Myxoedematous pre-coma and heart failure

Introduction

Hypothyroidism causes marked alterations in cardiovascular function. Impaired myocardial contractility, bradycardia, reduced cardiac output and increased systemic vascular resistance are all contributory (Klein and Danzi, 2007).

Patients may present with physical signs and symptoms similar to primary heart failure and the clinician should be alert to this possible differential.

Discussion

In hypothyroidism, cardiac output may fall by up to 50%. Systemic vascular resistance is increased as hypothyroidism impairs relaxation of vascular smooth muscle which may cause diastolic hypertension. Blood volume is decreased, and heart rate and cardiac contractility fall. Patients may also be anaemic as erythropoietin secretion is inhibited. Electrocardiographic features include prolongation of the QT interval and consequent risk of ventricular arrhythmia (Fredlund and Olsson, 1983).

The heart is primarily affected by serum tri-iodothyronine levels, as little conversion of the less active thyroxine occurs in cardiac myocytes. Tri-iodothyronine combines with receptor proteins in the nucleus which then bind to the promoter region of various genes to modulate transcription. Genes affected include those for the myosin heavy chain, calcium-ATPase and sodium/potassium-ATPase in the sarcoplasmic reticulum and the β-adrenoreceptor. Tri-iodothyronine can also act directly on extranuclear parts of the myocyte to alter ion channel function and intracellular signalling.

Hypercholesterolaemia with a high level of low density lipoprotein occurs in around 90% of patients (Duntas, 2002). The mechanism is thought to involve down-regulation of low density lipoprotein receptors in the liver. There is a correspondingly raised incidence of ischaemic heart disease and stroke if left untreated.

Specific management of severe hypothyroidism

Treatment of hypothyroidism with levothyroxine results in reversal of all aspects of this pathology. As many patients are rela-

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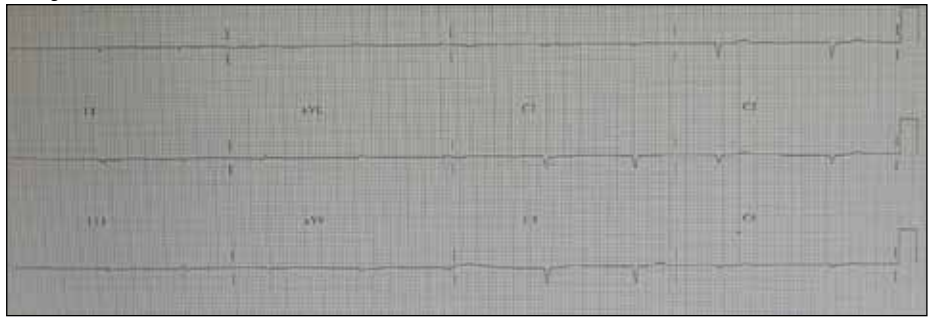
Figure 1. Electrocardiogram on presentation, showing bradycardia (55 beats/min), extreme low limb lead voltage (mean of 0.1 mV) and Q waves in chest leads C1–C6.



Case Report

A 62-year-old man with a background of atrial fibrillation, aorto-femoral bypass surgery, type 2 diabetes and hypothyroidism presented with increasing shortness of breath, orthopnoea and oedema over several months. On examination, his face appeared 'puffy' with a violaceous hue. He was grossly oedematous to the mid chest and peripherally cyanosed. His body temperature was 35.3°C, the heart rate was 50/min and blood pressure was 138/43 mmHg. Neck and facial veins were distended with frank ascites. He was conscious but only replied to questions, after considerable delay, with single words in a hoarse voice.

The electrocardiogram showed atrial fibrillation with bradycardia, low voltage complexes and widespread Q waves (*Figure 1*). A chest radiograph showed pulmonary oedema. Echocardiography demonstrated moderate to severe global left ventricular dysfunction (left ventricular ejection fraction of 30%) and significant tricuspid regurgitation. He was diagnosed with likely congestive cardiac failure and treated with diuretics.

Initial investigations (normal range) revealed a troponin I of 0.20 ng/ml (<0.04 ng/ml), markedly elevated thyroid stimulating hormone >60 mu/litre (0.5–4.5 mu/litre) and low free thyroxine of 5.6 pmol/litre (9–24 pmol/litre). The alkaline phosphatase level was 399 mmol/litre (35–125 mmol/litre), creatinine kinase 188 u/litre (32–234 u/litre) and C-reactive protein 59 mg/litre (0–8 mg/litre). The full blood count and renal function were normal, although the sodium level was slightly low at 134 mmol/litre (135–145 mmol/litre). The diagnosis was modified to severe myxoedematous hypothyroidism.

The patient was treated with both liothyronine (T3) at 20 mg twice daily for the first 10 days and thyroxine at 100 μg daily (increasing to 150 μg daily thereafter) as well as intravenous diuretics. He made a gradual recovery, losing more than 12 kg in weight over the first 4 days and a total of 29 kg over 6 weeks. Clinically he became more alert and talkative. His temperature reached 37°C consistently only after 23 days of therapy. Further questioning revealed that he had stopped taking his prescribed thyroxine (dosage of 100 μg/day) several months previously. Recovery was complicated by an elevated alkaline phosphatase (liver isoenzyme) at 970 mmol/litre (35–125 mmol/litre) and a gamma glutamyl transferase of 185 mmol/litre (25–45 mmol/litre). Liver ultrasound and serum 'liver screen' (hepatitis, iron, ferritin, caeruloplasmin and alpha 1 antitrypsin) were normal.

A repeat echocardiogram showed improved left ventricular function with an ejection fraction of 41–50%. The electrocardiogram has shown some improvement, with limb lead voltage amplitude now 0.18 mV.

The patient remains in rehabilitation some 4 months following the initial admission.

tively elderly a low dose regimen is often started with dosage increments guided by thyroid-stimulating hormone and free thyroxine levels. A concern has always existed that high dose thyroxine might exacerbate any underlying ischaemic heart disease. Evidence suggests that the prognosis improves rather than deteriorates with such treatment (Keating et al, 1961). However, controversy still exists over the use of tri-iodothyronine (liothyronine) replacement in addition to thyroxine. Authors have suggested that the more biologically active tri-iodothyronine may give rise to more complete and rapid resolution of symptoms (Bunevicius et al, 1999). The American Association of Clinical Endocrinology guidelines state that insufficient evidence exists of any benefit from tri-iodothyronine and the short half-life may in fact cause unacceptable fluctuations in metabolic status (AACE Thyroid Task Force, 2006). Its use may be justified in myxoedema verging on coma.

The authors ascribe the abnormalities of liver function to non-alcoholic steatohepatitis, a feature reported as being a complication of hypothyroidism (Loria et al, 2009). This gradually resolved over the next 2 months.

A further consideration in the management of this condition is hypothyroid-induced adrenal insufficiency (Shulman et al, 2007), which when treated with thyroxine may precipitate an addisonian crisis (Shaikh et al, 2004). Some endocrinologists would advocate steroid 'cover' in the initial resuscitation of patients with such severe hypothyroidism.

Conclusions

The diagnosis of hypothyroidism should be considered in all patients presenting with apparent heart failure as some restoration of cardiac function is usually achievable. **BJHM**

AACE Thyroid Task Force (2006) American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hyperthyroidism and Hypothyroidism. www.aace.com/pub/pdf/guidelines/hypo_hyper.pdf (accessed 1 February 2010)

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