

Congestive Heart Failure Complicated with Chylothorax as the Manifestation in A Patient with Thyrotoxicosis: A Case Report

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Abstract

Although thyrotoxicosis is not rare, congestive heart failure as the manifestation of thyrotoxicosis is relatively uncommon. Coexistence of congestive heart failure and chylothorax is even rarer in hyperthyroid patients. A 37-year-old male patient had been well until 3 years ago when tachycardia and body weight loss developed and a diagnosis of Graves' disease was made. Due to an improvement in the patient's clinical condition, there was non-adherence to his antithyroid therapy. On admission, he presented with symptomatic congestive heart failure and bilateral pleural effusion. Thoracocentesis revealed a high triglyceride level in the pleural effusion, consistent with chylothorax. Survey for other common causes of congestive heart failure and chylothorax was negative. The only concurrent illness identified was thyrotoxicosis and the underlying cause of congestive heart failure and chylothorax was finally determined to be hyperthyroidism. Treatment of heart failure and hyperthyroid state led to a remarkable improvement in the clinical status including recovery of heart function and disappearance of chylothorax. To the best of our knowledge, there were only two adult cases in the literature presenting with congestive heart failure and chylothorax resulting from hyperthyroidism. (J Intern Med Taiwan 2011; 22: 57-62)

Key Words: Thyrotoxicosis, Congestive heart failure, Chylothorax, Graves' disease

Introduction

Chylothorax defined as chyle accumulation in the pleural space is a rare clinical condition. In adults, traumatic or surgical injury of the lymphatic drainage is still the leading cause of chylothorax, followed by lymphoma, other malignancies and various medical disorders¹⁻³. On very rare occasions, congestive heart failure (CHF) may

produce chylothorax^{2,4-6}. Thyrotoxicosis can aggravate an underlying cardiovascular disease and lead to the development of CHF⁷⁻⁹. Actually, thyrotoxicosis itself was reported to be the cause of CHF^{7,9-11}. Whether thyrotoxicosis alone without CHF can lead to chylothorax is still unclear. In this report, we describe a Graves' disease patient with a very unusual presentation including CHF and chylothorax.

Case Presentation

A 37-year-old man had initially presented to the emergency room with a 2-week history of progressive lower leg edema and shortness of breath on exertion. He had also experienced a weight loss of approximately 4 kilograms and tachyarrhythmia over the previous four weeks. Shortness of breath and general malaise had increased over the 3 days before admission. He had a 20-year history of cigarette smoking, but denied alcohol or illicit drug use. The patient did not have any previous medical history except he was diagnosed with Graves' disease three years previously. At that time, palpitation and body weight loss had been bothering him. Improvement to his hyperthyroid state often resulted in a non-adherence to his antithyroid therapy.

In the emergency room, his temperature was 36.3 °C, irregular pulse rate 142 per minute, respiratory rate 25 per minute, and blood pressure 112/76 mmHg. Head and neck examination revealed a symmetrically enlarged, non-tender thyroid gland. Proptosis was not found but jugular venous dilatation was observed. Cardiac examination demonstrated a laterally displaced apex and fast first and second heart sounds. Grade 3/6 holosystolic murmurs were heard at the apex and left sternal border. Chest examination revealed few basilar crackles over both lung fields. Moderate ankle pitting edema was noted bilaterally.

Twelve-lead electrocardiogram (ECG) showed atrial fibrillation (AF) with rapid ventricular response and diffuse ischemic change. Chest radiography demonstrated cardiomegaly and bilateral pleural effusion (Fig 1A). Echocardiogram documented diffusely hypokinetic right and left ventricles, severe mitral regurgitation (MR) and tricuspid regurgitation (TR) (Fig 2A). Left ventricular ejection fraction (LVEF) was reported as 31% (Fig2B) and the estimated systolic pulmonary

