The mysterious case of the lost pituitary: amiodarone-induced hypothyroidism

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CASE REPORT

A 60-year-old man with a history of ischaemic heart disease, myocardial infarction and previous coronary bypass grafting was admitted to hospital with sustained monomorphic ventricular tachycardia. He was treated with intravenous amiodarone and was later discharged on oral amiodarone 200 mg once a day in addition to his usual antianginal therapy, angiotensin-converting enzyme inhibitor and diuretic.

Approximately 6 months afterwards, he presented with profound tiredness, somnolence, weight gain constipation and fluid retention. He described fluctuating disorientation in time as well as vivid visual hallucinations of people and animals. He had also experienced auditory hallucinations of the voices of his relatives conversing with him in the second person.

Transient secondary delusions were evident. In particular, on the night before his readmission he became convinced that he had lost his pituitary and enlisted his wife to help search for it in the bed.

Thyroid function tests (TFTs) revealed a free thyroxine level of 2 pmol/litre (normal range 11–25 pmol/litre) and markedly raised thyroid-stimulating hormone (TSH) of more than 150 mU/litre (normal range 0.35–5.00 mU/litre). Microsomal thyroid antibodies were present — 670 IU/ml (normal range 0–200 IU/ml). Amiodarone was stopped and he was given thyroxine, with gradual dose titration up to 150 μg per day.

On reviewing his medical notes it was discovered that a diagnosis of hypopituitarism was made in 1984, and he had briefly been treated with steroid, testosterone and thyroxine replacement therapy. This diagnosis had later been refuted. Of relevance is that a thyrotropin-releasing hormone test was normal at this time. Plain X-ray of the skull showed an asymmetrical sella, and a diagnosis of 'empty sella syndrome' was made. There was no previous psychiatric history. Interestingly his basal TFTs at the time of amiodarone initiation showed a normal thyroxine level of 16 pmol/litre but TSH was not measured. A month later his free thyroxine was still 16 pmol/litre and TSH was noted to be elevated at 8.9 mU/litre. He appeared euthyroid and no changes were made to his treatment.

Following the treatment of his hypothyroidism his angina worsened, while his psychiatric symptoms settled within a matter of weeks and his TFTs showed adequate replacement after 5 months. To date there has been no recurrence of his arrhythmia.

In this report a case of amiodarone-induced hypothyroidism is described, in association with interesting psychiatric features.

DISCUSSION

Hypothyroidism is a well-recognized clinical diagnosis.

Amiodarone is an effective anti-arrhythmic drug. Its use, however, is associated with a number of troublesome side-effects, predominantly endocrine, neurological, pulmonary and dermatological. Endocrine side-effects are usually either hypothyroidism or thyrotoxicosis.

Amiodarone-induced hypothyroidism is seen in up to 20% of patients (Counihan and McKenna, 1990) and may occur between 2 weeks and 39 months after starting treatment (Nademanee et al, 1989).

While there is some evidence that antithyroid microsomal antibodies may develop soon after the start of amiodarone treatment (Monteiro et al, 1986), the development of amiodarone-induced hypothyroidism does not appear to be related to the occurrence of de novo thyroid antibodies, but rather to the presence of such antibodies before treatment. In fact, for women with microsomal and/or thyroglobulin auto-antibodies, the relative risk of developing hypothyroidism because of amiodarone therapy is 13.5 (95% confidence interval 3.2–57.4; Trip et al, 1991).

While neurological adverse effects, e.g. tremor, ataxia, peripheral neuropathy, paraesthesiae and vertigo, occur in about 20% of those on long-term amiodarone (Coulter et al, 1990), psychiatric effects are not reported.

We believe therefore that the psychiatric symptoms experienced by our patient were neuropsychiatric manifestations of his altered thyroid status, rather than a direct effect of amiodarone. In fact this was a case of 'myxoedematous madness'.

The concept of myxoedematous madness, whereby hypothyroidism may present with a variety of psychiatric symptoms, such as confusion and disorientation, depression, both visual and auditory hallucinations, persecutory, hypochondriacal and grandiose delusions, was documented by Asher (1949). In none of the cases that he described was the psychosis diagnostic of schizophrenia, although confusion and disorientation with persecutory delusions and hallucinations were common. Nowadays, with the availability of thyroid function tests, it is rare to see such extreme cases and pre-symptomatic diagnosis is usually made.

This man's peculiar delusion and the search for his 'lost pituitary' had its origins in the fact that he had previously been told that he had the 'empty sella syndrome'. The patients' psychopathology, i.e. of a transient secondary delusion, was understandable in terms of his past medical history. This demonstrates that the content of an individual's delusion may be influenced by culture.

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What therefore can be learnt from this case? In patients taking amiodarone, profound hypothyroidism can develop rapidly. Current recommendations for amiodarone initiation include measurement of baseline thyroid function, including serum thyroid-stimulating hormone (TSH) and thyroid antibodies, and TSH monitoring at 6-monthly intervals (at least) during treatment (Newman et al, 1998). In this case, amiodarone treatment was started urgently for a life-threatening arrhythmia and baseline TSH and autoantibodies were not measured. The raised TSH after 1 months' treatment should have alerted us to the impending hypothyroidism, regardless of the euthyroid state and thyroxine at that time.

The management of amiodarone induced hypothyroidism includes thyroxine replacement at doses that cause normalization of TSH level with optional cessation of amiodarone. Our patient elected to stop amiodarone. **HM**

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