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Painful gynecomastia in a patient with malignant thymoma

Malign timomalı bir hastada ağrılı jinekomasti

Gamze Gököz DOĞU,[1] Fatih TANRIVERDİ,[2] Mustafa DİKİLİTAŞ,[1] Metin ÖZKAN,[1] Kürşat ÜNLÜHİZARCI,[2] Özlem ER[1]

Erciyes Üniversitesi Tıp Fakültesi, [1]Medikal Onkoloji Anabilim Dalı, [2]Endokrinoloji ve Metabolizma Hastalıkları Anabilim Dalı

Gynecomastia is an abnormal increase in the volume of the male breast. This pathological change may occur unilaterally or bilaterally and is generally considered to be due to an increased estrogen/androgen ratio. Gynecomastia is more common in pubertal ages and in older men. Chemotherapy may injure gonadal and hormonal functions and are associated with development of gynecomastia. In this case, a 36-year-old man who had bilateral acute painful gynecomastia associated with malignant thymoma is presented together with a review of the literature. Tamoxifen 20 mg daily was started. Twenty days later, tamoxifen resulted in complete regression of gynecomastia. After an extensive literature search, we found that gynecomastia had not been previously documented in malignant thymoma.

Key words: Malignant thymoma; painful gynecomastia; tamoxifen.

Jinekomasti, erkek memesinde anormal volüm artışı ile kendini gösterir. Bu patolojik değişiklik tek veya çift taraflı olabilir ve genellikle artmış östrojen/androjen oranıyla ilişkilidir. Jinekomasti pubertal çağda ve yaşlılarda daha yaygındır. Kemoterapi ile gonadal ve hormonal fonksiyonlar hasara uğrayarak jinekomasti gelişebilir. Bu yazıda, iki taraflı akut ağrılı jinekomastili malign timoma tanısı olan 36 yaşındaki bir erkek hasta bildirildi, bu konudaki literatür bilgisi özetlendi. Hastaya tamoksifen günde 20 mg olarak başlandı. Yirmi gün sonra tamoksifenle jinekomastide tamamen gerileme gözlendi. Literatür araştırması yaptığımızda malign timomada jinekomasti bildirimine rastlamadık.

Anahtar sözcükler: Ağrılı jinekomasti; malign timoma; tamoksifen.

Gynecomastia is an abnormal increase in the volume of the male breast, characterized by a tender discoid enlargement 2-4 cm in diameter beneath the areola, with hypertrophy of the gland and the surrounding fatty tissue. This pathological change may occur unilaterally or bilaterally and is generally considered to be due to an increased estrogen/androgen ratio.

Gynecomastia is more common in pubertal ages and in older men. Chemotherapy may injure gonadal and hormonal functions and is associated with the development of gynecomastia.

CASE REPORT

A 36-year-old man with an anterior mediastinal mass and respiratory failure was admitted to our hospital 9 months ago. Debulking surgery was performed via median sternotomy. Histopathological diagnosis had revealed unresectable thymic cancer, and induction chemotherapy was administered (cyclophosphamide 500 mg/m^2, epirubicin 75 mg/m^2, and cisplatin 75 mg/m^2 on day 1; and prednisone 100 mg/per day on days 1-5). This cycle was repeated four times at three-week intervals. Surgery was not possible because of extensive vas-

Correspondence (İletişim): Gamze Gököz DOĞU, M.D. Erciyes Üniversitesi Tıp Fakültesi, Medikal Onkoloji Anabilim Dalı, Kayseri, Turkey.
Tel: +90 - 352 - 437 49 01 e-mail (e-posta): ggd2882@gmail.com

cular invasion. He was treated with radiotherapy (total dose 6000 Gy in 30 fractions in six weeks). One month later, the patient presented with bilateral acute painful gynecomastia. Physical examination showed slightly enlarged breasts (Fig. 1).

The patient presented with bilateral acute painful gynecomastia. On physical examination, he appeared well, and his vital signs were normal. The lungs were clear, heart sounds were normal, and the abdomen was soft, with no masses or tenderness. The results of a complete blood count and the levels of electrolytes, calcium, creatinine, urea nitrogen, protein, albumin, globulin, and bilirubin were normal. There was no adenopathy, and testicular examination was normal. Abdominal ultrasonography (USG), testicular USG, and magnetic resonance imaging of the sella turcica were normal. Follicle-stimulating hormone (FSH) 26.18 (1.4-18 mIU/ml) and luteinizing hormone (LH) 16.83 (1.5-9.3 mIU/ml) were high. Beta-human chorionic gonadotropin, testosterone, prolactin, dehydroepiandrosterone sulfate, alpha-fetoprotein, insulin-like growth factor 1, thyroid function tests and cortisol level were normal. In view of progression in this patient, ifosfamide was given as second-line chemotherapy. Tamoxifen (TAM) 20 mg daily was started. Twenty days later, TAM resulted in complete regression of gynecomastia and there has been no recurrence in follow-up physical examinations.

