



Residual Subclinical Left Ventricular Systolic Dysfunction in an Adolescent Patient with Primary Hypothyroidism and Dilated Cardiomyopathy

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Abstract

Dilated cardiomyopathy is a rare complication of hypothyroidism. Studies with standard echocardiography have established that compromised left ventricular systolic dysfunction associated with hypothyroidism is reversible after hormone replacement therapy. Speckle tracking strain imaging has been used to evaluate subtle myocardial dysfunction and regional wall-motion abnormalities in the context of normal ejection fraction.

We report a case of a 15-year-old female of primary hypothyroidism and dilated cardiomyopathy in which residual subclinical left ventricular systolic dysfunction was detected by two-dimensional speckle-tracking echocardiography after recovery of ejection fraction.

Keywords: Hypothyroidism; Dilated cardiomyopathy; Two-dimensional speckle tracking echocardiography; Cardiac function

Introduction

Hypothyroidism is a rare cause of reversible dilated cardiomyopathy. Both genomic and non-genomic actions of thyroid hormones are thought to be crucial to the pathogenesis of cardiovascular manifestations in both overt and subclinical hypothyroidism [1]. Conventional echocardiographic parameter, including LVEF, for the evaluation of left ventricular systolic dysfunction is unable to fully reflex facets of complex myocardial mechanics. Conventional qualitative and semi-quantitative evaluation of myocardial movements can be maneuver-dependent, and can be inaccurate due to the interaction of adjacent myocardium. Speckle-tracking echocardiography has offered the opportunity to further understand the complexity of myocardial movements in the context of various disease states.

We describe the case of residual subclinical left ventricular systolic dysfunction detected by two-dimensional speckle-tracking echocardiography after recovery of ejection fraction in a patient of primary hypothyroidism and dilated cardiomyopathy.

Case Presentation

A 15-year-old female (54 kg, 140 cm) affected by hypothyroidism and congestive heart failure was admitted to our hospital for dyspnea, abdominal bloating, generalized edema, poor stamina, and occasional paroxysmal nocturnal dyspnea. She had been on substitutive hormonal treatment with tab levothyroxine, diuretic treatment with furosemide and spiro lactone, along with angiotensin converting enzyme (ACE) inhibitor (perindopril) and beta blocker (metoprolol) for four months. The diagnosis of hypothyroidism was suspected due to solemnness and inactivity progressively developed over four years prior to admission, and was confirmed with elevated serum TSH level, depressed T4 and T3 levels, all indicative of severe primary hypothyroidism. On examination the patient was overweight, with a body mass index (BMI) at 27.5 kg/m², her skin was dry and infiltrated with edema in the bilateral lower extremities. Blood pressure was at 80/50 mmHg, the pulse was at 80 bpm/mn. There was a class II enlargement of goiter. Her apex beat was in 6th intercostal space in anterior axillary line. Cardiac dullness extended to the left and downward. There was no murmur. There was no hepatomegaly. Shifting dullness was elicited. Biological tests showed decreased high-density lipoprotein and elevated triglyceride level respectively at 0.68 mmol/L and 4.17 mmol/L, raised alkaline phosphokinase level at 396 IU/L and elevated uric acid level at 581

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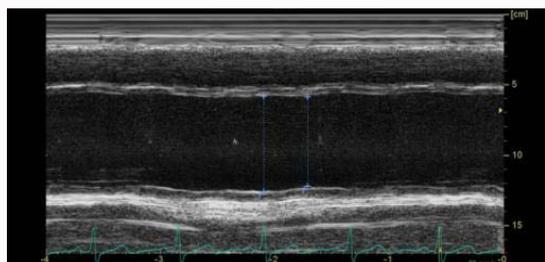


Figure 1A: M-mode image of parasternal long-axis view of standard echocardiography upon admission showed enlarged left ventricle and myocardial hypokinesia.

