Weight Loss-Based Nutraceuticals: A Rare Cause of Thyrotoxicosis and Thyrotoxic Periodic Paralysis

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Abstract

Thyrotoxic periodic paralysis (TPP) is characterized by muscle weakness, areflexia, and hypokalemia in the setting of thyrotoxicosis. We present the case of a 32-year-old male with multiple presentations to the emergency department for lower limb weakness, tremors, diaphoresis, and tachycardia. His initial blood work revealed T3-toxicosis and hypokalemia, and he was treated for TPP with intravenous fluids and potassium supplementation. He had been ingesting weight loss supplements containing iodine, kelp, licorice, and likely undeclared thyroid hormones or mimics. Following discontinuation of supplements, all laboratory investigations normalized and thyrotoxicosis symptoms resolved. This case illustrates that ingestion of thyroid hormone-based nutraceuticals should be considered as a cause of thyrotoxicosis and TPP.

Résumé

La paralysie périodique thyrotoxique (PPT) se caractérise par de la faiblesse musculaire, une aréflexie et une hypokaliémie dans le contexte de la thyrotoxicose. Nous exposons le cas d'un homme de 32 ans qui s'est présenté au service des urgences pour de multiples symptômes, soit une faiblesse des membres inférieurs, des tremblements, une diaphorèse et une tachycardie. Son bilan sanguin initial a révélé une toxicose-T3 et une hypokaliémie, et il a été traité contre la PPT par des solutés intraveineux et une recharge en potassium. Il ingérait des suppléments pour la perte de poids contenant de l'iode, de la laminaire, de la réglisse et probablement des hormones thyroïdiennes ou leurs analogues non déclarés. Après l'arrêt des suppléments, tous les examens de laboratoire sont revenus à la normale et les symptômes de thyrotoxicose ont disparu. Ce cas montre que l'ingestion de nutraceutiques à base d'hormones thyroïdiennes devrait être considérée comme une cause de la thyrotoxicose et de la PPT.

Introduction

Thyrotoxic periodic paralysis (TPP) is a rare disorder characterized by transient muscle weakness and hypo- or areflexia, with concurrent hypokalemia in the setting of thyrotoxicosis.¹⁻⁶ TPP is most often a complication of Graves' disease (GD) but it can arise from any cause of thyrotoxicosis. Signs and symptoms of thyrotoxicosis may be subtle and may present only after the onset of weakness. The mainstay of treatment includes beta-adrenergic blockade, cautious potassium

replacement to prevent rebound hyperkalemia, and treating the underlying etiology of thyrotoxicosis.¹⁻⁶ Previous case reports have described cases of TPP from thyroid hormone-based dietary supplements.^{3,7} We describe the clinical presentation, diagnosis, and management of a patient who developed TPP after taking weight loss supplements containing iodine, kelp, licorice, and likely undeclared thyroid hormone or mimics. This case aims to illustrate the use of nutraceuticals as a cause of thyrotoxicosis and TPP.

Case Report

In March 2019, a 32-year-old Caucasian male presented with a six-week history of clinical thyrotoxicosis including palpitations, diaphoresis, heat intolerance, hand tremors, increased bowel frequency, 75-pound weight loss, and proximal muscle weakness. Investigations for suspected thyrotoxicosis revealed a suppressed thyroid-stimulating hormone (TSH) of <0.01 mIU/L (reference range (RR) 0.40–4.50), with low free T4 (fT4) at 7 pmol/L (RR 9–19) and elevated free T3 (fT3) at 12 pmol/L (RR 4–6.8; Table 1). At that time, the patient was taking kelp and iodine weight loss supplements, which he was advised to discontinue. He was started on methimazole 5 mg daily for a likely diagnosis of GD. He had negative anti-thyroid peroxidase antibodies and TSH receptor antibodies, and low normal thyroglobulin level 7.0 pmol (RR 0–52.9), as well as a normal thyroid radioiodine uptake scan of 23% (2 weeks off methimazole, 2 months off iodine supplements, and on a low iodine diet). Thyroid indices 1 week prior to the scan revealed normal TSH at 2.01 mIU/L, low fT4 8 pmol/L, and normal fT3 at 3.8 pmol/L. He was followed regularly and his thyroid hormone indices remained normal while off methimazole and supplements. Therefore, he was thought to have had thyroiditis that recovered rather than GD.

The patient remained asymptomatic until early October 2019, when he presented to the emergency department (ED) with

lower limb muscle weakness. Blood work showed suppressed TSH <0.01 mIU/L, low fT4 6 pmol/L, and high fT3 15 pmol/L. He reported increased restlessness, and physical examination revealed mild tremors in both hands, diaphoresis, sinus tachycardia, and positive lid lag. Thyroid exam was normal with no palpable nodules or enlargement and no thyroid bruits. There were no physical examination features suggestive of GD including no acropachy, orbitopathy, or pretibial myxedema. Serum potassium (K^+) was low at 3.1 mmol/L (RR 3.7–5.3) and serum magnesium (Mg^{2+}) was 0.59 mmol/L (RR 0.66–1.07). The patient was given 10 mmol intravenous (IV) potassium chloride (KCl) and 2 g IV magnesium sulfate. His weakness resolved rapidly with normalization of serum K^+ and Mg^{2+} . He was prescribed bisoprolol 2.5 mg daily to control hyperadrenergic symptoms, and then discharged home with planned close endocrinology follow-up for further investigations and management.

