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## CASE REPORT

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# Diffuse Toxic Goiter Hyperthyroid with Atrial Fibrillation in Type 2 Diabetes Patient

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### ABSTRACT

*Goiter is an enlargement of the thyroid gland which can occur in euthyroid, hyperthyroid, or hypothyroid. Hyperthyroidism can cause symptoms, such as palpitations, fatigue, sleep disturbances, weight loss, and heat intolerance. There are various complications and symptoms of hyperthyroidism, one of which is cardiac arrhythmia. Thyroid dysfunction can coexist with type 2 diabetes, so special attention is needed. Male, 43 years old, complaining of palpitations in the chest since 2 days ago. Complaints were accompanied by weakness, hand tremors, and lack of appetite. Patient also complained there was a lump in the neck that moved when swallowing since 5 months ago. Patient has a history of type 2 diabetes and regularly takes metformin. Physical examination found diffuse enlargement of the thyroid gland, soft consistency, indistinct borders and irregular heart rhythm. Electrocardiography showed atrial fibrillation. Ultrasound examination revealed bilateral diffuse goiter. Free T<sub>4</sub> result is elevated. Therapy given is infusion, methimazole, beta-blockers, digoxin, and metformin. Thyroid hormones have significant effects on the heart, which include increasing resting pulse rate, blood volume, stroke volume, cardiac muscle contractility, and ejection fraction. Thyroid also causes sinus rhythm disturbances. Early thyroid treatment has a better prognosis for improvement. Treatment of hyperthyroidism can affect the condition of diabetes, so monitoring blood sugar is necessary. Early diagnosis and prompt treatment of hyperthyroidism can resolve complaints and prevent complications. Thyroxine concentrations higher than normal are more at risk of experiencing atrial fibrillation. Hyperthyroidism can occur together with type 2 diabetes so it needs special attention.*

**Keywords:** *Goiter, hyperthyroid, atrial fibrillation, type 2 diabetes*

## INTRODUCTION

Goiter is an enlargement of the thyroid gland.<sup>1</sup> The normal size of thyroid gland is 4 to 4.8 centimeters in The sagittal plane, 1 to 1.8 centimeters in the transverse plane, and 0.8 to 1.6 centimeters in anteroposterior dimension.<sup>1</sup> Goiters can occur in euthyroid, hyperthyroid, or hypothyroid.<sup>1</sup> The most common cause of goiter is iodine deficiency, with a prevalence of around 2.2 billion people worldwide.<sup>1</sup> Iodine is the main ingredient for the formation of thyroid hormone so iodine deficiency can cause a lack of thyroid hormone synthesis.<sup>1</sup>

Hyperthyroidism is characterized by increased synthesis and secretion of thyroid hormone from the thyroid gland.<sup>2</sup> The prevalence of hyperthyroidism is 0.8% in Europe and 1.3% in the United States.<sup>2</sup> The most common cause of hyperthyroidism is Graves' disease.<sup>2</sup> Graves' disease is triggered by an autoimmune process due to the presence of autoantibodies that bind to the TSH receptor thereby stimulating follicular cells to continue producing thyroid hormone.<sup>2</sup> Hyperthyroidism can affect various organ systems in the body.<sup>3</sup>

The most commonly complained symptoms are palpitations, fatigue, tremors, anxiety, sleep disturbances, and heat intolerance.<sup>3</sup> Physical examination can reveal tachycardia, tremors in extremities, and weight loss.<sup>3</sup> Graves' disease should be suspected in cases with symptoms of hyperthyroidism accompanied by clinical chemical findings of hyperthyroidism, such as decreased TSH level and free thyroxine (T4) level or increased triiodothyronine (T3) level.<sup>4</sup> Serum TSH level needs to be done first because it has higher sensitivity and specificity in diagnosing thyroid disorders.<sup>2</sup> Ultrasonography (USG) and TSH-receptor autoantibodies (TRAb) examinations can also be performed to support the diagnosis.<sup>2</sup>

