Introduction

Among the amiodarone-induced thyroid dysfunctions, thyrotoxicosis is the most troublesome with the highest rate of morbidity and mortality. Thyrotoxicosis is associated with increased cardiovascular morbidity and mortality, primarily due to heart failure and thromboembolism. Amiodarone-induced thyrotoxicosis (AIT) is a potentially serious condition that requires prompt diagnosis and careful treatment.

Amiodarone, used in the treatment of supraventricular and ventricular arrhythmias, is rich in iodine. A daily dose of 200 mg corresponds to an intake of 75 mg of organic iodine and generates about 7 mg of free iodine. In comparison, the normal dietary iodine requirement is only 100 to 200 mg/day. Accumulation of amiodarone in the thyroid gland may result in thyroid dysfunction, either hypothyroidism or thyrotoxicosis.

AIT is more prevalent in areas with low iodine intake (like many European countries), at the same time as hypothyroidism is more frequent in areas with high iodine intake (like the United States and the United Kingdom). In countries with high iodine intake, the incidence of AIT is about 2% among patients taking the drug, whereas in countries with low iodine intake it may be as high as 10%.

The pathogenesis of AIT is complex and not completely understood. Three mechanisms have been postulated:

- Iodine may have an effect on thyroid autoregulatory mechanisms and cause an excessive

Abstract.

A female patient was admitted to our Department for total thyroidectomy in amiodarone-induced thyrotoxicosis. The drug was prescribed for ventricular arrhythmia and atrial paroxysmal fibrillation in dilated cardiomyopathy due to chronic aortic regurgitation with left ventricular dysfunction (ejection fraction 35%; Class Functional NYHA III) and moderate-severe respiratory insufficiency.

The cardiologist-anesthetist team has allowed to evaluate the surgical-cardiovascular-anesthesiologic risks and the balance between the improvement by the amiodarone administration for the arrhythmia, and the discontinuation of this treatment in order to prevent aggravation of the thyrotoxicosis.

These hypotheses were subsequently discharged for the two reasons listed below:

- several other antiarrhythmic drugs (that didn’t show equivalent efficacy as amiodarone in preventing or converting such ventricular and atrial arrhythmias) may be proposed in the place of amiodarone. However, this could expose the patient to an arrhythmia;
- a clear proof that the suspension of amiodarone can allow restoring normalization of the thyroid function doesn’t exist.

Therefore, the patient has been successfully submitted to the surgical intervention and in the follow-up we brought her back to a state of normalized thyroid function and cardiovascular conditions.

In patients that cannot safely discontinue amiodarone or when medical therapy is ineffective in controlling thyrotoxicosis, thyroidectomy is the treatment of choice.

Key Words:

Amiodarone, Thyrotoxicosis, Heart failure, Thyroid surgery, Ventricular arrhythmia.
hormone synthesis, particularly in patients with primary thyroid autonomy;
• Amiodarone may have a direct cytotoxic effect, suggested by the destructive, inflammatory histologic changes and increased levels of cytokines and thyroglobulin;
• Amiodarone may trigger an autoimmune response towards the thyroid gland, but this mechanism remains controversial.

The diagnosis is based on low concentrations of TSH with normal or free T4 and free T3 levels, negative thyroid-stimulating immunoglobulins, and low or absent tracer uptake on thyroid scintigraphy. TSH levels should be assessed in all patients before starting amiodarone therapy, at 6 months, and once or twice yearly thereafter2.

Amiodarone treatment should be stopped safely whenever possible. However, it’s not clear if the remission rate of thyrotoxicosis could be decreased if amiodarone treatment is stopped. So it’s very important to evaluate the risks of a discontinuation of amiodarone therapy especially in a patient with severe ventricular arrhythmias.

The choice of antithyroid treatment can be guided by distinguishing two forms of AIT1,2,4. In type 1, patients have a goiter, positive thyroid immunoglobulins, abnormal 24-hour radioiodine uptake, and only slightly increased interleukin-6 levels. Type 1 occurs in patients with primary thyroid disease and treatment consists of a combination of a thionamide (propylthiouracil, methimazole) to inhibit hormone biosynthesis, and potassium perchlorate to block thyroid iodine transport. Type 2 patients have no goiter, no thyroid immunoglobulins, normal radioiodine uptake, and markedly increased serum interleukin-6 levels. Type 2 occurs in patients with the result from a destructive thyroiditis. Corticosteroids, alone or in combination with thionamides, have been credibly demonstrated to be effective in this setting.

However, because a mixed form of AIT may occur frequently, patients should be approached rationally with an initial combination of propylthiouracil or methimazole and potassium perchlorate, with steroids added after 2 weeks if no improvement occurs. If the thyrotoxicosis does not respond to this therapy, lithium may be a valid alternative5.

A total or subtotal thyroidectomy is indicated in patients with large goiters causing airway obstruction, malignant or equivocal nodules on fine-needle aspiration and severe hyperthyroidism that does not respond to conservative treatment. Surgery has been associated with low rates of perioperative morbidity and mortality, even in the presence of thyroid storm, heart failure, and refractory arrhythmias.

In conclusion, surgical therapy may be performed safely and successfully in patients with AIT.