The patient re-presented to the ED 4 days later with sudden onset of generalized flaccid paralysis. He was diaphoretic and tachycardic at 100 bpm. He exhibited complete upper and lower limb paralysis, areflexia of the lower limbs, and bilateral fine hand tremors. He admitted to eating a high carbohydrate meal the night prior to his presentation but denied vigorous exercise. Blood work revealed severe hypokalemia at 1.7 mmol/L, low TSH 0.07 mIU/L, and low fT4 6 pmol/L, with fT3 initially pending. ECG demonstrated findings consistent with severe hypokalemia (Figure 1).

Figure 1. Initial ECG at time of presentation with K^+ 1.7 mmol/L. Significant changes include prolonged PR interval, prolonged QT interval, diffuse T-wave inversions, and U waves.

A pituitary panel was sent, which revealed normal growth hormone, prolactin, cortisol, and ACTH. Interestingly, total testosterone was elevated at 36.6 nmol/L (RR 6–34) with suppressed follicle-stimulating hormone (FSH) and luteinizing hormone (LH) suggesting secondary hypogonadism. He admitted to taking non-prescribed testosterone cypionate 350 mg intramuscularly weekly to increase his muscle bulk. He was admitted to hospital and was given a total of 150 mmol oral potassium and 50 mmol IV KCl. He, subsequently, developed rebound hyperkalemia with K^+ 6.1 mmol/L. Potassium supplementation was discontinued, and K^+ and ECG normalized at the time of discharge (Figure 2).

Bisoprolol was switched to propranolol 10 mg twice daily upon discharge. Based on his prior ED presentation with elevated fT3, he was suspected to have T3-toxicosis and as a result, methimazole 10 mg daily was started with endocrinology follow-up in 2 weeks' time. Surprisingly, 3 days later, the fT3 level drawn during hospital admission came back low at 2.2 pmol/L and he was advised to discontinue methimazole.

In addition to the testosterone injections, our patient took multiple supplements marketed for exercise tolerance and weight loss for the prior 4 weeks, which contained: (i) caffeine (160 mg) and green coffee blend (400 mg); (ii) ginseng with 150 µg iodine; (iii) multiple algae including 20 mg kelp, 10 mg nori, 20 mg wakame, 25 mg dulse; (iv) 450 mg yohimbe extract; and (v) 100 mg licorice root extract. He denied having taken diuretics or exogenous thyroid hormones, however it is possible that the

supplements contained undeclared thyroid hormone or mimics. We advised him to discontinue all supplements. Repeat thyroid indices completely normalized after 4 weeks. He remains off the supplements and has not had any recurrence of clinical or biochemical thyrotoxicosis or TPP.

Discussion

We describe a case of a Caucasian male who developed thyrotoxicosis and TPP. While the clinical presentation of TPP is similar to that of familial hypokalemic periodic paralysis (FHPP), classically caused by mutations in a calcium channel gene, no clear genetic predisposition exists for TPP.^{8–10} TPP occurs more commonly in the Asian male population, but it is also seen in 0.2% non-Asians with thyrotoxicosis.^{2,3} Paralysis in TPP occurs due to hypokalemia that results from increased Na^+/K^+ adenosine triphosphatase (ATPase) pump activity from thyrotoxicosis-mediated beta-adrenergic stimulation^{2,4–6}. Other Na^+/K^+ ATPase pump activators can exacerbate hypokalemia-induced muscle weakness in TPP such as vigorous exercise, endogenous insulin surge after ingestion of high carbohydrate meal, or androgens which explains the male predominance seen in TPP.^{1,2,4–6} The ingestion of a high carbohydrate meal and use of testosterone increased our patient's risk for developing hypokalemia and paralysis in the context of TPP.

TPP is most often a complication of GD; however, it can occur secondary to thyrotoxicosis of any etiology such as

Figure 2. ECG at time of discharge with K^+ 5.0 mmol/L.

