

Total thyroidectomy in a patient with amiodarone-induced thyrotoxicosis and thiamazole related hepatotoxicity

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ABSTRACT

Total thyroidectomy in a patient with amiodarone-induced thyrotoxicosis and thiamazole related hepatotoxicity

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Amiodarone-induced thyrotoxicosis is a rare but serious complication of amiodarone use, especially in patients with severe cardiac disease. We discuss the anaesthetic considerations and management of patients with severe cardiac disease who require lifesaving thyroidectomy. We present a patient who developed amiodarone-induced thyrotoxicosis, following administration of amiodarone and hepatotoxicity due to thiamazole. Patient's life depended upon surgery as soon as possible. Total thyroidectomy was performed under general anaesthesia with precautions related to hyperthyroidism and cardiac stability. Complete cardiac rehabilitation was achieved two weeks after surgery. Total thyroidectomy is, in selected cases, the only treatment option and should not be delayed based on the hypothesis that pre-operative medical preparation will optimize the patient's condition (endocrine and cardiac).

INTRODUCTION

Amiodarone is considered an optimal therapy to maintain sinus rhythm in patients with atrial fibrillation as it can be safely used in patients with left ventricular dysfunction. However, it has many side effects, being the most hazardous the thyroid dysfunction. Amiodarone-induced thyrotoxicosis (AIT)

is considered a rare complication¹. The only identified predictor of AIT is age <62years². AIT is classified as types 1 and 2^{1,3}. Type 1 is similar to iodine-induced thyrotoxicosis and type 2 is similar to sub-acute thyroiditis^{1,3}. Anti-thyroid drugs are used to treat type 1 and type 2 is treated using glucocorticoids and, if possible, amiodarone should be discontinued^{1,3}. Accurate determination of AIT type is not always possible and mixed disease forms also

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exist⁴. Most patients with moderate to severe AIT require glucocorticoids⁴. Hepatotoxicity is a well-known complication of anti-thyroid therapy. Prompt recognition of drug induced toxicity and cessation of therapy is crucial to decrease the risk of acute liver failure and avoid chronic consequences⁵. Total thyroidectomy sometimes is the only treatment option.

CASE REPORT

We report a case of a 52-year-old man admitted with an acute myocardial infarction, treated with coronary angioplasty and stent implantation. During the hospital stay, the patient developed atrial flutter/fibrillation and refused radiofrequency ablation. Medical treatment with amiodarone (300 mg per day) and acenocoumarol was initiated. One year later, thyroid function tests demonstrated an increased free T4 (4.06 ng/dL; normal values (NV): 0.61– 1.12), free T3 (9.23 pg/mL; NV: 2.5–3.9), and decreased TSH (0.01 μ UI/mL; NV: 0.34–5.6). Mixed AIT was diagnosed and amiodarone therapy was discontinued. The patient started therapy with bisoprolol (5 mg per day), thiamazole (10 mg twice a day) and prednisolone (5 mg per day). Electrical cardioversion was performed with success, after transesophageal echocardiogram excluded thrombus. Two months later, patient was admitted for medical treatment due to recurrent atrial fibrillation. Laboratory tests revealed the following biochemical results: free T4 1.49 ng/dL, free T3 3.22 pg/mL, TSH 0.03 μ UI/mL, aspartate transaminase

147 UI/L (<37), alanine transaminase 323 UI/L (<37) and gamma-glutamyltranspeptidase 103 UI/L (<49); lactate dehydrogenase 696 UI/L (266-500) and total bilirubin 1.20 mg/dL (<1.00). Extra-hepatic obstruction was ruled out with an abdominal ultrasonogram. Analytical evaluation suggested probable adverse drug reaction (CIOMS/RUCAM =8 points) to thiamazole. Radiofrequency ablation of the atrial fibrillation was proposed but the patient refused again.

Concerns regarding the duration of hyperthyroidism, the need of antiarrhythmic therapy and the risk of liver failure led to the decision of performing a total thyroidectomy. Lugol's solution (12 drops three times a day) was started two weeks before surgery, in an attempt to control thyroid hormone release. The hormones baseline levels on 7th and 14th increased, heart rate control was still inadequate and cardiac function declined despite therapeutic measures. Pre-operative echocardiography showed left ventricular ejection fraction of 34%, normal sized ventricular chambers, mild atrial dilatation, and mild tricuspid and mitral regurgitation. The patient was premedicated with midazolam 3 mg and hydrocortisone 200 mg. Patient was monitored with standard bispectral index (BIS), nasopharyngeal thermometer, electrocardiogram, invasive blood pressure, pulse oximetry and neuromuscular monitoring. Before anesthetic induction, patient was hemodynamically unstable due to atrial fibrillation with rapid ventricular response (180 bpm). Esmolol (20 mg), digoxin (0,5 mg) and

amiodarone (300 mg) were administered. Heart rate decreased to less than 100 bpm and medium arterial pressure was 90 mmHg. Pre-oxygenation with O₂ at 100% via facial mask was performed until O₂ end-tidal superior to 80% and general anesthesia was performed. Induction started with fentanyl (2 mcg/kg) and etomidate (0,25 mg/kg). Rocuronium (0, 6mg/kg) was given and intubation was performed after no responses on neuromuscular block monitoring. Central venous catheter on subclavian vein was inserted. Anesthesia was maintained with sevoflurane and remifentanyl, titrated to maintain a BIS between 40 and 50. After surgical incision, patient developed bradycardia (34 bpm) and hypotension (MAP<50 mmHg). Noradrenaline infusion was initiated because of insufficient response to intravenous bolus of atropine (1 mg) and phenylephrine (300 mcg). There were no other intraoperative complications until the end of the procedure.