artery pressure was 56 mmHg. His hematology parameters were normal. The serum total protein and albumin were 6.4 and 3.7 g/dL respectively. Lactate dehydrogenase (LDH) was 188 IU/L. The total cholesterol and triglyceride (TG) were 132 and 87 mg/dL respectively. Thoracentesis revealed a milky pleural effusion. Fluid analysis disclosed increased TG level (474 mg/dL), low total cholesterol (39 mg/dL), low protein (1.9 g/dL) and low LDH (84 IU/L), consistent with transudative chylothorax. Other microbiologic cultures and cytological studies were negative. Computed tomography of the chest and abdomen to detect the common causes of chylothorax was negative including malignancy, lymphadenopathy, inflammation and cirrhosis. Because our patient had a history of smoking and twelve-lead ECG showed diffuse ischemic change (Fig 1C), the cardiac catheterization was performed. Normal coronary

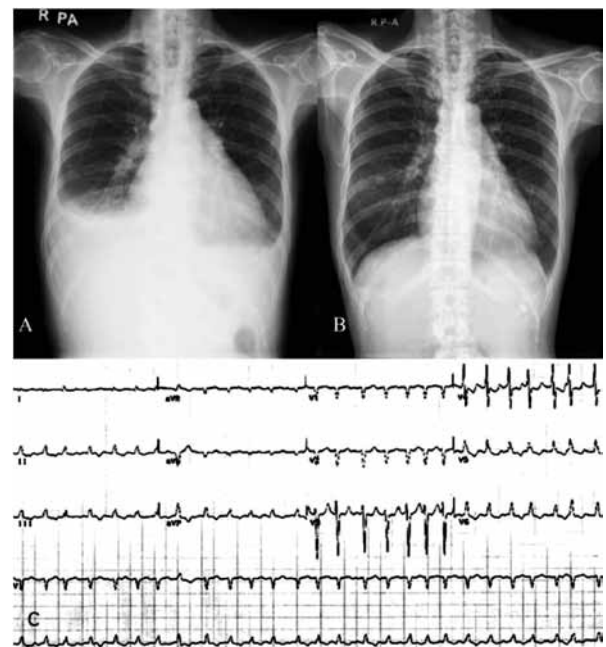


Fig. 1 A. Plain chest film revealing cardiomegaly with bilateral pleural effusion
 B. Plain chest film 5 days later showing the decrease in the size of heart and disappearance of bilateral pleural effusion.
 C. Twelve-lead electrocardiogram revealing atrial fibrillation with rapid ventricular rate and ST-segment depression and T inversion in leads II, III, aVF and V4 through V6.

arteries were impressed and ischemia-related heart failure was excluded. Survey for other common causes of CHF was negative, including coronary artery disease, hypertension, valvular heart disease and alcohol cardiomyopathy. In the absence of an apparent cause for this patient's heart failure and chylothorax, thyrotoxicosis-related cardiomyopathy was considered.

Thyroid function tests confirmed thyrotoxicosis with thyroid stimulating hormone (TSH) < 0.036 u IU/ mL (normal range: 0.35-4.94) and free thyroxine 2.38 ng/dL (normal range: 0.71-1.48). TSH receptor antibodies were 89% (normal range < 14%). The thyroid function tests and a thyroid scan were consistent with the diagnosis of

Graves' disease. Therefore, the endocrinologist started treatment with methimazole 10 mg three times a day for his thyrotoxicosis. In addition, the patient was also started on intravenous furosemide and orally loaded with digoxin, diltiazem and angiotensin-converting enzyme inhibitor. After a few days, the patient's pleural effusion and respiratory distress subsided (Fig 1B). Diuretics, digoxin and diltiazem were stopped and propranolol was started. One week after admission, repeated echocardiography showed a marked improvement in MR and TR and LVEF of 54% (Fig 2C and 2D). The systolic pulmonary artery pressure was decreased to 34 mmHg. The patient was discharged with a therapeutic regimen of methimazole and propranolol. The thyroid function tests slowly returned toward normal over the ensuing 7-8 weeks with continued methimazole. At the 3-year follow-up examination, the patient was doing well but he still had AF rhythm.