Table 1. Timeline of Clinical Presentation and Corresponding Biochemical Abnormalities

Date	Event	Intervention	TSH (mIU/L) (RR 0.40–4.50)	fT4 (pmol/L) (RR 9–19)	fT3 (pmol/L) (RR 4–6.8)	Potassium (mmol/L) (RR 3.7–5.3)
March 2019	Initial presentation of thyrotoxicosis	Started on methimazole and bisoprolol (unknown doses)	<0.01	7	12	Not done
April 2019	Initial consultation with Endocrinology	N/A	2.01	8	3.8	Not done
June 2019	N/A	Methimazole and bisoprolol discontinued 1 month prior	2.92	8	4.4	Not done
July 2019	N/A	N/A	2.45	11	Not done	Not done
August 2019	N/A	N/A	2.27	12	Not done	Not done
October 8, 2019	Initial ED visit with lower limb muscle weakness	Started on bisoprolol 2.5 mg daily, methimazole 10 mg daily	<0.01	6	15	3.1
October 13, 2019	Second ED visit with flaccid paralysis	Bisoprolol switched to propranolol 10 mg twice daily; methimazole discontinued	0.07	6	2.2	1.7
November 2019	First follow-up visit with Endocrinology	All medications and supplements discontinued	3.30	9	3.9	4.4
December 2019	Second follow-up visit with Endocrinology	All medications and supplements remain discontinued	3.07	10	4.4	4.2

the thyrotoxic phase of thyroiditis, exogenous use of thyroid hormone supplements, or toxic thyroid nodules.^{1–6} Our patient had objective muscle weakness on at least two separate occasions with documented hypokalemia, and suppressed TSH in the context of nutraceutical use for weight loss. Although some of our patient's symptoms could have been attributed to the side effects of certain ingredients in the supplements independent of thyroid function (e.g., adrenergic stimulation by caffeine,¹¹ pseudohyperaldosteronism secondary to chronic licorice consumption,¹² and so on), they would not cause concurrent abnormal thyroid function tests. Ingredients high in iodine, such as kelp and other algae,¹³ may directly lead to thyrotoxicosis and TPP.

Weight loss supplements are typically not regulated by federal health authorities and may therefore contain undeclared thyroid hormone or mimics.^{14,15} Poon et al. described three

patients who developed factitious thyrotoxicosis after taking supplements containing undeclared animal thyroid tissue.¹⁶ Kang et al. found that 9/10 analyzed herbal dietary supplements contained undeclared, but detectable T3 and/or thyroxine (T4) content.¹⁷ There are also a few reported cases of patients who developed TPP following the use of a thyroid hormone analog, tiratricol.^{3,7} Tiratricol is an active derivative of triiodothyronine (T3), which has enhanced thyromimetic effects compared to T4.⁷ There have been two warnings issued by the FDA about the risk of thyrotoxicosis with tiratricol use.^{7,18} Our patient denied having taken tiratricol, but it is possible that his supplements contained undeclared T3 (or analog) causing T3-toxicosis with elevated fT3, low fT4, and suppressed TSH on his first ED presentation, similar to previously reported cases.^{14,15} However, fT3 may be low in cases where the exogenous thyroid hormone source has been discontinued a few days prior to symptom onset, given the short

half-life of T3,⁷ as it was observed on his second ED presentation. Thyroglobulin level is a useful biochemical test to distinguish endogenous from exogenous thyrotoxicosis.¹⁹ It is suppressed in cases of thyrotoxicosis factitia but increased in endogenous thyrotoxicosis. However, thyroglobulin levels should be interpreted along with anti-thyroglobulin antibodies since positive antibodies will interfere with the thyroglobulin assay causing falsely high or low thyroglobulin levels.¹⁹ The patient's thyroglobulin level was checked when his anti-thyroglobulin antibody was 3 IU/mL (RR 0–3). Although the patient's thyroglobulin level was not suppressed, it was at the lower limit of normal with a low free T4, making it more likely a result of exogenous use of, possibly, thyroid hormones or thyroid hormone-based nutraceuticals.

Hypokalemia in TPP results from an intracellular potassium shift rather than total body depletion. Therefore, rebound hyperkalemia is a common complication following potassium repletion, and judicious replacement is warranted.^{1,2,4–6,20} Of the nine TPP cases reviewed by Clarine et al., six patients developed rebound hyperkalemia.⁵ Manoukian et al. reviewed 24 TPP cases and concluded that potassium replacement should not exceed 90 mEq KCl within 24 h, unless there is a concurrent reason for potassium wasting, such as gastrointestinal or renal losses.²⁰ Treatment of the underlying cause of thyrotoxicosis is the mainstay of prevention of recurrent episodes.

Conclusion

This case illustrates the thyrotoxic effects of weight loss-based nutraceuticals containing iodine, kelp, licorice, and likely undeclared thyroid hormones or mimics. In this case, their ingestion resulted in clinical and biochemical thyrotoxicosis and TPP in a young healthy male. This case demonstrates that the ingestion of thyroid hormone-based nutraceuticals should be considered as a cause of thyrotoxicosis and TPP, and it is important to ensure its timely, accurate diagnosis and management. A detailed history of over-the-counter supplements should be obtained, and most importantly, clinicians should educate patients about the risks of using these widely available but loosely regulated products.

Research Ethics Board

Research Ethics Board approval was not required for our case study. Informed consent was obtained from our patient.

Author Contributions

Conception and design: Shirley Shuster, Caitlyn Vlasschaert, Sara Awad

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Conflicts of Interest

The authors declare no conflicts of interest.

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