

Gynaecomastia as the First Complaint in A Case of Undiagnosed Graves' Disease

Tanı Almamış bir Graves' Hastalığı Olgusunda İlk Yakınma Olarak Jinekomasti

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Abstract

Gynaecomastia is defined as a generalised enlargement of the male breast. An alteration in the balance between the stimulatory effects of oestrogen on mammary epithelial tissues and the inhibitory actions of androgens is believed to underlie the pathophysiology of gynaecomastia. Although the association gynaecomastia and hyperthyroidism is well recognised, it is very rare that a hyperthyroid patient present with gynaecomastia as the chief and first complaint. Here we report a patient with Graves' disease, who applied to our clinic with complaints of gynaecomastia instead of classical hyperthyroidism symptoms. His gynaecomastia resolved after successful treatment of hyperthyroidism with radioiodine. *Turk Jem 2007; 11: 59-61*

Key words: Gynaecomastia, hyperthyroidism, Graves' disease, oestrogen, testosterone

Özet

Jinekomasti erkek meme dokusunun jeneralize büyümesi olarak tanımlanır. Jinekomasti patofizyolojisinin temelinde meme epitelyal dokusunda östrojenin uyarıcı etkileri ve androjenlerin inhibitör etkileri arasındaki dengedeki bir değişimin yattığına inanılmaktadır. Jinekomasti ve hipertiroidi arasındaki ilişki iyi bir şekilde tanımlanmış olmasına karşın hipertiroidili bir hastanın ilk ve ana yakınma olarak jinekomasti ile başvurusu nadir bir klinik sunumdur. Bu yazıda klasik hipertiroidi semptomları yerine jinekomasti yakınmasıyla kliniğimize başvuran bir Graves' hastası bildirilmiştir. Hastada var olan jinekomasti hipertiroidinin radyoiodin ile başarıyla tedavisi sonucunda düzelmiştir. *Turk Jem 2007; 11: 59-61*

Anahtar kelimeler: Jinekomasti, hipertiroidi, Graves' hastalığı, östrojen, testosteron

Introduction

Gynaecomastia is the benign enlargement of the male breast as a result of the proliferation of ductal tissue. Gynaecomastia is an often-encountered entity in clinical practice. It is thought to result from an oestrogen/ androgen imbalance at breast tissue level, which can be caused by various pathophysiological mechanisms. The majority of men with gynaecomastia are asymptomatic. Patients tend to present because of persistently tender breasts or unsatisfactory body image (1). Of all cases, who applied to a physician with gynaecomastia, 25% are idiopathic or related to ageing, 25% are classified as persistent after puberty, 10 to 15% are caused by drugs, 10% have a relation with nutritional factors or liver disease, 10% are caused by primary hypogonadism, and 3% are due to testicular neoplasms. The remaining cases are due to various diseases (2).

Gynaecomastia may be diagnosed in men during the course of hyperthyroidism. It is very rare to present as the chief complaint and the primary manifestation of hyperthyroidism (3, 4). Gynaecomastia in hyperthyroidism is mostly bilateral and the breasts are usually tender. Graves' disease is the most common cause of hyperthyroidism seen in association with gynaecomastia (3-5).

Here we report a patient with Graves' disease, who applied to our clinic with gynaecomastia instead of classical hyperthyroidism symptoms.

Case

A 36-year-old man applied to our outpatient clinic with complaints of bilaterally painful gynaecomastia. He was not on any medications and alcohol consumption. On further questioning, he revealed that he had lost six kg of weight over a period of about three months. He had fatigue, dyspepsia and decreased libido.

Physical examination of patient revealed bilateral tender gynaecomastia (Figure 1a, b). There were irritability, resting tachycardia and fine tremor. His thyroid gland was diffusely enlarged (grade-1B). Thyroid function test revealed a thyrotropin (TSH) level of 0.03 μ U/ml (normal: 0.4-5), free 3,5,3'-triiodothyronine (FT₃) of 25.7 pg/dl (normal: 1.8-4.2) and free thyroxine (FT₄) of 6.1 ng/dl (normal: 0.8-1.9). The results for serum anti-thyroid peroxidase antibody (ATPO), anti-thyroglobulin antibody (ATG) and thyroid receptor antibody (TRAb) were 87 IU/ml (normal: 0-10), < 20 IU/ml (normal: 0-20) and 78 U/L (normal: 0-10), respectively. In ultrasound examination, thyroid gland was diffusely heterogeneous and there was no nodule. Technetium 99m thyroid scintigraphy revealed diffuse hyperactivity. Gynaecomastia was confirmed by ultrasound. In ultrasound examination, proliferation of fibroglandular tissue was observed bilaterally (figure-1c). Serum free testosterone was 10 pg/ml (normal: 12-30 pg/ml) and oestradiol was 78.5 pg/ml (normal: 14-75 pg/ml; table-1). Hemogram, kidney and liver tests, serum prolactin (PRL: 9.4 ng/ml), luteinizing hormone (LH: 5.8 mIU/ml), follicle stimulating hormone (FSH: 5.2 mIU/ml) and sex hormone binding globuline (SHBG: 28.6 mmol/ml) levels were within normal ranges. The patient was treated with 300 mg/day propylthiouracil followed by 10 mCi radioiodine. Three months after radioiodine, transient hypothyroidism due to radioiodine developed. Six months after radioi-

