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Case Report

Management of Thyrotoxicosis and its Associated Atrial Fibrillation- A Case Report

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ABSTRACT

Background: Thyrotoxicosis is a condition occurs when excessive thyroid hormone level produced by overactive thyroid gland. It is the risk factor of getting atrial fibrillation (AF) as it could exert marked influences on electrical impulse generation and conduction which associated with shortening of action potential duration and contribute to AF. **Case:** A 57 years old Chinese female was diagnosed with thyrotoxicosis and atrial fibrillation when she was admitted to emergency department of hospital with complaints of shortness of breath, dyskinesia, on and off palpitation, fine tremor, tachycardia, warm skin, firm, enlarged and palpable thyroid, having patches of vitiligo on hands and feet and increase bowel movement. The CT scan has revealed small infarct near left band ganglia. **Aims:** The aims of management in this case were to resolve the symptoms presented and get the thyroid hormone levels restored to euthyroid state. **Results:** Aspirin and propranolol were given immediately after diagnosis for symptomatic relieve and rate control. Carbimazole and dexamethasone were given concurrently for hyperthyroid management. Aspirin was then replaced by warfarin before patient discharged to have better control and reduce risk of stroke. Furthermore, the patient's ECG and INR were monitored closely for stroke prevention.

Key words: Antithyroid drugs, Atrial fibrillation, Hyperthyroidism, Stroke prevention, Thyrotoxicosis.

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INTRODUCTION

Hyperthyroidism is a form of thyrotoxicosis in which there is inappropriate elevation of circulating thyroid hormone production.[1-3] It mostly caused by Graves' disease and thyroiditis.[2-4] A Nationwide Multicenter Study stated prevalence of thyroid disorders in Malaysia is 2% for hyperthyroidism and associated with iodine status amongst population.[5] Thyroid hormone influences many organs and tissues in the body and increase in thyroid hormone level can leads to common clinical state of thyrotoxicosis.[2] Based on Management Guideline of American Thyroid Association and American Association of Clinical Endocrinologists, hyperthyroidism affects cardiovascular system the most and untreated hyperthyroidism can leads to complications include loss of weight, osteoporosis, atrial fibrillation, embolic events, and even cardiovascular collapse and death. Thus, severity of the disease should be assessed and appropriate treatment should be formulated to prevent potential cardiovascular and neuromuscular complications.[5]

The aim to achieve euthyroid state is the most crucial step in managing thyrotoxicosis. In 2007, consumption of antithyroid preparations in Malaysia was 1.05 defined daily dose (DDD)/1000 population/day and the most utilized antithyroid preparation was carbimazole (82.8%), followed by propylthiouracil (17.2%). There is a high utilization of antithyroid drug in Malaysia because it is the first-line therapy in hyperthyroidism.[6]

Case History

A 57 years old Chinese female patient [weight 57 kg (2 months earlier: 62 kg)] was admitted to the emergency department due to shortness of breath and dyskinesia. This was the first time she experienced the symptoms and she did not experience any temporary loss of consciousness. On physical examination, patient was anxious, alert, conscious and pink. She was experiencing on and off palpitation, fine tremor, tachycardia, warm skin, and firm, enlarged and palpable thyroid, having patches of vitiligo on hands and feet and increase bowel movement. Her blood pressure was 150/95 mmHg, heart rate 191, body temperature 39°C, respiratory rate was 20 breaths per min. Her ECG report showed rapid ventricular response that indicates atrial fibrillation. Laboratory diagnosis shown that the patient is having TSH <0.1MU/L, T4 total is 185mmol/L with negative anti-T9 antibody; urea 7.2mmol/L, creatinine 116mmol/L; and haemoglobin value of 11.5g/dL. From CT scan, small infarct near left band ganglia was detected.

She has hypertension for the past 7 years and the condition was stabilized with tablet lisinopril 20 mg once daily (OD) and tablet metoprolol OD. The patient claimed to be adhered to the medications and do not have any drug allergy. She has self-monitored her blood pressure at home 2-3 times a week and the BP reading was around 135/70 mmHg. The medications that have been administrated to the patient during admission are shown in Table 1.

During admission, tab paracetamol was given in the first place to reduce patient's high body temperature. Carbimazole was given as an antithyroid drug to lower high thyroid hormone levels in patient while dexamethasone has been provided as an adjuvant to decrease the T_3 and T_4 levels faster to achieve euthyroid levels. Besides this, aspirin was administered to the patient initially to manage atrial fibrillation. However, warfarin was prescribed to replace aspirin because patient stroke risk factor was high based on CHA_2DS_2-VASc score.

