INTRODUCTION

Gynecomastia is the glandular enlargement of the male breast due to hypertrophy and/or hyperplasia. It is the most common benign disorder of the male breast. Gynecomastia occurs due to increase level of estradiol, decreased androgen level or imbalance between estrogen and androgen. Physiologic gynecomastia is commonly seen in new born, puberty, aging and obesity. Familial gynecomastia occurs because of increased peripheral aromatization in families and due to inversion in chromosome 15q21.2-3 resulting in increased estrogen production in fatty tissue. Differential diagnosis of gynecomastia includes lipomastia, carcinoma breast, breast abscess. Gynecomastia requires urgent and extensive evaluation if it is recent onset, rapidly growing, tender and occurs in lean subjects. It is rare for gynecomastia predisposing to carcinoma except in Klinefelter syndrome (KFS).

Oral tamoxifen is effective in the active phase of the disease. Surgery is indicated for cosmetic reasons like increase in size, tenderness and in suspected malignancy.

Endoscopically assisted transaxillary liposuction and subcutaneous mastectomy is the surgery of choice in gynecomastia.

Herein, we report a family with two siblings having bilateral gynecomastia.

Their causes and management issues are discussed. All familial gynecomastia may not be always physiological.

CASE REPORT

Two brothers, 18-years-old and 14-years-old, born out of non-consangious marriage, were brought by their father in endocrine out-patient department (OPD) with complaints of swelling in both breast since 6 years and 2 years, respectively. On investigation, the breast swellings were gradually increasing in size and painless with no discharge from the nipple. No history of chronic use of drugs, local applications of ointments or substance abuse was reported. No history of palpitation, weight loss, headache, diminution of vision, viral infections, trauma or similar complaints in any other family member. They never had liver, renal, and thyroid disease in the past. Patients’ father attained puberty at the age of 22 years and mother’s age of menarche was 12 years.

Examination of younger brother

Pulse = 84/min, Blood pressure (BP) = 122/82, 114/80 mm of Hg supine and standing, respectively height = 154 cm, weight = 52 kg, body mass index (BMI) = 21.94 kg/m², arm
span = 153 cm, upper segment = 78 cm, lower segment = 76 cm. Both the breasts were firm, 2.5 cm × 1.9 cm in size (tanner stage III), not attached to underlying tissue, non-tender. Patient did not have facial hair. He had normal axillary and pubic hair (Tanner stage IV). Testis volume 10/10, stretched penile length of 9 cm, coarse scrotal skin. Other general and system examination was unremarkable.

**Examination of elder brother**

Pulse = 88/min, BP = 116/78, 110/76 mm of Hg in supine and standing position, respectively, height = 160 cm, weight = 59 kg, BMI = 23.04 kg/m², arm span = 165 cm, upper segment = 77 cm, lower segment = 83 cm patient had eunuchoid physique, wide hip, narrow shoulders, no facial hair. Axillary hairs were sparse, pubic hair had feminine distribution (Tanner stage II). Genitals appeared prepubertal, testis volume 2/2 (Prader orchidometer) = 5 cm, stretched penile length of 4 cm, thin scrotal skin. Both the breasts were 4.1 cm × 3.8 cm (Tanner stage V), firm, non-tender, not attached to underlying tissue. Other general and system examination was normal.

**Investigations in younger brother**

| Parameter                  | Value                  |
|----------------------------|------------------------|
| HB                         | 13.4 gm%               |
| TC                         | 8900 cells/cu mm       |
| Blood glucose fasting      | 92 mg%                 |
| Post-prandial glucose      | 134 mg%                |
| Total bilirubin            | 0.6 mg%                |
| SGPT and SGOT              | within normal limits   |
| Serum creatinine           | 0.9 mg%                |
| Serum sodium               | 135 meq/L              |
| Serum potassium            | 4.1 meq/L              |
| Serum FSH                  | 5.42 mIU/ml            |
| Serum LH                   | 1.82 mIU/ml            |
| Serum prolactin            | 6.75 ng/ml             |
| Serum testosterone         | 500.8 ng/dl            |
| TSH                        | 2.01 mIU/ml            |
| FT4                        | 7.4 mgm/dl             |
| FT3                        | 129.18 ng/dl           |
| Serum cortisol (8 am)      | 14.5 mgm/dl            |

Serum cortisol (8 am) = 14.5 mgm/dl.

Ultrasonography of the chest showed fat deposition in subcutaneous plane, glandular tissue (right > left). Ultrasonography of the abdomen = normal, ultrasonography of the scrotum = right testis 1.1 × 1.1 × 0.8 cm, left testis 1 × 0.8 × 0.5 cm suggestive of atrophic hypoplastic testis. His karyotype revealed 47XXY.

In view of clinical, biochemical, hormonal, radiological investigations and karyotype, elder brother was diagnosed as gynecomastia (tanner stage V) secondary to KFS.

**DISCUSSION**

Familial gynecomastia is rare, with description of three brothers in a single family and was due to increased extraglandular aromatase activity.[1] In pubertal boys it is generally subaerolar nodule and may regress in half to approximately one and half year in majority of cases. Pubertal gynecomastia occurs due to increased estrogen androgen ratio. KFS described by Harry F. Klinefelter is the most common chromosomal abnormality associated with primary testicular failure and infertility. The prevalence is about 1:500 to 1:1000 live born boys. The most common karyotype is 47XXY. Gynecomastia is present in about >40% of KFS patients.

In physiological or familial gynecomastia, estradiol levels may be high due to conversion from testosterone. But in KFS, estradiol levels are high already in the prepubertal age, irrespective of development of gynecomastia. Testosterone treatment, testicular volume, bone density, as well as the social status of the patients are inversely related to gynecomastia. Whereas, height and gynecomastia are positively correlated. Causes of bilateral gynecomastia,[2] may be familial, physiological, KFS, thyrotoxicosis. It may also be present in pre and post pubertal onset of hypogonadism. Bilateral gynecomastia in KFS is seen in 42% patients in pubertal age, with small testes and neurodevelopmental disorders.[3] Whereas gynecomastia is the presenting symptom in 10% and sign in 33% of adults KFS.

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From an endocrinological standpoint, patient’s complaints may vary, according to gonadal dysfunction, from signs of sex hormone deficiency in young adults to infertility in a male without other signs of hypogonadism. Before puberty, the condition is usually under recognized due to the fact that childhood is a period characterized by normally low testosterone levels and no sperm.
Histologically, there is hyperplasia of interductal tissue, unlike ductal hyperplasia seen in other high estrogen states. There is a high risk of carcinoma breast, about 60-fold higher than normal men. This high risk is due to the hyperestrogenic state secondary to increase aromatization of testosterone to estradiol and over expression of oncogene on X chromosome that has escaped inactivation. Patient should be trained to do self breast examination to detect any nodule. Mammography though helpful is not superior to self-breast examination.

No treatment is required except reassurance of the patient which was given to the younger brother. The younger brother was advised dietary modification, weight loss in addition to increased physical activity, however, he later underwent for bilateral surgical resection. Elder brother in view of his clinical and biochemical profile was started on testosterone injection after discussion with patient and family members. For the family it was devastating to learn that over the years they were told gynecomastia was normal in the elder sib and would go away with age. However, after confirmation of diagnosis and extensive discussion and counseling of the family members they were relieved and proceeded with further treatment of their children. Our case was unusual as both brothers in one family developed gynecomastia in their adolescence, but had different etiologies and both required different management strategies. Management in such cases requires assurance, reassurance, therapeutic trial of drugs, family counseling, or surgical approach depending on an individual case.

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