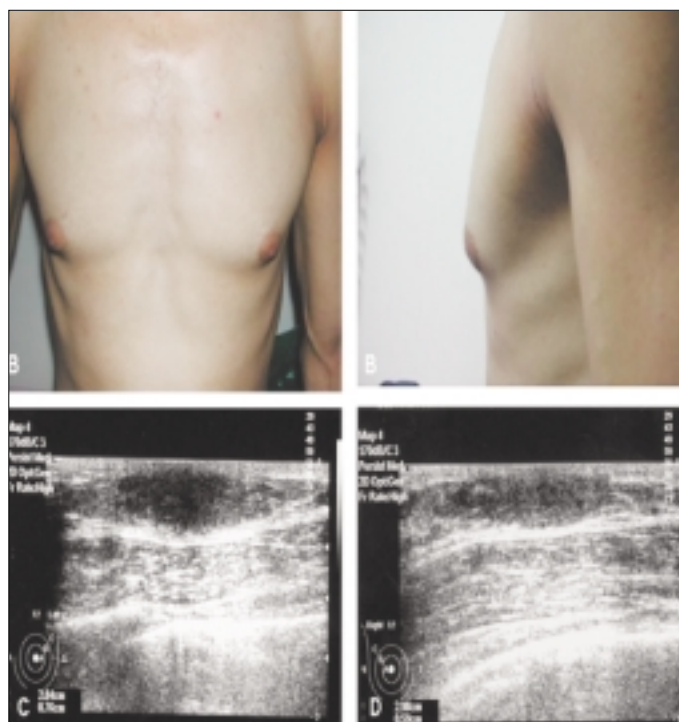


Figure 1. Bilateral gynaecomastia of the patient (a and b: on the physical examination; c: left breast and d: right breast by ultrasound) In ultrasound examination, the spindle-shaped increased amount of breast parenchyma shows homogenous echoes

dine, euthyroidism was achieved and his gynaecomastia resolved (figure-2a, b, and c). His libido increased and he had normal potency, simultaneously. In euthyroid state he had relatively higher free testosterone (17 pg/ml) and lower oestradiol (62.1 pg/ml) levels (Table 1).

Discussion

The frequency of gynaecomastia in hyperthyroidism was reported as high as 40% in some series (6). However, recent data suggest a much lower frequency (5). This difference may be related to the criteria used for defining the presence of gynaecomastia. Some people require the presence of breast tissue at least 20 mm in diameter for the diagnosis, although others believe that the diag-

