

## CASE STUDIES

# Low T<sub>3</sub> Syndrome in a Patient with Acute Myocarditis

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## INTRODUCTION

Thyroid hormones have multiple cardiovascular effects.<sup>1</sup> A variety of cardiac disease states, including heart failure, are associated with changes in thyroid hormone metabolism leading to declines in triiodothyronine (T<sub>3</sub>). Low T<sub>3</sub> levels are associated with poor prognosis and are strongly linked to mortality in hospitalized cardiac patients.<sup>2,3</sup> The worse prognosis of patients with low T<sub>3</sub> syndrome, in terms of cardiovascular morbidity and mortality, has spurred the completion of studies in patients undergoing heart surgery; these studies indicate that postsurgical outcomes can be improved by raising T<sub>3</sub> levels.<sup>4-7</sup> These promising data have led to the view that the normalization of low serum T<sub>3</sub> levels may be clinically and physiologically beneficial in the setting of chronic cardiac disease and with some acute conditions.

A low T<sub>3</sub> state may be particularly disadvantageous to patients with acute myocarditis. In this case, treatment with IV liothyronine in a patient with acute myocarditis and a low T<sub>3</sub> state resulted in marked improvement in clinical status and a favorable outcome several months later.

## CASE DESCRIPTION

### Presentation and History of Present Illness

A 40-year-old white male with a medical history of hypothyroidism and hypertension presented after a flu-like illness and severe chest pain for 3 days. He was currently taking levothyroxine 200 µg/d and hydrochlorothiazide 12.5 mg/d. The patient was found to have a temperature of 100.2°F, creatine kinase (CK) of 1579 U/L (normal range, 60–400 U/L), CK-MB of 180 ng/mL (normal, 0–7.0 ng/mL), CK-MB of 11.4% (normal, 0%–6%), and troponin I of 224 ng/mL (normal, 0.0–0.4 ng/mL) and was admitted to the hospital.

## Physical Examination and Laboratory Studies

On admission, an echocardiogram demonstrated inferior wall hypokinesis, suggesting a diagnosis of acute myocardial infarction. However, cardiac catheterization revealed normal coronary artery anatomy, as well as severe diffuse left ventricular dysfunction with a left ventricular ejection fraction (LVEF) of 20%. On day 2, the patient developed hypotension (~70/30 mm Hg), and was started on IV norepinephrine 10 µg/min plus dobutamine, as well as an intra-aortic balloon pump (IABP). On day 3, he became acidotic (pH, 7.19; pCO<sub>2</sub>, 60 mm Hg; pO<sub>2</sub>, 48 mm Hg; HCO<sub>3</sub><sup>-</sup>, 20 mEq/L) and developed respiratory distress requiring intubation. IV vasopressin at 4 U/h was started. The patient also developed nonoliguric acute renal failure, requiring initiation of continuous venous–venous hemodialysis, starting on day 3. Thyroid function tests were obtained on day 3 and revealed a thyroid-stimulating hormone (TSH) level of 0.09 µIU/L (normal range, 0.5–4.7 µIU/L), T<sub>3</sub> of 28 ng/dL (normal, 60–181 ng/dL), free thyroxine (T<sub>4</sub>) of 0.6 ng/dL (normal, 0.8–1.8 ng/dL), and total T<sub>4</sub> of 2.8 µg/dL (normal, 4.5–12.5 µg/dL).

## Diagnosis and Treatment Strategy

In view of the patient's extremely low T<sub>3</sub> level and the potential for thyroid hormone to improve cardiac function in this case of *acute myocarditis*, treatment with IV liothyronine sodium (T<sub>3</sub>) at a rate of 2 µg/h was initiated at the end of day 5.

## Treatment Outcome

Serum T<sub>3</sub> rose rapidly to about 100 ng/dL and remained within the normal range for the following 96 hours. Within 12 hours of administration of T<sub>3</sub>, the patient's cardiac output, cardiac index, central venous pressure, and pulmonary

artery catheter wedge pressure started rising and improved substantially, reaching normal values within 24 hours. Within 1 day after the initiation of  $T_3$  (day 6 of admission), the patient was weaned from the IABP, followed by a tapering off of vasopressin on day 8 and extubation on day 9. On day 10, the infusion rate of  $T_3$  was decreased to 1  $\mu\text{g}/\text{h}$ .  $T_3$  administration was discontinued on day 12, and the patient resumed treatment with oral levothyroxine 175  $\mu\text{g}/\text{d}$ . There were no episodes of arrhythmia observed during IV  $T_3$  administration. On day 13, the patient was weaned from inotropic/pressor support, and on day 20, he was discharged from the hospital.

At a follow-up visit 2 weeks after discharge, the patient had a TSH level of 0.39  $\mu\text{IU}/\text{L}$  and total  $T_4$  of 7.7  $\mu\text{g}/\text{dL}$ . Further follow-up at 3 months revealed TSH had increased to 0.80  $\mu\text{IU}/\text{L}$ , right ventricular ejection fraction was 48%, and LVEF was 51% with no regional decrease in contractility.

## DISCUSSION

The production of  $T_3$ , the biologically active thyroid hormone molecule, occurs mostly in the liver and kidneys by the enzymatic removal of 5'-iodine from the  $T_4$  molecule. Conversion of  $T_4$  to  $T_3$  does not occur to any measurable degree in cardiac myocytes, and the physiologic effect of thyroid hormone on the cardiovascular system depends on the peripheral availability of  $T_3$ . The cardiovascular and hemodynamic effects of normal thyroid hormone levels include a lower systemic vascular resistance and decreased isovolumic relaxation time, as well as increased blood volume, heart rate, ejection fraction, and cardiac output. Accordingly, the hypothyroid state is associated with decreased stroke volume, cardiac output, and cardiac contractility, and an increase in systemic vascular resistance.<sup>1</sup>

Among physicians, there is disagreement about the proper management of low  $T_3$  levels in patients with non-thyroid illnesses, including chronic cardiac disease. There is a theoretic risk of creating tachyarrhythmias, hypermetabolic myocardial state, and consequent ischemia with thyroid replacement therapy. Such concerns, however, have not been substantiated, and even high-risk patients have tolerated thyroid supplementation without adverse events.<sup>8</sup> In contrast, cardiac risk is increased in untreated patients with low  $T_3$ . Examination of thyroid function in

patients with heart disease showed that the prevalence of low  $T_3$  syndrome increased with the severity of cardiac disease and heart failure, and that cumulative and cardiac deaths were significantly higher in the low  $T_3$  group.<sup>2</sup> These results suggest that low  $T_3$  levels are a strong prognostic marker of poor outcome in cardiac patients and strengthen the hypothesis that  $T_3$  treatment may have some beneficial effects.<sup>2,8</sup> In particular, it has been postulated that oral  $T_3$  may benefit some patients, owing to the risk for long-term deleterious effects of inotropic agents. Several studies have shown that  $T_3$  treatment had a beneficial effect on morbidity and mortality in patients with cardiomyopathy or depressed LVEF, and in those undergoing cardiac surgery, and was not associated with serious adverse effects.<sup>4-8</sup> In the present case, an adult male with acute myocarditis and low  $T_3$  syndrome had greatly improved clinical status after the treatment with IV  $T_3$ . Although this hypothyroid patient responded positively to thyroid hormone therapy, a randomized prospective study is necessary to ascertain whether  $T_3$  treatment for acute myocarditis will improve mortality and morbidity of such patients overall.

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