ABSTRACT. Hypothyroidism is a common disorder which can have protean systemic manifestations including cardiac disease. Impairment in cardiac structure, function, and conduction can be seen in this disorder. Sinus bradycardia is the most commonly seen arrhythmia, but rare cases of serious ventricular arrhythmias such as ventricular tachycardia and torsades de pointes (TDP) have been reported in the literature. These arrhythmias can be fatal. However, if promptly identified and treated, complete recovery is possible with excellent long-term prognosis. We describe a patient with untreated hypothyroidism presenting with sudden cardiac death and prolonged QT not attributable to any other identifiable cause who responded to thyroid replacement therapy. Genetic analysis failed to detect common mutations for hereditary long QT syndromes.

KEYWORDS. sudden cardiac death, long QT, female, levothyroxine, steroids.

Case presentation

A 25-year-old African American female was brought to the emergency department (ED) in January 2011, after her mother found her unresponsive in bed. The mother noted she was pulseless, whereupon she promptly began cardiopulmonary resuscitation (CPR) and called 911. Paramedics found the patient in ventricular fibrillation (VF) and defibrillated her twice. En route to the ED, a third shock was administered with return of spontaneous circulation (ROSC). Her heart rate ranged from 40-50 beats/minute and she remained without measurable automatic blood pressure (BP) on initial arrival to the ED. Atropine was administered with resultant supraventricular tachycardia (SVT) at a rate of 185 beats/minute. This was followed by return of VF. She was defibrillated again, CPR was continued and epinephrine was given. ROSC was attained.

In the coronary care unit (CCU), an electrocardiogram showed sinus bradycardia with QTc of 624 ms, T-wave inversion, and low lead voltage (Figure 1). Further history was obtained, and it became apparent that the patient had undergone transnasal transsphenoidal endoscopic hypophysectomy for a pituitary tumor, measuring 2.5 cm. The biopsy had shown lymphocytic hypophysitis. She had been started on steroid therapy post surgery but had failed to continue treatment on an outpatient basis and was admitted to the hospital with adrenal insufficiency in July 2010. She was found to have central hypothyroidism in addition to central adrenal insufficiency and was started on levothyroxine. The mother revealed that she had stopped taking all her medications around a week prior to her current presentation for economic reasons. She had no other known medical problems and no psychiatric history or diagnosis. She was not on any medications except levothyroxine and hydrocortisone. There was no family history of sudden cardiac death (SCD) or cardiac dysrhythmias.

Initial laboratory work showed normal potassium of 4.0 mg/dl and magnesium of 1.4 mg/dl. The urine toxicology screen was positive for benzodiazepines (which were administered in the ED). Urine toxicology was negative for tricyclic antidepressants, cocaine, methadone, barbiturates, phenycyclidine, opioids, and barbiturates. An echocardiogram showed the left ventricle to be normal in structure and function. A computed tomography scan of the thorax showed no pulmonary embolism. Cardiac magnetic resonance imaging was normal, with no


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INNOVATIVE TECHNIQUES

FELLOWS CASE OF THE MONTH

Sudden Cardiac Death Due to Untreated Hypothyroidism

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evidence of myocardial scar or arrhythmogenic right ventricular dysplasia.

Thyroid function testing revealed decreased free levothyroxine (T4) at 0.22 ng/dl (normal range 0.9–1.7 ng/dl), decreased free tri-iodothyronine (T3) at 1.38 pg/ml (normal range 2.00–4.40 pg/ml), and normal thyroid stimulating hormone (TSH) at 1.89 μU/ml (normal range 0.27–4.2 μU/ml).

She was placed on the hypothermia protocol in view of SCD. Aggressive intravenous magnesium supplementation was started. Endocrine consultation was obtained and she was promptly begun on intravenous levothyroxine and stress dose steroids. With appropriate treatment, her heart rate improved, QTc normalized to 418 ms, and the lead voltage improved (Figure 2). There was no recurrence of any ventricular arrhythmias during her CCU stay. She was also treated for aspiration pneumonia. She improved progressively and was weaned off the ventilator and attained a full neurological recovery without any deficits except for mild residual memory impairment.

