Case Report

AMIODARONE-INDUCED THYROTOXICOSIS AFTER TOTAL THYROIDECTOMY FOR METASTATIC FOLLICULAR THYROID CANCER

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ABSTRACT

Objective: To describe the case of a man who developed amiodarone-induced thyrotoxicosis (AIT) after a total thyroidectomy for metastatic follicular thyroid cancer because of the effect of the drug on metastasis. To the best of our knowledge this is the first reported case of this condition.

Methods: We completed a retrospective review of medical records and laboratory results including thyroid function tests as well as imaging reports including plain radiographs, positron emission tomographs, computed tomographs, and histology reports.

Results: A 78-year-old man had undergone a total thyroidectomy for follicular thyroid cancer. He had metastatic disease in his chest and vertebrae, and after the operation he was started on suppressive levothyroxine treatment prior to ablative radioactive iodine treatment. Prior to thyroidectomy, his thyroid-stimulating hormone (TSH) concentration was 3.21 mU/L (reference range is 0.35 to 3.50 mU/L). On suppressive thyroxine replacement, his TSH concentration was 0.02 mU/L, his free thyroxine was 13 pmol/L (reference range is 8 to 12 pmol/L), and free triiodothyronine was 5.8 pmol/L (reference range is 3.8 to 6.0 pmol/L). He subsequently had a myocardial infarction and required antiarrhythmic treatment with amiodarone. Eleven days later he developed the clinical and biochemical features of thyrotoxicosis (TSH <0.01 mU/L, free thyroxine of 41 pmol/L, and free triiodothyronine of 14.7 pmol/L). His thyroxine dose was reduced and then discontinued 3 days later. AIT was the principal differential diagnosis, but before being able to determine the nature of the condition he died 18 days after his myocardial infarction.

Conclusion: AIT can still occur after total thyroidectomy if metastatic tissue is present. **(AACE Clinical Case Rep. 2020;6:e70-e72)**

Abbreviations:
AIT = amiodarone-induced thyrotoxicosis; **TSH** = thyroid-stimulating hormone

INTRODUCTION

Amiodarone is a class III antiarrhythmic drug that is used for managing a wide variety of cardiac arrhythmias. A well-recognized side effect of amiodarone treatment is the development of overt thyroid dysfunction. Frequently amiodarone causes thyrotoxicosis due to iodine-induced accelerated thyroid hormone synthesis (type 1), or a destructive thyroiditis (type 2). However, thyroid tissue is needed in order to develop thyrotoxicosis. We report a case of a man who underwent a total thyroidectomy for metastatic follicular thyroid cancer who required amiodarone treatment prior to ablative radioactive iodine treatment who developed amiodarone-induced thyrotoxicosis (AIT).

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CASE REPORT

A 78-year-old man was admitted to his local hospital in October of 2017 with a chest infection. He had a 6-year history of atrial fibrillation and benign prostatic hypertrophy for which he took medication. He was otherwise fit and well, except for a 5-pack year history of tobacco use.

A routine chest X-ray (Fig. 1) showed a well-defined, 12-cm, right upper chest wall mass with associated destruction of the adjacent rib. A computed tomography scan of his neck, chest, abdomen, and pelvis showed a solid lesion over his right fourth and fifth ribs and another within his fifth thoracic vertebra with elements indenting the spinal cord. He had no clinical or radiological evidence of cord compression. A 5.7-cm left thyroid solid nodule was also seen.

The provisional diagnosis was a primary thyroid cancer with bone metastasis, which was confirmed as a metastatic follicular thyroid carcinoma after a computed tomography guided biopsy of the chest mass. A positron emission tomography scan showed cord compression of his fifth thoracic vertebra, and a magnetic resonance image of the spine showed multilevel vertebral metastases.

One month prior to his total thyroidectomy, his thyroid function was normal with a thyroid-stimulating hormone (TSH) level of 3.21 mU/L (reference range is 0.35 to 3.50 mU/L). He underwent an uncomplicated operation and was started on 125 μg of levothyroxine daily. His histology was reported as a widely invasive follicular carcinoma (PT3 NX M1R0).

He was due to have a dose of radioactive iodine 2 months after his operation, but suffered a myocardial infarction 1 week prior to radioiodine treatment. Despite urgent percutaneous coronary intervention, he developed severe congestive heart failure and had a cardiac arrest 24 hours after his myocardial infarction. He was resuscitated and a permanent pacemaker was inserted 1 day later. His thyroid function tests on admission showed TSH of 0.02 mU/L, free thyroxine of 13 pmol/L (reference range is 8 to 12 pmol/L), and free triiodothyronine of 5.8 pmol/L (reference range is 3.8 to 6.0 pmol/L) suggesting his suppressive thyroxine dose was correct. Two days after the pacemaker insertion, he was started on 200 mg of amiodarone daily.

Eleven days after the initiation of amiodarone, his thyroid function was tested again and showed TSH was <0.01 mU/L, free thyroxine was 41 pmol/L, and free triiodothyronine was 14.7 pmol/L. Table 1 shows his thyroid function test results in relation to his amiodarone treatment. It was initially thought that he was over-treated with levothyroxine, and the dose was decreased to 100 μg. His thyroid status was clinically reassessed 3 days later and, because his hormone concentrations had been very elevated, his amiodarone treatment was suspended and an endocrine opinion sought.

Given that there was no longer a thyroid gland present, it was felt that the thyrotoxicosis was due to thyroid hormone release from the metastatic tissue precipitated by the recent amiodarone use. The dose of bisoprolol was increased and thyroid function was tested twice weekly. A pertechnetate scan was requested to look for uptake to help determine which type of AIT he had, but unfortunately his cardiac function continued to deteriorate and he died 18 days after his myocardial infarction.

