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Dilated Cardiomyopathy Related to Hyperthyroidism in Young Adults

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ABSTRACT

Introduction: DCM is characterised by myocardial structural and functional abnormalities not caused by ischemia. One cause is hyperthyroidism. Hyperthyroidism can lead to a hyperdynamic circulatory state, increasing cardiac output and metabolic demands, which can ultimately result in heart failure.

Case: A 35-year-old woman presented with complaints of acute shortness of breath that worsened at night, accompanied by bilateral lower limb oedema and palpitations. Her medical history revealed hyperthyroidism diagnosed in 2021, but the patient was not compliant with treatment. Physical examination showed low blood pressure (84/60 mmHg), tachycardia 110 Beats Per Minute (BPM), and elevated Jugular Venous Pressure (JVP). Auscultation detected fine bilateral crackles and mitral regurgitation. Bilateral lower limb oedema. Echocardiography showed global hypokinesia with an Ejection Fraction (EF) of 30%, consistent with DCM. Laboratory tests revealed hyponatremia, elevated creatinine, and significantly increased liver enzymes. Initial management included intravenous saline infusion, continuous dobutamine infusion, and high-dose furosemide drip, which did not respond to furosemide. Acetazolamide was introduced as an additional diuretic. The patient also received ramipril, spironolactone, and enoxaparin for comprehensive cardiovascular and electrolyte imbalance management. This case highlights the importance of recognising the multifactorial nature of heart failure, particularly in patients with hyperthyroidism.

Conclusion: This case illustrates the complexity of treating DCM with hyperthyroidism and the need for individualized therapy to optimize patient outcomes. The addition of acetazolamide proved effective in addressing the inadequate response to furosemide, emphasizing its role in enhancing diuretic response.

Keywords

Cardiovascular Disease, Cardiogenic shock, Dilated cardiomyopathy, Hyperthyroidism

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INTRODUCTION

Thyrotoxicosis is a clinical syndrome resulting from an excess of thyroid hormones in the blood, caused by either hyperthyroidism or other mechanisms that lead to the excessive release of thyroid hormones into the systemic circulation.[1] Thyroid hormones affect almost all nucleated cells and play a role in normal growth processes and energy metabolism. Hyperthyroidism is a condition characterized by the overproduction of thyroid hormones, leading to a hypermetabolic state.[2] This can significantly impact the cardiovascular system, including increased heart rate, myocardial contractility, and cardiac output. Over time, these effects may lead to cardiac complications such as atrial fibrillation, heart failure, and cardiomyopathy.[3] The relationship between hyperthyroidism and heart failure, particularly thyroid cardiomyopathy, is well

documented but often underrecognized in clinical practice.[4] Changes in thyroid hormone concentrations directly influence abnormal changes in the structure and/or function of the heart, leading to cardiomyopathy and increasing the risk of complications such as heart failure and arrhythmias that are life-threatening.[5]

DCM is characterized by myocardial structural and functional abnormalities not caused by ischemia. Its clinical features are defined by the absence of ischemic heart disease, hypertension, valvular disease, or congenital heart disease characterized by left-sided or biventricular dilatation and systolic dysfunction.[6] One of the causes of cardiomyopathy is metabolic or endocrine dysfunction, such as Cushing's disease, hypothyroidism, hyperthyroidism, pheochromocytoma, chronic hypocalcemia, hypophosphatemia, and congenital metabolic disorders. Thyroid cardiomyopathy is a form of heart muscle disease that occurs due to the toxic effects of excessive thyroid hormones on the heart. Patients with thyroid cardiomyopathy may exhibit symptoms of heart failure such as dyspnea, fatigue, and peripheral edema. Echocardiographic findings typically include left ventricular hypertrophy, chamber dilation, and reduced ejection fraction, as seen in this patient. The goal of treatment for patients with thyroid cardiomyopathy is to restore the euthyroid and manage cardiovascular manifestations using oral antithyroid medications. Proper management of hyperthyroidism is crucial in preventing these cardiac complications, but adherence to treatment remains a challenge for many patients.[7]

