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Successful Surgical Treatment of Refractory Amiodarone-Induced Thyrotoxicosis Causing Tachycardiomyopathy

A. Marinis, G. Vassilopoulos, A. Avraamidou, T. Vassilakaki, P. Bassioukas, S. Rizos

Abstract

Amiodarone is a well-established pharmacologic therapy used for several types of tachyarrhythmia. However, it is associated with potential adverse effects on thyroid function due to its high iodine concentration. Amiodarone-induced thyrotoxicosis (AIT) is considered a difficult diagnostic problem that requires careful therapeutic strategy in order to balance the cardiologic and endocrine dysfunction associated with this condition. Herein, we report the case of a 52-year-old male patient who suffered from tachyarrhythmia due to paroxysmal atrial fibrillation. The patient had experienced recurring episodes of atrial fibrillation despite medical therapy with propafenone, sotalol and pulmonary vein isolation with catheter ablation. Amiodarone was subsequently administered, and temporary control of the arrhythmia was achieved. Six months after amiodarone treatment, the patient presented with uncontrollable tachycardia leading to heart failure, a condition known as tachycardiomyopathy. The thyroid function was assessed, and amiodarone-induced thyrotoxicosis was diagnosed. Unfortunately, AIT was refractory to treatment with carbimazole and cortisone and a surgical approach was decided. The patient eventually underwent a total thyroidectomy with complete control of the underlying arrhythmia, without the necessity for β-blockers. Heart failure was reversed and the patient has resumed his normal daily activities.

Key words *Amiodarone, thyrotoxicosis, tachyarrhythmia, tachycardiomyopathy*

Introduction

Amiodarone is a well-established pharmacologic therapy used for several types of tachyarrhythmia. However, it is associated with potential adverse effects on thyroid function (hyperthyroidism) due to its high iodine concentration and its effects on thyroid hormones, a condition known as amiodarone-induced thyrotoxicosis (AIT) [1]. Overt thyrotoxicosis aggravates the underlying tachyarrhythmia and is managed by amiodarone discontinuation and administration of beta-blockers, antithyroid drugs and cortisone. Rarely, patients with AIT may fail to respond to medical therapy and should be managed by thyroidectomy before they become excessively debilitated by uncontrollable tachyarrhythmia and inadequately treated thyrotoxicosis. Herein, we report a case of AIT with deteriorating heart failure which was treated surgically.

A. Marinis, P. Bassioukas, S. Rizos
First Department of Surgery, Tzaneio General Hospital, Piraeus, Greece

G. Vassilopoulos
Department of Clinical Therapeutics, University of Athens Medical School, "Alexandra" General Hospital, Athens, Greece

A. Avraamidou
Department of Anaesthesiology Tzaneio General Hospital, Piraeus, Greece

T. Vassilakaki
Department of Pathology, Tzaneio General Hospital, Piraeus, Greece

Corresponding author: Athanasios Marinis, MD, PhD
1 Zanni & Afentouli street, 18536, Piraeus, Greece
Tel.: +30-4592493 / Fax: +30-2104592491
E-mail drmarinis@gmail.com

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Case report

A 52-year-old male patient was admitted to our Surgical Department for management of an AIT that was refractory to medical therapy. His history had started five years earlier when the patient presented with palpitations, fatigue, and shortness of breath and was found to be in atrial fibrillation. The patient had experienced recurring episodes of atrial fibrillation and had received warfarin for stroke prevention. He had required direct-current cardioversion to restore sinus rhythm on two occasions, despite treatment with propafenone and subsequently with sotalol. Catheter ablation failed to reduce the recurrences of atrial fibrillation, and amiodarone was consequently administered, and temporary control of the arrhythmia was achieved. Six months later, tachycardia relapsed in an uncontrollable fashion, progressively leading the patient to heart failure (tachycardiomyopathy).