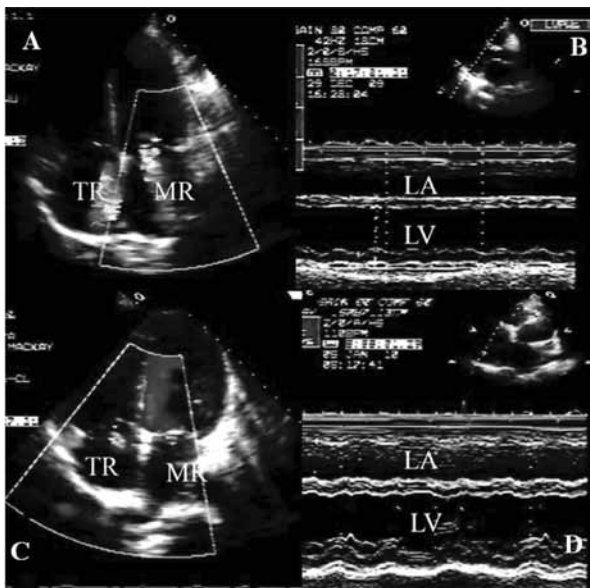


Fig.2 A. Color Doppler ultrasonography demonstrating severe mitral and tricuspid regurgitation. MR= mitral regurgitation; TR= tricuspid regurgitation.
 B. M-mode tracing showing the decrease in fractional shortening. LA= left atrium; LV= left ventricle.
 C. Color Doppler ultrasonography 1 week later demonstrating only mild mitral and tricuspid regurgitation. MR= mitral regurgitation; TR= tricuspid regurgitation.
 D. M-mode tracing 1 week later showing the improvement in left ventricular fractional shortening. LA= left atrium; LV= left ventricle.

Discussion

The diagnosis of chylothorax is made when the pleural fluid TG level is above 110 mg/dL¹. Though rare in incidence, chylothorax usually leads to significant morbidity and mortality and is mostly attributable to trauma (including surgery), malignancy, and miscellaneous disorders¹⁻³.

Rarely, heart failure secondary to various causes may produce chylothorax⁴⁻⁶. Two mechanisms of chylothorax formation in CHF were postulated. One was increased capillary filtration resulting from high venous pressure, which leads to augmented lymph production⁴⁻⁶. The second was decreased thoracic duct inflow and lymphatic collateral flow formation due to elevated central venous pressure^{4,6,12}. These two mechanisms cannot completely explain the chylothorax formation in CHF patients. The high prevalence of CHF and the rare presentation of chylothorax imply that other undiscovered factors may play a role in the

pathogenesis of chylothorax in patients with CHF.

Most patients with thyrotoxicosis have characteristic clinical pictures, many of which are related to the cardiovascular system^{13,14}. With the combination of genomic and non-genomic effects, thyroid hormone (TH) can increase inotropy and chronotropy of myocardia and decrease systemic vascular resistance of the peripheral circulation. The total effects of TH on the cardiovascular system usually lead to a high cardiac output state^{8,13,14}. Actually, thyrotoxicosis may aggravate the underlying cardiovascular disease and make CHF develop^{8,10,13-15}, especially in elderly and patients with AF, hypertension, or risk factors for coronary artery disease^{8,13,14,16}.

How did thyrotoxicosis lead to CHF? Some studies showed that the LV function was usually improved with adequate control of heart rates long before the euthyroid state was achieved which indicated tachycardia-induced cardiomyopathy as the underlying mechanism for CHF^{13,16}. In contrast, some studies demonstrated that there was only partial recovery of LV function despite successful rate or rhythm controlled in hyperthyroid patients which suggested that other mechanisms might contribute to the development of CHF^{8,9}. It was proposed that excessive TH might directly induce myocardial necrosis and subsequently result in the development of CHF^{9,13}. Pereira et al observed rapid reversibility of LV dysfunction in hyperthyroidism and proposed that myocardial stunning might lead to the development of CHF in some patients with hyperthyroidism¹⁷. To summarize, we conclude three possible mechanisms of CHF development in hyperthyroidism, including long-standing tachycardia^{9,16}, direct toxic effects of the TH on the myocardium^{8,9,13}, and myocardial stunning¹⁷. Each of the three factors seemed to play some role of the pathogenesis of CHF in our patient because this patient had a relatively long duration of tachyarrhythmia and hyperthyroid state and

exhibited a remarkable improvement of LVEF within a few days.

It is not clear whether thyrotoxicosis alone without CHF can lead to chylothorax. We cannot find any report about chylothorax due to pure thyrotoxicosis. The only two case reports that we can find both had CHF and chylothorax simultaneously^{12,18}. It seems to suggest that thyrotoxicosis itself hardly leads to chylothorax without the development of CHF. More evidence is needed to clarify the association between thyrotoxicosis and chylothorax.

In our patient, survey for other common causes of CHF was negative, including coronary artery disease, hypertension, valvular heart disease and viral or alcohol cardiomyopathy. Imaging studies did not find the common causes of chylothorax including malignancy, lymphadenopathy or liver cirrhosis. Moreover, he responded well to antithyroid treatment and short-term heart failure therapy. All the clinical condition and laboratory data implied that CHF secondary to thyrotoxicosis was the most probable cause of chylothorax.

In addition to an anti-hyperthyroid regimen, the treatment of CHF secondary to hyperthyroidism is chiefly based on a beta-blocker except in patients with hypotension, chronic obstructive pulmonary disease, asthma and bradycardia^{13,14}. Some reports revealed severe, adverse hemodynamic changes of beta-blocker administration in thyrotoxic heart failure patients^{7,11}. The first thing to be determined should be whether the patient was in a high-output or low-output state because the beta-blocker was only indicated in the former condition¹¹. Administration of digoxin is reasonable in patients with a low EF and/or AF with fast ventricular rate^{7,15}. However, high dosages may be required in patients with thyrotoxicosis as well as chylothorax for two reasons. One is increased numbers of sodium-potassium ATPase units and increased renal excretion in hyperthyroid state¹³. The second is

that near zero digoxin level may occur because of sequestration of digoxin in the chyle¹⁹.

In conclusion, we describe a very unusual presentation of hyperthyroidism in this report. Recovery of heart function and disappearance of chylothorax after correction of the thyrotoxicosis strongly suggests a cause-effect relationship between thyrotoxicosis and CHF associated with chylothorax. For two reasons, thyrotoxicosis should be included in the differential diagnosis in patients with unclear etiology heart failure and chylothorax. First, delayed diagnosis leads to poor prognosis because thyrotoxicosis-related heart failure responds poorly to the conventional treatments of CHF and chylothorax usually leads to significant morbidity and mortality^{1,3}. Second, early anti-thyroid regimen often leads to complete and rapid recovery of thyrotoxicosis-related heart failure^{11,14}.

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甲狀腺亢進以鬱血性心衰竭及乳糜胸為臨床表徵： 一病例報告

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摘要

雖然甲狀腺亢進並不少見，但是以鬱血性心衰竭為臨床表徵的甲狀腺亢進並不常見。在甲狀腺亢進患者中，同時存在鬱血性心衰竭和乳糜胸的情形更是罕見。一位原本健康的37歲男性病人，3年前因心搏過速，體重減輕而被診斷為葛雷夫氏症。因為他的臨床病情改善，所以他並不嚴格遵從甲狀腺亢進的治療。入院時，他表現出鬱血性心衰竭的症狀以及雙邊胸腔積液的情形。胸液抽吸發現高三酸甘油酯的胸腔積液，符合乳糜胸診斷。篩檢一般鬱血性心衰竭以及乳糜胸的常見原因，也都沒有進一步的發現。在此同時唯一可以找到的疾病是甲狀腺亢進。最後，鬱血性心衰竭和乳糜胸的根本原因被歸因是由於甲狀腺亢進所造成。治療甲狀腺亢進和鬱血性心衰竭後，有顯著的臨床狀況改善，包括心臟功能的恢復和乳糜胸的消失。據我們所知，在文獻中只有兩個成年病例因甲狀腺亢進而呈現出鬱血性心衰竭和乳糜胸的情形。