Amiodarone-Induced Thyrotoxicosis Type 2 : Utilization of Color-flow Doppler Sonography for Diagnosis

Sam Joseph, MD.1 ; Larissa Check, DO.2 ; Donald Eagerton MD1
1Endocrinology Fellowship Division, Grand Strand Medical Center, Myrtle Beach, SC, USA
2Department of Internal Medicine. Grand Strand Medical Center, Myrtle Beach, SC, USA

Abstract

Amiodarone is potent class III antiarrhythmic medication commonly used to treat atrial and ventricular arrhythmias. Amiodarone is a benzofuranic iodine-rich compound structurally similar to triiodothyronine (T3) and thyroxine (T4) thyroid hormones. An estimated 15-20% of patients on amiodarone therapy experience thyroid dysfunction in the form of iodine overload, more than 50-100 times the recommended daily intake. Clinical pathologies of amiodarone use include hypothyroidism as well as hyperthyroidism. This case report focuses on the hyperthyroid side effects of amiodarone, clinically described as amiodarone-induced thyrotoxicosis (AIT). The report further discusses the various types, clinical significance and a review of the most current literature on management. There are three subtypes of AIT and these include type 1, type 2 and mixed. Although AIT is a well described phenomenon, clinical recognition and immediate treatment is crucial to prevent severe consequences such as fatal arrhythmias, heart failure, atrial fibrillation and strokes. This review aims to highlight key clinical signs and symptoms of AIT and further emphasize an update on the diagnostic and treatment plans to prevent associated morbidity and mortality.

Objective

The objective of this case report is to discuss the importance of utilization of color-flow doppler sonography in the diagnosis of Amiodarone Induced thyrotoxicosis (AIT) and discuss the management of AIT.

Introduction

Amiodarone-induced thyrotoxicosis (AIT) is a diagnostic and therapeutic challenge. There are two main forms of AIT: type 1, a form of iodine-induced hyperthyroidism, and type 2, a drug-induced destructive thyroiditis. However, mixed/indefinite forms exist where patients acquire an overlapping condition of both types. AIT 1 usually occurs in structurally abnormal thyroid glands, whereas AIT 2 develops in apparently normal thyroid glands. AIT 2 is more prevalent in iodine-sufficient areas and, in general, is the most frequent form of AIT. Anti-thyroid antibodies, such as anti-thyroid peroxidase antibodies, are often positive in AIT 1 and negative in AIT 2, although their presence does not necessarily allow a diagnosis of AIT 1.[1] Color flow Doppler sonography shows absent hypervascularity in AIT 2 and increased vascularity in AIT 1 and can be used a tool to distinguish them. Thionamides are the first-line treatment for AIT 1. AIT 2 is best treated by oral glucocorticoids.[2]

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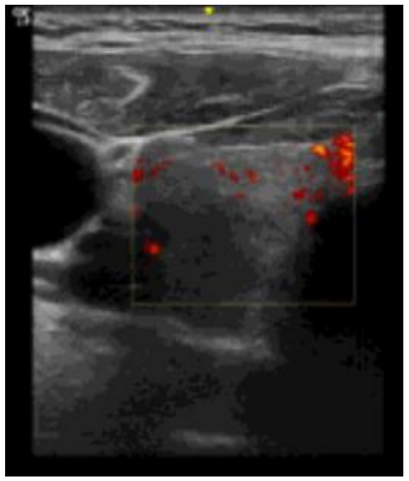
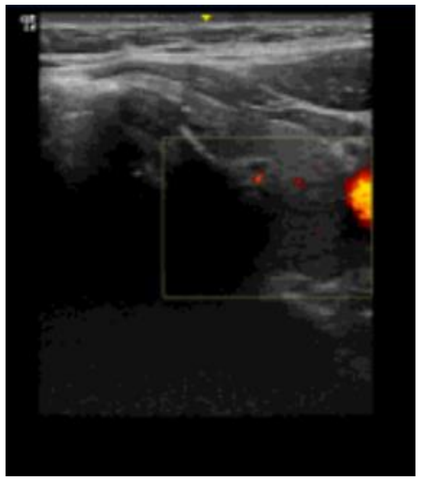
Case Presentation

