CASE REPORT

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# Therapeutic plasma exchange as a bridge to thyroidectomy in refractory amiodarone-induced thyrotoxicosis – Case Report

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## Abstract

Amiodarone-induced thyrotoxicosis (AIT) is a potentially life-threatening complication of amiodarone therapy, particularly challenging in patients with significant cardiovascular disease. The case is presented of a 77-year-old man with advanced cardiac comorbidities who developed severe thyrotoxicosis during amiodarone treatment. AIT type II was diagnosed based on clinical features, laboratory results, and Doppler ultrasonography. Despite intensive therapy with glucocorticoids, beta-blockers, antithyroid drugs, lithium carbonate, and sodium perchlorate, no improvement was achieved. Therapeutic plasma exchange (TPE) was introduced as a rescue strategy. 4 sessions resulted in significant hormonal reduction and clinical stabilization, enabling safe total thyroidectomy without perioperative complications. This case highlights the limitations of conventional therapy in severe AIT and supports early consideration of TPE in selected high-risk patients requiring rapid stabilization before definitive treatment.

## Key words

amiodarone, hyrotoxicosis, plasmapheresis, thyroidectomy, heart diseases, aged

## INTRODUCTION

Amiodarone-induced thyrotoxicosis (AIT) is a potentially severe adverse effect of amiodarone therapy, resulting from distinct underlying pathophysiological mechanisms. Based on these mechanisms, AIT is conventionally classified into type I, type II, or a mixed form [1, 2].

Type I AIT occurs in patients with pre-existing thyroid abnormalities associated with autonomous hormone production, such as nodular goiter or latent Graves' disease, and reflects iodine-induced thyroid hormone synthesis. In contrast, type II AIT represents a destructive thyroiditis caused by direct toxic effects of amiodarone on thyroid follicular cells, leading to the release of preformed thyroid hormones [1]. The mixed form of AIT exhibits features of both mechanisms, frequently complicating the diagnostic process and limiting the effectiveness of standard therapeutic strategies, often necessitating combined or non-standard treatment approaches [1, 3].

Amiodarone is a class III anti-arrhythmic drug widely used in patients with ventricular and atrial arrhythmias, particularly in those with structural heart disease and reduced left ventricular ejection fraction, in whom other anti-arrhythmic agents are often contraindicated. Despite its high efficacy, amiodarone poses a significant risk of thyroid dysfunction, which may have serious clinical consequences in cardiology patients. Approximately 37% of the molecular weight of amiodarone consists of iodine, leading to a substantial iodine load and long-term tissue accumulation. Amiodarone-induced thyroid dysfunction appears to occur more frequently in iodine-deficient regions and may precipitate severe thyrotoxicosis, significantly increasing the risk of arrhythmia exacerbation, heart failure decompensation, and cardiovascular morbidity [4, 5].

Therapeutic plasma exchange (TPE) has a well-established role in the management of several immune-mediated and systemic disorders. According to the 2023 guidelines of the American Society for Apheresis (ASFA), clinical indications for plasma exchange are categorized into four classes based on the strength of evidence and the clinical role of the procedure. Category I indications, such as myasthenia gravis or anti-glomerular basement membrane disease (Goodpasture syndrome), represent conditions in which plasma exchange is accepted as first-line therapy [6, 7].

In contrast, the use of plasma exchange in endocrine emergencies, including amiodarone-induced thyrotoxicosis, is classified as a Category II indication, reflecting its role as a second-line or adjunctive treatment option. Importantly, within this category, plasma exchange is positioned as a non-routine intervention, reserved for selected cases with severe or refractory disease in whom conventional therapy fails or is contraindicated [6]. Available evidence supporting its use in this setting remains limited and is largely based on isolated case reports and small case series.

## CASE REPORT

A 77-year-old male with an extensive cardiovascular history was admitted urgently due to progressive dizziness

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accompanied by chest pain. His medical history was significant for ischemic heart disease, including anterior myocardial infarction in 1988, previous coronary artery bypass grafting, and percutaneous coronary interventions with drug-eluting stent implantation. He was diagnosed with heart failure with preserved ejection fraction (HFpEF), arterial hypertension, dyslipidaemia, and paroxysmal atrial fibrillation treated chronically with rivaroxaban. The patient had also experienced two ischemic strokes (in 2015 and 2021), including one likely of cardioembolic origin. Additionally, ventricular and supraventricular ectopic beats were documented. Given the presence of paroxysmal atrial fibrillation in the setting of structural heart disease, prior myocardial infarction, heart failure, and a history of ischemic stroke, long-term antiarrhythmic therapy with amiodarone had been initiated more than three years prior to admission for antiarrhythmic therapy. The use of amiodarone in this context reflected the need for effective rhythm stabilization in a high-risk patient with significant structural cardiac abnormalities and elevated thromboembolic risk. Laboratory evaluation demonstrated overt thyrotoxicosis with complete suppression of thyroid-stimulating hormone (TSH), and markedly elevated free thyroid hormone concentrations (Tab. 1).