Hyperthyroid therapy options are divided into three, namely anti-thyroid drugs, radioactive iodine ablation, and surgery (thyroidectomy).<sup>5</sup> Anti-thyroid drug therapy is preferred in cases of Graves' disease, except in America which prefers radioactive iodine

ablation.<sup>5</sup> Methimazole is the main choice of anti-thyroid drug, except for first-trimester pregnant women, propylthiouracil (PTU) is the main choice.<sup>5</sup> Giving beta-blockers drugs, such as propranolol, is also needed to reduce patient complaints regardless of the cause of hyperthyroidism.<sup>5</sup> Complications and symptoms that arise in patients with hyperthyroidism vary.<sup>2</sup> Older patients show fewer symptoms than younger people but have a greater risk of cardiovascular complications.<sup>2</sup> When compared with elderly people without hyperthyroidism, elderly patients with hyperthyroidism have 3 times greater risk of experiencing atrial fibrillation.<sup>2</sup> Thyroid disorders can also be found in patients with type 2 diabetes related to insulin resistance.<sup>6</sup> Another condition that can be experienced in hyperthyroid patients is blood disorders because the thyroid also plays an important role in hematopoiesis.<sup>7</sup>

## CASE ILLUSTRATION

A male, 43 years old, came with chest palpitations 2 days ago and had been getting worse since this morning. Complaints accompanied by weakness, tremors in both hands, nausea without vomiting, and decreased appetite. Since 5 months ago, a lump appeared on the patient's neck. The lump enlarged and moved when swallowing. Complaints of weight loss were also recognized, but the amount of weight loss was not measured. The patient had a history of diabetes and routinely took metformin twice a day. History of similar disease in the family was denied. Examination of the patient's vital signs showed full awareness, blood pressure 135/88 mmHg, pulse rate 79 times per minute, respiratory rate 20 times per minute, and body temperature 37.5°C. Physical examination of the neck showed diffuse enlargement of the thyroid gland, soft consistency, with indistinct boundaries. Physical examination of the heart revealed single irregular 1st and 2nd heart sounds, without murmurs or gallops. An electrocardiography examination of the

patient showed atrial fibrillation. Ultrasound examination of the thyroid was also performed and found bilateral diffuse goiter suggestive of hyperthyroidism. Thyroid function examination showed increased levels of free thyroxine hormone (T<sub>4</sub>). A complete blood count examination showed an increase in hemoglobin, erythrocyte count and hematocrit parameters. Random blood sugar was increased. Treatment was given with ringer lactate infusion 28 drops per minute, methimazole 20 milligramsevery 12 hours orally, propranolol 20 milligrams every 12 hours orally, digoxin 0.25 milligrams every 24 hours orally, and metformin 500 milligrams every 12 hours orally. After being treated for four days, the patient's complaints were reduced and the condition was stable.

## DISCUSSION

Goiter is an enlargement of the thyroid gland.<sup>1</sup> Goiter can occur in euthyroid, hyperthyroid, or hypothyroid.<sup>1</sup> Hyperthyroidism is characterized by increased synthesis and secretion of thyroid hormone from the gland.<sup>2</sup> The most common symptoms complained by patients with hyperthyroidism are palpitations, fatigue, tremors, anxiety, sleep disturbances, and heat intolerance.<sup>3</sup> Physical examination can find tachycardia, tremors in extremities, and weight loss.<sup>3</sup> A 43-year-old male patient complained of a lump was the neck which had enlarged since 5 months ago. The lump is felt to move when swallowing, accompanied by weight loss and atrial fibrillation. Physical examination of the neck revealed diffuse enlargement of the thyroid gland, soft consistency, with indistinct boundaries.

Serum TSH level needs to be done first in cases with suspected hyperthyroidism because it has higher sensitivity and specificity in diagnosing thyroid disorders.<sup>2</sup> Ultrasound examination and TSH-receptor autoantibodies (TRAb) can also be performed to support the diagnosis and determine the etiology of hyperthyroidism.<sup>2</sup> Early screening and treatment of thyroid disorders with arrhythmias is important because it can affect long-term

prognosis.<sup>7</sup> Normal levels of free thyroxine (fT<sub>4</sub>) in the blood are 11-25 pmol/L or 0.85-1.94 ng/dL.<sup>9</sup> T<sub>4</sub> concentrations that are higher than normal have a higher risk of experiencing atrial fibrillation, especially in young patients.<sup>9</sup> The patient was then examined for free thyroxine hormone levels and found an increase in free T<sub>4</sub> with a result of 4.86 ng/dL (normal: 0.89 - 1.72 ng/dL). The patient also underwent an ultrasound examination, which obtained bilateral diffuse goiter suspicion of hyperthyroidism with a right thyroid size of 5 centimeters x 2.9 centimeters x 2.99 centimeters, left thyroid size of 6 centimeters x 2.9 centimeters x 2.8 centimeters; irregular surface; parenchymal echotexture looks more hypoechoic inhomogeneous; no nodules or cystic lesions were seen; no calcification is seen.

