Endocrinology, Diabetes & Metabolism CASE REPORTS

R D'Arcy and others | T3 toxicosis due to contaminated supplements

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Exogenous T3 toxicosis following consumption of a contaminated weight loss supplement

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Summary

A 42-year-old male presented with a one-week history of palpitations and sweating episodes. The only significant history was of longstanding idiopathic dilated cardiomyopathy. Initial ECG demonstrated a sinus tachycardia. Thyroid function testing, undertaken as part of the diagnostic workup, revealed an un-measureable thyroid-stimulating hormone (TSH) and free thyroxine (T_4). Upon questioning the patient reported classical thyrotoxic symptoms over the preceding weeks. Given the persistence of symptoms free tri-iodothyronine (T_3) was measured and found to be markedly elevated at 48.9 pmol/L (normal range: 3.1–6.8 pmol/L). No goitre or nodular disease was palpable in the neck. Historically there had never been any amiodarone usage. Radionucleotide thyroid uptake imaging (^{123}I) demonstrated significantly reduced tracer uptake in the thyroid. Upon further questioning the patient reported purchasing a weight loss product online from India which supposedly contained sibutramine. He provided one of the tablets and laboratory analysis confirmed the presence of T_3 in the tablet. Full symptomatic resolution and normalised thyroid function ensued upon discontinuation of the supplement.

Learning points:

- Free tri-iodothyronine (T_3) measurement may be useful in the presence of symptoms suggestive of thyrotoxicosis with discordant thyroid function tests.
- Thyroid uptake scanning can be a useful aid to differentiating exogenous hormone exposure from endogenous hyperthyroidism.
- Ingestion of thyroid hormone may be inadvertent in cases of exogenous thyrotoxicosis.
- Medicines and supplements sourced online for weight loss may contain thyroxine (T_4) or T_3 and should be considered as a cause of unexplained exogenous hyperthyroidism.

Background

Thyrotoxicosis is a common and frequently encountered condition both in the outpatient and emergency settings. The aetiology of this patient's thyrotoxicosis however is unusual particularly given the inadvertent nature of his exposure to T3. Such a dramatic elevation in Free T3 is rarely encountered even in the setting of thyrotoxicosis be it endogenous secretion or exogenous ingestion. The use of radionucleotide uptake scanning has been useful in confirming a physiological picture representative of exogenous thyroid hormone exposure.

Case presentation

A 42-year-old male presented to the emergency department with complaints of palpitations and paroxysmal sweating episodes of one-week duration. The only significant medical

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history was one of idiopathic dilated cardiomyopathy for which he was prescribed Perindopril, Carvedilol and Eplerenone. At presentation he denied any other medication or supplement usage. Further questioning revealed concomitant heat intolerance, insomnia and a degree of weight loss. There was no clear precipitant to the symptoms reported and no suggestion of recent infection.

On clinical examination he appeared tremulous and diaphoretic. There was a regular tachycardia of 110 bpm, and mild hypertension was noted with blood pressure of 155/91 mmHg. Examination of the neck was entirely normal with no goitre or nodular disease palpable. No signs of thyroid eye disease were evident.

ECG demonstrated a sinus tachycardia with well-established lateral ischaemic change and left ventricular hypertrophy. Chest x-ray was normal. The initial routine biochemistry was relatively unremarkable and admission under the care of cardiology was arranged for further investigation.

Investigation

Routine biochemical, renal and liver profiles were entirely normal. Serial troponin T assays excluded an acute ischaemic event. Initial thyroid function tests are shown in Table 1.

- These initial thyroid function results corresponded with a free T3 measured initially at 48.9 pmol/L quickly progressing to >50.0 (ref range: 3.1–6.8 pmol/L).
- Given that this patient presented with a symptom complex that may have been reflective of catecholamine excess, 24 h urinary metanephrines collections were also performed. These were returned within the normal range and are illustrated in Table 2.
- The presence of such a dramatically elevated free T_3, without an obvious cause at that stage, prompted the use of radioiodine uptake scanning. As shown in Fig. 1 this demonstrated total thyroid uptake is almost absent at 0.8% (normal range: 6–18%).
- In light of the above findings the case was re-evaluated with the patient who at this stage reported to taking a 'weight loss supplement' which had been sourced from an Indian online pharmacy. This on closer inspection had been sold as the now banned anorexiant sibutramine. On discussion with the patient it became clear that the onset and progression of his symptom complex followed shortly after commencing the supplement in question. The suspicion thus grew that the pills in question did in fact contain T_3. To examine this possibility, one of the tablets was dissolved with some difficulty and run in the local T_3 assay (ECL immunoassay (ECLIA), using Cobas e602, Roche). This indicated the presence of T_3 in the tablet.

