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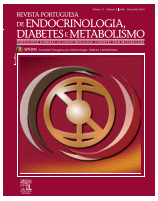

Caso Clínico

Severe Dilated Cardiomyopathy as the First Manifestation of Hypothyroidism: Case Report

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A B S T R A C T

A detailed clinical case of hypothyroidism-induced, reversible dilated cardiomyopathy is presented. A 31-year-old man was admitted with severely decompensated heart failure. At initial assessment, his condition was categorized as New York Heart Association (NYHA) functional class IV and the transthoracic echocardiography estimated 22% left ventricular ejection fraction. Blood tests revealed undetectable thyroid hormone levels as well as elevation of thyroid stimulating hormone, supporting the diagnosis of hypothyroidism. Both anti-thyroglobulin and anti-microsomial antibodies were positive. After one year treatment with L-thyroxin, clinical condition improved to a NYHA class I and transthoracic echocardiography showed left ventricular ejection fraction improvement up to 47%. The case report presents an unequivocal diagnosis of dilated cardiomyopathy secondary to hypothyroidism. Although rarely a cause of that cardiac disorder, thyroid function should systematically be accessed in all patients with a so far unclear etiology.

Miocardiopatia Dilatada Severa como Primeira Manifestação de Hipotiroidismo: Caso Clínico

Palavras-chave:
Miocardiopatia Dilatada
Hipotiroidismo
Insuficiência Cardíaca

R E S U M O

Apresenta-se um Caso Clínico de miocardiopatia dilatada (MCD) reversível, secundária a hipotiroidismo.

Doente do sexo masculino, 31 anos, admitido num Serviço de Cardiologia por MCD severa. Na avaliação inicial apresentava-se com quadro clínico de insuficiência cardíaca, classe funcional IV de New York Heart Association (NYHA), com fração de ejeção do ventrículo esquerdo (FEVE) de 22%, calculada por ecocardiograma transtorácico (ETT). A presença de níveis séricos das hormonas tiroideias indoseáveis e de hormona estimulante da tireoide elevada conduziram ao diagnóstico de hipotiroidismo primário. Os anticorpos anti-tiroglobulina e anti-microssomais revelaram-se positivos. Um ano após tratamento com levotiroxina, o doente apresenta-se em classe I de NYHA e com FEVE de 47% no ETT.

O quadro clínico descrito é inequívoco quanto ao diagnóstico de MCD, cuja descompensação clínica é secundária ao hipotiroidismo. Apesar de raramente ser uma manifestação inicial do hipotiroidismo, a função tiroideia deve ser sistematicamente avaliada em doentes com MCD.

Introduction

Dilated cardiomyopathy (DCM), the most common form of cardiomyopathy, is a heart muscle disorder defined by the presence of a dilated and poorly functioning left ventricle in the absence of abnormal loading conditions or extensive coronary artery disease (CAD). Patients with this condition generally have a poor prognosis due to a progressive and irreversible myocardial dysfunction. Nevertheless, with a detailed clinical history and a

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careful study, some rare treatable etiologies may be found such as endocrine disturbances.[1] The thyroid gland is embryological and physiological related to the heart.[2] Thyroid disorders, particularly hypothyroidism, have well established effects on the cardiovascular system,[3] although DCM seldom is the first manifestation.

We report a clinical case of reversible hypothyroidism-induced DCM. The long-term follow-up (1 year) and excellent echocardiographic documentation during follow-up represents an important contribution to clinical research of DCM's etiology.