We present a case of a 70-year-old Caucasian male who presented to our hospital with 3 days of acute onset shortness of breath and lower extremity edema. He also endorsed increased hair fall and weight loss of 18 lbs in two months prior to presentation. He has a known past medical history of myocardial infarction status post PCI x 3, ischemic cardiomyopathy, paroxysmal atrial fibrillation on amiodarone and anticoagulation with apixaban, CVA with residual speech finding difficulty. Amiodarone was started 3.5 years prior to presentation. He was noted to have hyperthyroidism with TSH 0.05 µIU/ml (0.465 – 4.68) , free T4 3.78 ng/dL (0.78 – 2.19), total T3 1.53 ng/mL (0.97 – 1.69). Thyroid peroxidase antibody, antithyroglobulin antibody and Thyrotropin receptor antibody were negative. He was diagnosed with amiodarone induced thyrotoxicosis (AIT) and treated as a mixed type with 30 mg prednisone and 10 mg Methimazole daily. Amiodarone was discontinued. Ultrasound of thyroid performed two days after discharge as outpatient at the endocrinology office showed normal thyroid gland with absence of hypervascularity on color-flow doppler sonography. His diagnosis was then modified to AIT 2 and methimazole was discontinued. He was euthyroid after 3 weeks of prednisone with TSH 0.8 µIU/ml , free T4 1.38 ng/dL and total T3 0.66 ng/dL. Prednisone was tapered and stopped.

Figure 1, 2: Color-flow Doppler Sonography of left and right thyroid lobes





Characteristics	AIT1	AIT2
Underlying thyroid abnormalities	Yes	Usually No
Color-flow Doppler sonography	Increased vascularity	Absent hypervascularity
Thyroidal Radioactive Iodine Uptake	Low/normal/increased	Suppressed
Thyroid autoantibodies	Present if AIT is due to Graves disease	Usually absent
Onset time after starting amiodarone	Short (median 3 months)	Long (median 30 months)
Spontaneous remission	No	Possible
Subsequent hypothyroidism	No	Possible
First – line medical treatment	Antithyroid drugs	Oral glucocorticoids
Subsequent definitive thyroid treatment	Generally yes	No

Table 1 . **2018 European Thyroid Association (ETA) Guidelines for the Management of Amiodarone-Associated Thyroid Dysfunction**
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Discussion

Proper and timely differentiation of AIT 1 and 2 is of utmost importance in the management of the disorder. The diagnosis of AIT usually requires increased serum Free T4 and Free T3 and suppressed serum TSH levels. In rare cases of AIT associated with severe non-thyroidal illness, FT3 may be normal. Thyroid ultrasonography can rapidly assess thyroid volume, nodularity, parenchymal echogenicity, and vascularity. Overall, most evidence shows that standard thyroid ultrasonography has low diagnostic value in AIT. Color-flow Doppler sonography (CFDS) provides a non-invasive, real-time assessment of thyroid vascularity.[2] Bogazzi et al. first used CFDS to differentiate patients with AIT 1 from AIT 2. A total of 27 patients with AIT underwent CFDS. The possible patterns were as follows: pattern 0 (absent intraparenchymal vascularity or minimal spots), pattern I (presence of parenchymal blood flow with patchy uneven distribution, or intranodular spots), pattern II (mild increase in Doppler signal with patchy distribution, or prominent flow at the periphery of the nodule) and pattern III (markedly increased Doppler signal with diffuse homogeneous distribution, or marked flow throughout the entire nodule).CFDS identified all 11 patients with AIT 1 who had increased vascularity of patchy distribution, while all 16 patients with AIT 2 showed absent vascularity.[3]
CFDS is the investigation of choice in AIT in Europe and North America.[4] However, the usefulness of CFDS depends on its availability and the necessary operator skills being available.
AIT 1 is treated with thionamides (40–60 mg/day of methimazole or equivalent doses of propylthiouracil). AIT 2 is treated with oral glucocorticoids. The proposed initial dose is 30 mg/day of prednisone (or equivalent doses of other glucocorticoids) tapered down based on clinical and/or biochemical euthyroidism.[2]

Conclusion

In this case report, our patient was treated in the inpatient setting as a mixed AIT with methimazole and prednisone. Using CFDS, which showed absent intraparenchymal vascularity and negative antithyroid antibodies, the diagnosis of AIT 2 was confirmed. This led to narrowing down the treatment to Prednisone which was tapered and stopped after euthyroid state was achieved.

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