Original Article

Clinical features, presentation and hormonal parameters in patients with pubertal gynecomastia

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Abstract

Objective: Gynecomastia is benign enlargement of breast in male. It is postulated that its development is primarily due to a mismatch in ratio of oestrogen and androgen at breast tissue. The aim of this study was to highlight the clinical features, presentation and hormonal parameters at the time of consultation. **Methods:** All adolescent patients who attended endocrinology department with the complaint of breast enlargement were taken into study. We analysed their thyroid function test, oestrogen, testosterone, prolactin, alpha-fetoprotein, follicle-stimulating hormone, luteinizing hormone, beta HCG (human chorionic gonadotropin) and liver function. Clinical features and anthropometry were recorded. **Results:** Out of 50 patients enrolled, 34 (68%) had bilateral gynaecomastia while 16 patients (32%) had unilateral disease. Mastalgia was seen in 44 patients (88%). Psychological disturbance in the form of depression was seen in 60% of adolescent boys with gynecomastia. Tanner stage B had positive correlation with oestrogen to testosterone (E2/TTE) ratio (r = 0.47; P = 0.034). All other hormonal parameters were normal. **Conclusion:** Mastalgia was one of the presenting complaints in majority of patients and many had bilateral enlargement. Altered oestrogen to testosterone ratio is altered in majority of patients thus may be reason for pubertal gynecomastia.

Keywords: Gynecomastia, oestradiol, puberty, testosterone

Introduction

Gynecomastia is defined as a benign enlargement of male breast due to proliferation of breast glandular tissue. It may be unilateral or bilateral, but mostly bilateral.[1,2] It is the most common breast disorder in males and it can occur at any age, but mostly in pubertal period, but can be seen in neonatal period and elderly males. Gynecomastia may be seen in up to 70% of boys during their adolescence. Most cases of pubertal gynaecomastia usually disappear within 6 months to two years. If it persists, then we need to rule out pathological causes for gynaecomastia.[3-6]

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The most common pathophysiologic reason responsible for pubertal gynaecomastia is imbalance between oestrogen and androgen activity in the breast tissue.[7,8] Gynecomastia occurs either when there is increased production of oestrogen or may be decreased production testosterone.[9] A sudden increase in oestradiol early in puberty or delayed rise in testosterone may derange oestrogen testosterone ratio may occur in puberty. Usually oestrogen has stimulatory and proliferative effect ductal and glandular tissue in breast. But testosterone exerts generalised suppressive effect of growth and differentiation of breast tissue through its antiestrogenic action.[10]

There is another important enzyme that plays its role in gynaecomastia, that is, aromatase. Aromatase converts androstenedione to estrone and testosterone to oestradiol.[11] It has been found out that there is overexpression and enhanced activity of aromatase enzyme in pubertal gynaecomastia. As a result of this upregulation, there is increased local synthesis of

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oestrogen, reduced oestrogen elimination, increased oestrogen receptors or decreased androgen receptors.[12,13]

Gynecomastia is usually most commonly associated with obesity either may be true gynaecomastia or pseudo gynaecomastia.[14,15] We know that adipose tissue has elevated aromatase enzyme, thus causing increased production of oestrogen. This may be the main reason for higher production and activity of aromatase in obese boys leading to gynecomastia.[6,16] Furthermore, elevated leptin level due to obesity may cause increased proliferation of breast tissue. Since nowadays most of the adolescent boys are obese it is important to identify true gynaecomastia form pseudo gynaecomastia. Gynaecomastia has a huge psychological impact on adolescent boy's behaviour. Many patients become depressed because of gynaecomastia. So early diagnosis and effective counselling and management will help in relieving their symptoms.[17]

