

Hyperthyroidism with Gynaecomastia as the Initial Complaint: A Case Report

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Abstract

Although gynaecomastia is a well-documented manifestation among male patients with hyperthyroidism, it is extremely rare to present as the initial or chief complaint in a subject with undiagnosed hyperthyroidism. We report a case of a 38-year-old Chinese man presenting with painful enlargement of both breasts of one month's duration. Examination revealed bilateral tender gynaecomastia. In addition, he was noted to have warm and moist peripheries, resting tachycardia and an enlarged goitre. Hyperthyroidism was confirmed biochemically. Treatment of thyrotoxicosis resulted in resolution of the gynaecomastia. This case report demonstrates that gynaecomastia may predominate over the commonly recognised, more manifest and urgent symptoms of hyperthyroidism.

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Key words: Breast enlargement, Graves' disease, Presenting feature, Thyrotoxicosis

Introduction

Gynaecomastia is not a commonly recognised feature among the myriad symptoms and signs associated with hyperthyroidism. A review of the literature disclosed only eight reported cases of gynaecomastia as a presenting feature in thyrotoxicosis,¹⁻⁵ and herein we describe an additional case. However, recognition of such an unusual presentation in a common disease like hyperthyroidism is important to ensure appropriate management and to avoid unnecessary investigations.

Case Report

A 38-year-old Chinese man complained of painful enlargement of both breasts for one month. He had no history of drug or steroid ingestion, alcohol intake, or systemic illness. He originated from southern China and had worked as a construction worker in Singapore for one year. Physical examination revealed tender, palpable glandular tissues, measuring about 2.5 cm beneath and around each areola. There was no discharge from the nipples. Hyperthyroidism was suspected based on clinical findings of warm and moist extremities with fine hand tremors, and a resting tachycardia of 120 beats per minute. He also had a mildly enlarged, diffuse and symmetric goitre. He had no obvious thyroid-associated

eye signs. His body habitus, hair distribution, and testicular volume were normal for an adult male. On direct questioning, he had experienced hand tremors, increased sweating, occasional palpitations and breathlessness on exertion for 3 to 4 months, although these symptoms did not bother him as much as the more recent onset of breast tenderness. He had unaffected libido and potency.

Laboratory investigations showed an elevated free thyroxine level of 62.2 pmol/L (range 10.3 to 31.0) and a suppressed thyroid stimulating hormone of less than 0.06 mU/L (range 0.32 to 5.00). Anti-thyroperoxidase antibody measured by semi-quantitative method was positive at 1/400 dilution. His serum testosterone level was elevated at 41.9 nmol/L (range 10.4 to 34.7), whereas his estradiol level was 117.3 pmol/L (range 22 to 161). His serum prolactin level was normal at 7.3 µg/L (range 5.0 to 27.7).

The patient was started on tablet carbimazole 40 mg daily for thyrotoxic Graves' disease. He was clinically euthyroid when reviewed two months later, together with complete resolution of gynaecomastia. He missed his thyroid function testing at 6 weeks of treatment, whereas the result at 3 months showed over-treatment with free thyroxine falling to 8.7 pmol/L and a normal thyroid stimulating hormone of 0.96 mU/L. Repeat sex steroid measurements were not done due to cost considerations.

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Discussion

Clinically evident gynaecomastia has been variously reported in 2% to 44% of male patients with thyrotoxicosis.^{2,6,7} However, its occurrence as the initial or chief complaint in patients with undiagnosed thyrotoxicosis is extremely uncommon. When gynaecomastia is noted as the initial manifestation of hyperthyroidism, it may be because it is the earliest symptom, it is the dominant symptom, or that other symptoms are not being appreciated by the patient. In our case, other symptoms of hyperthyroidism had been present for a longer duration that the patient accepted them as normal until specifically questioned about such symptoms. Our review of the literature revealed only 8 similar cases besides our current case report, as summarised in Table I. The age of these patients ranged from 20 to 75 years, with all of them suffering from Graves' disease.¹⁻⁵ Interestingly, all the reported cases complained of significant breast soreness or tenderness, and one patient also developed galactorrhoea despite a normal serum prolactin level.⁴ Gynaecomastia was noted to be unilateral in 4 reported cases and bilateral in the remaining 4, and all resolved upon treatment of thyrotoxicosis.

Although the association of gynaecomastia and hyperthyroidism was long noted by von Basedow more than 100 years ago, it was not until 1968 that Becker and co-

workers¹ first reported on the histological findings of the breast tissue in patients before and after treatment of hyperthyroidism. In hyperthyroid men with gynaecomastia, they demonstrated that the ducts were elongated and tortuous, the epithelium hyperplastic and papillary, and the periductal stroma loose and myxomatous. Regression was noted with treatment of hyperthyroidism, with the histology showing the epithelium receded in height, the ducts became less branched, and stroma less dense and collagenous.¹ Subclinical gynaecomastia may assume an even greater prevalence among male patients with hyperthyroidism, as suggested in another study by Becker and colleagues.⁶ They found histologic evidence of gynaecomastia in 15 (83%) of the 18 hyperthyroid men who underwent bilateral breast biopsies at the time of subtotal thyroidectomy, whereas breast enlargement was noted clinically in only 6 patients (33%).