Amiodarone-induced thyrotoxicosis was diagnosed due to excess serum thyroid hormones and suppressed TSH (<0.01 mU/L). Thyroid ultrasound revealed a slightly enlarged thyroid, with heterogeneous echogenity and increased vascularity with colour Doppler (Figure 1). Tc-99m thyroid scintigraphy with γ-camera demonstrated decreased

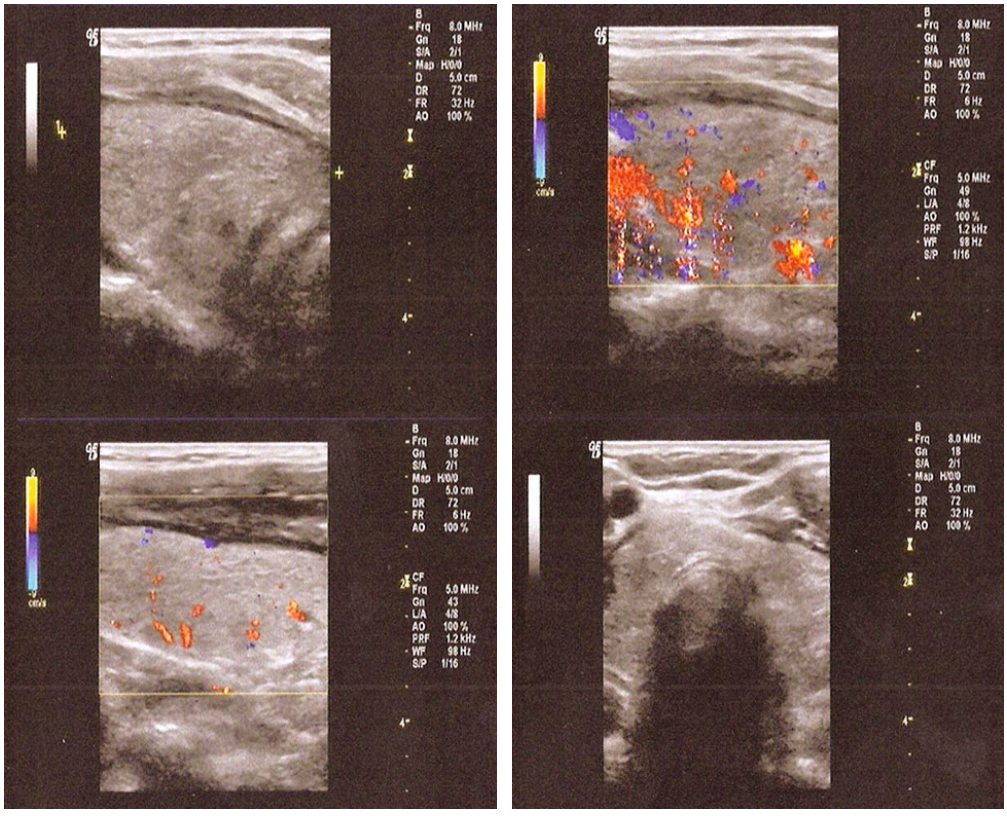

Figure 1. Thyroid ultrasonography demonstrating heterogeneous echogenity and increased vascularity on color Doppler.

absorption of the radionuclide without any localized lesions (Figure 2). Fine-needle aspiration cytology (FNAc) was non-diagnostic. The patient was treated with high doses of carbimazole (40mg tid) initially and cortisone addition (prednisolone 16mg daily), as well as propranolol 100mg bid without an acceptable response of either the tachycardia or the thyroid dysfunction. Consequently, the patient was referred for surgical treatment of refractory thyrotoxicosis which had caused debilitating heart failure (ejection fraction 30-35%). Prior to receiving amiodarone, the patient had no history of thyroid dysfunction or abnormality. A total thyroidectomy was offered, and the patient was discharged on postoperative day 2 without any perioperative morbidity or complications associated with the operation. Histopathologic examination of the surgical specimen revealed a nodular goiter with follicular hyperplasia (Figure 3).

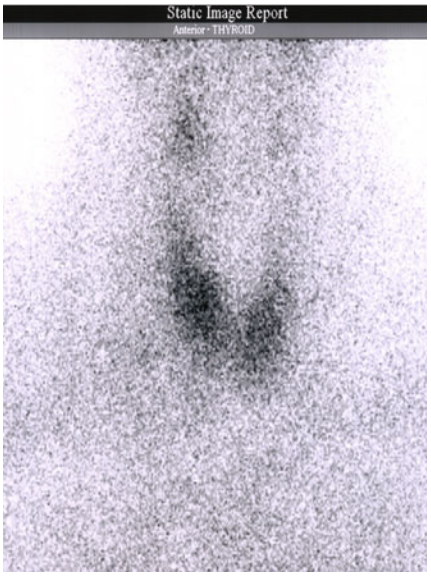

Figure 2. Thyroid scintigraphy with Technetium 99m and γ-camera showing decreased absorption of the radionuclide without any localized lesions.