Other rare causes of gynaecomastia are testicular tumours and adrenal tumours. These tumours sometimes secrete oestrogen, changing the oestrogen/testosterone ratio[18,19] thus causing gynaecomastia. In patients with hypogonadism, deficiency of testosterone lead to imbalance in the hormonal parameters leading to gynaecomastia.[4] During puberty there is fast linear growth due to secretion of growth hormone and insulin-like growth factor 1 (IGF-1) in presence of testicular hormones. These GH and IGF-1 are not only responsible for linear growth, but also cause proliferation of breast tissue by acting on their receptors present in breast tissue.[4] Since most cases of gynaecomastia occur during peak height velocity it is postulated that there may be relationship between GH/IGF-1 surge and gynaecomastia.[20,21]

There are many pathologic causes for gynaecomastia. We need to rule out them. One important cause is drug-induced gynaecomastia. Common drugs responsible are antiretroviral, spironolactone, antipsychotics and any drug acting as antiandrogen.[22,23] Gynaecomastia is also seen in patients with chronic liver disease and human immunodeficiency virus infection.[24,25] So, we need to take complete medical history of all adolescent boys presenting with gynaecomastia and should conduct a thorough physical examination to look for physical signs of systemic diseases.

Methods

We analysed 50 patients aged 10 to 18 years who presented to endocrinology outpatient department of super speciality hospital from January 2010 to December 2019. We had total 60 patients with breast enlargement. On investigation 6 patients proved to be having lipomastia on ultrasonogram and 4 patients diagnosed to have hypogonadism by clinical and biochemical evaluation. Thus, we had total 50 patients with pubertal gynaecomastia with mean age of 14.2 ± 3.8 years. We took detailed history and did a thorough physical examination. Anthropometric measurements included weight and height measurements. Body mass index (BMI) was calculated using standard formula. Weight was measured using a scale with a precision of 100 g. We measured the height using stadiometer. We collected report of thyroid function tests, follicle-stimulating hormone, luteinizing hormone, testosterone, oestradiol, prolactin.[26] We measured alpha-fetoprotein (AFP), beta HCG, alanine transaminase (ALT) and aspartate transaminase (AST) to rule out other rare causes of pathological gynaecomastia. We did ultrasonography in all patients to rule out lipomastia. Patients are classified according to Tanner breast staging.

Statistical analysis

All statistical analyses were performed using SPSS software (2015). We compared the two parametric variables using Student's *t*-test. The correlation between quantitative values was analysed by using Pearson's correlation. Whenever *P* value was less than 0.05, it was considered statistically significant. Demographic data and hormonal parameters represented as mean ± SD. We obtained ethical committee clearance from our institutional ethical committee obtained, 18/9/2020.

Results

The mean ± SD age of the patients was 14.2 ± 3.8 years at the time of the first consultation. Out of 50 patients who presented to us 7 were obese (14%), 22 were overweight (44%), 19 were normal weight (38%) and 2 of them were underweight (4%). Gynecomastia was bilateral in 34/50 (68%) of the subjects and 16 had unilateral disease (32%). 44 patients complained of mastalgia which includes all patients with unilateral gynaecomastia and 28 patients with bilateral disease. About 60% of the patients had some form of psychological disturbance due to breast enlargement. 21 patients were in tanner stage B2 (42%) and 24 patients were in stage B3 (48%). The remaining five patients were in stage B4 (10%). In terms of Tanner pubic hair staging P2 was seen in 20, P3 was seen in 22 and P4 in 8 patients. Mean testicular volume in patients with pubertal gynaecomastia at the initial assessment was 10.4 ± 5.2 cm

Hormonal parameters

We did hormonal parameters in all 50 patients with pubertal gynaecomastia. Oestradiol levels are elevated in 12 patients and it was with in reference range in rest of the patients. Testosterone levels are lower than the reference range in 8 patients and in rest of them it was above lower range of reference range. Mean FSH and LH levels are within reference arrange. T and TSH are normal in all the patients. Prolactin levels are normal in all the patients. When we observed these patients with elevated oestradiol about 6 (50% patients) were either obese or overweight. In 8 patients with lower testosterone level, 6 of them were either obese or overweight. This may suggest that obese patients with increased aromatase activity may precipitate development of gynaecomastia.

