



CASE REPORT

Amiodarone-Induced Thyroid Storm Treated with Plasmapheresis and Thyroid Artery Ablation

Mark J. Oertel, M.D.¹

Rajib Bhattacharya, M.D.²

¹Lawrence, KS

²University of Kansas Medical Center

Department of Internal Medicine

Division of Endocrinology, Metabolism & Genetics, Kansas City, KS

Introduction

Amiodarone is a class III anti-arrhythmic drug commonly used for treatment and prevention of cardiac arrhythmias. It is associated with a number of side effects including thyroid dysfunction due to its high iodine content and direct toxic effects.

In the United States, 3 to 5 percent of patients treated with amiodarone develop hyperthyroidism.¹ Amiodarone-induced thyrotoxicosis (AIT) is divided into 2 types. Type 1 is associated with increased synthesis of thyroid hormone, whereas type 2 is associated with excessive release of thyroxine (T4) and triiodothyronine (T3) from a destructive process. The diagnosis of thyroid storm is based upon clinical findings which are exaggerations of typical hyperthyroidism involving the central nervous, gastrointestinal, and cardiovascular systems.

The most accepted criteria to diagnose thyroid storm was created by Burch and Wartofsky who introduced a scoring system in 1993.² It provided a criterion to grade severity of thermoregulatory, cardiovascular, and central nervous system dysfunctions with scores greater than 45 being highly suggestive of thyroid storm. Medical therapy for thyroid storm is centered on thionamides, glucocorticoids, and beta-blockers. Plasma exchange and thyroidectomy have been used in patients whose hyperthyroidism is refractory to aggressive medical therapy. In our case,

thyroid artery ablation also was utilized when too ill to undergo surgical thyroidectomy.

Case Report

A 64-year-old Caucasian male with a history of ischemic cardiomyopathy and recurrent ventricular arrhythmia was maintained on amiodarone therapy. He had no known prior thyroid disease. He was admitted to an outside facility after experiencing three separate automatic implantable cardioverter defibrillator (AICD) events. An AICD interrogation showed recurrent episodes of ventricular fibrillation. Left heart catheterization, with associated iodinated contrast exposure, revealed no ischemic disease.

On transfer to our facility, the patient had a temperature of 38.0 degrees Celsius, respiratory rate of 28 breaths per minute, heart rate of 99 beats per minute, and blood pressure of 100/58 mmHg. His examination showed an anxious, mildly diaphoretic male with irregular tachycardia, a fine tremor, trace lower extremity edema, and no thyromegaly or nodularity. His Burch and Wartofsky score was 40, suggestive of impending thyroid storm. The thyroid stimulating hormone (TSH) level was 0.01 mIU/mL, with a free thyroxine (FT4) level greater than 6.0 ng/mL, and a free triiodothyronine (FT3) level of 13.3 ng/dL.

Thyroid autoantibodies were not detected. He was started on prednisone, methimazole (MMI) 20 mg by mouth three times daily, and an intravenous (IV) esmolol drip.

The patient continued to have frequent episodes of ventricular fibrillations and AICD shocks. Given his clinical instability and lack of sufficient response to medical therapy, we pursued additional possible treatments. He received three, 1:1 total exchanges on three separate days with improved thyroid function studies (TFTs), but his mental status and hemodynamics worsened, culminating in cardiac arrest requiring five minutes of cardiopulmonary

resuscitation. In lieu of conventional surgical thyroidectomy given his unstable clinical status, urgent bilateral thyroid artery ablation was performed in interventional radiology on hospital day 5. Plasmapheresis was resumed the next day along with medical therapy. The patient underwent nine total plasma exchanges with improvement of TFTs (Figure 1), resolution of arrhythmias, and improvement in his clinical status. He eventually underwent thyroidectomy on post-hospital day 17 with pathology showing a benign multinodular thyroid gland. He was started on weight-based levothyroxine replacement after his TFTs normalized.