Thyroid hormones have significant effects on cardiac function, both genomic and non-genomic.<sup>10</sup> Hyperthyroidism is characterized by an increase in resting pulse rate, blood volume, stroke volume, heart muscle contractility, and ejection fraction.<sup>10-11</sup> Atrial fibrillation can occur due to various mechanisms, such as an increase in right atrial pressure which can increase right ventricular workload and impaired ventricular relaxation, ischemia due to increased resting heart rate, and increased ectopic atrial activity.<sup>11</sup> Atrial fibrillation can also occur due to disturbances in sinus rhythm caused by suppression or replacement of sinus mechanism by a diffuse and irregular rhythm.<sup>8</sup> In this case, the patient complained of chest palpitations. This complaint was related to atrial fibrillation. Physical examination of the patient's chest revealed single but irregular in both first and second, heart sounds. The patient then underwent an electrocardiogram examination and atrial fibrillation was found with a pulse rate of 92 beats per minute.

In this case, the patient also had a history of diabetes mellitus and routinely consumed 500 milligrams of metformin twice a day. The patient was randomly checked for blood sugar and the result was 245 mg/dL.

(normal: <200 mg/dL). Diabetes mellitus and thyroid disorders are endocrine disorders that are often found and can occur together.<sup>12</sup> Both of these endocrine disorders can increase the risk of heart disease.<sup>12</sup> Thyroid disorders are more common in type 1 diabetes than type 2.<sup>12</sup> This is related to the autoimmune process that underlies thyroid disorders and type 1 diabetes<sup>12</sup>, whereas type 2 diabetes is associated with insulin resistance.<sup>6</sup>

Anti-diabetic drugs can affect thyroid function and anti-thyroid drugs can interfere with glycemic control.<sup>12</sup> Hyperthyroidism is associated with poor glycemic control, characterized by hyperglycemia and insulinopenia.<sup>12</sup> Thyroid hormone can increase gastrointestinal motility and increase glucose absorption in the gastrointestinal tract.<sup>13</sup> An increase in the process of gluconeogenesis also occurs in the liver due to the effects of thyroid hormones.<sup>6,13</sup> Thyroid hormone also increases the process of lipolysis in adipose tissue.<sup>6</sup> Diabetes can interfere with thyroid function by affecting TSH hormone levels and interfering with the conversion of T<sub>4</sub> to T<sub>3</sub> in peripheral tissues.<sup>14</sup>

Thyroid hormone plays an important role in hematopoiesis so blood disorders often occur in patients with thyroid disorders.<sup>7</sup> Thyroid hormone can have a direct effect on blood by stimulating erythrocyte precursors and indirectly by increasing erythropoietin production.<sup>7</sup> The study conducted by Ahmed et al. demonstrated that thyroid disorders can affect all blood parameters except platelets.<sup>7</sup> Anemia often occurs in patients with thyroid disorders, especially hypothyroidism.<sup>7</sup> Another study conducted by Liu et al. showed the presence of erythrocytosis in hyperthyroid patients with Graves' disease.<sup>15</sup> This result is associated with an increase in hypoxia-inducible factor-1- $\alpha$  (HIF-1 $\alpha$ ) which causes an increase in erythropoietin.<sup>15</sup> Polycythemia can occur in cases of hyperthyroidism. A case report by Souresho et al., explained that patients with a history of hyperthyroidism and hypertension experienced polycythemia with a hemoglobin level of 16.4 g/dL and a hematocrit of 52.1%.<sup>16</sup>

However, there was no examination of erythropoietin or JAK2 cell mutations to confirm the cause of erythrocytosis.<sup>16</sup> In this case, the patient underwent a complete blood count, obtained a hemoglobin level of 18.6g/dL (normal: 11.5–16.2 g/dL), erythrocytes 6.76 million/ $\mu$ L (normal: 4.00–5.90 million/ $\mu$ L), hematocrit 53.1% (normal: 35–45%), leukocytes 7.24 thousand/ $\mu$ L (normal: 4.50–11.00 thousand/ $\mu$ L), and platelets 181 thousand/ $\mu$ L (normal: 150–450 thousand/ $\mu$ L). Patients experiencing erythrocytosis or polycythemia are characterized by an increase in erythrocytes, hemoglobin, and hematocrit. Relative polycythemia can occur due to lack of intake. To rule out the differential diagnosis, patients can be planned for examination of erythropoietin and JAK2 hormone levels.