Case Description

This case concerns a 31-year-old male with irrelevant personal or familiar past medical history, who presents to the emergency department with a progressive two week-long dyspnea, orthopnea and fatigue. He had also a progressive worsening of bilateral lower extremity edema over the last two months. At clinical examination the patient showed pale and dry skin with infiltrated edema, mainly of both lower limbs, a normal blood pressure (120/80 mmHg) and tachycardia (120 beats/min). His body mass index (BMI) was normal (BMI: 21.5 kg/m^2; height: 170 cm; weight: 62 kg), no murmur heard at cardiac auscultation, and pulmonary auscultation showed reduced breathing sounds on both lung bases. Room air arterial oxygen saturation was 95%. Chest radiography showed an increased cardiothoracic index (0.64), indicating cardiomegaly, and signs of mild perihilar congestion (Fig. 1). The initial EKG showed normal sinus rhythm with low voltage of limb leads, intraventricular conduction delay and non-specific ST-segment and T-wave changes (Fig. 2). Blood tests revealed normal platelets and white blood cell count, normocytic, normochromic anemia [hemoglobin: 10.1g/dL; reference range (RR): 13.0–17.7g/d], elevated serum levels of B-type natriuretic peptide (BNP) – 59 0 pg/mL (RR: < 100 pg/mL), slightly elevated serum creatinine kinase (260 U/L; RR: 10–171 U/L) and normal troponin I, normal renal function, mild elevated aspartate transaminase (47 U/L; RR: 15–50 U/L) and normal serum electrolytes, including sodium, potassium, magnesium and ionized calcium. Lipid profile showed total cholesterol of 259 mg/dL (RR: < 190 mg/dL), high-density lipoprotein cholesterol 44 mg/dL (RR: 40–60 mg/dL), low-density lipoprotein cholesterol 196 mg/dL (RR: < 100 mg/dL) and triglyceride 110 mg/dL (RR: < 150 mg/dL). Bedside focused transthoracic echocardiography (TTE) revealed a severe dilated left ventricular cavity with an end-diastolic diameter of 71 mm and end-systolic of 64 mm, with severe systolic dysfunction (estimated LVEF: 22%), hypocontractility and circumferential mild pericardial effusion.

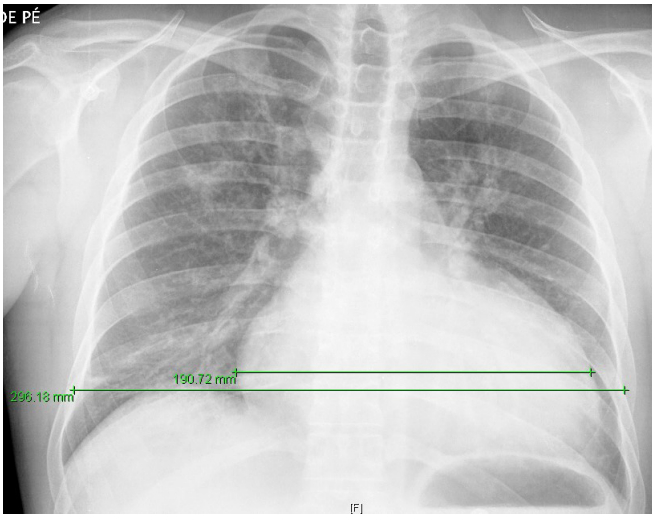


Figure 1. Initial chest X-ray. A posteroanterior chest X-ray view shows cardiomegaly, with a cardiothoracic ratio of 0.64 and mild perihilar congestion.

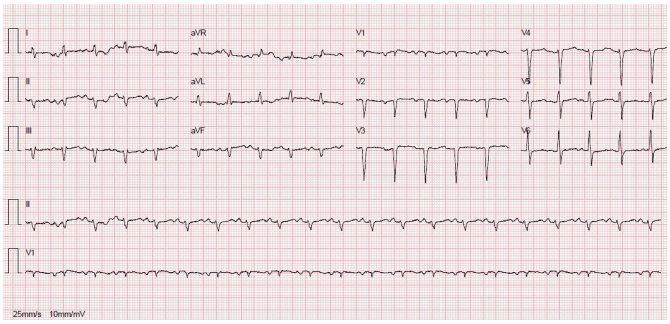


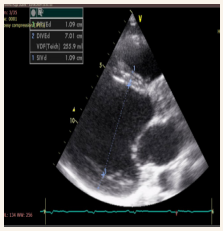
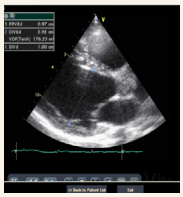
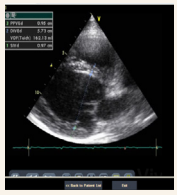
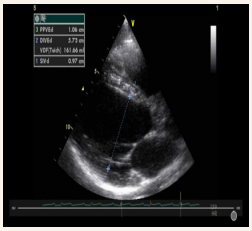
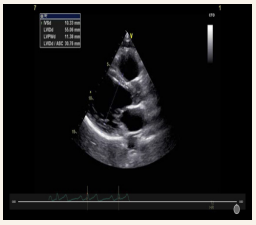
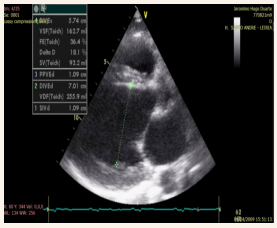
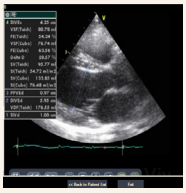
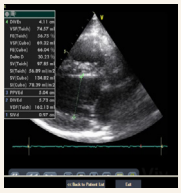
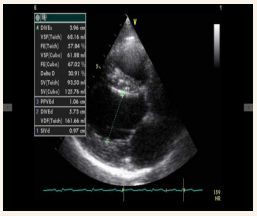
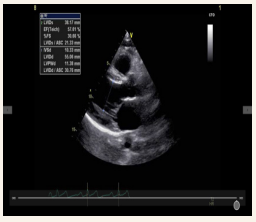
Figure 2. The 12-lead electrocardiography findings: normal sinus rhythm with low voltage of limb leads, interventricular conduction delay and nonspecific ST-segment and T-wave changes.

