclear antibody test. Echocardiogram revealed dilated right atrium, right ventricle and left atrium, severe tricuspid regurgitation, moderate mitral regurgitation, pulmonary artery systolic pressure of 78 mmhg with normal left ventricular cavity size and function Left ventricular ejection fraction was 55%. No structural heart valve abnormalities were noted

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

DISCUSSION

The most common cardiovascular changes arising from hyperthyroidism are increased blood volume, decreased peripheral vascular resistance, and increased resting heart rate and LV contractility, which together result in a hyperdynamic circulatory state and may increase Cardiac output by 50-300% over that of normal subjects. The manifestations usually include palpitations, tachycardia and exercise intolerance.

Association between hyperthyroidism and pulmonary hypertension was first reported in the early 1980s.[3] Possible mechanism includes High cardiac output-induced or autoimmune-induced pulmonary vascular endothelial injury which may lead to pulmonary hypertension.[4-8] Increased pulmonary vascular resistance could also result from increased metabolism of intrinsic pulmonary vasodilating substances (prostacyclin and nitricoxide).[8,9] The regression of pulmonary hypertension following attainment of euthyroid state may support this mechanism.

Many similar cases of isolated right-sided heart failure and pulmonary hypertension secondary to graves' disease have been infrequently reported.[10-28]

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.[29] In an echocardiographic study by Marvisi et al., mild pulmonary hypertension was found in 43% of the 114 hyperthyroid patients and in none of the healthy control group.[30] In another study of 23 consecutive patients with hyperthyroidism caused by Graves' disease, 65% of patients had pulmonary hypertension. Almost all patients normalized the increased pulmonary artery pressure with definitive treatment of the Graves' disease.[31]

These studies 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.

Grave's disease is an unusual and underdaignosed reversible cause of pulmonary hypertension. Detail knowledge of this fact is of utmost importance and high level of suspicion should always be kept in mind to arrive at the diagnosis early.

Our patient had signs resembling aortic regurgitation on the background of clinical diagnosis of hyperthyroidism. Both aortic regurgitation and Graves disease are high output states and if not intervened in time can cause high output cardiac failure. Our patients manifestations of right heart failure responded chiefly to antithyroid drugs; indicating direct connection between Graves disease and heart failure due to pulmonary hypertension. An astule physician should always keep this possibility in mind while treating Graves disease thereby avoiding diagnostic confusion and further unnecessary investigations.

CONCLUSION

Severe pulmonary hypertension leading to tricuspid regurgitation and right heart failure, are rare atypical manifestations of Graves' disease.

Our patient did not present with typical symptoms of hyperthyroidism, and is example of various atypical manifestations of grave's disease, lack of knowledge and understanding of which can mislead the treating physician and result in unnecessary investigations and delay in diagnosis or incorrect diagnosis.

Few cases of graves disease leading to reversible severe pulmonary hypertension leading to severe tricuspid regurgitation and isolated right heart failure have been

reported and we make an attempt to provide a detailed review of this condition.

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