Pre-operative embolization of thyroid arteries in a case of refractory amiodarone-induced thyrotoxicosis. Case report

Embolización preoperatoria de las arterias tiroideas en un caso de tirotoxicosis refractaria por amiodarona. Reporte de caso

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Abstract

Introduction: Amiodarone has become one of the main anti-arrhythmic drugs. However, it may cause a wide variety of adverse effects, sometimes severe. Amiodarone-induced thyroid dysfunction is one of the best known problems, resulting in either thyrotoxicosis or hypothyroidism.

Case presentation: A patient who, after 2 years of using amiodarone for the control of atrial fibrillation, developed thyrotoxicosis, refractory to conventional medical treatment. To optimize the patient’s clinical condition before total thyroidectomy, embolization of thyroid arteries was performed.

Conclusion: Embolization of the thyroid arteries as bridge therapy to thyroidectomy is an uncommon alternative in patients with amiodarone-induced hyperthyroidism. However, this treatment was useful to improve our patient’s symptoms and to optimize the anesthetic/surgical procedure.


Keywords: Amiodarone, Embolization, Thyroid crisis, Thyroidectomy, Thyrotoxicosis

Palabras clave: Amiodarona, Embolización terapéutica, Crisis tiroidea, Tirotoxicosis, Tiroidectomía

Resumen

Introducción: La amiodarona se ha convertido en uno de los principales fármacos empleados en el manejo de las arritmias cardiacas. Sin embargo, puede llegar a presentar una amplia variedad de efectos adversos, en ocasiones graves. La alteración de la función tiroidea es uno de sus problemas más conocidos, que puede causar tanto hipertiroidismo como hipotiroidismo.

Presentación del caso: Se presenta el caso de un paciente que, después de recibir durante dos años amiodarona para el control de una fibrilación auricular, desarrolló una tirotoxicosis refractaria al tratamiento médico clínico, por lo que se decidió realizar una embolización de las arterias tiroideas previa a tiroidectomía total, para lograr una optimización preoperatoria de su situación clínica.

Conclusión: La embolización de las arterias tiroideas como terapia puente a la tiroidectomía es una alternativa poco empleada en pacientes con hipertiroidismo, más aún si es debido a la...
administración de amiodarona, con escasos datos publicados en la literatura. En nuestro caso fue de utilidad para mejorar la sintomatología del paciente y optimizar el procedimiento anestésicoquirúrgico.

Introduction

Amiodarone is an anti-arrhythmic drug belonging to group III in the Vaughan Williams classification. Its mechanism of action is based on the prolongation of the action potential and the refractory period by blocking the sodium channels responsible for phase 3 repolarization. It is effective for the treatment of certain cardiac arrhythmias such as tachyarrhythmias associated with the Wolff–Parkinson–White syndrome, atrial fibrillation and flutter, supraventricular, nodal and ventricular paroxismal tachyarrhythmias, and ventricular fibrillation. However, it may cause multiple side effects.

Potential adverse effects include thyroid dysfunction, with varying incidence and prevalence depending on the literature. In the majority of cases, it leads to hypothyroidism, amenable to medical treatment and, exceptionally, to thyroiditis. In the most recent reviews, the estimated incidence of hypothyroidism and hyperthyroidism in patients receiving amiodarone is 5% to 10% and 0.9% to 10%, respectively.

Amiodarone-induced thyrotoxicosis (AIT), although rare, is associated with high morbidity and mortality because it may lead to severe cardiac dysfunction. For this reason, thyroid function monitoring is recommended before and during treatment in patients receiving this medication. There are 2 types of AIT: the first is produced by increased thyroid hormone synthesis and release, and the second is produced by a destructive thyroiditis of the gland that releases previously produced thyroid hormones. The medical treatment for AIT, which may be very challenging for the practitioner, is based on amiodarone discontinuation and the use of thioamides, perchlorates, and steroids. However, a small group of patients do not respond to these drugs and will continue to experience severe hyperthyroidism, leaving thyroidectomy as the only option for definitive treatment.

The thyroid storm deserves special mention. Though rare (incidence of 0.2/100,000 inhabitants/year), it constitutes a medical emergency, considering that the mortality rate is as high as 25% and may be triggered by various factors such as infections, pregnancy, trauma, stress, or surgery. The diagnosis of this condition is made primarily based on clinical findings, complemented by the application of the Burch and Wartofsky scale.