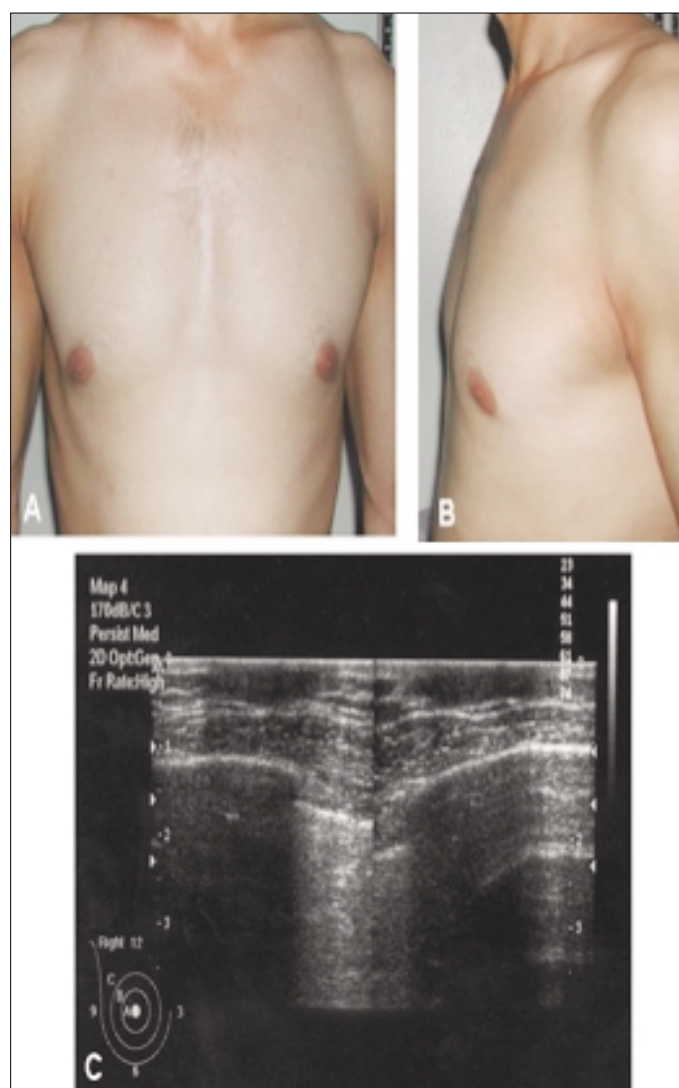


Figure 2. Recovery of gynaecomastia after achieving euthyroidism with radioiodine (a and b: on the physical examination; c: by ultrasound)

Table 1. Sex hormone profile before and after treatment of hyperthyroidism

	Before Treatment	After Treatment	Normal values
Free testosterone	10 pg/ml	17 pg/ml	12-30 pg/ml
Oestrogen	78,5 pg/ml	62,1 pg/ml	14-75 pg/ml

nosis of gynaecomastia may be done when only 5 mm of tissue is present (7).

The pathogenesis of gynaecomastia in hyperthyroidism is unclear. An altered ratio between serum free oestradiol and testosterone is believed to underlie the pathophysiology of gynaecomastia (2). The concentrations of total and unbound oestradiol are higher in subjects with gynaecomastia (1, 2). Similarly, our patient had increased oestradiol levels during hyperthyroid period and those levels decreased after euthyroidism was achieved. Although he had decreased free testosterone levels, total testosterone levels were normal, may be due to slightly increase in SHBG levels. Low free testosterone levels increased after restoring of euthyroidism and related symptoms such as impotence and decreased libido were recovered. In thyrotoxicosis, the changes in sex hormone profiles in men are raised total testosterone, SHBG, dihydrotestosterone, total oestradiol and LH (8, 9). Studies indicate that increased activity of oestrogen may play a significant role in the genesis of breast enlargement in hyperthyroidism (3). In addition to increased serum oestradiol decreased bioactive testosterone levels and decreased progesterone levels in hyperthyroidism have been reported (10). Chopra et al. (11) discovered that the ratio of serum free oestrogen and testosterone was significantly higher in patients with gynaecomastia than those without gynaecomastia. Increased androstenediol 3-sulfate levels, which is an active metabolite of dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS) and have oestrogenic activity, might contribute to gynaecomastia in hyperthyroidism (12). Hyperthyroidism causes marked alterations of the gonadotropic and prolactin axis and affects spermatogenic function (13). Kidd et al. (9) showed that men with hyperthyroidism have blunting of the feedback effects of oestradiol.

Despite decreased free testosterone levels in hyperthyroidism total testosterone levels are higher than in normal men. Serum concentration of sex hormone binding globulin may be also high in hyperthyroidism. This can explain the high serum total testosterone levels among hyperthyroid patients (8, 9, 11). Therefore, free testosterone measurement seems useful to identify hypoandrogenism in these patients in spite of the high concentration of total testosterone. Our patient had low free testosterone levels when he was hyperthyroid. After the treatment of hyperthyroidism his free testosterone levels increased and gynaecomastia resolved simultaneously.

While the increase in SHBG leads to a reduction in free testosterone, increased peripheral conversion of androgen to oestrogen appears to contribute to the high oestradiol concentration in hyperthyroidism (8). In man, adipose tissue is the main source of circulating oestradiol, which is derived from the aromatization of androgen precursors, mainly testosterone (3, 7). An increase in fat mass may lead to an increase in production of oestradiol. Oestradiol inhibits both pituitary and testicular production of testosterone (14). However, hyperthyroid patients are usually underweight. They usually lose weight also during the active dis-

ease as in our case. Although increased adipose tissue does not seem as the source of increased oestradiol in hyperthyroidism, qualitative changes in adipose tissue due to hyperthyroidism may be related to high oestrogen levels. Increased glandular secretion of oestradiol may also be important (7).

Radiographic investigation using mammography or ultrasound is recommended for confirmation of the diagnosis of gynaecomastia in men. Mammography of the male breast accounts for <1% of all mammograms performed (1). Three mammographic patterns of gynaecomastia have been described: an early nodular phase; a latter dendritic pattern of the fibrous phase; and a diffuse glandular pattern (15). It is technically difficult to obtain mammograms of the small male breast. This problem may be alleviated by the use of ultrasound, which has been used successfully to differentiate between gynaecomastia and other causes of swelling of the breast area in men (1, 2).

In conclusion, although gynaecomastia is rare as the initial symptom of hyperthyroidism, the diagnosis of hyperthyroidism in patients with gynaecomastia is very important as it resolves when the patient becomes euthyroid.

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