An Interesting Case of Amiodarone-Induced Thyrotoxicosis

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Abstract

An interesting case of a known side effect of a common medication. Providing an evidenced based structure for assessment and management of this condition.

Presenting Problem & Summary of History

PC: Mrs X a 44-year-old female with known dilated cardiomyopathy presented with increasing fatigue, weakness, and weight loss.

HPC: Over the past 2 months Mrs X had begun to feel increasingly tired and unable to carry out her normal daily activities without stopping for increasing rests and breaks. These feelings had come on gradually and were getting worse. She had not felt like this before and was concerned that it was her dilated cardiomyopathy getting worse. The symptoms were particularly evident on climbing stairs and other exertion. Also despite an increased appetite Mrs X had experienced weight loss and she was feeling more sensitivity to heat. Other symptoms of note were palpitations, nausea, and light-headedness. Mrs X also stated that she had become more changeable in mood.

PMH:
- Laproscopic cholecystectomy 5 years ago
- Diagnosed with dilated cardiomyopathy (DCM) 2 years ago (suspected post viral aetiology)
- VF arrest 1 year ago led to ICD fitted
- Put on heart transplant list 6 months ago (ejection fraction 11.2%)
- Intra-atrial thrombus found 6 months ago

DH:
-NKDA
- Amiodarone 200mg od (started 1 year ago following VF arrest)
- Carvedilol 3.125 mg od
- Perindopril 4 mg od
- Spironolactone 50 mg od

SH: Housewife who lives with her husband and 2 daughters in their own house with 1 flight of stairs. She is a non-smoker and doesn’t drink alcohol. Before this current presentation Mrs X’s activity was limited to light to moderate exertion due to DCM but she was able to carry out all of her normal activities of daily living and “jobs around the home”.

Examination Findings

General: On examination Mrs X had a blood pressure of 95/65 mmHg, heart rate of 80 bpm and a respiratory rate of 16 breaths per minute, SpO2 98%. Mrs X appeared comfortable but nervous at rest. She was sat in a wheelchair because of marked proximal weakness that had developed. A fine tremor was noted in the hands. Examination of the neck revealed a diffusely enlarged thyroid gland. No associated eye signs or bruit were observed.

Cardiovascular examination revealed an enlarged heart with a laterally displaced apex. Heart sounds were normal (I+II+0). Respiratory examination was normal. Neurological exam revealed normal sensation but decreased proximal power (4/5) and hyper-reflexia.

Summary: A 44-year-old female with known cardiomyopathy taking amiodarone to prevent life-threatening arrhythmias. Presented with a diffuse goitre and the signs and symptoms consistent with thyrotoxicosis.

Differential Diagnoses

The main differential is amiodarone-induced thyrotoxicosis. Other primary causes of thyrotoxicosis should be ruled out such as toxic diffuse goitre (Grave’s), toxic adenoma, toxic multinodular goitre, painful subacute thyroiditis, and excessive pituitary TSH production. Also worsening of the patient’s cardiomyopathy should be considered.

Investigations

Bloods:
- Haematological: FBC
- Biochemical: U&E, LFTs, TFTs
- Immunological: Thyroid autoantibodies (including TSH receptor antibodies and thyroid stimulating immunoglobulin, if other causes of thyrotoxicosis are
considered as likely differentials). Monitoring:
- ECG and monitoring of vital signs (O2, BP, temperature, pulse respiratory rate)

Drug specific monitoring:
Regular monitoring of amiodarone levels and a regular TSH measurement so that comparison with the patients baseline can be made to detect possible amiodarone induced complications.
Monitor possible interactions between: carvedilol + amiodarone (risk cardiotoxicity with bradycardia), carvedilol + Spironolactone + Perindopril (all can increase serum potassium).

Imaging:
- CXR, Echocardiogram (to rule out exacerbation of cardiomyopathy)
- Ultrasound of thyroid, thyroid radioiodine uptake (to investigate the cause of the hyperthyroidism).

Investigations confirmed amiodarone-induced thyrotoxicosis. Increased thyroid hormones (T4) and an undetectable thyroid-stimulating hormone level (TSH) were detected. The thyroid ultrasound was normal and thyroid radioiodine uptake was low.