The following is a description of thyroid artery embolization used as treatment before surgery in a case of refractory AIT.

Case description

Patient information

A 59-year-old, Caucasian male patient, with a weight of 91kg, height of 180cm and body mass index of 28kg/m². In terms of significant personal history, the patient had hypertension under treatment with candesartan and familial hypertrophic cardiomyopathy, with a positive genetic test for a mutation of the myosin binding protein C MyBPC3 gene in the dilated phase. In addition, he wore an implantable cardioverter defibrillator (AICD) as primary prevention for sudden death because of severe left ventricular dysfunction (30% ejection fraction confirmed by echocardiography, cardiac magnetic resonance, and cardiac catheterization) and moderate pulmonary hypertension (mean arterial pressure of 37 mm Hg). One year after the implantation of the AICD, the patient developed atrial fibrillation, treated initially by means of electric cardioversion, followed by 2 years of treatment with amiodarone. Medical treatment of the heart condition included also the use of bisoprolol, torasemide, and dabigatran.

Clinical findings, diagnostic assessment, and interventions

Abnormal thyroid hormone values, consistent with hyperthyroidism, were detected during subsequent follow-up testing for the patient’s underlying heart disease. This prompted the discontinuation of amiodarone and the initiation of treatment with corticosteroids and methimazole.

Despite pharmacological treatment, the patient developed heat intolerance, tremors, nervousness, palpitations, loss of 8kg over the previous month, insomnia, and increased gastrointestinal movements. Moreover, thyroid hormone levels continued to evolve poorly, prompting admission to our institution. Initial thyroid hormone levels were 3.24ng/dL and 0.06mIU/L, respectively, for thyroxin (free T4) and thyrotropin (TSH), and they increased up to 9.9ng/dL and 0.05mIU/L at the time of admission to the hospital.

On physical examination, the patient had arrhythmic heart sounds, arterial pressure of 102/46mm Hg, with no evidence of heart failure. The thyroid gland was not enlarged, and no nodules were palpated. The electrocardiogram (EKG) showed evidence of atrial fibrillation at 130bpm, and the chest X-ray showed a discrete increase in the cardiothoracic ratio, with no radiological signs suggesting acute cardiac decompensation or conforming gross intestinal disease, and no consolidation or evidence of circumscribed nodular lesions. Test results, except for the hormonal values mentioned above, did not show abnormal values worth noting (creatinine 0.59mg/dL, glomerular filtration rate greater than 90mL/min/1.73m², hemoglobin 12.1g/dL, leukocytes 8.6 × 10e9/µL and platelets 143 × 10e9/µL).
Workup was completed with anti-thyroid stimulating immunoglobulin receptor and anti-thyroglobulin antibody tests, which were negative. Thyroid ultrasound showed asymmetry in the size of the gland, with right and left lobe anteroposterior diameters of 2.6 and 2cm, respectively, and heterogenous parenchyma with small colloid cysts, consistent with thyroiditis. Clinical and test findings continued to decline despite high doses of steroids and anti-thyroid agents, with free T4 levels of more than 12ng/dL and undetectable TSH levels. In addition, following the administration of thioamides, liver function tests became abnormal, prompting the discontinuation of these agents and the initiation of plasmapheresis. After 6 sessions, results were unsatisfactory.

The symptoms of persistent severe hyperthyroidism, the cardiac history and the risk of perioperative worsening led to the decision by the multidisciplinary team of performing thyroid artery embolizations before total thyroidectomy. Monitoring during thyroid embolization in the interventional radiology suite included blood pressure, EKG and oxygen saturation. Sedation was also used during the procedure, consisting of remifentanil perfusion (0.05–0.1μg/kg/min), midazolam boluses of 20μg/kg, dexamethasone 8mg (for postoperative nausea and vomiting control and also because of its effect on the reduction of peripheral conversion of T4 to T3, and to reduce the risk of adrenal insufficiency due to severe thyrotoxicosis), and oxygen through nasal prongs at a rate of 3L/min.