We found that patients with stage 3 tanner staging had elevated oestradiol level and relatively lower testosterone level for their

pubertal stage compared patient with tanner breast stage 2. Though we were not able quantify it and prove it as we didn't have age-specific normogram for hormone level at different stages of puberty. But from this study we can conclude that obese patients have higher chance of pubertal gynaecomastia and patients with stage 3 or more tanner breast stage patients have higher oestradiol and lower testosterone.

Discussion

Pubertal gynecomastia is one of the main reasons for psychosocial discomfort, anxiety and loss of self-esteem in adolescent boys. So, it is imperative to recognize these apprehensions in these patients to provide appropriate management. The available literature regarding diagnostic approach and management approaches for gynecomastia consists of expert opinion, case series and few retrospective studies. There are no randomised control studies regarding the management of pubertal gynaecomastia.

This study summarizes the clinical features, pubertal staging and hormonal evaluation in management of pubertal gynaecomastia in young and adolescent boys. We know that variation in the oestrogen testosterone ratio is thought to be major cause of pubertal gynaecomastia.[27,28] According to the literature, idiopathic gynaecomastia accounts up to 25% of all cases of gynecomastia.[14,29] In our study 20 patients (40%) had some form of hormonal disturbance either in the form of low testosterone or increased oestradiol. Meanwhile no clear cause could be identified in 60% of patients. But we observed that obese patients had higher chance of hormonal abnormality and gynaecomastia.

According to recent guidelines all patients with gynecomastia on physical examination without any demonstrable cause, should undergo hormonal investigation including determination of blood LH, FSH, prolactin, Testosterone, oestradiol, beta-hCG and T4, TSH.[30] Furthermore, we should look for warning signs of pathologic gynaecomastia like rapid growth of breasts, breast skin changes, firm breast mass, testicular mass, hepatomegaly, headache, galactorrhoea, eunuchoid stature etc. Most of our patients did not have any abnormalities in their hormone levels. We found that 40% patients had either elevated oestradiol or lower testosterone level. This finding helps us to assume that there may be a relative change in the hormone level may be at tissue level leading to gynaecomastia in spite of normal serum oestradiol and testosterone. Secondly, we don't have normal value of serum oestradiol and testosterone in different age groups and different stages of puberty.

As prevalence of paediatric obesity is increasing at alarming rate, we are seeing a greater number of patients with breast enlargement. Though obesity causes pseudo gynaecomastia with proliferation of adipose tissue rather than glandular tissue, we have seen that obese patients have higher chance of true gynecomastia. So by diagnosing pubertal gynaecomastia early in puberty will help in categorising the patients who require treatment and who require only counselling. Also early diagnosis and treatment will cause complete disappearance of gynaecomastia. Rivera *et al.* shown that higher the BMI centiles more is the pubertal gynecomastia. Kulshreshtha *et al.*[31] also reported that most of the patients (64%) with breast enlargement were obese as per Coles criteria. In our study, the subjects had higher BMI values than the general population in patients with gynaecomastia. We also observed more hormonal changes in obese gynaecomastia patients compared to normal weight patients. We should always encourage obese patients with pubertal gynecomastia weight, because obesity is associated with complications when they undergo surgical treatment. Handschin *et al.*[32] report that in adults with gynecomastia who are overweight had more severe surgical complications when compared to normal-weight patients.

We are conscious of the limitations of our study being a retrospective in nature. It was study done in single centre with limited number of patients. Despite these limitations study provided insight into clinical features, presentations, and hormonal assessment in patients with pubertal gynaecomastia.

Conclusions

In conclusion, most of the patients had bilateral gynaecomastia meanwhile almost all of them had mastalgia at the time of presentation. Pubertal gynaecomastia is more common in obese adolescents and change in the oestrogen/testosterone ratio may be reason for development of pubertal gynaecomastia. Early identification of pubertal gynaecomastia will help in effective management without any unnecessary investigation.

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Conflicts of interest

There are no conflicts of interest.

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