Dilated cardiomyopathy with long QT secondary to hypothyroidism and hypocalcaemia in patient with post total thyroidectomy: A case report

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Abstract. The linkage between cardiac dysfunction and the lack of thyroid hormones has been well elucidated. A case involving a woman aged 44 years suffering a dilated cardiomyopathy (DCM) and long QT secondary to hypothyroidism and hypocalcaemia emerges. Thyroid hormone acts on the myocardium of the heart and peripheral blood vessels. There are two types of thyroid hormone effects, such as genomic and non-genomic. These effects are associated with cardiovascular and hemodynamic function. The prolongation of the QT interval is the most overlooked and well-documented sign in hypothyroidism. Ventricular fibrillation is usually the leading factor for the long QT syndrome. The incidence is characterized by an increased risk of sudden death and the abnormal QT-interval prolongation on the surface of ECG. The mechanism of hypothyroidism on the occurrence of the ventricular tachycardia and the QT prolongation is unrecognized, and although coexistent, the effects might be distinctive.

1. Introduction
A dilated cardiomyopathy (DCM) is a type of heart muscle disease that is reversible and developable through endocrine dysfunctions, such as hypothyroidism, hyperthyroidism, and chronic uncontrolled tachycardia, pregnancy, alcohol drinking, and drug use [1,2]. Various effects can result in the heart and vascular system by the thyroid hormone. Changes in the thyroid hormones make the heart sensitive, and both hyperthyroidism and hypothyroidism are commonly associated with cardiac disorders [2,3].

Hyperthyroid condition is related to the reduction in peripheral vascular resistance and the increment in cardiac output that caused hemodynamic leading to the state of hyperdynamic cardiovascular [3,4]. It will be contrary to hypothyroidism. The hypothyroidism is linked to bradycardia, mild diastolic hypertension, narrow pulse pressure, and slightly increased mean arterial pressure. The most common symptom encountered in patients with hypothyroidism is diastolic dysfunction. The rare presentation of hypothyroidism refers to the dilated cardiomyopathy [5].

2. Case
A case involving a 44-year-old woman with dilated cardiomyopathy (DCM) accompanied with long QT secondary to Hypothyroidism is encountered. The patient presented with shortness of breath since two days ago. Shortness of breath was arising when the patient lifted and replaced three water gallons.
Complaints slightly decreased with rest. Previously, the patient had no complaints while doing the same activity. Shortness of breath was also appearing when the patient lied down, and she must use three pillows during sleep. In the night, the patient often wakes up suddenly due to shortness of breath.

Besides, the patient also complained about muscle pain and tingling in the hands and feet. The patient around the lips also felt tingling. Patients felt this complaint since two weeks ago. The patient denied any history of unconsciousness.

The patient had a history of hyperthyroid since young and have performed thyroidectomy surgery about 11 years ago. She also said that she had a history of uncontrolled hypertension even with hypertension drug therapy, but after the thyroidectomy, the patient's blood pressure was supposed to be normal.

The patient has checked her complaints to the general practitioner, and received vitamin B complex therapy that should be taken twice daily, and she has been taking it for two weeks but the complaints were not improved.

As shown by the results of physical examination, the patient was found to have a Body Mass Index of 27.1 kg/m$^2$ (overweight). The vital of the patient, such as blood pressure was 120/70 mmHg; the pulse rate was 78 beats/min; the respiratory rate was 28 breaths/min, and the O$_2$ saturation was 96% in room air. The heart rate was regular, the murmur was heard systolic on the apex, and the tricuspid is grade III/VI and the breath-sounds were decreased with inspiratory crackles on bilateral lung bases.

The chest X-ray result showed cardiomegaly and pulmonary vein congestion (Figure 1). As indicated by the results of eletrocardiography, the patient had a normal sinus rhythm with poor R progression and prolonged QT interval [QTc: 560 ms (Figure 2)]. The results of clinical laboratory examinations showed that the patient had a normal range of TSH level and a decreased of FT4 and Calcium serum level (Table 1).

