Reminder of important clinical lesson

Intermittent and recurrent episodes of subclinical hypothyroidism, central hypothyroidism and T3-toxicosis in an elderly woman

Marta Cano Megías,¹ Pedro Iglesias,¹ Mercedes García Villanueva,² Juan José Díez¹¹Department of Endocrinology, University Hospital Ramon y Cajal, Madrid, Spain²Department of Pathology, University Hospital Ramon y Cajal, Madrid, Spain

Correspondence to Marta Cano Megías, mcanomegias@gmail.com

Summary

Exogenous thyrotoxicosis is usually caused by ingestion of excessive amounts of thyroid hormone, which could be intentional or surreptitious (known as factitious thyrotoxicosis). Non-pharmacological exogenous thyrotoxicosis is an exceptional event. One example is alimentary thyrotoxicosis, which is caused by the ingestion of meat or sausage containing thyroid tissue, inadvertently mixed with traces of muscles and other tissues of the animal's neck (hamburger thyrotoxicosis). We report for the first time a patient who had recurrent episodes of triiodothyronine (T3) toxicosis for several years due to inadvertent chronic consumption of contaminated traditional Spanish cold meat with porcine thyroid.

BACKGROUND

Alimentary thyrotoxicosis could be an authentic challenge for physicians. This case exemplified a non-frequently described condition in the last few years. To our knowledge, it is also the first well-documented case in Spain, related to a traditional cold meat.

CASE PRESENTATION

A 82-year-old woman was admitted in March 2009 for the evaluation of thyroid dysfunction. There was no family history of thyroid disease. She was initially diagnosed of subclinical hypothyroidism in May 2006 by her primary care physician and followed up without levothyroxine therapy. She was first admitted in our hospital in May 2007 with the suspicion of central hypothyroidism due to the finding of low serum concentrations of free thyroxine, FT4 (0.45 ng/dl; N: 0.70–1.48) and thyrotropin, TSH (0.218 mU/l; N: 0.350–4.950). Investigations did not confirm it and she was discharged with the diagnosis of subclinical hypothyroidism (TSH 14.8 mU/l; FT4 0.8 ng/dl). Treatment with levothyroxine (50 µg/day) was started. Four months later, the patient showed biochemical data of T3-toxicosis (TSH 0.005 mU/l; FT4 0.57 ng/dl; and FT3 6.25 pg/ml; N: 1.71–4.53) and levothyroxine was withdrawn. After 3 months without therapy, hormonal study was compatible again with central hypothyroidism (TSH 0.008 mU/l; FT4 0.56 ng/dl; and FT3 3.45 pg/ml). Three months later, in May 2008, thyroid function tests again suggested the presence of T3-toxicosis (TSH 0.035 mU/ml; FT4 0.55 ng/dl; and FT3 8.44 pg/ml). In June 2008, a central hypothyroidism (TSH 0.0 mU/l, FT4 0.57 ng/dl; and FT3 3.71 pg/ml) was newly diagnosed. In December 2008 a new episode of T3-toxicosis (TSH 0.002 mU/l; FT4 0.91 ng/dl; and FT3 6.90 pg/ml) was developed. The patient did not take any known drug that affects thyroid function. On physical examination she appeared as a

euthyroid woman. She weighed 42.2 kg, her height was 155 cm and she had a blood pressure of 145/65 mm Hg, with a heart rate of 90 bpm. Neck examination did not show goitre or cervical nodes. At that time, her biochemical data showed again central hypothyroidism (TSH 0.04 mU/l; FT4 0.6; and FT3 3.43 pg/ml). Thyroid autoimmunity (thyroid peroxidase antibodies, antithyroglobulin antibodies and thyroid-stimulating immunoglobulin) was negative. Serum thyroglobulin level was normal (12.2 ng/ml; N: 3–40). The serum titres of anti-T3 and anti-T4 autoantibodies were also negative. Thyroid ultrasound showed a small thyroid gland without nodules and Tc-99m pertechnetate thyroid scan revealed a small thyroid with heterogeneous uptake pattern. She remained hospitalised for 23 days and during this admission, she had a hormonal pattern of central hypothyroidism that spontaneously became subclinical primary hypothyroidism (figure 1). The patient was discharged without treatment, and at the first outpatient visit 1 month later, hormonal study was again consistent with T3 toxicosis (TSH 0.003 mU/l; FT4 0.81 ng/dl; and FT3 14.1 pg/ml). Further anamnesis revealed an excessive daily consumption for years of *chopped pork*, a traditional Spanish food product made from coarsely chopped pork meat and fat. Three months after the patient stopped eating it, thyroid function tests became normal for the first time since her first visit, that is, 3 years. Although the presence of thyroid tissue in the pathological study of a small sample of commonly consumed meat could not be proved, pork neck tissues such as thymus, cartilage and salivary glands were detected, indicating the possibility of a chronic consumption of porcine thyroid tissue (figure 2).