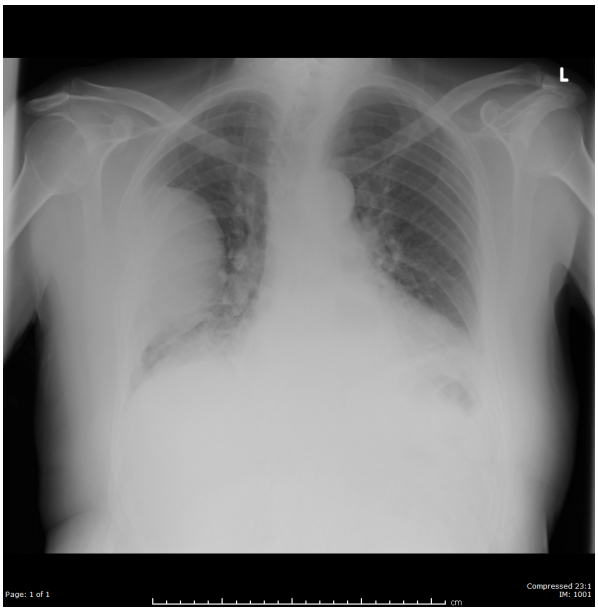

Fig. 1. X-ray showing a large opacity projected over the right thorax. It destructs the lateral fifth rib in keeping with a right chest wall mass.

DISCUSSION

Amiodarone is a benzofuranic, iodine-rich antiarrhythmic drug (class III) that causes thyroid dysfunction in 15 to 20% of patients (1). In each 200-mg tablet, there is 75 mg of iodine (37% of the amiodarone mass) of which approximately 10% of the iodine is released as free iodide daily. This affects thyroid hormone metabolism. A few days after amiodarone intake, patients can develop AIT type 1 or 2 (2). The drug has a long half-life of approximately 50 to 100 days, so AIT can also develop after withdrawal of the drug. Differentiating AIT type 1 from type 2 is important because it has therapeutic implications. Thyroid function tests are not helpful in differentiating AIT type 1 from type 2, therefore other investigations need to be carried out in order to clarify the diagnosis (3).

AIT type 1 is a form of iodine-induced hyperthyroidism, whereas AIT type 2 is a drug-induced destructive thyroiditis. AIT type 1 is more common in iodine-deficient parts of the world and often results in excessive, uncontrolled synthesis of thyroid hormone by autonomously functioning thyroid tissue in response to iodine. It mainly affects individuals with latent or known thyroid disorders,

Table 1
Time Course of Thyroid Function in Relation to Amiodarone Therapy

	Thyroid-stimulating hormone (mU/L)	Free thyroxine (pmol/L)	Free triiodothyronine[b] (pmol/L)
Reference range	0.35-3.50	2-21	3.8-6.0
January 8, 2016	3.13	8	Not measured
October 16, 2017	0.02	12	8.7
December 13, 2017	3.21	8	Not measured
March 4, 2018[a]	0.02	13	5.8
March 10, 2018	Amiodarone started		
March 21, 2018	<0.01	41	14.7

[a]The date of his myocardial infarction.
[b]At our institution free triiodothyronine is only measured if thyroid-stimulating hormone concentration is suppressed.

such as Graves disease, and diffuse or nodular goiters. Thioamide drugs, such as methimazole or carbimazole, are the first-line treatment for AIT type 1.

AIT type 2 is most prevalent in iodine-sufficient parts of the world. It develops in apparently normal thyroid glands. In AIT type 2, amiodarone exerts direct cytotoxic effects on thyroid follicles and triggers inflammation. As a result of this follicular disruption, preformed thyroid hormones are released into circulation. Because of the inflammatory nature of the condition, AIT type 2 is best treated by oral glucocorticoids.

Radioactive iodine is not a first-line treatment in AIT because iodine uptake by the gland is inhibited by the iodine load of amiodarone. In addition, radioactive iodine treatment does not work for destructive thyroiditis. Radioactive iodine can be used where thioamide drugs have been used initially to render an individual with AIT type 1 euthyroid, but who is unable to come off the oral agents. In more resistant cases, thyroidectomy may be an option (1,4).

The present case had already undergone a total thyroidectomy but still managed to developed thyrotoxicosis after a few days of being on amiodarone. There are aspects of this patient's care that could have been different, such as stopping the thyroxine treatment immediately on recognition that he was thyrotoxic rather than reducing the dose to 100 μg, but these decisions were made by the cardiology team looking after him rather than the endocrinologists. However, it is unlikely that this would have altered the outcome.

We also acknowledge that thyroid autoantibodies were not measured, which may have helped to differentiate between the types of AIT. We suggest (but accept that another limitation is that we did not have a pertechnetate scan to confirm) that this was due to AIT due to an effect on the metastatic thyroid tissue. An extensive literature search of the Medline, EMBASE, CINHAL, and EMCARE databases failed to find any reported cases of AIT following total thyroidectomy.

Because this is the first reported case of this condition, it is difficult to know the best therapeutic strategy. In our opinion, the best way to treat this condition would be as with any other case of AIT: withdrawal of the amiodarone, a pertechnetate scan, and the use of anti-thyroid drugs. In addition, it may be helpful to use high-dose steroids while waiting to see if the anti-thyroid drugs work (3). In this situation, ablative radioactive iodine therapy may also have helped.

CONCLUSION

We have reported a case of AIT despite a previous total thyroidectomy in a man with metastatic follicular thyroid cancer. We hypothesise that this developed due to the effect of amiodarone on his metastatic tissue.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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