Two weeks after thyroidectomy, the patient experienced better tolerance of physical activity, reduced his β-blocker regimen and demonstrated a higher ejection fraction (50%) on heart ultrasound. One month postoperatively, the patient has discontinued his β-blocker and has returned to normal daily activity.

Discussion

Amiodarone is a well-known class III anti-arrhythmic agent currently indicated for the management of several tachyarrhythmias due to its β-adrenergic inhibiting

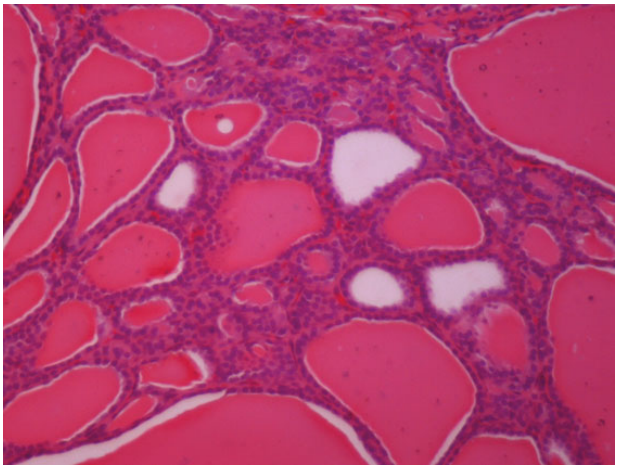

Figure 3. Nodular goiter with follicular hyperplasia (E&H, x200)

mechanism of action. However, the amiodarone molecule contains two iodine atoms which constitute 37.5% of the drug's mass, resulting in excess iodine consumption. More specifically, amiodarone-induced thyrotoxicosis complicates the arrhythmiologic problem of the patient, aggravating the underlying tachycardia for which the drug is administered. AIT has a relative predominance in men (M:F ratio 3:1) [2] and occurs in up to 6% of patients treated with amiodarone in iodine sufficient deprived countries and up to 10% in iodine deprived areas [1].

This condition is classified into two types [3]: type I, caused by the high iodine concentration of amiodarone and type II, an amiodarone-related destructive thyroiditis, although mixed forms occur as well. Type I usually occurs in patients with pre-existing non-toxic multinodular goiter or underlying Grave's disease and occasionally demonstrates measurable radioactive iodine uptake (RAIU) and increased vascular flow on colour-flow Doppler ultrasound [1]. In our case report, the patient did not have a known history of goiter, and he demonstrated increased vascularity on ultrasound and decreased Tc-99m uptake; hence, he could not be clearly classified as one of the two types.

The main consideration in AIT is that it usually becomes necessary to discontinue amiodarone, and this must be decided following cardiologic consultation. According to currently established recommendations [1], discontinuation of amiodarone is a difficult decision since it might be the only effective way to control tachyarrhythmia. It is often a controversial decision due to its delayed elimination from fat storages and its T3-antagonistic effect at cardiac level, increasing T3 conversion after stopping the drug which can aggravate the underlying arrhythmia. In our case, overt thyrotoxicosis necessitated immediate amiodarone discontinuation.

Current management guidelines [1] are based on the AIT type: type I is best treated with antithyroid drugs (usually methimazole 40mg daily), while type II is managed with anti-inflammatory agents (cortisone). In our case, in which a clear distinction between both types of AIT was not possible, initial treatment with carbimazole was followed by the addition of prednisone without, however, controlling the thyrotoxicosis. Refractory AIT to aggressive medical combination treatment is currently considered a clear indication for total thyroidectomy [1,4], as was the case in our patient. Although thyroidectomy in the setting of uncontrolled arrhythmia and thyrotoxicosis is associated with a significant morbidity and mortality rate (9%) [1], the patient should be advised that both rates are significantly higher in the absence of consent to surgical treatment. On the other hand, thyroidectomy effectively controls thyrotoxicosis and associated tachyarrhythmia, permitting further amiodarone use. In our patient, thyroidectomy resulted in control of thyrotoxicosis (discontinuation of antithyroid drug and cortisone) and complete reversal of tachyarrhythmia and, more importantly, the associated heart failure. Our patient gradually decreased the beta-blocker dose and, finally, discontinued it with his ejection fraction returning to normal levels.

