

Embarrassing breasts

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Your 20-year-old male patient has longstanding gynaecomastia with signs of testosterone deficiency and is not taking any prescription medications. Could this be a case of Klinefelter's syndrome?

Case scenario

Mark, 20 years old, comes to see you because he is embarrassed about his breasts. He first noticed a little swelling at age 14 but had not felt he was any different from his classmates until the last few years when his breasts had increased in size (Figure). He was in the taller quarter of his class, played tennis for the school and was doing well academically. His pubic and body hair started growing at the same time his breasts increased in size. He thinks his penis has always been small but he does have erections and ejaculations, although he has never had sexual intercourse. He now avoids getting undressed in public and takes care to wear a tight singlet and a loose shirt to hide his breasts.

Mark works in his family's grocery business, feels otherwise well and has no current or past medical problems. There is no family history of breast problems among his immediate family. He takes no prescription medication but has taken vitamin supplements and herbal preparations for several years in the hope that they will help. He does not smoke cigarettes and uses alcohol rarely (preferring marijuana since trying it at age 18).

On examination he is 194 cm tall and weighs 85 kg; his BMI of 22.6 kg/m³ is within the healthy range of 20 to 25 kg/m³. He does not have much body hair (but does need to shave most days). Both his

breasts are enlarged with rubbery firm tissue extending from under the nipples. There is no tenderness and Mark says there has been no milky or other discharge. His testes seem small (approximately 2.5 cm). He is very anxious and it is difficult to measure his penis but he says it is about 10 cm fully erect. Other examination is normal.

Mark's gynaecomastia, female escutcheon, generally sparse body hair, underdeveloped musculature and relatively long legs (more than half his height) make you suspect he might have Klinefelter's syndrome.

Questions

- Is breast cancer likely?
- Is the breast enlargement likely to spontaneously resolve?
- What drugs might be responsible?
- What investigations are indicated?
- What treatment can be offered?

Feedback

Is breast cancer likely?

A diagnosis of breast cancer is not likely. Features suggestive of breast cancer include recent onset of a unilateral, asymmetrical, firm, fixed mass and associated nipple discharge and axillary adenopathy. Mark's breasts do not fulfil any of these criteria. If there were suggestive features, fine needle aspiration or biopsy would be indicated. If breast cancer were diagnosed, close questioning about cancers in other family members might suggest a genetic syndrome (breast, ovary, colon, prostate).

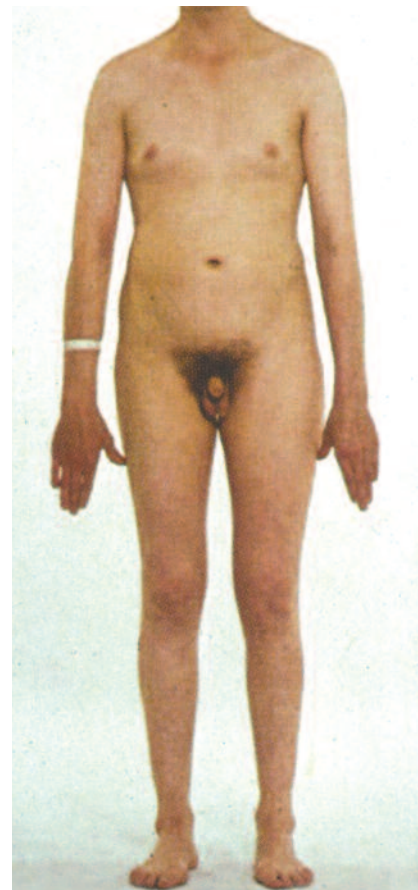


Figure. The patient's gynaecomastia together with his sparse body hair, underdeveloped musculature, small penis and testes, female escutcheon and relatively long legs is suggestive of Klinefelter's syndrome.

Is the breast enlargement likely to spontaneously resolve?

The enlargement is not likely to spontaneously resolve because Mark has had gynaecomastia for six years and the 'tincture of time' is usually associated with resolution in pubertal boys who have recently developed gynaecomastia. Most boys experience some breast enlargement during puberty but this

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generally resolves over the next two to three years. Mark is likely to have an underlying and ongoing problem.