Hyperthyroidism affects about 1-2% of the global population, with prevalence variations based on geographic, ethnic, and age factors. Women are significantly more likely to be affected by this condition compared to men, and it is most commonly diagnosed in individuals aged 20-40 years.[7] Several epidemiological studies show varying rates of heart disease incidence in thyrotoxicosis. Although there are no publications in Indonesia reporting the incidence rate of cardiomyopathy in patients with thyrotoxicosis, global data indicates that about 1% of thyrotoxicosis patients develop DCM, leading to severe left ventricular dysfunction and resulting in cardiogenic shock.[1]

The management of hyperthyroidism in Indonesia poses unique challenges due to varying levels of access and awareness of healthcare services, highlighting the need for public health interventions that can hit the right target and improvements in diagnostic and treatment facilities. In this case, a 35-year-old woman with a history of hyperthyroidism presented with symptoms of heart failure and cardiogenic shock. Although she was diagnosed with hyperthyroidism in 2021, she had not been compliant with her treatment. This lack of compliance likely contributed to the progression of her condition, culminating in her acute symptoms. The clinical manifestations of her disease, including shortness of breath, leg swelling, and chest pain, underscore the severe impact of untreated hyperthyroidism on heart function. This case report emphasizes the importance of recognizing and managing hyperthyroidism to prevent severe cardiac complications. This also illustrates the need for regular follow-up and patient education to ensure adherence to prescribed treatments. Through this case, we aim to raise awareness about the cardiovascular risks associated with hyperthyroidism and the importance of early and sustained intervention.

CASE

A 35-year-old woman presents with acute onset shortness of breath that began one day ago. The dyspnea initially occurred during light activities and did not improve with rest, leading to significant discomfort and causing her to wake up frequently at night. Alongside the shortness of breath, the patient also reports swelling in both legs that started simultaneously with the dyspnea. Additionally, she experiences palpitations and occasional chest pain.

The patient's medical history reveals a previous hospitalization in 2021 for similar complaints, during which she was admitted to the Intensive Cardiac Care Unit (ICCU). It was then that she was diagnosed with hyperthyroidism. Despite the diagnosis, she has not been diligent in taking her prescribed medication, thiamazole, 3x10mg, and has not taken it for a significant period. The patient denies any history of diabetes mellitus, hypertension, or stroke, which are often associated with cardiovascular issues. There is no relevant family medical history of similar conditions, indicating that her current health issues may be isolated rather

than hereditary. The lack of medication adherence since her last hospitalization could have contributed to the worsening of her symptoms, leading to her current acute presentation. Given the combination of respiratory distress, peripheral oedema, palpitations, and chest pain, along with a history of untreated hyperthyroidism, a comprehensive evaluation and management plan is essential to address her condition and prevent further complications.

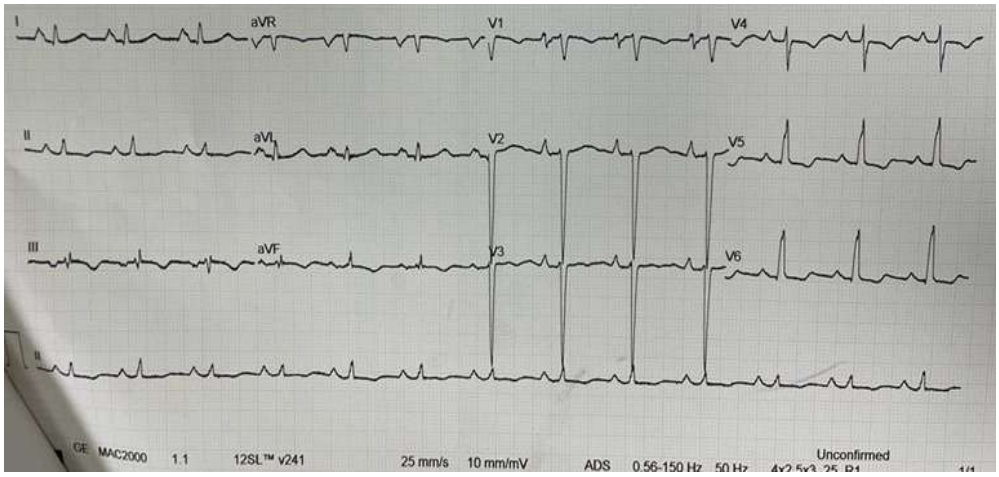

Figure 1. The electrocardiogram (ECG) of the patient reveals sinus tachycardia at a rate of 110 BPM

