A Case of Amiodarone Induced Thyrotoxicosis Presenting with Methimazole Induced Agranulocytosis

Suhail Saad-Omer [1,2], Moises Matos [1,2], Mustafa Kinaan [1,2]

(1) UCF HCA Healthcare GME, Orlando, FL. (2) Department of Internal Medicine, UCF College of Medicine, Orlando, FL.

UCF College of Medicine
UNIVERSITY OF CENTRAL FLORIDA

HCA Florida Osceola Hospital

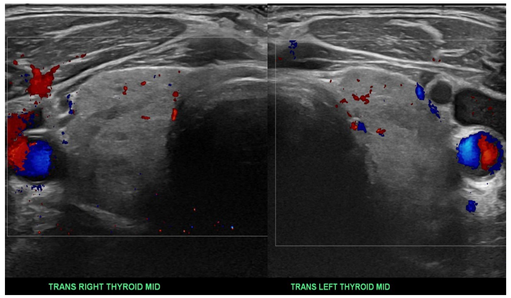
Background

- Amiodarone is a frequently used anti-arrhythmic drug which may often cause thyroid dysfunction. Management of amiodarone induced thyrotoxicosis (AIT) often hinges on distinguishing between type I and II AIT which is not often possible. When antithyroid drugs (ATD) are used, higher than average doses are often needed, increasing risk for complications, specifically agranulocytosis.

Case Presentation

- We report a case of a 67-year-old man who presented with palpitations, tremors, diarrhea and weight loss, consistent with thyrotoxicosis.
- He had been on amiodarone for paroxysmal atrial fibrillation (a-fib) for several years.
- Admission labs showed TSH < 0.01 uIU/ml (0.36-3.74 uIU/ml), free T4 3.32 ng/dL (0.76-1.46), total T3 237 ng/dL (86-192), thyrotropin receptor blocking antibodies < 1.10 IU/L (0.0-1.75), thyroglobulin antibodies < 20 IU/mL (0.0-40.0), and thyroid peroxidase antibodies < 10.0 IU/mL (0.0-35.0).
- Ultrasound showed a mildly enlarged, heterogeneous thyroid without discrete nodules and normal vascularity. (Figure 1)
- He was treated empirically for both type I and type II AIT with methimazole 40 mg and prednisone 40 mg.
- Despite treatment, he returned one month later with symptoms concerning for impending thyroid storm. EKG showed a-fib with a heart rate of 120 bpm. Repeat labs showed TSH < 0.01 uIU/ml, free T4 4.01 ng/dL and total T3 146 ng/dL.
- CBC was notable for a WBC 4.0 10^3 cells/µL and absolute neutrophil count (ANC) of 520 cells/µL. The following day, those decreased further to a nadir of 2.6 10^3 cells/µL and 62 cells/µL, respectively.
- Due to poor response to ATDs and development of severe agranulocytosis, emergent thyroidectomy was necessary.
- His WBC improved with discontinuation of methimazole and resolved completely a day after administration of G-CSF.
- He was treated with potassium Iodide, prednisone, cholestyramine and metoprolol in preparation for surgery.
- He did well after total thyroidectomy and was discharged home in stable condition on postoperative day two.
- His prednisone was tapered over two weeks and he was started on a weight-based dose of levothyroxine.

Imaging



• Figure 1: Thyroid ultrasound - transverse view

Amiodarone Induced Thyrotoxicosis

	Type 1	Type 2
Mechanism	Excessive thyroid hormone production due to iodine overload	Destructive thyroiditis leading to release of preformed thyroid hormone into circulation
Pre-existing thyroid disease	Yes, patients may have latent autoimmune thyroid disease	No
Prevalence	Most common type in iodine-deficient regions	Most common type in U.S.
Imaging	Radioiodine Uptake scan shows increased uptake Normal or increase vascularity on US	Radioiodine Uptake scan shows decreased uptake Decreased vascularity on US
Labs	May have positive TSI, TRAB No IL6 elevation Normal/high thyroglobulin	No detectable thyroid antibodies May have IL-6 elevation Low thyroglobulin
Treatment	Antithyroid medications	Steroids

• Table 1: Features of type 1 and 2 Amiodarone Induced Thyrotoxicosis

Discussion

- AIT has been classified into two major categories (Type 1 and Type 2) which differ in underlying mechanisms and treatment approach (see Table 1).
- Differentiation of these two types of AIT often poses a unique challenge for clinicians as some patients may have a mixture of both mechanisms. Nevertheless, determining which type of AIT a patient can determine treatment approach. For cases where AIT is mixed or unidentified, treatment should typically begin with ATD and oral corticosteroids
- While the risk of agranulocytosis from ATDs is mostly dose dependent, patients with amiodarone-induced thyrotoxicosis are at much higher risk. A large cohort study revealed that the prevalence and incidence of ATD related agranulocytosis was 10 times higher in AIT patients compared with thyrotoxicosis due to other etiologies.
- Although neutropenia resolves in most patient in 1-3 weeks after cessation of ATDs, use of G-CSF may shorten recovery times, decrease risk for infections and shorten hospital stays [1]
- Total thyroidectomy is usually considered when there is insufficient response to drug treatment with ATD and corticosteroids, development of side effects to ATDs, rapid deterioration of cardiac function, or advanced heart disease.
- In a recent observational study with 207 AIT patients, those who underwent thyroidectomy showed lower mortality and significant improvement in LVEF than those who were only treated medically, especially in patient's with LVEF<40% [2]

Conclusion

- It is important for clinicians to be aware of the thyroid-related side effects of amiodarone therapy, the different types, and management approach.
- Do not discontinue amiodarone without first consulting with a cardiologist given risk of worsening cardiac condition.
- Carefully monitor for agranulocytosis in this patient population given significantly higher risk.

References

1. Gershinsky M, Saliba W, Lavi I, Shapira C, Gronich N 2019 Increased risk of antithyroid drug agranulocytosis associated with amiodarone-induced thyrotoxicosis: a population-based cohort study. Thyroid 29:193–201.
2. Cappellani D, Papini P, Pingitore A, Tomisti L, Mantuano M, Di Certo AM, et al. Comparison Between Total Thyroidectomy and Medical Therapy for Amiodarone-Induced Thyrotoxicosis. J Clin Endocrinol Metab. 2020 Jan 1;105(1):242-51.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

HCA Healthcare®