Patient was admitted to the cardiology department in order to be clinically compensated and also to perform additional diagnostic tests aiming to identify potentially treatable causes. Virus serologies (Epstein-Barr, cytomegalovirus, human immunodeficiency virus -HIV and hepatitis B and C virus - HBV and HCV) were negative and thus viral etiology was excluded. Given the suspicion of hemochromatosis iron metabolism was assessed: ferritin was significantly elevated (1380 ng/mL; RR: 23.9–336.2 ng/mL), with normal serum iron and transferrin saturation [12.0 µmol/L (RR: 11.6–31.3 µmol/L) and 14.6% (RR: 10.6–69.2%), respectively]; liver ultrasound imaging evidenced hepatomegaly with increased density; nevertheless genetic study was negative to hemochromatosis (heterozygous for H63D). Thyroid function test showed elevated serum levels of thyroid stimulating hormone (TSH: 86.22 µUl/mL; RR: 0.34–5.6 µIU/mL), decreased serum levels of free T3 (2.9 pmol/L; RR: 3.8–6.0 pmol/L) and undetectable serum levels of free T4 (0.0 pmol/L; RR: 7.9–14.4 pmol/L). Thyroid echography showed an atrophic gland, with hypoechogenic parenchyma and a small nodule about 12 mm in size. Both antithyroglobulin and antimicrosomal antibodies were elevated [4136 Ul/mL (RR: < 280.0 Ul/mL) and 993 Ul/mL (RR: < 60.0 Ul/mL) respectively]. These findings supported the diagnosis of hypothyroidism and were suggestive of Hashimoto's thyroiditis.

Right after admission, medical treatment according to the European Society of Cardiology (ESC) heart failure guidelines was started, including loop diuretic (furosemide), angiotensin converting enzyme (ACE) inhibitor (captopril), beta-blocker (carvedilol) and aldosterone antagonist (spironolactone). When the diagnosis of hypothyroidism was achieved, replacement hormonal treatment with L-thyroxin was initiated and titrated up to 100 µg/day. Patient was discharged on maximum tolerated drug doses, with furosemide 40 mg od, carvedilol 6.25 mg bid, ramipril 2.5 mg od, spironolactone 25 mg od, ivabradine 5 mg bid, atorvastatin 40 mg od and L-thyroxin 100 µg od therapy.

Over the following year, thyroid function progressively improved to euthyroidism, along with an improvement on left ventricular function up to an estimated ejection fraction of 47%, on TTE. One year follow-up TTE findings and thyroid function analyses are shown in Table 1. Furthermore, clinical laboratory findings such as anemia, elevated transaminases and creatinine

Table 1. Transthoracic echocardiographic findings with thyroid function levels.

		Follow-up period (months)				
	Index	**1st**	**5th**	**7th**	**9th**	**12th**
Hemoglobin (g/dL)	10.1	10.9	12.5	13.3	NA	13.6
FT3 (pmol/L)	2.2	4.1	NA	NA	NA	4.6
FT4 (pmol/L)	Un	7.7	10.6	10.6	NA	12.2
TSH (µUl/mL)	86.22	41.44	9.82	5.91	NA	1.98
LVDd (mm)	71.0	70.1 	59.5 	57.3 	57.3 	55.06 
LVDs (mm)	64.0	57.4 	42.5 	41.1 	39.6 	38.2 
LVSF (%)	9.0%	18.1%	28.5%	30.2%	30.9%	30.6%
LVEF (%)	22.0%	35.0%	NA	NA	NA	47.0%

FT4 - free thyroxine T4; FT3 - free thyroxine T3; TSH - thyroid stimulating hormone; LVDd - diastolic left ventricle dimension; LVDs - systolic left ventricle dimension; LVSF - left ventricle shortening fraction; LVEF - left ventricle ejection fraction; NA - non-available; Un - undetectable

kinase and lipid profile normalized. One year later, patient was in heart failure NYHA class I. Regarding pharmacological treatment furosemide, spironolactone and ivabradine were withdrawn but the patient continued on ramipril, carvedilol and thyroid hormone replacement therapy.

