Amiodarone-Induced Destructive Thyroiditis Associated with Coronary Artery Vasospasm and Recurrent Ventricular Fibrillation

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What Is Known about This Topic

- Hyperthyroidism is a recognised cause of coronary artery spasm and routine thyroid function testing should be performed in all patients.
- Thyroid dysfunction secondary to amiodarone therapy is common.
- The prevalence and cause (type I or II) of amiodarone-induced thyrotoxicosis (AIT) varies significantly depending on geographical location.
- The need to withdraw amiodarone therapy in patients with type 2 amiodarone-induced thyrotoxicosis (AIT) remains unclear but may hasten restoration of a euthyroid state.

What This Case Report Adds

- This case adds to the current small volume of literature highlighting the association between thyrotoxicosis and coronary artery spasm with the additional rare features of having AIT as the cause and been complicated by recurrent ventricular fibrillation.
- Coronary artery spasm typically confers excellent long-term prognosis, however episodes can precipitate malignant ventricular arrhythmias.

Key Words

Coronary artery spasm · Ventricular fibrillation · Amiodarone-induced thyrotoxicosis

Abstract

A 55-year-old male on long-term amiodarone therapy presented with ischaemic chest pain and recurrent witnessed syncope. Interrogation of his internal cardiac defibrillator, which had been inserted 4 years earlier, revealed two episodes of ventricular fibrillation, the timing of which corresponded to his syncopal events. Severe spontaneous

coronary artery vasospasm was observed on coronary angiogram. Thyroid function testing revealed severe hyperthyroidism with a diagnosis of type 2 amiodarone-induced thyrotoxicosis (AIT) subsequently made. Treatment with prednisolone therapy was commenced and thyroid function rapidly normalized. Prednisolone was weaned without recurrence of hyperthyroidism and on last review, 6 months after initial presentation, he remains free from further chest pain and arrhythmias. Our patient's presentation is a very rare case of AIT-associated coronary artery spasm and documented ischaemic ventricular fibrillation with fortunate survival.

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Fig. 1. **a** Cranial left anterior oblique view of the left coronaries with minor atherosclerotic plaque (arrows) at the ostium of the distal left circumflex artery. **b** A long segment of severe spontaneous vasospasm involving the distal left circumflex artery with poor distal vessel flow. **c** Intracardiac electrogram recording during one of his syncopal episodes showing ventricular fibrillation terminated by a single shock from his ICD (arrow).

Table 1. Thyroid function prior to and throughout amiodarone therapy

	Prior to presentation			Admission with ventricular fibrillation	Follow-up		
	10/12/2008	08/01/2009	24/01/2012	05/04/2012	22/06/2012	10/07/2012	11/09/2012
TSH (0.1–4.0 mIU/l)	1.37	2.19	0.97	<0.01	0.06	0.41	1.04
FT ₄ (9–26 pmol/l)				75.1	17.5	17.5	17.7
FT ₃ (3.5–6.5 pmol/l)				14.9	5.0	5.0	5.5

Case Report

In April 2012, a 55-year-old male was admitted to our cardiology unit following two unwitnessed syncopal episodes. Both episodes were preceded by chest pain, which was ischaemic in character. He was a current smoker and his past history was significant for a non-ischaemic cardiomyopathy. A primary prevention internal cardiac defibrillator had been inserted 4 years earlier in the setting of severe persistent global left ventricular systolic dysfunction despite empirical heart failure therapy. Amiodarone was introduced shortly after when a high burden of ventricular ectopy was detected on device interrogation. Successful ectopy suppression was observed and correlated with a dramatic improvement in left ventricular systolic function, leading to the retrospective diagnosis of tachycardia-mediated cardiomyopathy. Amiodarone therapy was continued at 200 mg twice daily. No previous device therapies had been delivered.