Moreover, bearing in mind the possibility of a thyroid storm, a management plan was put in place, based on reducing thyroid hormone synthesis and release, as well as control of systemic manifestations, consisting of the following:

- Fluid and electrolyte replacement and support measures.
- Anti-thermal measures (physical and pharmacological, using paracetamol and avoiding salicylates).
- Glucocorticoids (initial hydrocortisone dose of 300mg, followed by 100mg every 8hours).
- Anti-thyroid agents (initial dose of propylthiouracil of 500mg, followed by 250mg every 4hours).
- Beta-blockers (esmolol at an initial dose of 500μg/kg, followed by continuous perfusion at a rate of 50–200μg/kg/min).
- Iodine solutions such as potassium iodide, 5 drops (0.25mL or 250mg) by mouth every 6hours.

The technique was performed following retrograde puncture of the right common femoral artery with the aim of conducting angiography to identify the superior (first branches of the external carotid artery) and inferior (branches of the thyrocervical trunks arising from the subclavian artery) thyroid arteries.

Thyroid artery catheterization was performed using a microcatheter and embolization was accomplished by means of polyvinyl alcohol particles 250 to 355μL in size, mixed with contrast.

On follow-up, a good morphological result was observed, with significant flow reduction in the arteries and thyroid parenchyma. However, adequate reduction of free T4 levels was not accomplished over the next few days after the procedure, since they dropped only to 7.77ng/dL. Consequently, a second embolization was planned, again under deep sedation, using smaller particles to reach the terminal branches and achieve better results. Almost complete suppression of the thyroid parenchyma was achieved.

After performing each of the procedures, the patient was transferred to the postanesthetic recovery unit to maintain tight monitoring during the first few hours, considering the increased risk of a thyroid storm episode: the literature describes a potential increase in thyroid hormone release following gland necrosis.

Later, the only side effects of embolization were a self-limiting episode of hiccoughs that persisted for several hours, odinophagia (with normal oropharynx on exploration), and neck pain radiating to the ear and the zygomatic area, probably explained by microparticles passing to collateral branches of the superior and inferior thyroid arteries, for example, the infrahyoid, esophageal and pharyngeal branches.

**Follow-up and outcome**

Symptoms were partially under control after the 2 embolizations, with improved tolerance of tremors and palpitations, but no clear improvement of nervousness or drop in serum values of thyroid hormones which remained at 9.07ng/dL and 0.004mIU/L for free T4 and TSH, respectively. Three days later, the patient was scheduled for thyroidectomy which was performed under balanced general anesthesia (with etomidate for induction and desflurane for maintenance), with uneventful anesthetic and surgical procedures, except for the finding of a brownish gland probably due to ischemia.

After the surgery, the patient remained asymptomatic with absence of the clinical manifestations that led to admission. Vital signs remained stable and there was a favorable reduction in serum hormonal levels. The patient was discharged and initiated replacement therapy with 100μg of sodium levothyroxine. Free T4 values dropped to 1.16ng/dL and TSH values remained at 1.19mIU/L.

**Discussion**

In our case, necrosis of the thyroid was induced by means of embolization with the aim of lowering blood levels of thyroid hormones before surgery, and of achieving lower hormonal release during surgical manipulation of the gland. According to the published literature, thyroid hormone levels may increase within hours or days following embolization, either because of their release by...
the necrotic thyroid tissue or due to direct toxicity of iodine-based contrast material used during catheterization. In our patient, thyroxin and TSH values remained high during the first day and dropped by the second day, although not sufficiently (recommended level of free T4 is 3 ng/dL).

We could have waited for complete thyroid necrosis and a larger drop of hormonal values, but the patient’s clinical condition did not allow it. Therefore, we opted for a second embolization, achieving lower hormonal levels than before, allowing for a successful intervention under safer conditions, even though free T4 levels did not approach 3 ng/dL.

This therapeutic approach helped improve the clinical condition of a patient with a significant associated comorbidity, optimizing the anesthetic/surgical procedure.

The patient’s situation on arrival was the result of the administration of amiodarone for atrial fibrillation control. For this reason, thorough knowledge of the drug-associated adverse effects is crucial. Likewise, it is mandatory to maintain close monitoring and follow the course of the patient’s condition to avoid such effects and, in the event they occur, find solutions based on the most recent scientific and technical advances, using a multidisciplinary approach.

Ethical responsibility

Human and animal protection. no experiments were conducted in humans or animals for this study.

Right to privacy and informed consent. the authors obtained the authorization and informed consent from the patient. This document is kept by the authors.

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Conflict of interest

The authors declare having no conflict of interest.

References