During the physical examination, the patient was conscious (compos mentis) but in severe distress. Her Glasgow Coma Scale (GCS) score is E4V5M6. Vital signs reveal a blood pressure of 84/60 mmHg, a heart rate of 110 beats per minute, a respiratory rate of 26 breaths per minute, a temperature of 36.6°C, and an oxygen saturation of 99% on a Non-Rebreather Mask at 12 litres per minute. General examination shows no signs of anaemia or jaundice in the eyes, but an elevated JVP is observed in the neck. Examination of the ear, nose, and throat reveals no abnormalities. Cardiovascular assessment reveals normal S1S2 heart sounds with the murmur regurgitation. Respiratory examination indicates vesicular breath sounds with fine crackles bilaterally but no wheezing. The abdominal examination shows normal bowel sounds, no distension, and no tenderness on palpation. Examination of the extremities reveals bilateral leg oedema, warm extremities, and a capillary refill time of fewer than 2 seconds. Overall, the physical examination indicates signs of severe distress with cardiovascular and respiratory system involvement, highlighting the critical nature of the patient's condition.

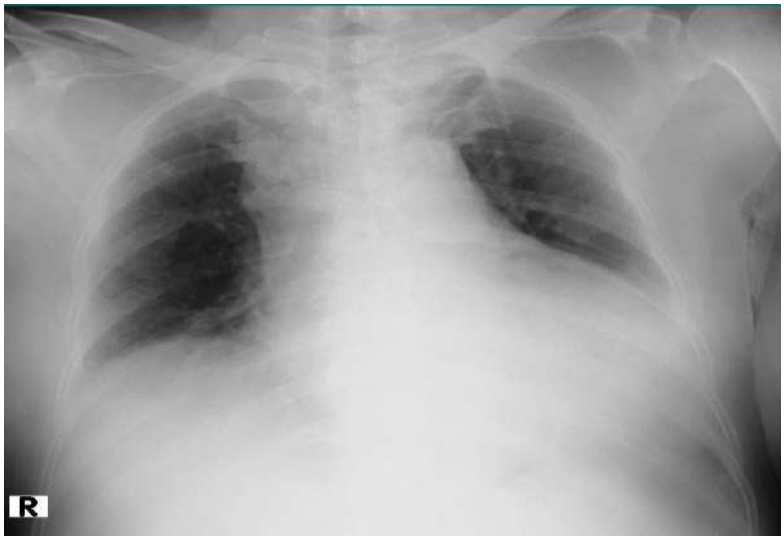

Figure 2. Chest X-ray shows an enlarged heart, which is consistent with the image of cardiomegaly.

The additional examinations conducted provide further insight into the patient's condition. The ECG reveals sinus tachycardia at a rate of 110 BPM (Figure 1). A chest X-ray shows cardiomegaly (Figure 2), indicating an enlarged heart, which is consistent with the patient's symptoms and history of hyperthyroidism.

Thyroid function tests show a low Thyroid-Stimulating Hormone (TSH) level at 0.22 µIU/mL and elevated Free T4 (FT4) at 26.29 pmol/L, consistent with hyperthyroidism. Echocardiography (Figure 3) performed reveals dilatation of all cardiac chambers, eccentric Left Ventricular Hypertrophy (LVH), severely reduced left ventricular systolic function with an EF of 30%, grade III diastolic dysfunction, normal right ventricular contractility, global hypokinesis, mild mitral regurgitation, an Estimated Right Atrial Pressure (eRAP) of 15 mmHg, and a normal pericardium. The findings are consistent with cardiomyopathy. Overall, these additional examinations suggest a complex interplay of cardiovascular, respiratory, renal, and metabolic dysfunctions, likely exacerbated by the patient's untreated hyperthyroidism, contributing to her acute presentation.