DIFFERENTIAL DIAGNOSIS

Alimentary thyrotoxicosis should be suspected in cases of self-limiting and recurrent episodes of hyperthyroidism with low Tg levels and negative antithyroid antibodies.

Figure 1 Changes in serum TSH and FT3 concentrations over the 3-year follow-up. The shaded and white areas show the normal range for TSH and FT3, respectively.

Thyroid scintigraphy usually shows a low uptake pattern.¹ Furthermore, in clinical practice, sometimes a patient's symptoms are not associated with the laboratory findings, as it happened in our case. We should also take into account that immunoassays do not always give correct results.² Even antibodies could successfully interfere with laboratory measurements. So an assay's results could vary depending on the type of the commercial kit and the binding site of the antibody to the antigen, resulting in falsely high or low hormone levels. In conclusion, our case illustrates the importance of adequate and detailed anamnesis in cases of recurrence episodes of symptoms that simulate silent thyroiditis.

OUTCOME AND FOLLOW-UP

Three months after the patient stopped eating chopped pork, thyroid function tests became normal for the first time since her first visit. However, later during follow-up, she developed a subclinical hypothyroidism. In the last visit in March 2012, the patient showed a mild subclinical

hypothyroidism (TSH<10 mU/l) without needing treatment with levothyroxine.

DISCUSSION

Alimentary thyrotoxicosis is a rare cause of exogenous thyrotoxicosis. Its prevalence and incidence are not known, because medical reports are related to isolated cases or community outbreaks. It is usually caused by ingestion of meat or sausage containing thyroid tissue, inadvertently mixed with traces of muscles and other tissues of the animal's neck. Only five reports of alimentary thyrotoxicosis, all of them due to consumption of bovine thyroid gland in ground beef, have been reported so far.³⁻⁷ Hedberg *et al.*³ reported in 1987 one of the first alimentary thyrotoxicosis community outbreaks in areas of Minnesota, South Dakota and Iowa related to the consumption of ground beef prepared from neck trimmings that contained thyroid bovine gland, during a process called gullet trimming in a single slaughtering plant. One year later (1988), Kinney *et al.* described another case of community outbreak in Nebraska probably in patients

Figure 2 H&E. Pathological study of chopped: salivary gland (A) and thymus tissue (B).

who had been eaten ground beef that was contaminated with bovine thyroid gland. The meat came from a non-regular supplier in Nebraska, which had reportedly instituted the practice of trimming gullets.⁴ In 2008, Conrey *et al.* described a case-control study of community outbreaks in Minas, Uruguay, caused by the consumption of minced beef and chorizo contaminated with thyroid gland. A beef supplier selling meat cuts containing thyroid gland was identified.⁵ Additionally, it has also been described isolated cases of alimentary thyrotoxicosis. Parmar *et al.*⁶ reported a recurrent hamburger thyrotoxicosis case, in a patient who lived on a farm and every couple of years she slaughtered a cow from her herd, which was the main source of meat, and it was inadvertently contaminating with thyroid tissue. Lastly, Hendriks *et al.*⁷ documented another case caused by excessive intake of sausages contaminated with thyroid tissue. After the patient stopped eating them, he became and remained euthyroid. Our patient could be the first clinical case of alimentary thyrotoxicosis induced by chronic consumption of contaminated pork with porcine thyroid.