Management of hyperthyroidism depends on the etiology, severity, age, comorbidities, and treatment options. The main options for therapy are beta-blockers and anti-thyroid drugs, namely propylthiouracil and methimazole.<sup>8</sup> Beta-blockers, such as propranolol, are used to control adrenergic symptoms.<sup>8</sup> Early screening and thyroid treatment are important because they can affect long-term prognosis.<sup>8</sup> Patients were given methimazole 20 milligrams every 12 hours orally and propranolol 20 milligrams every 12 hours orally to reduce thyroid hormone levels in the blood and overcome complaints.

Treatment of atrial fibrillation patients with hyperthyroidism aims to prevent symptoms by controlling heart rate and rhythm and preventing complications, such as heart failure and stroke.<sup>8</sup> A study in 1982 showed that 62% of patients with atrial fibrillation were able to return to sinus rhythm after the first three to four months of thyroid treatment.<sup>8</sup> Patients with early thyroid treatment can experience improvement in heart rhythm after two to three months.<sup>17</sup> Cardioversion, both electrically and pharmacologically, can be given if atrial fibrillation has not improved.<sup>17</sup> Patients are given digoxin 0.25 milligrams every 24 hours orally as a therapy to control heart rate and rhythm.

Diabetic patients on metformin treatment have smaller thyroid volumes and a smaller risk of developing thyroid nodules compared to controls.<sup>18-19</sup> Metformin is known to have the effect of lowering TSH levels, reducing thyroid nodule volume, and preventing the development of thyroid carcinoma.<sup>18</sup> Giving sulfonylureas should be avoided in diabetic patient with thyroid disorders because they can increase the risk of thyroid carcinoma.<sup>20</sup> Metformin medication which was taken by the patient continues. Anti-thyroid drugs can also cause hypoglycemia, related to insulin autoimmune syndrome which can make insulin ineffective due to binding with insulin autoantibodies.<sup>12</sup>

Cases of erythrocytosis or polycythemia can be divided into relative and absolute polycythemia.<sup>16</sup> Relative polycythemia occurs in patients with low plasma volume due to insufficient intake or excessive output.<sup>16</sup> While absolute polycythemia occurs in patients with polycythemia vera, a mutation in the JAK2 gene which causes an increase in the number of erythrocytes, and patients with increased levels of erythropoietin, a hormone that can stimulate the production of erythrocytes.<sup>16</sup> Patients were given a ringer lactate infusion of 28 drops per minute to increase intake.

## CONCLUSION

A 43-year-old male, came with complaints of chest palpitations since 2 days ago and had been getting worse since this morning. Complaints accompanied by weakness, tremors in both hands, nausea, and decreased of appetite. Since 5 months ago, a lump appeared on the patient's neck. The lump enlarged and moved when swallowing. Complaints of weight loss was recognized by the family but was not measured. Patient has a history of diabetes and routinely takes metformin 500 milligrams twice a day. Physical examination of the neck showed diffuse enlargement of the thyroid gland, soft consistency, with indistinct boundaries. Physical examination of the heart revealed single irregular first and second heart sounds. The result of the heart record examination showed

atrial fibrillation. Ultrasound examination of the thyroid was also performed and found bilateral diffuse goiter suggestive of hyperthyroidism. Examination of thyroid function showed increased levels of free thyroxine (T<sub>4</sub>) hormone. Complete blood count showed an increase in the parameters of hemoglobin, erythrocyte count, and hematocrit. Examination of random blood sugar of patients showed increased results. The treatment given was an anti-thyroid drug and beta-blockers to reduce thyroid levels and reduce complaints, an anti-diabetic drug in the form of metformin to control sugar levels, infusion of physiological fluids to treat polycythemia, and anti-arrhythmic drugs to control heart rhythm. After being treated for 4 days, the patient's complaints were reduced and his condition was stable.

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