Table 1: Medication summary.

Medication	Dose	Form
Paracetamol	500mg qds	Tablet (Tab)
Warfarin	2.5mg od	Tab
Propranolol	40mg qds	Tab
Carbimazole	20mg qds	Tab
Aspirin	300mg bd	Tab
Dexamethasone	2mg qid	Tab

DISCUSSION

The patient was diagnosed with thyrotoxicosis integrated with atrial fibrillation and transient ischemic attack. Atrial fibrillation is the most common cardiac complication of hyperthyroidism and occurs in 15% of patients with hyperthyroidism.[4-7] For the management, beta blocker should be considered first in all patients with symptomatic hyperthyroidism, especially thyrotoxicosis patients with resting heart rates more than 90 beats/min or coexistent cardiovascular disease.[4-7,8] Treatment with propranolol, atenolol and metoprolol could lower heart rate, systolic blood pressure, muscle weakness and tremor, as improvement in the degree of irritability, emotional liability and exercise intolerance.[4-9] However, non-selective beta blockers that mostly used for management of symptoms are generally contraindicated in patients with bronchospastic asthma. Thus, relative beta-1 selective agent can be used with careful monitoring of pulmonary status.[4-8,9] For this patient, tablet propranolol 40mg QDS has been given as a rate control because propranolol has advantage of reducing the peripheral conversion of T_4 to T_3 and reduce circulating tri-iodothyronine (T3) concentration by 10 and 40% respectively.[7-10] The details of dosage and frequency of beta blockers used for symptomatic relieve are presented in Table 2.

Besides that, the goal of treatment in this case was to achieve euthyroid state of the patient. Normally, antithyroid agents such as methimazole (MMI) and propylthiouracil (PTU) should be used for management of thyrotoxicosis.[7,8,10-12] They are thionamides group that act to decrease production of thyroid hormones by inhibiting the iodination of thyroglobulin, which occurs via inhibition of thyroperoxidase. Carbimazole is the first line thionamide choice in almost all patients because it results in a more rapid improvement in thyroid hormone levels, has less hepatotoxicity, and can be given once daily due to its longer half-life.[4-7,8-10] Carbimazole is a precursor of MMI and 10mg of carbimazole is metabolized into 6mg of MMI[4].

At the start of MMI therapy, higher dose was given to the patient to achieve a euthyroid state. However, a rough guide was used to initiate MMI daily dosing as shown in Table 3.

These rough guidelines should be tailored to individual patient, incorporating additional information on symptoms, thyroid gland size, and total T_3 levels. Serum T_3 levels are important to monitor initially because normalized free T_4 levels with MMI will have persistently elevated serum T_3, indicating continuing thyrotoxicosis.[4-10] In this case, patient T_4 total reading was 185 mmol/L (reference range = 70 to 140 mmol/L), which was 1.32 times higher than reference range. Hence, she has taken 5-10mg of MMI or 10-20mg of carbimazole once daily to manage her hyperthyroidism. MMI needs to take for about 1-2 months to restore euthyroidism as plasma half-lives of thyroid hormones in the body are long and require several weeks to inhibit and reduce their synthesis.[11] Once the euthyroid state is achieved, maintenance therapy with MMI at a lower dose (generally 5 to 10 mg daily) may be used, typically for 18 months with the beta blocker withdrawn gradually.[4-10-12] After initiation of carbimazole, thyroid function tests (estimated free T4, total T3, TSH) should be obtained monthly at first, and then every 2-4 months[4].

Moreover, administration of dexamethasone 2mg orally QDS in acute medical patient could significantly lowered the serum T_3, T_4, and thyroglobulin (T_g) below baseline values within 24 to 48h after the first dose of dexamethasone in hyperthyroid patients.[13,14] This is due to ability of corticosteroids to inhibit peripheral conversion of T_4 into T_3, where more persistent drop in T_3 in the hyperthyroid patients will then decrease T_4 and T_g level[14]. This suggested an additional effect of dexamethasone administration on thyroid secretion in the patient. Treatment should be tapered appropriately based on the required duration of steroid therapy.