Management
Attempts for medical control were unsuccessful. The patient was resistant to the withdrawal of amiodarone and treatment with propylthiouracil and high dose steroids (dexamethasone) and Carbimazole (40 mg od) were unsuccessful. The drugs chosen were appropriate for this patient’s condition and were prescribed and given correctly. Thus, due to the patient’s co-morbidities and continued thyrotoxicosis despite attempts at medical management, it was decided that stat control of the patient’s thyrotoxicosis was required. Thus, Mrs X was referred to an endocrine surgeon for consideration for thyroid surgery.

Clinical Decision Making
The important clinical decisions in this case are:

- Was amiodarone the appropriate choice of anti-arrhythmic drug for this patient, considering its well-known side effect profile?

DCM is associated with a 5 year mortality of ~20%. Sudden cardiac death (SCD) accounts for 30% (8-51%) of these deaths and VT and/or VF is the most common mechanism. Controlled trials support the use of Amiodarone and ICDs to reduce the incidence of SCD in patients with nonischaemic DCM and advanced heart disease (ejection fraction less than or equal to 35%). The ICD has been shown to be superior to amiodarone for secondary prevention of VT/VF5, however amiodarone may be effective as an adjunct to ICD to reduce the number of shocks.6 Thus, despite the serious adverse effects of amiodarone e.g. corneal microdeposits (90%), optic neuropathy/neuritis (1%-2%), blue-gray skin discoloration (4%-9%), photosensitivity (25%-75%), hypothyroidism (6%), hyperthyroidism (0.9%-2%), pulmonary toxicity (1%-17%), peripheral neuropathy (0.3% annually), and hepatotoxicity (elevated enzyme levels, 15%-30%; hepatitis and cirrhosis, 3% [0.6% annually]6 the prescription of amiodarone is inline with the European guidelines and metanalysis evidence for the management DCM and prevention of SCD5, but close surveillance of these patients is recommended.

- Could more have been done to classify the likely pathophysiology of the amiodarone-induced thyrotoxicosis, and would this have helped to optimise the management strategy?

Guidelines for the management of amiodarone-induced thyrotoxicosis could not be identified. The following discussion of management is based upon clinical review evidence and case studies of surgery presented in the literature.

Two predominant types of amiodarone induced thyrotoxicosis have been identified and suggested management is different reflecting there underlying pathophysiology:
- Type 1 amiodarone-induced thyrotoxicosis is most commonly seen in patients with preexisting or latent
thyroid disorders and is caused by unregulated hormonal synthesis. - Type 2 is thought to occur in patients with a previously normal thyroid and is due to the release of preformed hormone by an inflammatory destruction of the gland.

These two types can be distinguished by clinical, laboratory, and imaging studies and management initiated accordingly. The suggested medical management for type 1 is with thionamides (e.g. carbimazole and propylthiouracil) and potassium perchlorate. Whereas in the inflammatory type 2 corticosteroids are recommended. Some patients may present with a mixed form or a severe form (as in Mrs X’s case). In these circumstances combination therapy with both thionamides and corticosteroids is recommended in an attempt to establish a rapid clinical response. Thyroidectomy is advised for patients with worsening thyrotoxicosis after failure of medical management to gain control and for those who must be kept on amiodarone (both of these criteria were met by Mrs X). The evidence from case studies described in the literature suggests that control is often inadequate with medical management and surgery is an effective alternative for amiodarone-induced thyrotoxicosis.

Effect of illness episode on patient and family / carers:

Mrs X found the deteriation in her function alarming. She was unable to perform her daily activities and interact as she had previously done with her young family. This was distressing for Mrs X and her family.

Ethical / Governance Issues:

This case has important ethical issues because the patient actually came to harm from the medication given. The risks and benefits of medications need to be fully evaluated before a treatment strategy is offered. This may require a multidisciplinary approach to formulate the best treatment options for a patient. This case also highlights the importance of concordance in medical practice. The potential benefits along with the potential side effects need to be discussed adequately with the patients to facilitate informed consent for a treatment to be started (as long as the patient is competent to evaluate and form this decision). Otherwise serious medical and legal questions could be asked of the prescribing doctor if the patient experiences side effects without adequate warning or prior discussion.

Conclusions

This was an interesting clinical case, which stimulated further research into the patient’s co-morbidities and pharmacological treatment. It demonstrates the difficulty of prescribing medications in patients taking multiple medications and with serious co-morbidities.

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