In conclusion, patients with AIT and aggravating tachyarrhythmias should be initially managed with antithyroid drugs and cortisone, substituting amiodarone with other beta-blockers and, if both conditions (thyrotoxicosis and arrhythmia) are not appropriately controlled, thyroidectomy should be considered as it is the safest and most effective method of treatment for controlling thyrotoxicosis and reversing tachyarrhythmia and associated heart failure.

Conflict of interest

There is no conflict of interest

Informed consent

Written informed consent was obtained from the patient

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Επιτυχής Χειρουργική Θεραπεία Ανθεκτικής Θυρεοτοξίκωσης από Αμιοδαρόνη που Προκαλούσε Ταχυκαρδιομυοπάθεια

Α. Μαρίνης, Γ. Βασιλόπουλος, Α. Αβραμίδου, Θ. Βασιλακάκη, Π. Μπασιούκας, Σ. Ρίζος

Περίληψη

Η αμιοδαρόνη αποτελεί σήμερα μια καλά τεκμηριωμένη φαρμακολογική θεραπεία για την αντιμετώπιση ποικίλων ταχυαρρυθμιών. Παρ' όλα αυτά, σχετίζεται δυνητικά και με την εμφάνιση ανεπιθύμητων δράσεων στη λειτουργία του θυρεοειδή, κυρίως λόγω της μεγάλης περιεκτικότητάς της σε ιώδιο. Η θυρεοτοξίκωση από αμιοδαρόνη θεωρείται δύσκολο διαγνωστικό πρόβλημα κι απαιτεί μια προσεγμένη θεραπευτική στρατηγική, προκειμένου να επιτευχθεί ισορροπία μεταξύ της καρδιολογικής κι ενδοκρινικής δυσλειτουργίας που σχετίζονται με την κατάσταση αυτή. Στην αναφορά αυτή παρουσιάζουμε έναν άνδρα 52 ετών με ιστορικό ταχυαρρυθμιών λόγω παροξυσμικής κολπικής μαρμαρυγής, η οποία υποτροπίαζε παρά τη θεραπεία με προπαφενόνη, σοταλόλη και την απομόνωση της πνευμονικής φλέβας και τη διακαθετήρια κατάλυση με υψίσυχνο ρεύμα (RFA). Αισίως, η χορήγηση αμιοδαρόνης είχε ως αποτέλεσμα τον παροδικό έλεγχο της αρρυθμίας. Έξι μήνες μετά ο ασθενής επανεμφάνισε μη ελεγχόμενη ταχυκαρδία που οδήγησε σε καρδιακή ανεπάρκεια, μια κατάσταση που ονομάζεται ταχυκαρδιομυοπάθεια. Η θυρεοειδική λειτουργία ελέγχθηκε και διαγνώσθηκε θυρεοτοξίκωση από αμιοδαρόνη. Δυστυχώς, η κατάσταση αυτή ήταν ανθεκτική στη θεραπεία με καρβιμαζόλη και κορτιζόνη, οπότε αποφασίσθηκε η χειρουργική θεραπεία. Τελικά, ο ασθενής υποβλήθηκε σε ολική θυρεοειδεκτομή με αποτέλεσμα τον πλήρη έλεγχο της αρρυθμίας χωρίς την ανάγκη λήψης β-αναστολέων. Η καρδιακή ανεπάρκεια υποστράφηκε τελείως και ο ασθενής έχει πλέον επιστρέψει σε κανονικές καθημερινές δραστηριότητες.

Λέξεις κλειδιά *Αμιοδαρόνη, θυρεοτοξίκωση, ταχυαρρυθμία, ταχυκαρδιομυοπάθεια*

Α. Μαρίνης, Π. Μπασιούκας, Σ. Ρίζος
Α΄ Χειρουργική Κλινική, Γενικό Νοσοκομείο Πειραιά «Τζάνειο», Πειραιάς, Ελλάδα

Γ. Βασιλόπουλος
Θεραπευτική Κλινική του Πανεπιστημίου Αθηνών, Γενικό Νοσοκομείο «Αλεξάνδρα», Βασιλίσσης Σοφίας 80, 11528, Αθήνα, Ελλάδα

Α. Αβραμίδου
Αναισθησιολογικό Τμήμα Γενικό Νοσοκομείο Πειραιά «Τζάνειο», Πειραιάς, Ελλάδα

Θήβη Βασιλακάκη
Παθολογοανατομικό Εργαστήριο, Γενικό Νοσοκομείο Πειραιά «Τζάνειο», Πειραιάς, Ελλάδα