Since the patient was diagnosed with AF and small infarct near left band ganglia, she might have increased risk of getting stroke. Thyrotoxicosis can be the sole cause of AF and may predispose to AF-related complications for instances stroke.[15,16] The irregular fast heartbeat caused by AF increase risk of blood clot formation and travel to arteries of brain, block the blood circulation and leads to stroke.[15] To prevent thrombus

Table 2: Dosage and frequency of beta blockers used for symptomatic relieve in thyrotoxicosis.

Drug[a]	Dosage	Frequency	Considerations
Propranolol[b]	10-40 mg	3-4 times per day	Nonselective beta-adrenergic receptor blocker Longest experience May block T_4 to T_3 conversion at high doses Preferred agent for nursing and pregnant mothers
Atenolol	25-100 mg	1-2 times a day	Relative beta-1 adrenergic receptor blocker More compliance Avoid during pregnancy
Nadolol	40-160 mg	1 time per day	Non-selective beta-adrenergic receptor blocker May block T_4 to T_3 conversion at high doses Least experience to date
Metoprolol[b]	25-50 mg	2-3 times per day	Relative beta-1 adrenergic receptor blocker
Esmolol	50-100 µg/kg/min IV infusion		In intensive care unit for severe thyrotoxicosis or storm

[a]Each of these drugs has been approved for the treatment of cardiovascular diseases, but none has been approved for the treatment of thyrotoxicosis to date. [b]Also once daily dose preparations available

Table 3: Dosage of methimazole to be given based on free T4 level[4].

Dose of methimazole	Free T_4 level
5-10mg	1-1.5 times higher than upper limit of normal
10-20mg	1.5-2 times higher than upper limit of normal
30-40mg	2-3 times higher than upper limit of normal

Table 4: Calculation of CHA_2DS_2-VASc score and its points.

	Condition	Points
C	Congestive heart failure (or Left ventricular systolic dysfunction)	1
H	Hypertension: blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	1
A2	Age ≥75 years	2
D	Diabetes Mellitus	1
S2	Prior Stroke or TIA or thromboembolism	2
V	Vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque)	1
A	Age 65–74 years	1
Sc	Sex category (i.e. female sex)	1

formation and increase risk of ischemic stroke, aspirin (antiplatelet) and warfarin (anticoagulant) remain the mainstays of the therapy.[17] Before recommending medication for AF management, stroke risk in AF patient should be estimated through introduction of the CHA_2DS_2-VASc score as it can simplify the initial decision for oral anticoagulant use in AF patients. The calculation of CHA_2DS_2-VASc score and the points are presented in Table 4.

Patients without clinical stroke risk factors do not need antithrombotic therapy, while patients with stroke risk factors (CHADS-VASc score of 1 or more for men, and 2 or more for women) are likely to benefit from oral anticoagulant.[16] For our patient, her CHADS2-VAC score was 4, it indicates she is in high risk of stroke attack. Thus, suggest her to be on oral anticoagulant therapy.[16-18] From the case, aspirin 300mg BD was given when patient first admitted preventing thromboembolic events. However, warfarin was prescribed to replace aspirin as it is more benefitted to patient with stroke risk score more than 2 and could reduce the risk of stroke by two-thirds and mortality by one-quarter compared to aspirin use.[19-23] Subsequent doses of warfarin dependent on the prothrombin time, reported as INR (international normalised ratio). Hence, regular testing of the INR in first three months of treatment is essential for patient who never received warfarin. The dosage should be adjusted to maintain a target INR of 2.5 (range 2-3).[16]

Last but not least, patient was prescribed with paracetamol 500mg QDS to manage her high body temperature. Fever can be treated with cooling measures and antipyretics but aspirin should be avoided to prevent decreased protein binding and subsequent increases in free T3 and T4 levels. Nonetheless, the standard dosage given as antipyretic for paracetamol should be 500mg q6h prn[24] because severity of fever is not encouraged to be masked and affect diagnosis.

CONCLUSION

The treatment goals for thyrotoxicosis are to achieve euthyroidism, manage the symptoms and prevent risk of getting stroke. Propranolol and aspirin were given as immediate pharmacotherapy. There should be an early introduction of antithyroid drugs and warfarin in order to manage thyroid hormone levels and for stroke prevention. There is also a need to keep on review on her T_3 and T_4 levels, ECG and INR values 2 weeks after she get discharged to regulate the dose of medications.

CONFLICT OF INTEREST

No conflict of interest is declared

ABBREVIATIONS USED

od - once a day; bd - twice a day; qid/qds - four times a day, q6h -every 6h; prn - as needed; T_4 - Thyroxine

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