Table 1. Laboratory findings reveal several abnormalities.

Parameter	Results
Leukocytes	16.04 10^3/uL
Erythrocytes	4.62 10^6/uL
Haemoglobin	11.6 g/dL
Hematocrit	36.0 %
Platelets	127 10^3/uL
Sodium	127 mmol/L
Potassium	4.1 mmol/l
chloride	101 mmol/L
Urea	89.3 mg/dL
Creatinine	1.22 mg/dL
SGPT	1130 U/L
SGOT	43 U/L
TSH	0.22 µIU/mL
FT4	26.29 pmol/L

Upon admission to the hospital, the patient with a diagnosis of DCM related to hyperthyroidism was started on a comprehensive treatment regimen. The therapeutic approach aimed to stabilise her hemodynamic status, manage her heart failure symptoms, address her thyroid condition, and prevent thromboembolic complications. The patient was initiated on intravenous fluid therapy with normal saline (IVFD NS) at a rate of 8 drops per minute to maintain adequate hydration and support her intravascular volume status. Additionally, a continuous dobutamine infusion was administered at a dose of 5 µg/kg body weight per minute to improve her cardiac output and address the cardiogenic shock. Dobutamine, a beta-adrenergic agonist, helps enhance myocardial contractility and increase cardiac output, which is crucial in managing cardiogenic shock. Given the patient's significant fluid overload and oedema, a continuous infusion of furosemide at 20 mg per hour (the maximal dose) was initiated. Furosemide, a potent loop diuretic, is essential for promoting diuresis and reducing fluid retention. However, due to furosemide in maximal dose, acetazolamide was added at 250 mg once daily. Acetazolamide, a carbonic anhydrase inhibitor, enhances the diuretic effect by promoting the excretion of bicarbonate, sodium, and water, thus aiding in effective fluid management.

The patient was also started on spironolactone at a dose of 50 mg once daily and ramipril at a dose of 2.5 mg once daily. Spironolactone, an aldosterone antagonist, helps reduce fluid retention and prevent cardiac remodelling, while ramipril, an *Angiotensin-Converting Enzyme* (ACE) inhibitor, aids in lowering blood pressure and reducing afterload, thereby improving cardiac function. Enoxaparin, a low molecular weight heparin, was given at a dose of 0.4 cc subcutaneously once daily to prevent thromboembolic events, which are a significant risk in patients with heart failure and reduced mobility. This comprehensive therapeutic approach aims to stabilise the patient’s condition, optimise cardiac function, manage symptoms, and prevent

complications. The patient's response to this treatment regimen was closely monitored, with adjustments made as necessary to ensure the best possible outcomes.

