Hypothyroidism-induced reversible dilated cardiomyopathy

Rastogi P, Dua A, Attri S, Sharma H

ABSTRACT
Dilated cardiomyopathy (DCM) is an idiopathic condition that results from impaired ventricular systolic function. Thyroid diseases have been known to cause myriad changes in the structure and function of the heart. Diastolic dysfunction is a common abnormality reported in hypothyroidism. However, hypothyroidism-induced DCM and systolic dysfunction is an uncommon phenomenon, especially as the initial presenting manifestation of hypothyroidism. The current article describes the case of a young female who presented with symptoms of heart failure and was diagnosed as having DCM as echocardiography revealed left ventricular global hypokinesia and severely depressed systolic function. Thyroid profile revealed a grossly elevated thyroid-stimulating hormone (TSH) value of 313 μIU/ml; free thyroxine (fT4) was 0.220 ng/dl. The present case presented with DCM as the initial presentation of hypothyroidism and improved significantly after five months of levothyroxine replacement therapy.

KEY WORDS: Dilated cardiomyopathy, heart failure, hypothyroidism

Introduction
Cardiomyopathies are defined as a heterogeneous group of diseases of the myocardium, associated with mechanical and/or electrical dysfunction that usually exhibit inappropriate ventricular hypertrophy or dilation. They are due to a variety of causes and frequently are genetic in nature. Cardiomyopathies are traditionally defined on the basis of structural and functional phenotypes, notably dilated, hypertrophic, and restrictive. Dilated cardiomyopathy (DCM) is an idiopathic condition that results from impaired ventricular systolic function, leading to progressive cardiac remodeling and dilatation.

Thyroid diseases have been known to cause myriad changes in the structure and function of the heart. Both hyperthyroidism and hypothyroidism produce changes in cardiac contractility, myocardial oxygen consumption, cardiac output, blood pressure, and systemic vascular resistance [Table 1]. Diastolic dysfunction is a common abnormality reported in hypothyroidism. Although alterations in myosin heavy chain isoform expression have been documented, hypothyroidism-induced DCM is an uncommon phenomenon. Here, we report a case of a young female who presented with hypothyroidism-induced DCM which improved significantly after levothyroxine replacement.

Case Report
A young married female aged 30 years presented to the Medical Emergency Department of our institute with chief complaints of decreased appetite, gradually progressive shortness of breath on exertion, and swelling all over body for 6 months. For the past 15 days, she had been complaining of dyspnea even on mild exertion and progressive abdominal distension. There was no history of fever, exertional chest pain, diabetes, hypertension, or jaundice. The family history was against any inherited causes of DCM. There was no history of any drug intake or alcohol or toxic substance addiction. Her obstetric history was noncontributory with three uneventful pregnancies and normal vaginal deliveries. The last delivery was 2.5 years back.

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On examination, the patient was tachypneic, normotensive, and afebrile. The body mass index was 24.8 kg/m². She had a hoarse voice which had changed over the past 2 years and had bilateral pitting pedal edema. The neck veins were engorged, and there were bilateral basal crepitations in the chest. The cardiovascular system examination revealed that apex beat was hyperdynamic in character and was localized in the 6th intercostal space outside the midclavicular line. The first and second heart sounds were normal; left ventricular (LV) third heart sound (S3) was present. There was no murmur or pericardial rub. There was no sign of nutritional deficiencies such as glossitis, cheilitis, limitation of ocular movements, memory impairment, or muscle weakness.

During the course of investigations, hemogram, fasting and postprandial blood glucose, kidney function tests, electrolytes, and liver function tests including serum proteins were found to be within normal limits. Chest X-ray revealed gross cardiomegaly and electrocardiogram showed left bundle branch block. Ultrasound abdomen revealed mild ascites and minimal bilateral pleural effusion. Echocardiography was done and it revealed DCM with severe global LV hypokinesia and ejection fraction 15% along with a minimal pericardial effusion and Grade II LV diastolic dysfunction. Thus, a diagnosis of DCM with heart failure was made, standard treatment for the same was started, and further investigations were carried out to focus on the etiology.

Considering the possibility of autoimmune pathology, antinuclear antibody testing by immunofluorescence was done which was not significant. Negative human immunodeficiency virus and hepatitis C virus serologies eliminated potential viral causes. Thyroid profile revealed a grossly elevated thyroid-stimulating hormone (TSH) value of 313 µIU/ml; free thyroxine (fT4) was 0.220 ng/dl. The patient was promptly initiated on levothyroxine 50 µg/day which was gradually increased to 100 µg daily replacement therapy. Within 3 weeks of starting the thyroxine therapy, the patient started showing significant improvement in her symptoms of dyspnea and effort intolerance. A repeat echocardiographic examination after 5 months of replacement therapy revealed remarkable improvement in her LV chamber dimensions and ejection fraction to 45% [Table 2]. There was a concurrent improvement in thyroid profile with the therapy (TSH 12.30 µIU/ml, fT4 1.13 ng/dl).