![Figure 1. Initial chest X-ray. The posteroanterior chest X-ray indicates a cardiomegaly and pulmonary vein congestion.](image)
Table 1. Clinical laboratory examinations.

| Examination | Result | Normal Range   |
|-------------|--------|----------------|
| TSH         | 6.4    | 0.270-4.20 microIU/mL |
| FT4         | 0.95   | 0.93-2.0 ng/dl |
| Ca          | 4.0    | 8.8-10.4 Mg/dl |

Figure 2. The Results of 12-lead electrocardiography. Normal sinus rhythm, poor R progression, and prolong QT interval (QTc: 560ms) are contracted to the patient.

As indicated in the results of echocardiography examination, a dilated left ventricular cavity is suffered by the patient with a diastolic dimension of 5.9 cm. Additionally, a decreased global systolic function with an ejection fraction of 26%, a grade III diastolic dysfunction, and moderate grade functional and mitral tricuspid regurgitation are contracted to the patient (Figure 3). The coronary angiographic result is non-significant stenosis in mid LAD (stenosis 40% in mid LAD).

The patient started a loop diuretic therapy using furosemide and angiotensin-converting enzyme (ACE) inhibitors (ramipril) for heart failure.

Figure 3. Echocardiography and coronary angiography result.
Due to the laboratory results, replacement to the thyroid hormone with thyroxine was performed to the patient. The dose of the thyroxine was then titrated up and was accompanied by the thyroxine dose adjustment based on functions of the thyroid.

| Table 2. Echocardiography with TSH finding after 1 year follow up. |
|---------------------------------------------------------------|
| **Follow up period**                                         |
|                                                               |
| **TSH (MicroIU/mL)**  | 0     | 1 mo | 6 mo | 12 mo |
| 6.4 (↑)                  | 5.0   | 4.2 (N) | 3.6 (N) |
| **LVEF (%)**             | 26% (↓) | 28% | 40% | 44% |
| **LVIDd (cm)**           | 5.9 (↑) | 5.6 | 5.2 | 5.2 |

| Table 3. Calcium serum level with QT interval finding after a 1-year follow-up. |
|---------------------------------------------------------------|
| **Follow up period**                                         |
|                                                               |
| **Ca Serum (mg/dL)**  | 0     | 1 mo | 6 mo | 12 mo |
| 4.0                   | 6.0   | 8.9 | 9.6 |
| **QT interval (ms)** | 560   | 550 | 480 | 460 |

The total surgery of thyroidectomy in 12 years ago was found to be the leading factor for the hypothyroidism in the patient [1,2]. The decreased cardiac contractility, the increased systemic vascular resistance, as well as decreased cardiac output are associated with the hypothyroidism. In its clinical development, the manifestation of the hypothyroidism seems to be extremely dangerous and progressive [3-5]. Various situations can be the leading factors to the DCM, the most common form of cardiomyopathy. The intended situations in questions include immune system disorders, toxins, infection, inflammation, electrolyte imbalance, and metabolic or endocrine disorders. The thyroid hormone works on the myocardium of the heart and peripheral blood vessels. The effects of the thyroid hormone linked to the hemodynamic function of cardiovascular and the cardiovascular itself are both the genomic and non-genomic effects. The possible genomic effects resulted in a system of cardiovascular have been outlined, that is to say, in the regulation of the transcription of mRNA that is associated with the contractile system, they are involved [6-8].

On ionic membranes of cardiomyocyte, a non-genomic effect is impacted by the thyroid hormones. T3 acts on the cardiomyocytes in a genomic and non-genomic way. T3 works genomically through bonds with TR located within the cardiomyocyte nucleus [7,8]. Activation of the TR-RXR-TRE complex by T3 enhances the transcription and expression of genes encoding structural and regulatory proteins along with important enzymes in the cardiomyocyte. The genes in the cardiomyocyte whose expression is affected by the T3-TR-RXR-TRE complex can be grouped into two types. The first type is a gene that is positively regulated. T3 increases the expression of the ion transport regulator protein that plays a role in conducting electrical activity of the cardiomyocyte [6]. The beta-1 adrenergic receptor gene encodes the beta-1 receptor protein in the cardiomyocyte plasma membrane, which acts as the conductor of heart responses to sympathetic and adrenergic races. Expression of the beta-1 receptor is increased by T3 effect. The second type is the negatively regulated gene, the genes that have decreased transcription activity due to T3 [8,9].