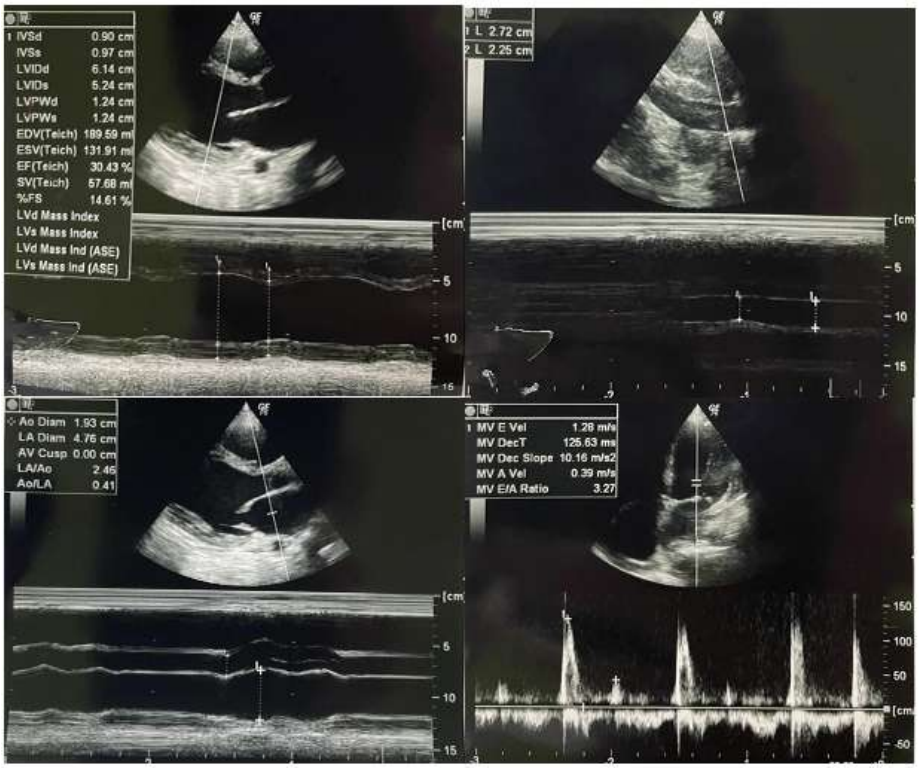

Figure 3. Echocardiography shows dilatation of all cardiac chambers, eccentric LVH, severely reduced left ventricular systolic function with an EF of 30%, grade III diastolic dysfunction, normal right ventricular contractility, global hypokinesis, and mild mitral regurgitation. The findings are consistent with cardiomyopathy.

DISCUSSION

Hyperthyroidism can cause heart failure through several mechanisms. Excess thyroid hormones increase the metabolic rate and oxygen consumption, placing greater cardiovascular demands. They also increase beta-adrenergic receptor sensitivity, heart rate, contractility, and cardiac output (8). Chronic exposure to high levels of thyroid hormones can lead to structural changes in the heart, such as left ventricular hypertrophy and dilation, as well as functional impairments, such as diastolic dysfunction. These changes can culminate in thyroid cardiomyopathy, a condition characterised by heart failure symptoms in the context of hyperthyroidism. The patient's echocardiographic findings of enlarged heart chambers and reduced ejection fraction are consistent with this pathophysiology.[9]

The mechanism of hyperthyroidism in cardiovascular disease is divided into two parts, namely, genomic and non-genomic mechanisms. In the genomic mechanism, The binding of T3 to TRH positively regulates the expression of several cardiac genes related to the contractile function of the heart, such as α-myosin heavy chains, sarco/endoplasmic reticulum free calcium (Ca^{2+}) ATPase 2 (SERCA2a), voltage-gated potassium channels, Na^{+}/K^{+} ATPase and β1-adrenergic receptor adenine nucleotide translocase. Conversely, they negatively regulate the expression of myosin β heavy chains, phospholamban (SERCA2a inhibitor), Na^{+}/Ca^{2+} exchangers (NCX1), adenylate cyclase types V and VI, and THR α1. The contraction and relaxation of cardiac muscle are regulated by the concentration of intracellular Ca^{2+}, which is determined by the release of sarcoplasmic calcium through ryanodine receptors and its reuptake by SERCA2a. Thyrotoxicosis markedly increases the expression of positively regulated genes and further decreases that of negatively regulated ones. These changes in gene expression contribute to enhanced diastolic function, as well as inotropism and chronotropism, increasing cardiac output. The non-genomic effects of thyroid hormones involve the membrane channels of sodium, potassium and calcium, and the endothelial smooth muscle and endothelial

nitric oxide synthase. Together, these effects can decrease systemic vascular resistance by 50–70%. This, added to the increase in cardiac output, stimulates the juxtaglomerular apparatus, increasing the production of renin and aldosterone and sodium renal absorption, thus increasing circulating blood volume and end-diastolic volume. Thyroid hormones also stimulate erythropoietin synthesis, increasing circulating blood volume by up to 25%. This contributes to increasing preload, decreasing afterload and increasing cardiac output by up to 300%.[8]