### Discussion

Effects of thyroid hormone on the heart are elicited by a number of genomic and nongenomic effects. Increase in thyroid hormone levels plays a role in transition from the fetal heart to adult phenotype of heart. The heart relies mainly on triiodothyronine (T3) because there is no significant deiodinase activity inside myocytes, and T3 is directly transported into the myocyte. During adult life, T3 modulates inotropic and lusitropic properties of the myocardium, myocardial contractility, and vascular function. T3 upregulates the transcription of many structural and functional proteins of the heart, namely, sarcomplamin reticulum calcium ATPase, alpha-myosin heavy chain, beta-1 adrenergic receptors, Na/K ATPase, voltage-gated potassium channels, and atrial and brain natriuretic peptides. It also downregulates some genes such as beta-myosin heavy chain, phospholamban Na/Ca exchanger, transcription-associated protein 1 (TRa1), and adenylyl cyclase type 5 and 6. Nongenomic effects of thyroid hormone on the heart relate to changes in ion transport, glucose and amino acid transport, and a number of intracellular signaling pathways.[4,5]

Hypothyroidism can produce clinical phenotype of heart failure from a number of diverse mechanisms which include: bradycardia, impaired contractility, impaired diastolic filling, increased systemic vascular resistance, diastolic hypertension, and endothelial dysfunction.[6] It has also been demonstrated that subclinical hypothyroidism may lead to the development of heart failure. Studies have shown that like the sick-euthyroid syndrome occurring in various nonthyroidal illnesses, for example, sepsis, patients with heart failure who have normal thyroid gland may have low circulating levels of T3 with normal levels of T4 and TSH. Low serum T3 in these patients strongly predicts all-cause and cardiovascular mortality.[7] The most consistent cardiac abnormality recognized in patients with overt hypothyroidism is impairment of LV diastolic function characterized by slowed myocardial relaxation and impaired early ventricular filling.[8,9] However, hypothyroidism presenting as cardiomyopathy and decreased LV systolic function is an uncommon feature. There have been few case reports till date in literature mentioning hypothyroidism-induced DCM with decreased LV systolic function. Since the first description of DCM in four hypothyroid patients in 1918,[10] few such cases have been published. Bezdah et al.[11] reported the case of a patient with severe hypothyroidism and a DCM complicated by heart failure, which recovered with levothyroxine therapy. They suggested that hypothyroidism should be evoked systematically when a DCM is diagnosed. Ladenson et al.[12] found reversible alteration in myocardial gene expression in a young man with DCM and hypothyroidism. Similarly, Khochtali et al.[13] reported two case studies demonstrating reversible DCM caused by hypothyroidism.[14]

### Table 1: Cardiovascular changes with thyroid disease

| Parameter                        | Normal     | Hyperthyroid | Hypothyroid |
|----------------------------------|------------|--------------|-------------|
| Systemic vascular resistance     | 1500-1700  | 700-1200     | 2100-2700   |
| Heart rate (beats/min)           | 72-84      | 88-130       | 60-80       |
| Cardiac output (L/min)           | 5.8        | > 7.0        | < 4.5       |
| Blood volume (percentage of normal) | 100       | 105.5        | 84.5        |

### Table 2: Echocardiographic parameters at presentation and at 5 months after levothyroxine replacement therapy

| Parameter                        | At presentation | After 5 months |
|----------------------------------|-----------------|---------------|
| Interventricular septum cm       | 0.867           | 1.02          |
| LV internal dimension cm         | 6.27            | 5.81          |
| LV posterior wall cm             | 1.02            | 1.27          |
| Ejection fraction (%)            | 15              | 45            |

LV: Left ventricular

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In the present case study, our patient’s case confirmed previous reports concerning the potential reversibility of heart failure after levothyroxine replacement. Our patient had presented with symptoms of heart failure and had LV global hypokinesia and severely depressed systolic function. She responded well to thyroid hormone replacement therapy along with conventional therapy for DCM, and during the course of treatment, her LV function and clinical symptoms improved suggesting that reversible LV dysfunction was due to hypothyroidism.

**Conclusion**

DCM is primarily an idiopathic disease with progressive and an irreversible outcome. In contrast, in some cases, DCM can be secondary to certain well-documented causes such as alcohol use, pregnancy, chronic uncontrolled tachycardia, hyperthyroidism, and drug use. Hypothyroidism can also cause DCM, and replacement treatment with levothyroxine can significantly improve myocardial function. Hence, thyroid function tests should be systematically performed in all patients with DCM to rule out hypothyroidism. Large-scale studies are needed to explore and elucidate further the mechanisms involved in the pathogenesis of hypothyroidism-induced DCM.

**Declaration of patient consent**

The authors certify that appropriate patient consent was obtained.

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**Conflicts of interest**

There are no conflicts of interest.

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