AMIODARONE INDUCED THYROTOXICOSIS — A CASE YOU MIGHT ENCOUNTER

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INTRODUCTION

Amiodarone is an effective antiarrhythmic agent with significant potential for adverse effects. We report a case who was treated with amiodarone for atrial fibrillation and who subsequently developed severe amiodarone induced thyrotoxicosis.

CASE REPORT

A fifty-five years old woman was referred in September 2000 because of atrial fibrillation. She was being treated with digoxin 0.25mg daily and aspirin 75mg daily. Examination revealed no clinical abnormalities and was euthyroid. Routine blood tests were normal and her lipids were controlled (cholesterol 4.5mmol/L, HDL 1.0mmol/L, LDL 3.5mmol/L, Triglyceride 2.0mmol/L). Blood sugar was 6.5mmol/L. ECG showed atrial fibrillation and chest X-rays was normal. Echocardiography ruled out valvular heart disease, good left ventricular function and no clot in the left atrium or ventricle. She was commenced on amiodarone 200 mg eight hourly for one week (started concurrently with iv loading) followed by 200mg twelve hourly for one week. She was then maintained 200mg daily. Follow up was arranged for two months. Approximately six weeks later she was seen urgently because of development of goiter. Examination of thyroid status revealed all the features of thyrotoxicosis - anxious look, sweating, tremors, lid lag.. Cardiovascular examination revealed sinus rhythm. Amiodarone was discontinued at once. Urgent thyroid function tests and thyroid scan were arranged. T3 was markedly elevated at 7.0 nmol/L with T4 elevated at 290nmol/L, TSH was less than detectable. Thyroid scan showed toxicnodular goiter. She was started on Carbimazole 30mg daily and Atenolol 50mg daily in order to maintain the sinus rhythm (as sotalol was not available in the market) and to control the adrenergic effects of thyrotoxicosis. She was then reviewed after six weeks in the medical out patients department. She was euthyroid clinically and in sinus rhythm. Repeat thyroid function tests showed T3 5.1 nmol/L, T4 190 nmol/L and TSH 2.5 u/L. She was then maintained on 15mg of Carbimazole daily.

PATHOGENESIS AND CLINICAL FEATURES OF AMIODARONE-INDUCED THYROTOXICOSIS

Feature	Type I	Type II
Underlying thyroid abnormality	Yes	No
Pathogenesis mechanism	Excessive hormone synthesis because of iodine excess	Excessive release of performed hormones because of thyroid destruction
Goiter	Multinodular or diffuse goiter normally present	Occasionally small, diffuse, firm, sometimes tender
Thyroidal radioiodine uptake	Normal/raised	Low/absent
Serum IL-6	Normal/Slightly raised	Profound increased
Thyroid ultrasound	Nodular, hypechoic	Normal

IL-6 = interleikin 6.

TABLE – 1

DISCUSSION

Amiodarone is the most effective antiarrhythmic agent for the treatment of life threatening ventricular arrhythmias and is also being used with increasing frequently in the treatment of patients with atrial fibrillation.[1]

Amiodarone has been implicated as a cause of both hypothyroidism and hyperthyroidism. It is structurally similar to thyroxine, with a benzene ring structure containing 2 iodine molecules, and each 200mg amiodarone tablet contain 75mg of iodine. Thyroid abnormalities result from the presence of iodine in the amiodarone molecule or secondary to a direct toxic effect of amiodarone on the thyroid gland.[2]

Hyperthyroidism occurs in fewer than 2% of amiodarone treated and occurs more commonly in countries with low iodine diets with prevalence of greater than 13%. Amiodarone "decreases the peripheral deiodination of thyroxine to triiodothyronine resulting in an increase of serum levels of thyroxine and reverse triiodothyronine and a decrease of serum levels of triiodothyronine. Clinical manifestations of amiodarone induced hyperthyroidism are similar to those of primary idiopathic hyperthyroidism. One of the earliest sign of hyperthyroidism is an increased heart rate. Many of the symptoms may be obscured by amiodarone's antiadrenergic actions. Laboratory findings include elevated T3 concentrations (>200 IU/dL) with TSH suppressed to undetectable levels.

Two main types of hyperthyroidism occur with amiodarone treatment[3] (Table 1). Type I occurs in patients with underlying thyroid disease. Subclinically autonomous thyroid tissue increases thyroid hormone production in response to the iodide load provided by amiodarone. These patients typically have multinodular or diffuse goiter, normal thyroidal radioiodine uptake, and abnormal thyroid ultrasound results.

Type II amiodarone-induced hyperthyroidism occurs secondary to a direct toxic effect of the drug in patients with normal thyroid glands. In these patients, amiodarone causes subacute destructive thyroiditis with preformed thyroid hormone released into the circulation.[4] Type II hyperthyroidism is characterized by low or

absent thyroidal radioiodine uptake, profoundly elevated interleukin 6 levels, and normal thyroid ultrasound results.

Management of amiodarone-induced hyperthyroidism is more complicated than management of hypothyroidism. Amiodarone discontinuation, if therapeutically possible, may be attempted, although hyperthyroid symptoms and cardiac status may worsen as the antiadrenergic effects of the drug wear off. Patients with type I hyperthyroidism rarely respond to amiodarone discontinuation alone; most patients remain symptomatic 6 to 9 months after drug discontinuation. As a result, treatment with high-dose methimazole or propylthiouracil is often required and continued for 3 to 6 months. Because most patients with type I hyperthyroidism have underlying Graves' disease or multinodular goiter, thyrotoxicosis usually recurs. Ultimately, radioiodine therapy is required.[5]

In patients with type II amiodarone-induced hyperthyroidism, amiodarone discontinuation alone may be effective. Most patients will become euthyroid in 3 to 5 months after drug discontinuatin. Steroid treatment speeds recovery and is indicated in patietns with severe symptoms.[6] Clinical resolution of type II hyperthyroidism begins within days of initiation of steroid treatment and is complete after 1 month of therapy. Addition of antithyroid drugs (methimazole, propylthiouracil) generally is not required in pure type II hyperthyroidism, and radioiodine therapy is not effective.

Mixed hyperthyroidism (multinodular goiter with toxic thyroiditis) is typically managed with antithyroid drugs and steroids. Occasionally, traditional management of hyperthyroidism fails or thyrotoxicosis recurs in patients who continue amiodarone therapy. Subtotal or near total thyroidectomy is required for both forms of hyperthyroidism if more conservative therapy fails.

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