Exogenous thyrotoxicosis should be suspected in the presence of hyperthyroidism, no struma, a low take in thyroid scintigraphy and a low serum thyroglobulin.⁷ This picture should be carefully considered by a physician before giving a wrong diagnosis of silent thyroiditis.

The presence of goitre and other typical medical sign and symptoms could be helpful in the diagnosis procedure. Exophthalmia, proptosis and goitre are commonly absent in exogenous thyrotoxicosis, although elderly patients could develop endogenous hyperthyroidism without such combination.^{6 7}

A low uptake in a thyroid scintigraphy is not only present in exogenous thyrotoxicosis, but also in thyroiditis or iodide-induced hyperthyroidism. Both causes were excluded in our case: antibodies were negative and the patient did not undergo any medical iodide administration procedure (or drug) during follow-up.

The thyroglobulin level measure is key to differentiate endogenous or exogenous hyperthyroidism.⁶ It is elevated in endogenous causes. But it is just low in exogenous ones. This point is a constant hallmark of thyrotoxicosis factitia or exogenous thyrotoxicosis and also of all previously reported cases of alimentary thyrotoxicosis.

This clinical picture of isolated cases is really hard to diagnose, and could take a long period of time (in our case, 3 years). Even other authors have also reported a 10-year diagnosis period.⁶

Alimentary thyrotoxicosis should be differentiated from other forms of exogenous thyrotoxicosis such as intentional (or accidental, such as diet pills or children) suppression of TSH and surreptitious intake of thyroid hormones (thyrotoxicosis factitia), such as intentional purpose of losing weight.

In conclusion, alimentary thyrotoxicosis should be suspected in the presence of recurrent episodes of spontaneously resolving thyrotoxicosis associated with low or normal-low thyroglobulin levels, negative thyroid autoantibodies and low uptake pattern in thyroid scan. In most cases, a detailed and focused anamnesis is the key to diagnose this uncommon clinical entity.

Learning points

- ▶ Non-pharmacological exogenous thyrotoxicosis is an exceptional event.
- ▶ Alimentary thyrotoxicosis is caused by the ingestion of meat or sausage containing thyroid tissue.
- ▶ Alimentary thyrotoxicosis should be suspected in the presence of recurrent episodes of spontaneously resolving thyrotoxicosis associated with low or normal-low thyroglobulin levels, negative thyroid autoantibodies and low uptake pattern in thyroid scan.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Mittra ES**, Niederkoher RD, Rodriguez C, *et al.* Uncommon causes of thyrotoxicosis. *J Nucl Med* 2008;**49**:265–78.
2. **Jones AM**, Honour JW. Unusual results from immunoassays and the role of the clinical endocrinologist. *Clin Endocrinol (Oxf)*. 2006;**64**: 234–4.
3. **Hedberg CW**, Fishbein DB, Janssen RS, *et al.* An outbreak of thyrotoxicosis caused by the consumption of bovine thyroid gland in ground beef. *N Engl J Med* 1987;**316**:993–8.
4. **Kinney JS**, Hurwitz ES, Fishbein DB, *et al.* Community outbreak of thyrotoxicosis: epidemiology, immunogenetic characteristics, and long-term outcome. *Am J Med* 1988;**84**:10–19.
5. **Conrey EJ**, Lindner C, Estivariz C, *et al.* Thyrotoxicosis outbreak linked to consumption of minced beef and chorizo: Minas, Uruguay, 2003–2004. *Public Health* 2008;**112**:1264–74.
6. **Parmar MS**, Sturge C. Recurrent hamburger thyrotoxicosis. *CMAJ* 2003;**169**:415–17.
7. **Hendriks LEL**, Looij BJ. Hyperthyroidism caused by excessive consumption of sausages. *Neth J Med* 2010;**68**:135–7.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Megías MC, Iglesias P, Villanueva MG, Díez JJ. Intermittent and recurrent episodes of subclinical hypothyroidism, central hypothyroidism and T3-toxicosis in an elderly woman. *BMJ Case Reports* 2012;10.1136/bcr-2012-006260, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow