



Primary Hypothyroidism: Uncommon Presentation With Reversible Dilated Cardiomyopathy in a Young Subject

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ABSTRACT

Most patients with dilated cardiomyopathy have a poor prognosis that is associated with progressive and irreversible myocardial dysfunction. Rarely, a reversible metabolic etiology that is amenable to specific therapy is identified. Thyroid hormones have many effects on the heart. Although cardiac output is reduced in hypothyroidism, heart failure is relatively rare due to the lower demand for peripheral oxygen delivery. We report a 14-year-old girl who presented with dilated cardiomyopathy (DCM) and was determined to have primary hypothyroidism, for whom cardiac function improved significantly after levothyroxine replacement therapy. Our case underscores the necessity of thyroid function testing to examine the etiology of nonischemic DCM, even in young subjects.

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► Implication for health policy/practice/research/medical education:

Hypothyroidism is a rare cause of dilated cardiomyopathy and hormonal treatment with levothyroxine can significantly improve myocardial function. Hence it is felt that thyroid function tests should be systematically performed in all patients with DCM in order to rule out hypothyroidism.

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1. Introduction

Cardiomyopathies constitute a group of diseases that primarily affect the heart muscle and are not the result of congenital, acquired valvular, hypertensive coronary arterial, or pericardial abnormalities. Dilated cardiomyopathy (DCM) is an idiopathic condition that results from impaired ventricular systolic function, leading to progressive cardiac remodeling and dilatation (1). A reversible form of DCM can develop

due to alcohol use, pregnancy, chronic uncontrolled tachycardia, hypothyroidism, hyperthyroidism, drug use, and other endocrine dysfunctions (2-7). Since the first description of DCM in 4 hypothyroid patients in 1918, few such cases have been published (8, 9); most reports have described adults, the youngest of whom was 20 years (8). We report a case of hypothyroidism in a young patient with DCM.

2. Case report

A 14-year-old girl complained of dyspnea on exertion for 1 month. The dyspnea was progressive, with the patient becoming symptomatic at gradually lower levels of exertion. She had a history of 3 episodes of paroxysmal nocturnal dyspnea without any chest pain or syncope. Over the past

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15 days, she developed increasing pedal edema. In the past year, the patient noticed weight gain, facial puffiness, constipation, dry skin, and intolerance to cold.

On examination, the patient was obese, with a body mass index (BMI) of 28.4 kg/m², and her skin was pale and dry. Her blood pressure was 120/80 mm Hg, and her pulse was 54/min. We noted bilateral pitting pedal edema with raised jugular venous pressure. A symmetrical and firm grade 2 goiter was palpable. Bilateral ankle jerks showed delayed relaxation. Heart sounds were distant, with a chest examination revealing bibasilar end inspiratory crackles and an abdominal examination showing tender hepatomegaly. A chest x-ray showed cardiomegaly and a reverse bat wing appearance of a pulmonary edema (Figure 1). There were non-specific ST-T changes with low voltage QRS complexes on the electrocardiogram. Echocardiography revealed a DCM with severe dysfunction of the left ventricle (ejection fraction 25%) and global hypokinesia (Figure 2).

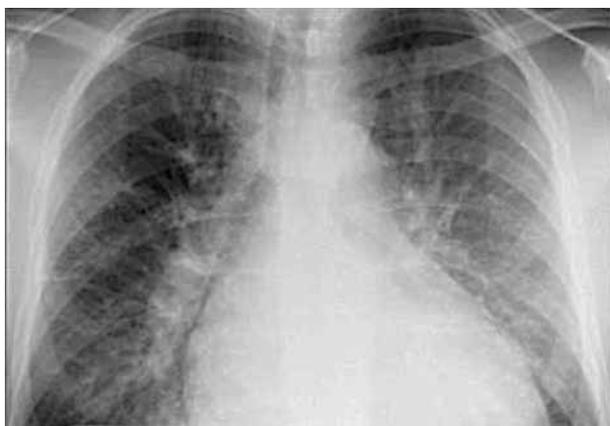
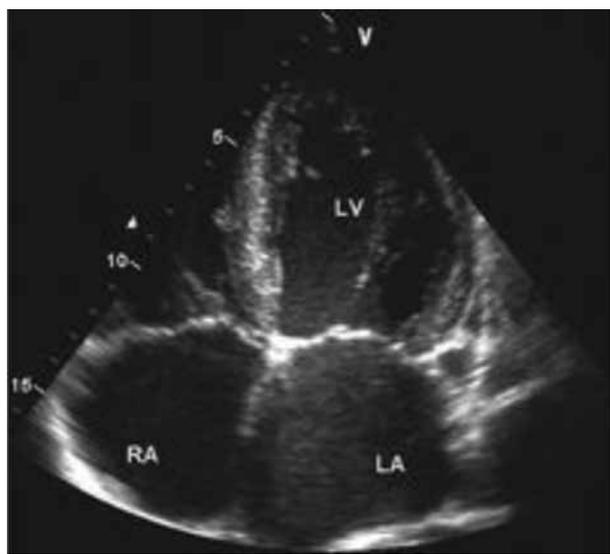