What drugs might be responsible?

Although Mark is not taking any of the drugs that commonly cause gynaecomastia, some of the herbal preparations he is taking might contain phytoestrogens that have oestrogenic effects. He is also using marijuana which contains phytoestrogens and is known as a possible cause of gynaecomastia (Table 1).¹ (Marijuana also increases prolactin levels but gynaecomastia is caused by the oestrogenic effect; prolactin does not cause growth of breast tissue despite increasing milk production in established breast tissue.) However, Mark's gynaecomastia preceded his use of herbal preparations and marijuana.

If medication did seem responsible, stopping or changing it and applying the 'tincture of time' would be appropriate.

Table 1. Medications that may cause gynaecomastia¹

Common

- Anabolic steroids
- Antiandrogens
- Cancer chemotherapy
- Cimetidine
- Ketoconazole
- Oestrogens
- Spironolactone

Less common

- Antipsychotics
- Diazepam
- Digoxin
- Marijuana
- Methadone
- Omeprazole
- Some antiemetics (e.g. metoclopramide)
- Some calcium channel blockers (e.g. verapamil)
- Tricyclic antidepressants

What investigations are indicated?

Gynaecomastia reflects an imbalance in the proportions of oestrogens and testosterone with an absolute or relative excess of oestrogens stimulating growth of breast tissue.

Mark has small testes and signs suggestive of testosterone deficiency (sparse body hair, poor muscular development and a small penis). He is tall and has relatively long legs for his height. His history is characteristic of Klinefelter's syndrome, in which the extra X chromosome (the karyotype is usually 47,XXY) results in testicular underdevelopment. At puberty, varying amounts of testosterone are produced in response to luteinizing hormone and result in varying levels of pubertal development. In Klinefelter's syndrome, testosterone levels are low or below normal (and tend to fall with age) but oestrogen levels are normal or even a little high. As noted, Mark has evidence of testosterone deficiency and the relative excess of oestrogen has resulted in gynaecomastia.

Primary hypogonadism could be confirmed by measuring testosterone levels (which would be expected to be low because of abnormal testicular function) and gonadotrophins (particularly

Table 2. Other causes of gynaecomastia¹

Common

- Physiological (up to 70% of cases in newborns, 30% in pubertal and 80% in men over 80 years)
- Idiopathic (approximately 25 to 50% of longstanding cases)

Less common

- Cirrhosis
- Hyperthyroidism
- Hypogonadism (primary or secondary)
- Renal disease
- Testicular or adrenal tumours

luteinizing hormone, which would be expected to be high reflecting the hypothalamic pituitary response to testosterone deficiency). Chromosome analysis on a blood smear would demonstrate the abnormal karyotype.

In other cases where gynaecomastia is longstanding, outside pubertal age and not attributable to medication, investigations would be guided by the history (Table 2).¹ Renal, liver and thyroid function tests as well as testosterone levels will assess the most likely causes. If these are normal, discussion with an endocrinologist might guide further investigation (for example, measurement of human chorionic gonadotrophin and oestradiol levels to check for adrenal or testicular tumours). In a significant number of cases no cause is ever found.

What treatment can be offered?

Treatment is guided by the underlying cause. Unfortunately, medical approaches; such as antioestrogens (for example, tamoxifen and clomiphene) and androgen supplements do not usually result in complete regression of the gynaecomastia. Testosterone replacement for hypogonadism may be needed.

Plastic surgery is often indicated for psychological reasons and total mastectomy reduces the risk of later breast cancer (which is more common in men with gynaecomastia).

Keypoints

Gynaecomastia is common at birth and puberty and in old age. The increase in breast tissue is caused by an imbalance of sex hormones (absolute or relative excess of oestrogen over testosterone). Drugs are often responsible and common medical causes include cirrhosis and hypogonadism.

Reference

1. Phillips P, Braddon J. Dangerous drugs in endocrinology. Current Therapeutics 1999; 40(6): 56-67.