Gynaecomastia is believed to develop in hyperthyroid subjects as a result of the increase in the physiologically active oestrogen to androgen ratio. Hyperthyroidism is associated with a several-fold increase in levels of sex hormone binding globulin (SHBG) as a result of primary hepatic stimulation by thyroid hormones.⁸⁻¹⁰ This could have tipped the sex hormone balance as testosterone (T) binds to SHBG with greater affinity and is much nearer

TABLE I: SUMMARY OF REPORTED CASES OF HYPERTHYROID MEN WITH GYNAECOMASTIA AS THE PRESENTING FEATURE

Author (year of publication)	Age	Thyroid function results (see footnotes)	Clinical features (<i>presenting complaint in italics</i>)
Becker et al ¹ (1968)	75 y	PBI = 14 ug/100ml; RAIU = 58%	<i>Right breast tenderness for several weeks;</i> other symptoms of hyperthyroidism for 8 months
	52 y	PBI = 14 ug/100ml; RAIU = 64%	<i>Left breast tenderness for two weeks;</i> other symptoms of hyperthyroidism for 6 months
	66 y	PBI = 14 ug/100ml; RAIU = 57%	<i>Bilateral breast tenderness and enlargement for one week;</i> other symptoms of hyperthyroidism for 6 months
Cheah ² (1971)	33 y	PBI = 10.5 ug/100ml; RAIU = 66%	<i>Bilateral breast tenderness and enlargement for one month;</i> other symptoms like tremors, sweating and weight loss for 24 months
Bercovici et al ³ (1972)	20 y	PBI = 11.5 ug/100ml; RAIU = 84%	<i>Bilateral breast tenderness and swelling for two weeks;</i> other symptoms like palpitation, sweating, muscle weakness and weight loss for 4 months
Muthusamy ⁴ (1991)	37 y	Total T4 = 260 nmol/L	<i>Bilateral breast enlargement and secretion for one month;</i> other symptoms include tremors, increased appetite and weight loss
Gordon et al ⁵ (1997)	64 y	Total T4 = 304 nmol/L TSH <0.1 mU/L	<i>Left breast pain and swelling;</i> other symptoms of hyperthyroidism became evident only 8 weeks later
	35 y	Total T4 = 191 nmol/L TSH <0.06 mU/L	<i>Left breast tenderness and enlargement for three weeks;</i> other symptoms of hyperthyroidism present but were assumed to be "normal" by the patient

PBI: serum protein bound iodine (normal 4 to 8 ug/100ml);

RAIU: radioactive iodine uptake at 24 hours (normal 15% to 30%);

Total T4: total thyroxine (normal 64 to 154 nmol/L);

TSH: thyroid stimulating hormone (normal 0.5 to 5.0 mU/L)

saturation. The physiologically active (free and albumin-bound) T therefore falls as SHBG rises, and the pituitary responds by increasing luteinizing hormone (LH) production. This in turn stimulates the Leydig cells, which increase their production of T and estradiol (E_2), until the bioavailable T is returned to normal. This, however, may result in an abnormally high level of unbound E_2 , because of the weaker binding of E_2 to SHBG. Changes in sex hormone balance in hyperthyroidism were clearly demonstrated by Chopra and Tulchinsky,¹¹ who found that the mean ratio of serum unbound E_2 to T was significantly greater in hyperthyroid men with Graves' disease compared to normal subjects (0.65 ± 0.10 versus 0.34 ± 0.02 ; $P < 0.01$). While we were unable to measure the physiologically active T and E_2 in our patient due to the lack of facility, the finding of an elevated serum total testosterone level is consistent with the above hypothesis.

Several other mechanisms could have contributed to the imbalance of sex hormones in hyperthyroidism. Elevated E_2 levels in hyperthyroid subjects also seem to result from increased peripheral tissue aromatisation of androgens as well as increased glandular secretion of oestrogens.^{7,9,12} The excessive oestrogens will further elevate SHBG levels and alter the bioavailable E_2 to T ratio.³ It has also been demonstrated that serum LH remained elevated in men with hyperthyroidism despite increased serum unbound E_2 and normal unbound T levels.¹¹ The mechanism of LH elevation is not clear, although it has been postulated to result from either an abnormality in Leydig cell function or an altered setting of the hypothalamo-hypophyseal-gonadal axis, or a combination of both factors.¹¹ This situation may increase aromatization;¹² however, serum LH is noted to gradually decrease to normal levels with the return of the euthyroid state.^{7,10}

It is interesting to note that not all male patients with hyperthyroidism have demonstrable gynaecomastia despite finding elevated ratios of unbound E_2 to T.¹¹ This could signify the existence of "subclinical" gynaecomastia

that is not detected clinically or that other factors, such as the duration of the exposure and/or variations in individual target tissue responsiveness.⁷

In conclusion, our case with painful gynaecomastia depicts an unusual presenting symptom of hyperthyroidism. Its pathogenesis is believed to be due to an increase in the ratio of physiologically active oestrogens to androgens, and it is fully reversible with treatment of hyperthyroidism. Recognition of this uncommon presentation in a common disease like hyperthyroidism will help to expedite therapy and avoid unnecessary investigations.

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