Figure 1. Chest X Ray PA View Showing Cardiomegaly and Reverse bat Wing Appearance of Pulmonary Edema.

Figure 2. Apical Four Chamber Echocardiographic View Shows Marked Enlargement of all Four Chambers, as Well as Spontaneous Echo Contrast in the Left Sided Chambers Because of a Very low Ejection Fraction and Sluggish Flow.



LA- Left Atrium, LV- Left Ventricle, RA- Right Atrium

Biological tests showed cholesterol and triglyceride levels of 250 mg/dl and 285 mg/dl/l, respectively, and elevated creatinine phosphokinase (430 U/l). Thyroid function test showed reduced T3 (60 ng/dl, normal: 80-180 ng/dl) and T4 (3.6 µg/dl, normal: 5-12 µg/dl) and elevated thyroid-stimulating hormone (TSH = 135.5 mU/l, normal: 0.5-5 mU/l), establishing a diagnosis of primary hypothyroidism. The thyroid was enlarged, heterogeneous, and multinodular by ultrasonographic imaging. The patient was positive for anti-thyroperoxidase and anti-microsome. The final diagnosis was Hashimoto thyroiditis.

The pulmonary edema was treated with oxygen inhalation, digoxin, diuretics, and angiotensin-converting enzyme inhibitors (ACEIs). Hormonal replacement therapy with levothyroxine was begun at an initial dose of 25 µg/day, increasing over 9 months to 150 µg/day, until the TSH levels normalized. Despite gradual symptomatic improvement, the echocardiography, performed 6 months after levothyroxine supplementation was initiated, revealed left ventricle ejection fraction of 45%, and the patient was asked to take only ACEIs and omit digoxin and the diuretic. Three months after the 150-µg/day dosage of levothyroxine was begun, the echocardiography showed a significant improvement in left ventricle systolic ejection fraction to 57% (Table 1). All other medications, including ACEIs, were withdrawn at this point. Echocardiography, performed twice at 6-month intervals then after echocardiography showed ejection fraction of 57%, revealed ejection fractions of 56% and 59%, respectively, with the patient remaining symptom-free.

3. Discussion

Our case confirms previous reports concerning the potential reversibility of heart failure after substitutive hormone treatment (2, 8, 9). The patient's young age at presentation with DCM led us to search for a reversible etiological factor. Additional findings of goiter, dry skin, and delayed relaxation of tendon reflexes led us to suspect coexistent hypothyroidism. Other similar cases have been reported primarily adults, with the youngest patient at age 20 years (7-9). We believe our case is unique, based on its presentation in a young subject aged 14 years.

Thyroid hormones interact with the sympathovagal balance but also act on peripheral vascular resistance. The effect of thyroid hormones on the cardiovascular system can be explained by the transcriptional regulation of genes that are implicated especially in contractile system synthesis. Rapid nongenomic effects of thyroid hormones on ionic channels in the cardiomyocyte membrane have recently been reported (10). The effects of thyroid hormone on the heart occur primarily through a change in protein synthesis. Some abnormalities of cardiac function in patients with thyroid dysfunction directly reflect the effects of thyroid hormone on calcium-activated ATPase and phospholamban, which are involved

Table 1. Comparison of Baseline Parameters of the Patient With That of Post Thyroxine Replacement Parameters.