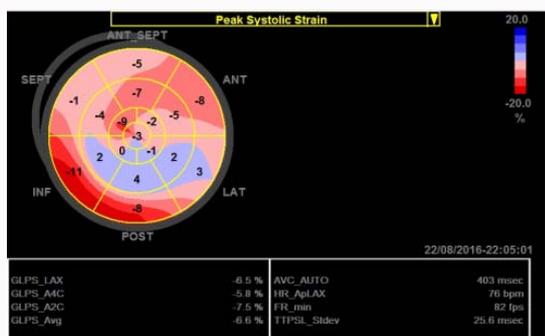


Figure 1B: Bull-eye presentation of 2-dimensional speckle tracking strain imaging upon admission showed diffusely compromised left ventricular longitudinal myocardial strain upon admission. The apical segments showed remarkable deterioration.

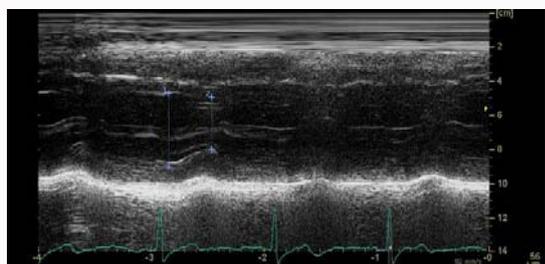


Figure 1C: M-mode image of parasternal long-axis view of standard echocardiography 13 months after showed normalization of left ventricle dimension and improvement in myocardial systolic function.

μmol/L. In addition, there was an elevated brain natriuretic peptide level at 1999 ng/L and normal range of cardiac enzymes. Renal functions were normal with blood urea nitrogen of 6.14 mmol/L and creatinine of 45 μmmol/L. The patient was euthyroid with TSH, TT4 and TT3 levels at 4.30 mU/L (reference range: 0.38 mU/L to 4.34 mU/L), 1.56 pg/ml (reference range: 0.81 pg/ml to 1.89 pg/ml) and 3.78 pg/ml (reference range: 1.8 pg/ml to 4.1 pg/ml), respectively. The anti-thyroid peroxidase and antithyroglobulin antibodies were positive at 45.45 IU/ml (reference range: <34 IU/ml) and 453.1 IU/ml (reference range: <115 IU/ml). The thyroid gland was diffusely heterogeneous with reduction of blood flow on ultrasound imaging. The EKG revealed a heart rate of 70/min with normal sinus rhythm, left axis deviation and non-specific ST-segment and T-wave changes. Coronary computed tomography angiography was unremarkable. Standard cardiac ultrasound revealed that the patient had a dilated left ventricular cavity with a diastolic dimension of 63 mm, with severe LV global hypokinesia and ejection fraction of 13% (Figure 1A). In addition, there was a mild pericardial effusion, and a moderate

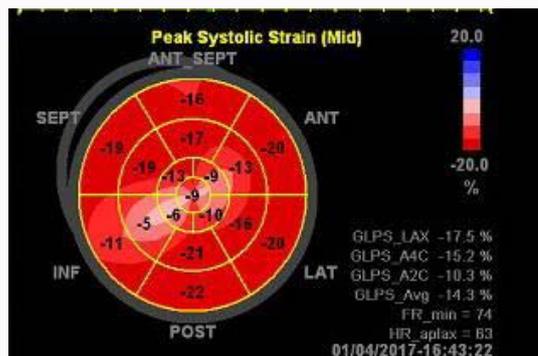


Figure 1D: Bull-eye presentation of 2-dimensional speckle tracking strain imaging 13 months after showed persistent impairment in myocardial longitudinal strain in apical segments.

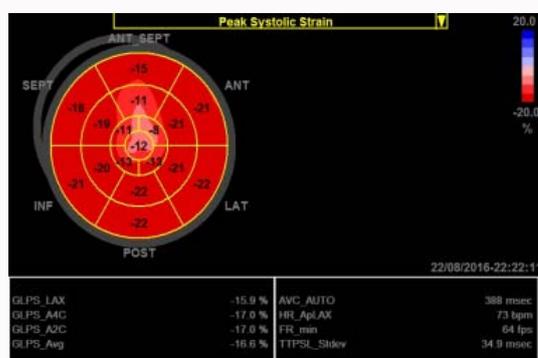


Figure 1E: Bull-eye presentation of 2-dimensional speckle tracking strain imaging three years after showed persistent impairment in myocardial longitudinal strain in apical segments.

mitral regurgitation. Speckle-tracking strain imaging revealed diffuse left ventricular myocardial dysfunction, particularly in the apical segments (Figure 1B), with global peak systolic longitudinal strain at -7% (normal, greater than -18%).