DISCUSSION

Gynecomastia is common, present in 30% to 50% of healthy men. Conditions associated with gynecomastia are shown in Table 1. Men with recent-onset gynecomastia or mastodynia need a more detailed evaluation, including selected laboratory tests, to search for an underlying cause. Treatment depends on the cause and may include observation, withdrawal of an offending drug, therapy of an underlying disease, administration of androgen or antiestrogen drugs, or plastic surgery. Most cases of gynecomastia result from an imbalance between estrogenic (stimulatory) and androgenic (inhibitory) effects on the breast. Drug-induced gynecomastia accounts for 20% to 25% of cases.[1] Some drugs can cause gynecomastia through multiple mechanisms. For example, drugs mimicking or having estrogenic or antiandrogenic effects may also be associated with development of gynecomastia.[2-4] Even with detailed evaluation, there is no identifiable cause

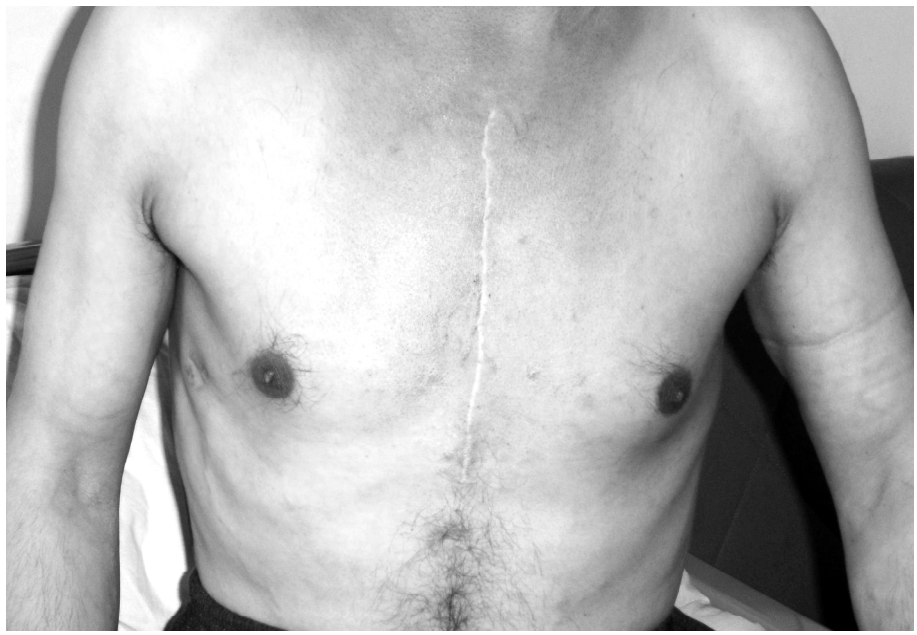

Fig. 1. The patient presenting with bilateral gynecomastia.

Table 1

Causes of gynecomastia

Physiological	**Pathological**
Neonatal	Idiopathic
Pubertal	Drug-induced
Aging	
Increased serum estrogen	**Decreased testosterone synthesis**
Increased aromatization (peripherally or glandular)	Primary gonadal failure, congenital
Sertoli cell tumors	Anorchia
Sex cord tumors	Klinefelter syndrome
Testicular germ cell tumors	Hermaphroditism
Leydig cell tumors	Hereditary defects in testosterone synthesis
Adrenocortical tumors	Primary gonadal failure, acquired
Hermaphroditism	Viral orchitis
Obesity	Castration
Hyperthyroidism	Granulomatous disease (including leprosy)
Liver disease	Testicular failure due to hypothalamic and/or pituitary disease
Testicular feminization	Androgen resistance due to androgen receptor defects
Refeeding after starvation	
Primary aromatase excess	
Displacement of estrogen from SHBG	
Spironolactone	
Ketoconazole	
Decreased estrogen metabolism	
Cirrhosis (?)	
Exogenous sources	
Topical estrogen creams and lotions	
Ectopic hCG production	
Lung carcinoma	**Other**
Choriocarcinoma	Chronic renal failure
Liver carcinoma	Chronic illness
Kidney carcinoma	HIV
Gastric carcinoma	Enhanced breast tissue sensitivity

SHBG: Sex hormone-binding globulin; HIV: Human immunodeficiency virus.

in about 25% of cases. Causes may include excessive local production of estrogen due to increased aromatase activity, decreased estrogen degradation, or changes in androgen or estrogen receptors.

Primary hypogonadism due to Leydig cell damage from any cause (e.g., mumps orchitis, trauma, cytotoxic chemotherapy, alkylating agents, vincristine, nitrosoureas, methotrexate) is commonly associated with gynecomastia. First, levels of total and free testosterone decrease. Second, the resulting increase in serum LH stimulates the aromatase enzyme in testicular Leydig cells to produce more estrogen. In addition, peripheral aromatization of the adrenal androgen androstenedione to estrogen remains unaffected.

Preliminary efficacy data from a retrospective chart review of patients with gynecomastia indicated that TAM was associated with reductions in breast size and decreased pain.[5] TAM, in an uncontrolled study, resulted in complete regression of gynecomastia in 70% of cases.[6]

LH and FSH are secreted by adenocarcinoma and large cell carcinoma. However, to our knowledge, there is no case in the literature describing paraneoplastic gynecomastia with malignant thymoma. It can be speculated that LH and FSH are secreted in malignant thymoma and that gynecomastia developed as a paraneoplastic entity.

REFERENCES

1. Braunstein GD. Gynecomastia. N Engl J Med 1993;328(7):490-5.
2. Carlson HE. Gynecomastia. N Engl J Med 1980;303(14):795-9.
3. Croce P, Montanari G, Zinzalini G, Iacona A. Gynecomastia. [Article in Italian] Minerva Med 1992;83(10):609-14. [Abstract]
4. Glass AR. Gynecomastia. Endocrinol Metab Clin North Am 1994;23(4):825-37.
5. Ting AC, Chow LW, Leung YF. Comparison of tamoxifen with danazol in the management of idiopathic gynecomastia. Am Surg 2000;66(1):38-40.
6. Parker LN, Gray DR, Lai MK, Levin ER. Treatment of gynecomastia with tamoxifen: a double-blind crossover study. Metabolism 1986;35(8):705-8.