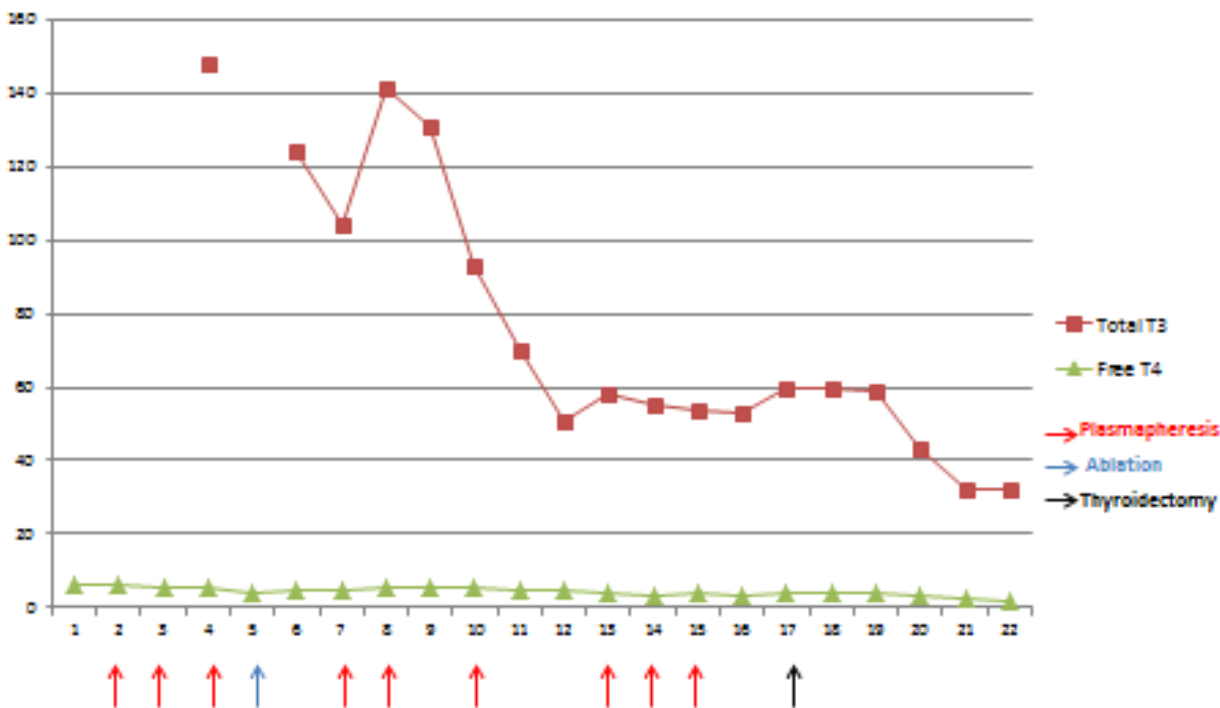


Figure 1. Variations in total T3 and free T4 over the course of treatment.

Discussion

Amiodarone induced thyrotoxicosis has occurred in 3% of patients treated with amiodarone.³ In hospitalized patients, the incidence of thyroid storm was 0.20 per 100,000 patients per year.⁴ In patients with underlying thyroid abnormalities, type I AIT

occurred due to iodine-induced excessive thyroid hormone synthesis. Its pathogenesis could be related to effects of iodine overload on an abnormal thyroid gland, such as latent Graves’ disease, autonomous nodules, or multinodular goiter.⁵

Beta blockers, thionamides, and glucocorticoids are typically the first line treatment for thyroid storm.⁶ Beta blockers work by inhibiting 5'-monodeiodinase, thus inhibiting conversion of T4 to T3. Propranolol is a nonselective beta blocker and can be given emergently and intravenously as well as in oral form for long term use. Esmolol competitively blocks response to beta 1 adrenergic stimulation and beta 2 receptors at high doses, but is limited to IV use.

Thionamides include propylthiouracil (PTU) and methimazole and work slowly by blocking de novo thyroid hormone synthesis without affecting levels of preformed thyroid hormones.⁶ PTU also has additional effects of blocking T4 to T3 conversion. Glucocorticoids reduce conversion of T4 to T3.

Given our patient's recent iodinated contrast exposure, he was not a candidate for radioactive iodine ablation. In addition to conventional therapy with MMI, esmolol, and prednisone, lithium and cholestyramine were discussed, but not utilized, because of their side effects and lack of efficacy. Plasmapheresis was initiated in lieu of thyroidectomy given his unstable clinical status.

The purpose of plasmapheresis is to remove plasma containing preformed thyroid hormones from circulation and replace it with plasma containing normal levels of thyroid hormones. Removal of circulating autoantibodies against the thyroid gland also could contribute to improvement in patient's TFTs and subsequent clinical status.⁷ However, there have been no clinical trials evaluating plasmapheresis as a treatment modality in thyrotoxicosis.

In published reports using plasmapheresis for treatment of thyrotoxicosis,⁷⁻¹¹ some used two exchanges while others used up to eight exchanges. No

reports studied the optimal number of plasma exchanges and most discontinued plasmapheresis after clinical improvement rather than improvement in TFTs. Most demonstrated benefit from plasmapheresis.⁷⁻¹⁰ Of note, the use of plasmapheresis often improved the patients' clinical status until they could undergo thyroidectomy.^{7,8,10} The use of plasmapheresis in treatment of other conditions is associated with thyroid hormone disorders.^{13,14}

Pasimeni et al.⁸ reported a 57-year-old female with a known multinodular goiter who developed thyrotoxicosis induced by an iodinated contrast agent received for a computed tomography scan, a mechanism similar to type 1 AIT. She ultimately was treated with two sessions of therapeutic plasma exchange. Her FT3 and FT4 levels and clinical symptoms improved to enable a thyroidectomy without complications.