The patient was continued on levothyroxine of 75 μg qd, and was treated with carvedilol at an initial dose of 6.25 mg bid, perindopril at an initial dose of 4 mg qd, spiro lactone 20 mg qd, and trimetazidine 20 mg tid. Fifteen months after, follow-up cardiac ultrasound showed a significant improvement of the left ventricle systolic ejection fraction to 55% and normalized diastolic dimension of 43 mm (Figure 1C). However, on speckle tracking strain analysis, the global peak systolic longitudinal strain was still below normal reference at -14.3%. On bull-eye presentation, the mid inferior and anterior segments, and the apical segments displayed severe attenuation of myocardial longitudinal strain (Figure 1D). The patient was weaned from the diuretic medications; however, due to residual left ventricular systolic dysfunction detected by speckle tracking echocardiography, she was continued on carvedilol 25 mg bid and perindopril 6 mg qd. Levothyroxine dosage for thyroid hormone replacement therapy was titrated based on thyroid function tests to 150 μg qd. Three years after, standard echocardiography showed a further improvement of the left ventricle systolic ejection fraction to 73%; On speckle tracking strain analysis, the global peak systolic longitudinal strain showed parallel improvement to -16.6%, which was still below normal reference. Persistent impairment in myocardial longitudinal strain in apical segments were noted (Figure 1E).

It has been established that hypothyroidism may cause multiple

cardiac manifestations including pericardial effusion, depressed chronotropy, increased peripheral vascular resistance, decreased myocardial contractility, compromised diastolic function, accelerated coronary atherosclerosis, and, rarely, dilated cardiomyopathy, which is reversible after substitutive hormonal treatment [1]. Both genomic and non-genomic actions of thyroid hormones upon cardiovascular system, including calcium flux, beta-adrenergic-receptor function, synthesis of various contractile proteins, function of multiple ion channels, mitochondrial membrane and mitochondriogenesis, and signalling pathways of cardiomyocytes and vascular smooth muscle cells, are thought to be crucial to pathogenesis of cardiovascular manifestations in hypothyroidism [2]. It is also reported that edema and the accumulation of mucopolysaccharides in the endocardium, and the ensuing diffuse myocardial fibrosis, also plays a role in dilated cardiomyopathy associated with hypothyroidism [3].

In this case, the patient had no family history of dilated cardiomyopathy. There were no histories of drug abuse, alcohol addiction, no nutritional deficiency. Clinical investigations were against viral causes. The patient responded to hormone replacement and anti-cardiac remodeling therapy, supporting the association of hypothyroidism with cardiomyopathy.

The reversibility of cardiac dysfunction associated with hypothyroidism is well documented based on studies with standard echocardiography [4]. In our case, residual focal left ventricular systolic dysfunction was detected, despite normalization of left ventricular systolic dysfunction and improvement in global peak longitudinal strain. The standard analysis of regional myocardial function can be maneuver-dependent, and can be inaccurate due to the interaction of adjacent myocardium. Two-dimensional speckle tracking echocardiography is an angle-independent, quantitative method for the evaluation of the myocardial movements. Attenuation and reversibility of left ventricular longitudinal strain has been implicated in various disease states including hypothyroidism [5-7]. Speckle tracking longitudinal myocardial strain mostly represents endomyocardial function [8]. Persistent attenuation of left ventricular longitudinal myocardial strain three years after euthyroid state suggest unresolved endomyocardial damage, which may be overlooked with standard echocardiography. What's more, whether neuroendocrine antagonists should be continued along with thyroid hormone replacement therapy in the treatment of such patients warrants further investigation.

Our observation highlighted the importance additional noninvasive investigation such as two-dimensional speckle tracking myocardial longitudinal strain imaging in hypothyroid patients with left ventricular systolic dysfunction. In such patients, strain imaging can help to guide treatment and improve the monitoring of therapeutic effects of hormone replacement and anti-remodeling cardiac therapy.

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