These genes include heavy-chain beta-myosin genes, phospholamban, adenyl cyclase types V and VI, thyroid hormone receptor-1, and Na + /Ca2+ exchanger. T3 lowers the expression of the heavy chain beta-myosin gene while raising heavy chain alpha-myosin expression, resulting in hypertrophy and increased cardiomyocyte contractility [9,10]. In hypothyroidism, phospholamban expression in the cardiomyocyte increases, causing a blockage of calcium uptake into the sarcoplasmic reticulum so that cytoplasmic calcium increases and disrupts the diastolic phase. Hypothyroidism causes interruption of cardiomyocyte calcium exchange and alteration of the contractile protein arrangement of the
cardiomyocyte [2-4]. The effect is a decrease in cardiomyocyte relaxation and left ventricular diastolic filling disorder so that, clinically, there is a reduction in cardiac contractility and cardiac output.

Patients with hypothyroidism have clinical manifestations of bradycardia, decreased myocardial contractility, increased systemic peripheral vascular resistance and pericardial effusion [10]. In addition, patients with hypothyroidism are at high risk for atherosclerosis, and ischemic heart disease. The patients with hypothyroidism are less likely to experience heart failure even if cardiac output decreases. This is due to low oxygen demand levels. In the current case, patient does not have a family history of DCM [11]. In addition, patients also have no history of alcohol abuse or history of drug addiction or other substances. Echocardiography findings indicated the presence of DCM. From literature stated that myocardial function in DCM secondary to hypothyroidism can be restored by normalizing thyroid function and heart failure management. In conclusion, through this case, doctors should consider the possibility of DCM secondary to hypothyroidism in patients with congestive heart failure [12,13].

LQT is the most common cardiac repolarization disorder caused by drug administration or electrolyte disturbance, one of which is hypocalcemia [14]. In this patient, it was obtained with a low serum iron concentration of 5 mg/dL. This hypocalcemia state was associated with a total thyroidectomy in the patient so that the operation was not only elevating the patient's thyroid gland but also elevating the patient's parathyroid glands. The function of the parathyroid gland is to regulate the levels of calcium and phosphate in the blood. Parathyroid increases levels of calcium in the blood by increasing the mechanism of osteoclast (through RANK / RANKL mechanism) to break bones and release calcium. In the gastrointestinal tract, parathyroid increases calcium absorption by activating vitamin D. While in the kidney, parathyroid increases calcium reabsorption [14].

Hypocalcemia causes prolonged QT interval because hypocalcemia will produce low calcium concentrations in extracellular fluid. According to cardiac physiology, the inclusion of calcium through the L-type calcium channel supports depolarization to create a plateau phase (also known as phase 2). During this phase, there is no change in electrical charge through the cell membrane [15,16]. The number of positive ions coming in and out is in equilibrium. Plateau is caused by the flow of calcium ions into the cell slowly. Usually, extracellular calcium levels are higher than intracellular potassium. In this phase, there is an increase in the number of potassium ions and calcium ions in which calcium ions go into intracellular. The inclusion of calcium ions into intracellular is offset by the release of potassium ions to the extracellular, resulting in a change of membrane potential. The entry of calcium into intracellular is a trigger of cardiac muscle contraction. The plateau phase ends when the calcium channel is closed and calcium exits the cell and repolarization of the cell membrane occurs. Low levels of calcium extracellular cause calcium ions to enter intracellular to be slower. The entry of slow calcium ions takes longer to reach the intracellular calcium ions threshold to close the L-type calcium channel, so the duration of the action potential extends, and ultimately prolongs the QT interval on electrocardiographic examination [14-16].

3. Conclusion
One of the secondarily leading factors for disease incidence is the DCM, in addition to other factors like hypothyroidism and, hypocalcemia which, can cause prolonged QT interval. The present study implies that considerations on the possibility of DCM secondary to hypothyroidism should be upheld by every clinician, particularly in patients contracting a congestive heart failure and prolong QT interval secondary to hypocalcemia.

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