Indications for thyroid artery embolization in AIT are not well elucidated. Few cases described thyroid artery embolization for treatment of thyroid disease. Xiao et al.¹⁴ described the utilization of thyroid artery embolization in 22 patients with Graves' disease in patients unable to tolerate or not accepting of current therapies (oral medication, radioactive iodine, or surgery). Six received embolization followed by thyroidectomy with the remaining 16 receiving embolization only. Fourteen remained euthyroid. Only two patients required maintenance doses of anti-thyroid drugs. No adverse effects were described from the thyroid artery embolization.

Zhao et al.¹⁵ used thyroid arterial embolization in 37 patients with Graves' disease to study pathological changes of the thyroid gland. They discovered ischemia, then necrosis, of the gland at seven days post-embolization. Of the 37 patients, 26 were rendered euthyroid at follow-up in

three years and all improved TFTs in seven days along with some improvement in clinical status.

In our case, the patient was clinically unstable despite three plasma exchanges and he continued to have elevated TFTs. His TFTs briefly increased after ablation which was attributed to destruction and necrosis of

his thyroid gland and release of preformed thyroid hormones. After two additional plasma exchanges, his clinical status and TFTs improved, allowing the patient to undergo thyroidectomy. Our case illustrated the potential severity of AIT and the successful use of plasmapheresis and thyroid artery embolization in its treatment.

References

- ¹ Batcher EK, Tang XC, Singh BN, et al. Thyroid function abnormalities during amiodarone therapy for persistent atrial fibrillation. *Am J Med* 2007; 120(10):880-885. PMID: 17904459.
- ² Burch HB, Wartofsky L. Life-threatening thyrotoxicosis. Thyroid storm. *Endocrinol Metab Clin North Am* 1993; 22(2):263-277. PMID: 8325286.
- ³ Cardenas GA, Cabral JM, Leslie CA. Amiodarone induced thyrotoxicosis: Diagnostic and therapeutic strategies. *Cleve Clin J Med* 2003; 70(7):624-626. PMID: 12882384.
- ⁴ Akamizu T, Satoh T, Isozaki O, et al. Diagnostic criteria, clinical features, and incidence of thyroid storm based on nationwide surveys. *Thyroid* 2012; 22(7):661-679. PMID: 22690898.
- ⁵ Harjai KJ, Licata AA. Effects of amiodarone on thyroid function. *Ann Intern Med* 1997; 126(1):63-73. PMID: 8992925.
- ⁶ Bahn RS, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis: Management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologist. *Endocr Pract* 2011; 17(3):456-520. PMID: 21700562.
- ⁷ Ezer A, Caliskan K, Parlakgumus A, Belli S, Kozanoglu I, Yildirim S. Preoperative therapeutic plasma exchange in patients with thyrotoxicosis. *J Clin Apher* 2009; 24(3):111-114. PMID: 19484727.
- ⁸ Pasimeni G, Caroli F, Spriano G, Antonini M, Baldelli R, Appetecchia M. Refractory thyrotoxicosis induced by iodinated contrast agents treated with therapeutic plasma exchange. A case report. *J Clin Apher* 2008; 23(2):92-95. PMID: 18293390.
- ⁹ Vyas AA, Vyas P, Fillipon NL, Vijayakrishnan R, Trivedi N. Successful treatment of thyroid storm with plasmapheresis in a patient with methimazole-induced agranulocytosis. *Endocr Pract* 2010; 16(4):673-676. PMID: 20439250.
- ¹⁰ Koball S, Hickstein H, Gloger M, et al. Treatment of thyrotoxic crisis with plasmapheresis and single pass albumin dialysis: A case report. *Artif Organs* 2010; 34(2):E55-58. PMID: 20420590.
- ¹¹ Sakata S, Komaki T, Kojima N, Miura K. The effect of double filtration plasmapheresis on thyroid hormone economy and thyroid function. *Jpn J Med* 1986; 25:246-249. PMID: 3095574.
- ¹² Nieuwenhuis L, Santens P, Vanwallegghem P, Boon P. Subacute Hashimoto's encephalopathy, treated with plasmapheresis. *Acta Neurol Belg* 2004; 104(2):80-83. PMID: 15508271.
- ¹³ Dandona P, Marshall NJ, Bidey SP, Nathan A, Havard CW. Successful treatment of exophthalmos and pretibial myxedema with plasmapheresis. *Br Med J* 1979; 1(6160):374-376. PMID: 581653.
- ¹⁴ Xiao H, Zhuang W, Wang S, et al. Arterial embolization: A novel approach to thyroid ablative therapy for Graves' disease. *J Clin*

Endocrinol Metab 2002; 87(8):3583-3589.
PMID: 12161479.

¹⁵Zhao W, Gao BL, Tian M, et al. Graves' disease treated with thyroid artery

embolization. Clin Invest Med 2009; 32(2):E158-E165. PMID: 19331805.

Keywords: thyroid storm, plasmapheresis, ablation techniques, amiodarone