CASE REPORT

Hypothyroid heart: myxoedema as a cause of reversible dilated cardiomyopathy

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SUMMARY

Hypothyroidism may cause several cardiac manifestations including conduction abnormalities, pericardial effusion, decreased myocardial contractility and accelerated coronary atherosclerosis. Although cardiac output is reduced in hypothyroidism, frank heart failure (HF) is relatively rare because of the low peripheral oxygen demand. Several mechanisms have been postulated in hypothyroid-induced HF, including genomic as well as non-genomic actions of thyroid hormone. Dilated cardiomyopathy (DCM) of other aetiologies is usually progressive, and is associated with significant morbidity and mortality. We report a case of DCM associated with severe hypothyroidism with marked improvement on restoration of euthyroid state. Our case is unique in that the patient had no known risk factors for cardiac disease and experienced marked improvement despite being on minimal doses of HF medications, illustrating the relationship between hypothyroidism and development of left ventricular dysfunction, and its reversible nature with restoration of euthyroid status.

BACKGROUND

Dilated cardiomyopathy (DCM) is the most common form of cardiomyopathy; it is usually a progressive disease and associated with a poor prognosis.¹ It may be idiopathic, familial or secondary to several acquired conditions, including pregnancy, alcoholism, chronic anaemia, adriamycin and other chemotherapeutic agent toxicity, ischaemic heart disease, myocarditis and infectious causes.¹ It is uncommon to identify a metabolic aetiology responsive to specific therapy, rendering the cardiomyopathy potentially reversible. Although many studies have suggested that thyroid hormone deficiency is associated with a reversible decrease in cardiac contractility, it remains controversial when it is hypothyroidism alone, with no pre-existing heart disease, and can cause a DCM and profound clinical heart failure (HF).

We describe a case of a woman with undiagnosed longstanding hypothyroidism, presenting with HF due to DCM that improved substantially on correcting the hypothyroidism.

CASE PRESENTATION

A 49-year-old woman presented to our hospital, with progressive weakness and dyspnoea rated as New York Heart Association (NYHA) functional class IV. She reported a 1-year history of weight gain, hair loss, coarse dry skin, constipation, cold intolerance and leg swelling. Vital signs showed a temperature of 31.1°C, blood pressure 134/

83 mm Hg, heart rate 88 bpm, respiratory rate 18 breaths/min and oxygen saturation 90% on room air. She had cool, dry skin, significant pretibial, periorbital and bilateral lower extremity non-pitting oedema, and left ankle lichenification. The thyroid was not palpable. Cardiovascular examination showed muffled heart sounds, an S3 and a grade 2/6 systolic ejection murmur at the apex radiating to the left axilla. Lung examination revealed rales bilaterally. Chest X-ray findings were consistent with pulmonary oedema and small bilateral pleural effusions (figure 1). Transthoracic echocardiography (figure 2A) showed a markedly dilated left ventricle (LV) with a diastolic dimension of 5.7 cm, a severely depressed LV systolic ejection fraction (LVEF) of 15–20%, severe diffuse hypokinesia, a moderate to severe degree of mitral regurgitation and a small pericardial effusion.

The white cell count was 4.1/nL (3.5–11/nL), haemoglobin 10.4 g/L, mean corpuscular volume 103.7 fL (80–100 fL) and platelet count 215/nL (150–440/nL). Thyroid function tests (normal range) revealed thyroid-stimulating hormone 52 mIU/L (0.47–6.90), free T4 0.18 ng/dL (0.75–2) and T3 0 ng/dL (60–181). The antithyroid peroxidase antibody titre was 287 IU/mL (<40). Other serum levels were sodium 140 (135–145) mEq/L, potassium 4.1 (3.5–5.0) mEq/L, chloride 104 (98–108) mEq/L, bicarbonate 27.9 (24–30) mEq/L, blood urea nitrogen 14 (5–26) mg/dL, creatinine 0.8 (0.1–1.5) mg/dL, total protein 8.1 (6.0–8.5) g/dL, albumin 4.1 (3.5–5.5) g/dL, alkaline phosphatase 152 (30–115) U/L, aspartate aminotransferase 71 (5–40) U/L, alanine aminotransferase 30 (1–40) U/L, creatine kinase 260 (5–150) U/L, troponin I 0.017 (<0.15) µg/L, cortisol 22 (5–25) µg/dL, total

Figure 1 Initial chest X-ray.

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Figure 2 Colour Doppler of mitral regurgitation: (A) initial and (B) follow-up after 7 months.

cholesterol 231 (120–200) mg/dL, high-density lipoprotein cholesterol 39.6 (34–87) mg/dL and triglycerides 68 (35–135) mg/dL.

The patient initially received intravenous furosemide. However, within a few hours of admission, she developed cardiogenic shock requiring inotropic support and tracheal intubation for acute hypoxic respiratory failure. As soon as the laboratory results indicating the severe hypothyroid status became available, treatment was begun with intravenous levothyroxine and liothyronine.

Thyroid ultrasonography (on day 3) showed multiple hypoechoic micronodules throughout the thyroid gland, measuring up to 0.2 cm, consistent with lymphocytic micronodules of Hashimoto's thyroiditis, with diminished thyroid parenchymal vascular flow on colour Doppler imaging.

The patient was successfully weaned off inotropes, extubated and discharged 4 weeks after admission, in stable condition. Ischaemic causes of DCM and HF were ruled out by normal findings on CT angiography with a calcium score of zero.

OUTCOME AND FOLLOW-UP

The patient has been maintained on levothyroxine and has had close endocrine and cardiology outpatient follow-up. Dosing of

Table 1 Thyroid function tests

	Day 0	Day 30	4 Months later	13 Months later
TSH	52.1	30.6	1.4	0.7
Free T4	0.18	1.14	1.21	1.28
T3	0		121	119

TSH, thyroid-stimulating hormone.