A well-documented follow-up with regular monitoring of pharmacological compliance, periodic TTE and thyroid function blood tests are fundamental for a correct treatment. Month by month, patient recovery to euthyroidism aside with a gradual improvement on LV function. Symptomatic improvement to HF NYHA class I, as well as analytical and echocardiographic improvement over the first month, were the main reasons for a watchful waiting approach. After one-year follow-up with pharmacological therapy with a notable clinical improvement, a reversible DCM was assumed.

Discussion

The current report describes a patient with a typical congestive heart failure (HF) of recent onset. The evidence of a severe dilated left ventricular cavity with LVEF of 22% on TTE was consistent with the diagnosis of DCM. Other diagnosis tools such as cardiac magnetic resonance (CMR) have higher accuracy in the diagnosis of patients with DCM, showing and quantifying functional abnormalities in DCM, assessing ventricular volumes and LVEF and providing morphologic information (detecting myocardial scar, useful to characterize myocardial tissue).[4] Other than that, CMR has excellent reproducibility so it can be used for serial monitoring of cardiac function. However, widely available TTE remains the cornerstone in the algorithm for the diagnosis of patients with HF with reduced ejection fraction.[5] In the current case lack of CMR could be pointed out as a limitation, as TTE was the main tool for the diagnosis and follow-up evaluation of DCM.

In this young patient the absence of major cardiovascular risk factors led to a low probability of ischemic heart disease. Valve disease or congenital heart defects were both easily excluded by the cardiac ultrasound evaluation. Other causes potentially related with transient DCM were excluded or considered unlikely supported on personal and family history, physical examination and blood tests. Thyroid hormone replacement restored thyroid function and normalized lipid profile after one year treatment.

The thyroid's function tests results, thyroid gland ultrasound imaging features and the detection of positive auto-antibodies were consistent with the diagnosis of primary hypothyroidism, and Hashimoto's thyroiditis. In addition, thyroid hormone replacement restored thyroid function and normalized lipid profile after one year treatment. Hashimoto's thyroiditis is an autoimmune process. Through a destructive mechanism, thyroid antibodies lead to gradual depletion of stored thyroid hormones and hypothyroidism.[6]

Thyroid gland functional disorders are relatively common in HF patients and thyroid function is highly recommended in order to detect reversible/treatable causes of HF, monitor treatment and establish a prognosis.[5] Through genomic and non-genomic mechanisms, biologically active thyroid hormones increase inotropism and chronotropism, decreases systemic vascular resistance and increases cardiac output.[2,3] The microcirculation

of the myocardium also seems to be affected.[7] Hyper and hypothyroidism can both produce changes in the heart and cardiovascular system.[2,3] In hypothyroidism, cardiac output may be reduced from 30% to 50%.[8] Nevertheless, congestive HF is rare due to a reduction in metabolic demands for peripheral oxygen delivery.[3] However, some cases of DCM have been described with regression of HF manifestations and reversal of dilated pattern after replacement hormonal treatment and correction of thyroid function. In fact, ESC guidelines mention hypothyroidism as a precipitant cause of acute HF.[5] In this case the treatment of thyroid abnormality with L-thyroxin was determinant for HF management and improvement in cardiac systolic function.[9]

Although ESC guidelines do not mention therapy indications after patient recovery/improvement, furosemide, spironolactone and ivabradine were all discontinued after one-year follow-up. At that time, patient was in NYHA class I, LVEF was 47.0% on TTE and thyroid function normalized. ACE inhibitors and beta-blockers were maintained, as the patient still showed evidence of slight impairment of ventricular systolic function.

In conclusion, DCM is frequently of unknown etiology and marked by progressive LV dysfunction and irreversible poor outcome. Hypothyroidism may be a cause of DCM decompensation, and hence hormonal replacement treatment with L-thyroxin improves the prognosis. This case highlight the importance of thyroid function tests in the first assessment of DCM.

Ethical Disclosures

Conflicts of Interest: The authors report no conflict of interest.

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Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

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