The patient reported more than three years of continuous amiodarone therapy without regular monitoring of thyroid function. Autoimmune thyroid disease was excluded based on negative thyroid-stimulating hormone receptor antibodies (TRAb), anti–thyroid peroxidase antibodies (anti-TPO), and anti-thyroglobulin antibodies (anti-Tg). Thyroid ultrasonography revealed inflammatory features with reduced vascularity on power Doppler imaging. On the basis of clinical presentation, laboratory findings, and imaging, amiodarone-induced thyrotoxicosis type II was diagnosed.

## RESULTS

Initial management included beta-adrenergic blockade and antithyroid therapy with thiamazole administered orally. Autoimmune hyperthyroidism was excluded and thyroid ultrasonography demonstrated an enlarged gland with inflammatory features and reduced vascularity on Doppler imaging, supporting the diagnosis of amiodarone-induced thyrotoxicosis with a destructive mechanism (type II). Due to lack of clinical and biochemical response, systemic glucocorticoid therapy was added. During the course of treatment, rising liver injury markers prompted exclusion of viral hepatitis and escalation of antithyroid therapy to intravenous thiamazole. As thyroid hormone concentrations remained markedly elevated despite combined treatment, additional agents were introduced sequentially, including lithium carbonate followed by sodium perchlorate, reflecting concern for a possible mixed pathogenic component.

Despite intensified pharmacological therapy, the patient showed no meaningful improvement. He developed dysphagia and experienced rapid, unintended weight loss of approximately 6 kg within one week, requiring nutritional support.

Given persistent severe thyrotoxicosis refractory to multimodal medical therapy and the patient's substantial cardiovascular burden, TPE was initiated as a rescue intervention to rapidly reduce circulating thyroid hormone levels. A central venous catheter was placed in the left subclavian vein. Four TPE procedures were performed.

**Table 1.** Changes in thyroid hormone levels during hospitalization and therapeutic plasma exchange

| Time point | fT3 (pg/mL) | fT4 (ng/dL) |
|---|---|---|
| At hospital admission | 700 | >6.030 |
| Before plasma exchange | 690 | >6.030 |
| After 1st plasma exchange | 970 | >6.030 |
| After 2nd plasma exchange | 595 | >6.030 |
| After 3rd plasma exchange | 660 | >6.030 |
| After 4th plasma exchange | 830 | 900 |

Replacement therapy included fresh frozen plasma and human albumin solutions. The procedures were completed without major complications.

Following TPE, clinical and biochemical stabilization was achieved, allowing qualification for definitive surgical management. Total thyroidectomy was subsequently performed without perioperative complications.

Reference ranges: free triiodothyronine (fT3) 2.34–4.92 pg/mL, free thyroxine (fT4) 0.52–1.44 ng/dL Values above or below the analytical range of the laboratory are reported as '>' or '<' according to laboratory limits.

## DISCUSSION

Differentiation between type 1 and type 2 AIT remains challenging and is essential for appropriate management. Amiodarone alters thyroid hormone metabolism even in euthyroid patients by inhibiting peripheral conversion of T4 to T3, which may complicate interpretation of thyroid function tests. Both AIT types typically present with suppressed TSH and elevated free T4 levels, while free T3 may be normal or increased, limiting the diagnostic value of routine biochemical parameters.

Although type 1 AIT is classically associated with underlying thyroid disease and type 2 AIT with destructive thyroiditis in a previously normal gland, laboratory markers such as thyroid autoantibodies lack sufficient specificity. The presence of antithyroid antibodies does not exclude type 2 AIT, supporting the concept of mixed or overlapping forms, particularly in patients with poor response to standard therapy. Thyroid ultrasonography and colour-flow Doppler sonography are useful adjuncts, as increased vascularity favours type 1 AIT, whereas reduced blood flow suggests type 2 disease. However, imaging findings may be inconclusive. Moreover, clinical evolution and incomplete response to initial therapy may suggest coexistence of overlapping pathogenic mechanisms, highlighting that differentiation between AIT subtypes remains dynamic rather than strictly categorical in clinical practice. Overall, the absence of a single reliable marker necessitates a comprehensive and individualized diagnostic approach [2, 4, 5].