She was discharged home with a life vest and a follow-up appointment with the electrophysiologist. A genetic analysis done to screen for hereditary long QT syndromes was negative for SCN5A, KCNH2, KCNQ1, KCNE1, KCNE2, and KCNJ2 mutations. She was followed carefully to ensure treatment compliance and no further arrhythmias were documented. She was taken off the life vest and continues to do well.

**Discussion**

Hypothyroidism can cause structural, functional, and conduction abnormalities in the heart. Bradycardia, low voltage, and heart block are the more commonly described effects, and sustained life-threatening ventricular arrhythmias are rarely seen. Our review of the literature did not reveal any previously reported cases of successfully resuscitated out-of-hospital SCD due to hypothyroidism-induced prolonged QT, although torsades de pointes (TDP) has been described previously. None of these cases reported genetic analysis to rule out hereditary long QT syndromes. Interestingly, all the reported cases of TDP in hypothyroidism have been in women, mostly between the ages of 30 and 50 years.

Cardiac effects of hypothyroidism are related to the severity and duration of the disease. Functional effects include decreased inotropy and chronotropy. Decrease in stroke volume, heart rate, and ejection fraction (EF), and increase in peripheral vascular resistance and circulation time are seen. Structural effects can include dilated cardiomyopathy, septal and ventricular hypertrophy, and pericardial effusions.

Physiologic chronotropic response and normal tension of the heart muscle in diastole depend on the proper expression of T3 in the heart cells and its stimulating influence on the Na⁺–K⁺ ATPase and Ca²⁺ ATPase in the endoplasmic reticulum. Normal heart contractility is also related to proper T3 stimulated transcription of the myosin heavy-chain alpha gene and inhibition of the myosin heavy-chain beta gene. Proper T3 expression in the cardiac muscle affects the number of beta adrenergic receptors and their sensitivity to catecholamines. Hypothyroidism causes decreased expression of T3 in the cardiac myocytes, resulting in decreased contractility, slower heart rate, and decreased conduction. Overall, hypothyroidism is believed to induce a sympathovagal imbalance, characterized by decreased cardiovascular sympathetic and...
vagal modulation. However, the sympathetic influence is believed to predominate. High plasma norepinephrine levels have been seen in hypothyroidism, but the responsiveness to endogenous catecholamines is decreased, because of a decrease in the number of beta adrenergic receptors and their desensitization to the effect of catecholamines. This autonomic dysfunction can be partly restored after replacement treatment with levothyroxine.7

Hypothyroidism has also been associated with prolongation of QT and increased QT dispersion. This has been shown to be reversible with levothyroxine. The sympathovagal imbalance and increased inhomogeneity of ventricular recovery times can both predispose to potentially life-threatening arrhythmias.7

In patients with hypothyroidism, the occurrence of TDP in the milieu of a prolonged QT interval has been reported in only a few reports in the English literature. In most of these cases, no other predisposing factors could be ascertained, and the arrhythmogenic tendency abated with levothyroxine replacement. Predisposition to malignant arrhythmias appears to be promptly eradicated with thyroxine therapy, unlike most other cardiac abnormalities seen with hypothyroidism that are slow to resolve with replacement. Stress dose glucocorticoid coverage should be provided in the acute situation and the levothyroxine dose should be increased gradually to avoid precipitating angina in patients with underlying coronary artery disease.

**Conclusion**

The awareness of the protean effects of hypothyroidism on the heart is necessary for the prompt treatment of patients with life-threatening complications of hypothyroidism as seen in our patient. Rapid recovery is possible with appropriate treatment with a favorable long-term prognosis.

**References**


**Figure 2:** Electrocardiogram shows her heart rate improved, QTc normalized to 418 ms, and the lead voltage improved.