Case report

In this study we report the case of a 65 years old female patient, with a history of dilated cardiomyopathy (CMPD) due to moderate-severe aortic regurgitation (AR) complicated by ventricular arrhythmia (VA) and paroxysmal atrial fibrillation (FAP), who developed severe AIT.

The patient was admitted to our Department for an hyperfunctioning multi-nodular goiter.

The patient dates back the clinical history concerning her thyroid disease to about 20 years ago when, performing a thyroid echography, multiple nodular formations in both lobes are noticed and for such motive she is submitted to a therapy with the dose of 5 mg/die of Methimazole.

In the last 2 years, because of her CMPD complicated by VA e FAP, both associated with severe haemodynamic changes, was started a different antiarrhythmic drugs but successful was only Amiodarone 200 mg orally resulted in this case in a successful and safety controlling of both arrhythmias and safe and effective for the maintenance of normal sinus rhythm.

Afterwards a series of symptoms to tied a hyperfunctioning of the thyroid gland, like loss in weight (12 kg in the arc of the 2 years), hair loss, insomnia, nervousness, etc., started to reveal.

In December of the 2004, while performing the analysis of the thyroid hormones, values of FT4 23.33 pmol/l, FT3 3.63 pmol/l, TSH 0.970 µIU/ml, Ab anti-TSH < 5 U/l TSH were revealed.

In 2005 June, the patient underwent a thyroid scintigraphy with iodine 131 that revealed captation values of the radioiodine lower than normal because of a presumable interference caused by the contemporary assumption of Amiodarone.

In the same period another thyroid echography was performed and revealed a thyroid with dimensions moderately increased (right lobe APD: 23 mm and left lobe APD: 21 mm ) with
outline finely irregular, slightly disomogeneous eco-structure and, in particular, a few sub-centimeter nodular formations of colloidal-cystic aspect (at least 3 in the right lobe of 10.6 mm; 3.6 mm; 5.4 mm and 2 in the left lobe of 10.3 mm and 10 mm) and a greater one of about 1 cm in diameter placed in the left of the isthmus center of solid aspect and isoechoic structure with thin rarefaction halo of the echoes. The trachea appeared in axle and there was no notice of lymphadenopathy in latero-cervical compartments.

After some month from the beginning of the therapy with Amiodarone the patient reported pharmacological intolerance to Methimazole which was substituted with Propylthiouracil 50 mg/die.

During the hospitalization we pointed out an ECG with an Atrioventricular Block I degree and complete Left Bundle Branch Block, a moderately dilated left ventricular with hypertrophy, ejection fraction 35-40%, moderate-severe aortic valvular regurgitation, light-moderate mitral insufficiency and light tricuspidal insufficiency with normal systolic pressure in pulmonary artery. At this time the patient was in III NYHA functional Class; there was besides a severe broncopathy with hypoxic emphysema. The patient underwent an operation of total thyroidectomy and, after a short hospitalization in the Intensive Care Unity where the vital parameters were constantly watched, agreed the basic arrhythmic pathology, returned in our Department from which she was then discharged.

**Discussion**

It is standard practice to render thyrotoxic patients euthyroid preoperatively. Despite the obvious difficulties with management of patients with Amiodarone-associated thyroid disease, anaesthesia and surgery may be performed safely and successfully.

For many authors radioiodine treatment is recommended as a definitive treatment for this form of disease. The timing and dose of radioiodine treatment will depend on the severity of thyrotoxicosis and the response to anti-thyroid drugs. Radioiodine treatment is not effective in type II AIT.

Amiodarone-associated thyroid disease may be severe and refractory to medical therapy. Despite the potential risks of anaesthesia associated with uncontrolled thyrotoxicosis, thyroidectomy should be considered in the scene of severe thyrotoxicosis. Near total thyroidectomy is ideally a definitive and often preferred treatment option in both forms of thyrotoxicosis, especially when is not possible to discontinue Amiodarone-therapy. Thyroidectomy has been carried out in type I AIT patients, but thyroid surgery in thyrotoxic patients, especially those with cardiac problems, carries a high surgical risk. Thyroidectomy is also an option if amiodarone has to be continued or reintroduced.

In this case, we have thought that the substitution of the Amiodarone with other second choice drugs like Sotalol or Propafenone would have been risky because of second choice and less effective instead of Amiodarone. Besides, from the various published works in literature, there is no proof that discontinuing Amiodarone-therapy of a patient suffering from AIT, this one regresses. After all, in our specific case, we have been forced to operate to avoid possible cardiac problems caused by the suspension or by the substitution of amiodarone-therapy. We had forced to follow a surgical way because we haven’t other possible ways. The treatment with Amiodarone would have damaged the thyroid function and the hyperthyroidism would have damaged the cardiac functionality.

So the question that we posed to ourselves is: in a patient with a less serious arrhythmic pathology and with lesser risks, would it be rational to change the Amiodarone antiarrhythmic therapy waiting for a return to the normal thyroid functionality?

At last we believe that in patients who cannot safely discontinue amiodarone or when medical therapy is ineffective in controlling thyrotoxicosis, thyroidectomy is to be considered the treatment of choice.

**References**


