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ORIGINAL ARTICLE

Treatment of Amiodarone-Induced Thyrotoxicosis with Plasmapheresis and Thyroidectomy

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Amiodarone is an antiarh ythmic drug which may produce secondary effects on the thyroid function. We report a case of severe amiodarone-induced thyrotoxicosis in a 56-year-old patient. Because of dramatic clinical manifestations, plasmapheresis was performed as a first step in management of thyrotoxicosis and an improvemen t of clinical status was observed. Pharmacological therapy with thionamide, dexamethasone, betablocker and lithium carbonate was started. Clinical status worsened progressively and the decision to operate was made after 9 weeks of inefficient pharmacological therapy. Before surgery, the patient was submitted to plasmapheresi s daily and she became euthyroid after the 5th plasmapheresis. Subsequently, total thyroidec tomy was performed which resulted in an absolute cure of thyrotoxicosis withou t complications. We suggest that a combination of plasmapheresis and thyroidectomy warrants consideration as definitive treatment for resistant amiodarone-induced thyro toxicosis.

Key words: **Amiodarone, amiodarone-induced thyrotoxicosis, plasmapheresis, thyroidec tomy**

Introduction

Amiodarone is an iodine rich drug used in the treatment of various tachyarhythmias which has many effects on the thyroid function test and/or thyroid hormone metabolism (1). Amiodarone-induced thyrotoxicosis (AIT) occurs more frequently in areas with low iodine intake that may be refractory to conventional pharmacological therapy even in the event of discontinuation of amiodarone treatment (1, 2). The evolution of AIT can be very severe requiring an aggressive therapy with multiple drugs which may in some cases be ineffective or fail to alter the dramatic course of clinical manifestations (1, 3-6).

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We report a case of AIT successfully treated with a combination of plasmapheresis and surgery because of the failure of pharmacological treatment consisting of propylthiouracil (PTU), dexamethasone (DXT), lithium carbonate and betablocker.

Case Report

A 56-year-old female presented with a ten days history of severe clinical hyperthyroid signs and symptoms such as mild fever, tachycardia, tremor, persistent sweating, intolerance of heat easy fatiguability and generalised weakness. She had a history of amiodarone treatment during the last 6 months for paroxysmal atrial fibrillation. On physical examination, she appeared jittery, restless, irritable and emotionally labile. Blood pressure was 120/80 mmHg, pulse rate 104/min with a regular rhythm and fever was 37.5°C. The thyroid-stimulating hormone (TSH) level was low (0.027 mU/l), free thyroxine (FT_4) and triiodothyronine (FT_3) levels were high (>77.22 and 0.399 nmol/l). Antithyro-

globulin and antimicrosome antibodies were negative. Ultrasound of the thyroid showed an echogenic nodule, 5x10 mm in size and minimal enlargement of both lobes.

Amiodarone-induced thyrotoxicosis was diagnosed and amiodarone was discontinued. Because of dramatic clinical manifestations, the patient was submitted to plasmapheresis and pharmacological therapy with PTU (600 mg), DXT (3 mg), lithium carbonate (600 mg) and propranalol (60 mg) daily at was started. After plasmapheresis, serum FT_3 level decreased promptly (0.950 nmol/l), while FT_4 level did not alter (>77.22 nmol/l), but a clear-cut clinical amelioration was observed. Although she received high dose antithyroid treatment for up to 2 months, serum levels of thyroid hormones increased and clical status worsened progressively during this period. In the patient the decision to operate was made after 9 weeks of inefficient pharmacological therapy. Before surgery, plasmapheresis was performed daily in an attempt to decrease operative risk. Serum levels of FT_3, FT_4 and TSH after plasmapheresis are shown in Table 1. On the 5th day of plasmapheresis, total thyroidectomy was performed. In the intra and postoperative period, we did not observe any arhythmia or complication. Surgery resulted in absolute cure of thyrotoxicosis.

Table 1. Serum hormone levels* before and after plasmapheresis.

	FT_3(nmol/l)	FT_4(nmol/l)	TSH(mU/l)
Before plasmapheresis	0.144	66.28	0.019
After plasmapheresis			
1st day	0.094	62.41	0.012
2nd day	0.051	54.69	0.176
3rd day	0.036	35.00	0.212
4th day	0.041	31.91	0.204
5th day	0.037	26.51	0.288

* Normal values: FT_3: 0.022-0.053 nmol/l, FT_4: 9.23-23.80 nmol/l, TSH: 0.49-4.67 mU/l.

Discussion

Amiodarone is a benzofuran derivative containing two atoms of iodine molecule (37.5% of molecular weight). In iodine-deficient areas, AIT occurs in 2-12% of patients receiving amiodarone (1). Amiodarone may induce excessive thyroid hormone synthesis since the drug induces an iodine overload (type I) or destructive thyroiditis (type II). Differentiation between type I and type II may not always be feasible and there may be a combination of two forms of AIT (1, 2). Because of severe clinical status and refraction to the aggressive therapy, we thought that our case was an AIT type I. The treatment strategies of AIT remain controversial but it must be tailored individually. The discontinuation of amiodarone therapy may in some patients be fatal because of underlying cardiac arhythmia. Most cases may have persistent thyrotoxicosis even several months after amiodarone withdrawal since it has a prolonged half-life (2).

Although the present case had dramatic clinical manifestations of AIT, luckily, discontinuation of amiodarone therapy did not start cardiac arhythmia during follow-up. It would seem that the initial plasmapheresis may be useful in order to obtain a rapid amelioration of the severe clinical picture of thyrotoxicosis. Subsequently, it was decided to continue with pharmacological therapy including high doses of PTU, DXM, low doses of beta-blocker and lithium carbonate. High doses of thionamides are required as thionamides are less effective in the presence of high intrathyroidal iodine concentrations (1, 4). High dose corticosteroid treatment may be beneficial in AIT (1,7) by inhibiting conversion of T_4 to T_3 and by leading to a rapid recovery from thyroiditis. It has been shown that a combination of lithium carbonate and PTU is an effective therapy in patients with severe AIT by leading to faster normalisation of the hyperthyroid state (8). Although there are many reports suggesting that these treatment modalities may be successful in patients with AIT, we found that all of these drug treatments were ineffective after 9 weeks in our patient.

The effectiveness of plasmapheresis is controversial. It has been suggested that plasmapheresis is effective when drug treatment of thyrotoxicosis fails (9). In some case reports, however, plasmapheresis failed to control thyrotoxicosis (7, 10). Some authors have described a decrease in active thyroid hormone levels and a rapid deterioration of patients' clinical condition following plasmapheresis (9, 10).

We showed that plasmapheresis is effective on more rapid normalisation of thyroid hormone levels and a rapid amelioration of dramatic clinical status, however, the efficacy of plasmapheresis was not permanent. For this reason, when the patient became euthyroid after the 5th day of plasmapheresis, we performed total thyroidectomy. Some authors have suggested that total or near-total thyroidectomy is an alternative therapy for AIT (3-6). In our case, total thyroidectomy resulted in the resolution of thyrotoxicosis without complications.

In conclusion, we think that a combination of plasmapheresis and total thyroidectomy is safe and rapidly effective in controlling thyrotoxicosis in aggressive forms of AIT which are refractory to intensive pharmacological therapy and, perhaps, in patients who need continued amiodarone treatment.

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