After the surgery, the patient was transferred to Intensive Care Unit due to the need of vasoactive drugs support. During the first postoperative day, heart rate remained high with hypotension. Bisoprolol and amiodarone were initiated for rhythm control. On the 3rd postoperative day, sinus rhythm with controlled heart rate (50-60bpm) was achieved and cardiovascular drugs were stopped. Thyroid function tests improved gradually in the first week and the patient started on thyroxine, oral calcium and calcitriol (iatrogenic hypoparathyroidism). Two weeks after surgery, he was asympto-

matic, hemodynamically stable in sinus cardiac rhythm under bisoprolol therapy. Control echocardiography was normal, with left ventricular ejection fraction of 59%. The patient was discharged from hospital with follow-up appointment in Cardiology and Endocrinology.

DISCUSSION

Thyrotoxicosis may be a consequence of chronic amiodarone therapy. Accurate determination the type of AIT is not always possible and treatment should be directed for both types of AIT. The first line treatment includes amiodarone discontinuation and therapy with thiamazole and prednisolone according to response and severity^{3,4}. Previously uncontrolled rhythm disorders can reappear due to cardiac thyrotoxicosis.⁶ A rebound rise in T₃ and loss of beta blockade may exacerbate thyrotoxicosis upon stopping amiodarone therapy^{3,6}. Beta-blocker was started for rhythm control and successful electrical cardioversion was performed after transesophageal echocardiogram. Anti-thyroid drugs have risks and although hepatotoxicity is rare, it is possible. In this case, the inability to continue anti-thyroid drugs, the need of anti-arrhythmic therapy and the risk of liver failure caused concerns regarding patient's prognosis. It was then decided to perform a total thyroidectomy.

Clinical manifestations of uncontrolled thyrotoxicosis can, occasionally, be a reason for surgery before obtaining a euthyroid state. Preoperative

evaluation and optimization were extremely important, but only few improvements were possible. In regard to hyperthyroidism, Lugol's solution was administered two weeks prior to surgery to inhibit the release of thyroid hormone into the circulation and hydrocortisone was given in the beginning of surgery to suppress T4 conversion to T3. Anti-thyroid medication was continued in the perioperative period. Benzodiazepines were used for anxiolysis. Cardiovascular instability is influenced by thyroid hormones^{1,6}. High levels of T3 and T4 increase systemic vascular resistance and decrease relaxation time with repercussions in heart rate, ejection fraction, cardiac output, and blood volume¹. Hyperthyroidism predisposes the development of supraventricular arrhythmias, especially if the patient has already rhythm disturbances¹. Our patient presented for surgery with atrial fibrillation with rapid ventricular response (180 bpm). Esmolol, digoxine and amiodarone were administered and heart rate was controlled. Besides hemodynamically instability, it was decided to perform surgery since the patient had clinical manifestations of uncontrolled thyrotoxicosis. In these cases, total thyroidectomy may be the only treatment and should not be delayed based on the patient's condition⁶. It is generally advised to control cardiovascular responses evoked by sympathetic nervous system stimulation with beta-blockers, especially short acting agents. However, this patient was refractory to beta-blocker alone. The potential risk of severe bradycardia and sinus

arrest (resulting from the interaction between beta-blockers and amiodarone) must be taken into account⁶. Thyrotoxicosis can progress to a thyroid storm, which is associated with high mortality rates. Thyroid storm may be induced by surgery or changes in sympathetic nervous system.

Etomidate and fentanyl were used for induction because they have little cardiodepressor effect. Because thyrotoxicosis is associated with an increased incidence of myopathies neuromuscular block should always be monitored. As thyrotoxic state is a hypermetabolic clinical syndrome, catecholamines are secreted in abundance. Indirectly acting adrenergic agonists can cause unexpected rises in blood pressure and arrhythmias. Phenyphrine or noradrenaline are more appropriate choices if necessary. Early recognition of thyroid storm is of extreme importance so body temperature and invasive pressure monitoring are gold standard monitoring.

CONCLUSION

Amiodarone is increasingly used for ventricular and supraventricular arrhythmias. Therefore, AIT may be found more often in patients with cardiac disease. Medical treatment of thyrotoxicosis should be started, in first instance, in an attempt to render euthyroid state. It is desirable for the patient to be euthyroid prior to surgery. However, thyroidectomy may be necessary and live saving in patients with thyrotoxicosis and severe cardiac disease. In these circumstances, and if done rapid-

ly, may result in complete cardiac recovery. Thyroidectomy allows for rapid control of the thyrotoxicosis and safe re-introduction of amiodarone.

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Author Disclosures:

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