The antithyroid drugs that are widely used are PTU and imidazole (methimazole, thiamazole, and carbimazole). These two drugs belong to the thionamide group whose action is to inhibit thyroid hormone synthesis, but do not affect the secretion of thyroid hormone that has already been formed. Propylthiouracil can prevent the conversion of T4 to T3 in the periphery. The initial dose of PTU used is 300-600 mg/day with a maximum dose of 1200-2000 mg/day or methimazole 30-60 mg per day. Improvement in symptoms of hyperthyroidism usually occurs within three weeks, and euthyroidism can be achieved in 6 to 8 weeks [10]. The goal of treatment for patients with thyroid cardiomyopathy is to restore the euthyroid and manage cardiovascular manifestations using oral antithyroid medications. The treatment of cardiomyopathy follows the standard heart failure therapy, initially involving salt restriction with diuretics if there is excessive fluid volume, vasodilator therapy such as ACE Inhibitors or *Angiotensin Receptor Blockers* (ARBs), beta-blockers in hemodynamically stable patients, and adding aldosterone antagonists for patients with persistent symptoms. Thyroid cardiomyopathy poses unique therapeutic challenges. Hyperthyroidism can lead to a hyperdynamic circulatory state, increasing cardiac output and metabolic demands, which, over time, can result in heart failure. Adding acetazolamide, a carbonic anhydrase inhibitor, can benefit such cases. Acetazolamide enhances diuresis by inhibiting bicarbonate reabsorption in the proximal tubules, thereby increasing sodium and water excretion [10]. Acetazolamide is used as an adjunctive diuretic therapy in cases of furosemide resistance in heart failure. It works by inhibiting carbonic anhydrase in the proximal tubules, leading to increased excretion of bicarbonate, sodium, and water. This mechanism is complementary to the action of loop diuretics like furosemide, which acts on the ascending limb of the loop of Henle [11]. The combined use of these diuretics can enhance overall diuretic efficacy, particularly in patients who have developed resistance to loop diuretics alone. In this case, adding acetazolamide helped achieve better fluid balance and symptom control, illustrating its role in managing diuretic-resistant heart failure [12].

In the presented case, the patient's furosemide resistance is indicated by the persistence of oedema in both legs and the severity of her symptoms despite receiving high doses of furosemide. Specifically, the patient exhibited significant bilateral lower limb oedema and signs of fluid overload, which are typical indicators of inadequate diuretic response. The continued presence of these symptoms suggests that the furosemide, despite being administered at a maximum dose of 20 mg/hour, was insufficient to achieve the desired diuretic effect and relieve the patient's fluid retention. Acetazolamide was introduced as an adjunctive therapy to address this issue. Acetazolamide's mechanism of action differs from that of furosemide, as it inhibits carbonic anhydrase in the proximal tubules, thereby promoting the excretion of bicarbonate, sodium, and water. This complementary approach helps overcome diuretic resistance and improve overall fluid management in patients with DCM who do not respond adequately to loop diuretics alone.

Cardiogenic shock is a severe form of heart failure where the heart is unable to pump sufficient blood to meet the body's needs, resulting in inadequate tissue perfusion and oxygenation [13]. This condition is characterised by hypotension, elevated central venous pressure, and signs of end-organ dysfunction. In this case, the patient's severe low blood pressure, along with symptoms of severe dyspnea and peripheral oedema, indicated cardiogenic shock. The management of cardiogenic shock involves hemodynamic support with inotropes like dobutamine, which increases cardiac contractility and output. Diuretics and vasodilators also reduce preload and afterload, thereby improving cardiac efficiency. The use of comprehensive supportive measures, including fluid management and inotropic support, was crucial in stabilising the patient’s condition and addressing the underlying causes of her heart failure [14].

CONCLUSION

Effective management of heart failure in the context of thyroid dysfunction requires a multidisciplinary approach that encompasses the disease's cardiac and endocrine components. This case illustrates the complexity of treating DCM with hyperthyroidism and the need for individualised therapy to optimise patient outcomes. Managing cardiomyopathy related to hyperthyroidism presents unique challenges, as it requires treatment for both hyperthyroidism and heart failure, especially when cardiogenic shock is present with an inadequate response to diuretics. This case highlights the complex interaction between thyroid dysfunction and heart failure, as well as the therapeutic strategies used to manage this condition.

DECLARATIONS

This study was approved by Ethical Committee.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest in this report.

AUTHORS' CONTRIBUTIONS

KAS contributed to the preparation of the manuscript (background, case presentation, results, and discussion). NLESW gave guidance in this study.

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