ACE inhibitor (ACE-I) and β -blocker was suboptimal due to relative hypotension observed on attempted dose escalation. The patient attained euthyroid status within 4 months of levothyroxine therapy (table 1), with complete resolution of her cardiac and hypothyroid symptoms. Echocardiography 7 months after hospitalisation showed significant improvement in LVEF and of mitral regurgitation (figure 2B and table 2).

DISCUSSION

Thyroid hormone is an important regulator of cardiac function and cardiovascular haemodynamics.² It has long been recognised that hypothyroidism has profound effects on the cardiovascular system. These effects include bradycardia, conduction abnormalities, pericardial effusion,³ reduced chronotropy and inotropy with an increase in systemic vascular resistance, resulting in increase in afterload. All these consequently reduce stroke volume and cardiac output.^{2 4 5} In addition, hypothyroidism reduces tissue oxygen consumption secondary to decreased oxidative metabolism.⁶ Thus, despite reduction in cardiac output, frank HF is relatively rare, as the lowered cardiac output is often sufficient to meet the decreased peripheral oxygen demand.⁷ Thyroid hormone deficiency has also been linked to accelerated atherosclerosis and coronary artery disease.^{2 8 9}

The exact mechanism of hypothyroid-induced cardiovascular manifestations is unclear. Several mechanisms have been proposed, including genomic and non-genomic effects. Thyroid hormones exert their genomic effects by regulating the transcription of a number of cardiac genes, including myosin heavy chain α , sarcoplasmic reticulum calcium ATPase (SERCA), Na-K-ATPase, β -adrenergic receptor and atrial natriuretic peptide.^{2 4} In particular, the reduced expression of sarcoplasmic reticulum calcium ATPase and myosin heavy chain and increased expression of phosphobalman caused by hypothyroidism have, in animal studies, been associated with consequent impairment in contractility as well as in lusitropic properties of the myocardium.^{10 11}

Non-genomic or extranuclear actions of thyroid hormone target cardiac myocytes and peripheral vasculature, and regulate several physiological structural and regulatory functions, with impact on mitochondria, the actin cytoskeleton and cell morphology. In addition, these actions control vascular smooth muscle

Table 2 Transthoracic echocardiography

	Day 0	7 Months later
LVIDd (cm)	5.7	5.14
LVIDs (cm)	5.41	3.59
LVEF (%) by method of disks	18	46
LVEF (%) by Teichholz method	15	56
MIR	Moderate to severe	Mild

LVEF, left ventricular systolic ejection fraction; LVIDs, left ventricular internal diameter end systole; LVIDd, left ventricular internal diameter end diastole.

cell function, and Ca and Na ion homoeostasis, thereby regulating myocardial contractile function and diastolic relaxation.¹² Moreover, several lines of evidence have suggested an association of hypothyroidism with increased oxidative stress¹³ secondary to reduced glutathione levels in the myocardial tissue, leading to direct myocardial damage.¹⁴ These effects are primarily mediated by alteration in serum T3 levels, as cardiac myocytes are known to be unresponsive to changes in serum T4 levels.¹¹

Additionally, studies have demonstrated that about 30% of patients with congestive HF have low serum T3 levels.^{11 15 16} This low T3 state has been found to be an independent risk factor for progression of disease^{16 17} and increased mortality in these patients.¹⁵ There remains uncertainty as to whether hypothyroidism alone can cause HF or if it is merely an association. Some animal models have shown that hypothyroidism alone can cause progressive systolic dysfunction severe enough to lead to HF.¹⁸ It is possible that cardiomyopathy of purely thyroid origin remains an underdiagnosed entity because its recognition requires a high index of suspicion in the absence of clinical or radiological features to reliably distinguish it from other dilated cardiomyopathies, except for clinical signs of myxoedema.

In our case, the patient, with no known coronary risk factors, no history of cardiac disease, no family history of cardiac disease and no evidence of alcohol or toxic substance abuse, developed a DCM of apparently purely myxoedematous origin. There is evidence in support of improvement in ventricular function on normalisation of T3-responsive gene expression with thyroid hormone replacement therapy.^{19–21} Although the exact mechanism responsible for this improvement remains elusive, it emphasises the potentially life-saving therapeutic role of thyroid hormone replacement in such cases. In our patient, repletion of thyroid hormone deficiency led to complete resolution of clinical signs and symptoms of HF despite the use of minimal doses of HF medications. This was objectively supported by regression of ventricular dilation and significant improvement in LVEF on follow-up transthoracic echocardiography.

On review of the literature, we found that, in most of the few previously reported cases, underlying ischaemic heart disease still remained a plausible confounding factor. Although several cases have demonstrated cardiac function recovery with thyroid

replacement therapy, our case stands unique among the very few where coronary artery disease was conclusively ruled out with objective evidence.

Thus, this case demonstrates that severe hypothyroidism alone may lead to a potentially reversible DCM, emphasising the importance of recognising hypothyroidism in patients with non-ischaemic systolic dysfunction. Given the progressive nature of DCM of other aetiologies, we strongly suggest thyroid function testing in all patients with HF and non-ischaemic DCM, to rule out hypothyroidism as an underlying reversible cause.

Competing interests None declared.

Patient consent Obtained.

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Learning points

- A hypothyroid state alone can cause dilated cardiomyopathy and heart failure.
- Dilated cardiomyopathy induced by a hypothyroid state is potentially reversible with correction of hypothyroidism and achievement of euthyroid status.
- It is important to recognise hypothyroidism in patients with non-ischaemic systolic dysfunction by performing thyroid function testing in these patients to rule out hypothyroidism as an underlying cause given its potentially reversible nature.

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