Table 1 Initial thyroid function tests.

	Values	Reference
Free T_4, pmol/L	<5.0	12–22
TSH, U/L	<0.01	0.27–4.2

Table 2 Urinary metanephrines.

	Values	Reference
Normetanephrine, nmol/24h	2402	440–2960
Metanephrine, nmol/24h	607	141–1289

Treatment

Beta blockade provided useful symptomatic control in the interim and quickly normalised heart rate. Ultimately upon discontinuation of the offending supplement there was a complete resolution of the presenting symptoms and a normalising of free T_3, free T_4 and TSH.

Outcome and follow-up

Figures 2 and 3 outline the trends in thyroid function parameters over the course of presentation and follow-up to date. These illustrate a rapid decline in free T_3 measurements in keeping with its relatively short half-life. The subsequent unexpected rise in free T_3 in mid-September corresponds well to the patient commencing a similar supplement from an alternative online supplier. The recurrence of the symptom complex which had triggered his initial presentation prompted him to quickly discontinue these supplements also. Thereafter follows a rapid decline in free T_3 with a corresponding rise in TSH and free T_4 until ultimately all three markers have returned to their respective normal ranges. The patient has maintained an avoidance of weight loss supplements.

Discussion

Many patients with hyperthyroidism be it autoimmune or nodular disease will be found to have an elevated serum T_3 concentration due to combinations of increased production in the thyroid and increased peripheral conversion from T_4 (1). This is typically accompanied by elevations in free T_4 and suppression of TSH. The presence of symptoms suggestive of thyrotoxicosis in the setting of

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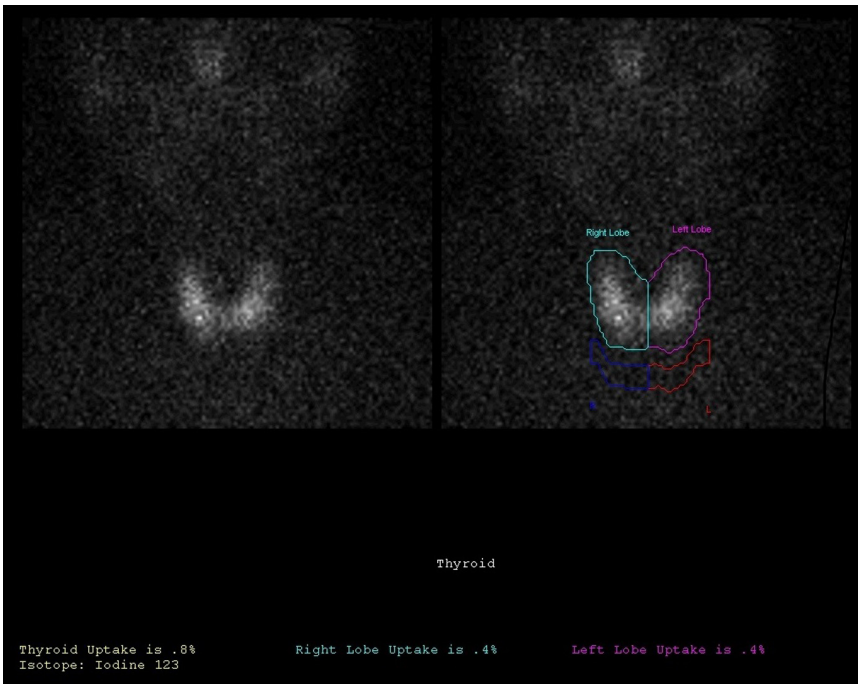

Figure 1
Iodine^{123} tracer uptake.

undetectable free T_4 and suppressed TSH is however quite atypical and should prompt consideration of a T_3 assay.

Whilst isolated T_3 toxicosis is well described, levels as dramatically elevated as seen in this patient are quite unusual and not typical of those expected with autonomous nodular disease or acute thyroiditis. Suppression of TSH and undetectable free T_4 concentrations, although unusual, could be explained in the setting of exposure to such elevated concentrations of T_3.