In AIT II, glucocorticoids are considered first-line therapy due to their anti-inflammatory effect and their ability to reduce the release of preformed thyroid hormones from the destroyed thyroid gland. However, treatment failure or suboptimal response is not uncommon. The therapeutic effect of glucocorticoids is often delayed and variable, resulting in prolonged exposure to excess thyroid hormones, which may be clinically unacceptable in patients with severe thyrotoxicosis and cardiovascular instability [8].

The limitations of conservative therapy are further emphasized by the pathophysiology of AIT II, which is driven by destructive thyroiditis rather than increased hormone synthesis. Consequently, antithyroid drugs have limited efficacy, as they do not prevent the release of preformed hormones. In elderly patients with multiple comorbidities, aggressive pharmacological treatment is associated with an increased risk of adverse effects, including metabolic complications, immunosuppression, and deterioration of cardiovascular status. These limitations highlight the need for alternative strategies in refractory cases, particularly when rapid biochemical and clinical stabilization is required [9].

TPE has been increasingly reported as an effective rescue therapy in patients with severe thyrotoxicosis who fail to respond to conventional medical management. TPE rapidly reduces circulating thyroid hormones and protein-bound hormone fractions by removing plasma and replacing it with colloid solutions, thereby lowering the biochemical burden and mitigating clinical instability prior to definitive treatment [10].

The effectiveness of TPE in thyrotoxicosis is primarily related to the removal of protein-bound thyroid hormones, as the majority of circulating thyroxine and triiodothyronine are bound to plasma proteins, including thyroxine-binding globulin, transthyretin, and albumin. By eliminating these hormone-protein complexes, TPE leads to a prompt reduction in biologically available hormone levels and a rapid improvement in metabolic and cardiovascular status [11].

Although the use of TPE in AIT is less well defined than in other forms of thyrotoxicosis, several case reports and small case series demonstrate its utility in patients with refractory AIT, where standard therapies, including corticosteroids and antithyroid drugs, have failed to achieve clinical or biochemical control [12]. In such scenarios, TPE has facilitated rapid reduction in hormone levels, improved haemodynamic stability, and served as a bridge to safe definitive therapies, such as thyroidectomy, in patients at high risk for perioperative complications [13].

These findings support early consideration of TPE in selected patients with severe, treatment-resistant AIT to expedite stabilization and improve clinical outcomes. TPE should therefore be considered early in carefully selected patients with severe AIT when rapid stabilization is required and conventional therapy is insufficient. In the presented case, persistent severe thyrotoxicosis despite intensive pharmacological treatment made immediate surgical intervention excessively risky. Plasma exchange enabled partial hormonal and metabolic stabilization, creating a safer window for definitive surgical management.

Thyroidectomy is considered in patients with amiodarone-induced thyrotoxicosis who are refractory or intolerant to optimal medical therapy, require rapid control of thyrotoxicosis, or present with progressive cardiovascular deterioration. Surgical intervention performed during active thyrotoxicosis is associated with a markedly increased risk of perioperative complications, including haemodynamic instability, malignant arrhythmias, heart failure decompensation, and increased mortality, particularly in elderly patients with limited cardiac reserve [14].

In this context, TPE may serve as an effective bridge therapy, enabling rapid reduction of circulating thyroid hormones and metabolic stabilization prior to surgery. Adequate preoperative preparation is crucial to minimize surgical risk and allow safe definitive treatment. Management of such patients requires a coordinated interdisciplinary approach involving endocrinologists, nephrologists, cardiologists, and experienced thyroid surgeons to optimize timing, perioperative safety, and overall outcomes. Therefore, early consideration of plasma exchange should be made in selected high-risk patients with severe or treatment-resistant AIT, particularly when rapid stabilization is required prior to definitive therapy.

## CONCLUSION

Plasma exchange can be an effective supportive treatment in severe, drug-resistant AIT II. In this case, it helped stabilize the patient's metabolic condition and allowed safe preparation for definitive treatment. Successful management requires a coordinated, multidisciplinary approach involving endocrinologists, nephrologists, and surgeons.

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