Interrogation of his internal cardiac defibrillator revealed two episodes of ventricular fibrillation terminated with device shocks (fig. 1c), the timing of which corresponded to his syncopal episodes. Electrocardiogram showed sinus rhythm with a pre-existing left bundle branch block. Laboratory data revealed a peak CK of 828 IU/l (normal <175) and troponin I 24 µg/l (normal <0.04). Coronary angiogram was performed and an atherosclerotic plaque with minor luminal stenosis was present in the distal left circumflex artery (fig. 1a). Severe spontaneous vasospasm of the distal left circumflex was observed on subsequent acquisitions and was associated with recurrence of his chest pain (fig. 1b). The vasospasm was successfully treated with intracoronary nitroglycerin. The remaining coronary arteries were normal. A diagnosis of coronary artery spasm-induced myocardial infarction and ventricular fibrillation was made and our patient was treated with a nitroglycerin patch and amlodipine. He was also counselled regarding the importance of smoking cessation, with active smok-

ing a well-established risk factor for coronary artery spasm [1]. Transthoracic echocardiogram revealed stable mild global left ventricular hypokinesis.

Thyroid function performed on presentation revealed severe hyperthyroidism with a free T₄ 75.1 pmol/l (normal 9.0–26.0), free T₃ 14.9 pmol/l (normal 3.5–6.5) and TSH <0.01 mIU/l (normal 0.1–4.0). A mild peripheral tremor was present but there was no recent history of weight loss, heat intolerance or diarrhoea. There was no evidence of myopathy, Graves' ophthalmopathy and the thyroid was normal in size with no palpable nodules or bruit. A euthyroid state had been present on serial assessment of thyroid function throughout his amiodarone therapy, including 2 months prior to presentation (table 1). Initial treatment with prednisolone 37.5 mg and carbimazole 15 mg twice daily was commenced. TSH receptor, thyroglobulin and thyroid peroxidase antibodies were normal. A subsequent thyroid ultrasound revealed normal thyroid size and echogenicity with no focal masses. Reduced flow was seen on colour Doppler assessment and ^{99m}Tc sodium pertechnetate thyroid scan revealed low tracer uptake 0.3% (normal 1–4%), consistent with type II AIT. β -Blocker therapy was not started in this case. Whilst most cardiac manifestations related to hyperthyroidism respond well to β -blocker therapy [1], these agents can provoke attacks or prolong vasospasm episodes and thus should be avoided in patients with variant angina [2]. Thyroid function normalized within 8 weeks, with a prompt response to therapy typically observed [3]. Prednisolone was weaned without recurrence of hyperthyroidism and on last review, 6 months after initial presentation, he remains free from further chest pain and arrhythmias. Amiodarone therapy was withdrawn in our patient. Whilst the need to cease amiodarone remains controversial, some studies have suggested continued therapy increases the recurrence rate of thyrotoxicosis causing a delay in restoration of euthyroidism [4, 5].

Coronary artery vasospasm is a recognized but rarely described cardiovascular manifestation of hyperthyroidism [6–10]. The primary mechanism of the malignant ventricular arrhythmias

observed in this case was acute myocardial ischaemia during the occlusive vasospasm episodes. Hyperthyroidism in the absence of coronary artery vasospasm is also proarrhythmic, although most commonly associated with supraventricular rhythm disturbance such as atrial fibrillation in 5–15% of cases [11]. In contrast, malignant ventricular arrhythmias are rarely associated with hyperthyroidism and typically only occur in the setting of a thyrotoxic storm [12], hypokalaemia associated with thyrotoxic periodic paralysis [13] and/or an additional underlying proarrhythmic substrate (cardiomyopathy or significant coronary artery disease).

Both endothelial dysfunction (particularly through abnormalities of nitric oxide synthase and its reduced bioavailability) and primary vascular smooth muscle cell hyperreactivity are thought to be major causative mechanisms in coronary artery vasospasm [1]. However, the specific mechanism in hyperthyroidism-related vasospasm is not well understood.

Our case adds to the current small volume of literature highlighting the association between thyrotoxicosis and coronary artery spasm. Whilst AIT is not uncommon, documented coronary artery spasm has rarely been described in this patient subgroup. Non-thyrotoxicosis-related coronary artery spasm typically confers an excellent long-term prognosis, but episodes can precipitate malignant ventricular arrhythmias. Ventricular arrhythmias in thyrotoxicosis-induced coronary artery spasm however have rarely been reported. Patients with severe cardiovascular complications associated with AIT can present difficult management challenges and our report highlights that rapid restoration of euthyroid state can be achieved in type 2 AIT with prednisolone and immediate cessation of amiodarone therapy.

Disclosure Statement

No competing interests exist.

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