Radioiodine uptake scanning has been particularly useful in this patient in pointing towards exposure to exogenous T_3. The near absence of uptake on imaging is entirely in keeping with exogenous hormone exposure rather than true hyperthyroidism. Had the aetiology not become apparent at that point then the use of serum thyroglobulin may have been useful in differentiating exogenous hormone ingestion from a thyroiditis picture.

Inadvertent exposure to thyroid hormones, both T3 and T4, through contaminated supplements has previously been reported. A number of commercially available weight loss aids and so-called thyroid supplements have all been found to contain undeclared quantities of thyroid hormones (2, 3). Their presence in such quantities as to precipitate overt thyrotoxicosis as seen in this patient poses an obvious public health risk. It was unfortunately not possible to quantify the T_3 content of the pills involved here due to the structure of the tablet and limitations in the locally available assay.

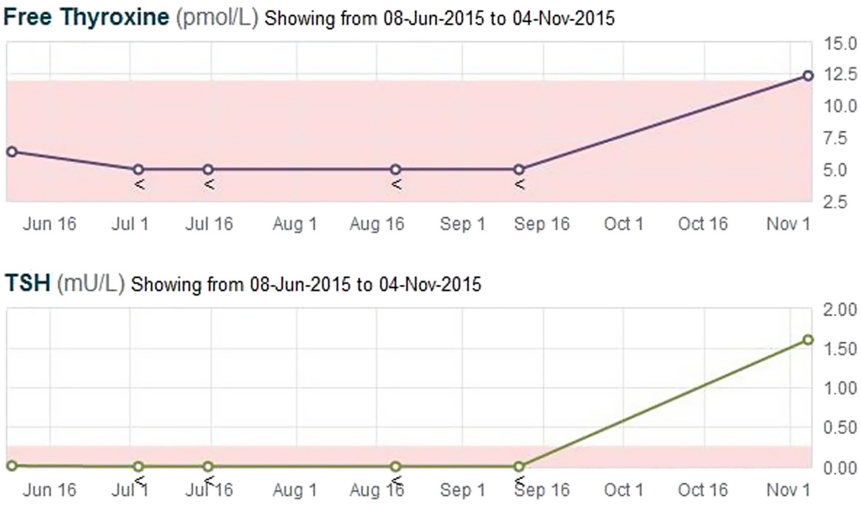

Figure 2
TSH and free T_4 evolution.

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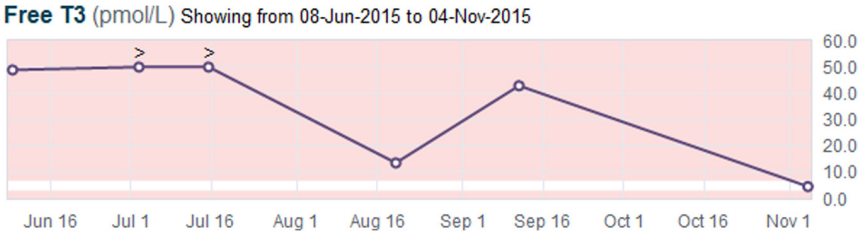

Figure 3
Free T_3 evolution.

It was clear upon discussion with the patient that the ease of access to this product and the seemingly open and professional setup of the suppliers involved had led him to believe he had purchased a safe and regulated product. Of note there has been a recent deterioration in the patient's cardiac function. Whilst this may well have been a progression of his underlying cardiomyopathy, there remains the possibility that his exposure to high concentrations of T3 has hastened that decline.

This patient's atypical hormone profiles and their evolution over the clinical course described provide an unusual but useful case when considering exogenous thyrotoxicosis.

For many patients presenting with this condition, as was seen here, beta blockade provides prompt symptomatic relief whilst waiting for hormone clearance. The relatively shorter serum half-life of T_3 allowed for relatively rapid improvement both biochemically and clinically. For cases involving either T_3 or T_4 administration in large quantities the use of Cholestyramine has proven useful. Given orally, typically 4 g q.i.d., it binds both hormones intestinally to diminish their usual enterohepatic circulation. In rarer cases plasmapheresis has been used for large-dose T_3 and T_4 consumption but is rarely required (4). For the vast majority of patients discontinuation of the offending supplement and conservative management should suffice as was seen here.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this research reported.

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Patient consent
The patient has provided written informed consent.

Author contribution statement
R D'Arcy is the primary author of the case and was a specialist registrar involved in the patient's management, and C H Courtney is the supervising consultant who has provided oversight. M McDonnell and K Spence are local endocrine laboratory managers who have provided assistance and oversight with tablet analysis.

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