Gynecomastia

Gynecomastia, a benign enlargement of the male breast due to proliferation of the gland, is a common clinical condition. It may be an incidental finding on routine examination or may present as an acute unilateral or bilateral painful tender mass beneath or as a progressive painless enlargement of the breast. In 75% of the cases, it is bilateral. The tissue could be as small as 1 cm or as large as a female breast. To be visible, the breast must be 2 cm or more. Type 1 (pubertal gynecomastia) is defined as enlargment less than 3-4 cm ; type 2 as enlargment greater than 3-4 cm (pubertal macromastia). Rarely nipple discharge will occur ; there could be mild discomfort during certain activities.

Prevalence

Palpable breast tissue is so prevalent in studies of men and boys that some authors suggest differentiating between it and clinically important gynecomastia. The peak occurs during puberty, with a rise beginning at approximately the age of 10 and peaking around 14, followed by a decline during the late teenage years. Studies found prevalences between 4% and 69%, with an average of around 40% in most studies. Type 1 gynecomastia occur in 60 to 70% of boys. It is transient and usually correlates with tanner stage 3-4. Type 2 gynecomastia occur less frequently (4.5% incidence).

Conditions associated with gynecomastia

Considering the high prevalence of gynecomastia, it may coexist with many disorders without there being a clear causal relation :

- neoplasms (adrenal tumors, seminome, leydig's cell tumor, hepatoma, etc.),
- chronic diseases : Rheumatic fever, renal, neurologic, pulmonary, liver disease
- primary testicular failure : radiation, chemotherapy, orchitis, trauma, leukemia, hemophilia, etc.
- alcoholism
- starvation
- endocrine : hyperthyroidism, congenital adrenal hyperplasia
- idiopathic.

Classes of drugs have been implicated in the conditionand tose with an asterix have a strong relation : hormones, anabolic steroids, cyproterone*, isoniazid, ketonazole*, metronidazole, cimetidine*, meprazole, ranitidine, digoxin*, captopril, enalapril, methyldopa, verapramil, diazepan, haloperidol, tricyclic antidepressants, phenothiazines, alcohol, amphetamines, marijuana, heroin, phenytoin, penicillamine.

However, most cases in adolescents are idiopathic, type 1 or 2.

Pathogenesis

The breast tissues of both sexes appear histologically identical at birth and remain relatively quiescent during childhood, undergoing further differentiation at the time of puberty. In the majority of males, transient proliferation of the ducts and surrounding mesenchymal tissue takes place during the period of rapid sexual maturation, followed by involution and ultimately atrophy of the ducts. In contrast, the breast ductal and periductal tissues in females continue to enlarge and develop terminal acini, which require both estrogen and progesterone.

Since estrogens stimulate breast tissue whereas androgens antagonize these effects, gynecomastia has long been considered the result of an imbalance between these hormones. The transition from the prepubertal to the postpubertal state is accompanied by a 30-fold increase in the concentration of testosterone, with only a 3-fold increase in estrogen levels. Therefore, a relative imbalance between serum estrogen and androgen levels may exist during a portion of the pubertal process and may result in gynecomastia. Alterations in the ratio of estrogen to androgen have been found in patients with gynecomastia in association with medications, adrenal and testicular neoplasms, Klinefelter's syndrome, thyrotoxicosis, cirrhosis, primary hypogonadism, malnutrition, and aging.

Gynecomastia would be expected to occur if the breast tissue of some men and boys had an enhanced sensitivity to normal circulating levels of estrogen. Indeed, increased aromatase activity has been found in pubic skin fibroblasts derived from patients with isolated gynecomastia, suggesting that aromatization of androgens to estrogens within breast tissue may be responsible for idiopathic gynecomastia. It has also been suggested that patients with protracted neonatal gynecomastia may be more susceptible to persistent pubertal gynecomastia, supporting the concept that breast glandular tissue is inherently more sensitive to estrogenic stimulation in some boys than in others. However, to date, studies of estrogen and progesterone receptors in pubertal macromastia have not been conclusive.

Evaluation

The most difficult condition to differentiate from gynecomastia is fatty enlargement of the breasts without glandular proliferation (pseudogynecomastia). The discrimination can usually be made with the patient in a supine position by an examiner who grasps the breast between the thumb and forefinger and gently moves the two digits toward the nipple. If gynecomastia is present, a firm or rubbery, mobile, disk-like mound of tissue arising concentrically from beneath the nipple and areolar region will be felt, whereas if the enlargement is due to adipose-tissue deposition, no such disk of tissue will be apparent.

Asymmetric gynecomastia is common, and unilateral gynecomastia may actually represent a stage in the development of bilateral disease. Although other disorders such as neurofibromas, lymphangiomas, hematomas, lipomas, and dermoid cysts may lead to unilateral, often eccentric breast enlargement, the most important condition that needs to be differentiated is breast carcinoma, which accounts for less than 1 percent of cancers in men. Male breast cancer usually presents as a unilateral eccentric mass, hard or firm, that is fixed to the underlying tissues. It may be associated with dimpling of the skin, retraction or crusting of the nipple, a nipple

discharge, or axillary lymphadenopathy. In patients with KInefelter's syndrome the risk of breast cancer is 16 times higher than in other men. However, gynecomastia due to other conditions is not associated with an increased risk of breast cancer.

Painful, tender gynecomastia appearing during mid-to-late puberty requires only a history and physical examination, including measurement of height, weight, blood pressure, Tanner stage and palpation of the testicles, and, if the results are normal, reassurance and periodic follow-up. In the majority of boys the condition resolves spontaneously and no further evaluation is necessary.

Since gynecomastia is so common in older men, the mere presence of nontender, palpable breast tissue on a routine examination should not lead to a major laboratory evaluation. In most instances taking a careful history pertaining to the use of medication, drugs, and alcohol, with specific questions about symptoms of hepatic dysfunction, testicular insufficiency (decreased libido or impotence), pulmonary symptoms suggestive of lung cancer, and hyperthyroidism is sufficient to uncover most of the conditions associated with gynecomastia. If no abnormalities are found on physical examination or after the assessment of hepatic, renal, and thyroid function by serum chemistry profiles, further specific evaluation is unlikely to be useful. The patient should be reexamined in six months.

If the patient reports the recent onset of progressive breast enlargement, with or without pain and tenderness, and is receiving a drug, he should discontinue the drug, if possible, and be reevaluated in one month. If the gynecomastia is drug-induced, there should be at least a decrease in breast discomfort.

Treatment

Most patients with gynecomastia require no therapy other than the removal of any identified cause. Specific treatment of the enlarged breast tissue is indicated if the gynecomastia causes sufficient pain, embarrassment, or emotional discomfort to interfere with the patient's daily life.

Chemical treatment with clomiphen (estrogen antagonist), danazol (antigonadotrophic), tamoxifen (antiestrogen) and dihydrotestosterone have been attempted and their efficacy remains to be proven.

Before one considers surgery, it is important to keep in mind that gynecomastia has a high rate of spontaneous regression. Two thirds of type 1 gynecomastia resolved within two years and 90% within three years.

Adapted from :

Gynecomastia, Glenn D. Braunstein, NEJM, 328 ;490-494

Stanford B Friedman, Martin fisher, S. Kenneth Schonberg, eds. Comprehensive adolescent health care. Quality Medical Publishing ; St-Louis, 1992