Parameters	Baseline	After Levothyroxine, 150 µg/ Day Treatment (12 weeks)	Reference Ranges
TSH ^a	135.5	10.5	0.5 - 5 (mIU/L)
Hemoglobin	10.2	12.5	13-16 g/dl
CPK	430	90	< 250 (U/L)
Ejection Fraction	25%	57%	55-60 %

^a Abbreviations: TSH, Thyroid stimulating hormone; CPK, Creatine phosphokinase

primarily in the regulation of systodiastolic calcium concentrations in cardiomyocytes. Myocardial relaxation is effected by calcium uptake into the sarcoplasmic reticulum, mediated by calcium-activated ATPase. Thyroid hormone also modifies the expression of other ion channels, such as Na⁺/K⁺-activated ATPase, Na⁺/Ca⁺⁺ exchanger, and some voltage-gated K⁺ channels (Kv1.5, Kv4.2, Kv4.3), thereby coordinating the electrochemical and mechanical responses of the myocardium (11). The majority of cardiac manifestations in hypothyroidism results from bradycardia, decreased myocardial contractility, and increased peripheral vascular resistance. (12). Pericardial effusion is the most frequent cardiac manifestation. Many patients with overt hypothyroidism have abnormal standard ECGs, including QT prolongation and flattening/inversion of the T wave (12), which reflect prolonged cardiac action potential. Sinus bradycardia with low voltage QRS complexes in our patient's ECG led to hypothyroidism as a possible etiology. The most frequent cardiac abnormality in patients with overt hypothyroidism is impairment of left ventricular (LV) diastolic function, which is characterized by slower myocardial relaxation and impaired early ventricular filling (13). LV systolic function is only marginally subnormal. Rawat *et al.* (14), in their study on overt hypothyroid patients, did not find any difference between severity of hypothyroidism and LV systolic function or LV size. Bhupathi *et al.* (15) found that systolic time intervals, such as pre-ejection period and ejection time, and diastolic functions, such as isovolumic relaxation time, were affected in hypothyroid children. However, ejection fraction (EF) and circumferential fiber shortening were not significantly affected. Other such cases that have presented with reversible DCM due to hypothyroidism (7-9) have responded to levothyroxine replacement therapy, ameliorating symptoms in 6 to 9 months. Our patient had a low EF of 25%, which increased to 57% after levothyroxine treatment for 12 months ie, 12 weeks after normalization of TSH. Hypothyroidism itself is one of the risk factors for atherosclerosis (16). Alterations in T₃-mediated gene expression lead to various cardiac manifestations in hypothyroidism (17). In hypothyroidism, although cardiac output is reduced, heart failure is relatively rare, because there is lower oxygen demand in the periphery (18). In a study by Rodondi *et al.*, subclinical hypothyroidism was associated with an increased risk of congestive heart failure among older adults with a TSH level of ≥ 7.0 mIU/L but not with other cardiovascu-

lar events or mortality (19). No similar observations were noted in young subjects. The baseline TSH level in our subject was 135.5 mIU/L.

In our patient, the family history argued against inherited causes of dilated cardiomyopathy. There was no history of drug abuse or alcohol or toxic substance addiction. The personal history and clinical exam ruled out nutritional deficiency, and negative HIV and HCV serologies eliminated potential viral causes of dilated cardiomyopathy. Our observations highlight the importance of hormone dosage in the first assessment of DCM, even in the absence of major symptoms of TH, because clinical presentation is not always obvious and because the diagnosis can only be made by thyroid function testing. Fortunately, the diagnosis of hypothyroidism was clinically evident in our patient and confirmed by the thyroid function test.

The challenge is to determine whether TH has an occasional association with DCM or is a cause of it (17). Bezdah *et al.* (2) and Khochtali I *et al.* (8) have suggested that hypothyroidism should be systematically evoked when DCM is diagnosed. The improvement in cardiac function after hormone treatment in our patient implicates hypothyroidism in the genesis of DCM. However, the earliest age of presentation of DCM in hypothyroidism in the literature is 20 years (8). Our case report highlights this unusual occurrence of hypothyroidism-induced, reversible DCM at age 14 years.

DCM is typically an idiopathic disease with a progressive course and an irreversible, poor prognosis and outcome. In contrast, in some cases, DCM can be secondary to various causes, such as hypothyroidism, and hormone treatment with levothyroxine can significantly improve myocardial function. Hence, we feel strongly that thyroid function tests should be performed systematically in all patients with DCM to rule out hypothyroidism. Most commonly, DCM becomes clinically apparent in the third or fourth decade of life. However, one needs to be alert for such occurrences in young subjects with hypothyroidism.

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