

## Severe Pubertal Gynaecomastia - Case Report and Review of the Literature

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### Abstract

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A 15-year-old adolescent male with severe and persistent pubertal gynaecomastia is presented to highlight the clinical presentation, and management challenges of the condition. The patient was well built for age with a weight of 75kg, height of 166cm and a BMI of 27kg/m<sup>2</sup>. He had bilateral breast enlargement at Tanner stage IV with milky discharge from both breasts. Hormone profile showed normal levels of serum follicle stimulating hormone, luteinising hormone and testosterone. Prolactin, progesterone and oestradiol levels were elevated. No pituitary mass was demonstrated on brain computed tomography scan. He was treated medically with Danazol (200mg) for six months and bromocriptine (12.5mg nocte) for two months with minimal response. He was offered reduction mammoplasty, but the parents declined. Severe gynaecomastia in a pubescent male poses a great management challenge. Medical treatment is often unsuccessful, with surgery being the best option. General unacceptability of surgery in our environment poses a further challenge.

### Introduction

GYNAECOMASTIA is a benign enlargement of the male breast resulting from proliferation of the glandular elements of the breast.<sup>1,2</sup> It results from an imbalance between the stimulatory effects of oestrogen and inhibitory effects of testosterone.<sup>1,2</sup> It is a common occurrence in puberty as nearly half of all boys are affected during puberty and can therefore be considered normal. Its incidence varies from 3.9 to 69 percent in various communities.<sup>1,4</sup> As far as we are aware, the incidence in our environment is yet to be documented. Pubertal gynaecomastia disappears within two years in 75 percent of cases, and three years in 90 percent of cases.<sup>1,7</sup> In a few cases however, breast enlargement may be severe and persistent, and become a matter of real concern and distress. Gynaecomastia has a negative impact on self-esteem in affected boys leading to avoidance of social activities and depression.<sup>2,5</sup> As would be expected of adolescents, many of these concerns are not discussed with parents. When gynaecomastia is severe i.e. breast tissue more than 4cm in diameter (female Tanner stage 4) and has persisted beyond 12

months, there is usually poor response to medical treatment, and surgery is recommended especially if there is significant pain or there are psychosocial problems.<sup>10</sup> The poor acceptability of surgery in our environment especially for problems that are perceived as benign, however, limits its use as a form of treatment. The aim of this report is to highlight the clinical presentation and management challenges of severe pubertal gynaecomastia, including a review of the literature.

### Case Report

A 15-year-old male presented to the paediatric endocrinology clinic of the University of Port Harcourt Teaching Hospital, with a two-year history of bilateral breast enlargement. The breasts had progressively increased in size, with a history of pain at the onset. There was no history of use of illicit drugs. There was also no history of use of oestrogen or contact with oestrogen containing substances. He denied any history of manipulation of the breast by himself or his peers. He would not undress in public places and preferred to wear loose clothing. His past medical history was unremarkable. He was the second of three children in a monogamous setting, two males and one female. His younger brother who was 12 years old, did not have similar problems nor did any other member of his family. Examination revealed a well grown but unhappy child, with a weight of 75kg, height of 166cm and a body mass index (BMI) of 27kg/m<sup>2</sup>. He had no

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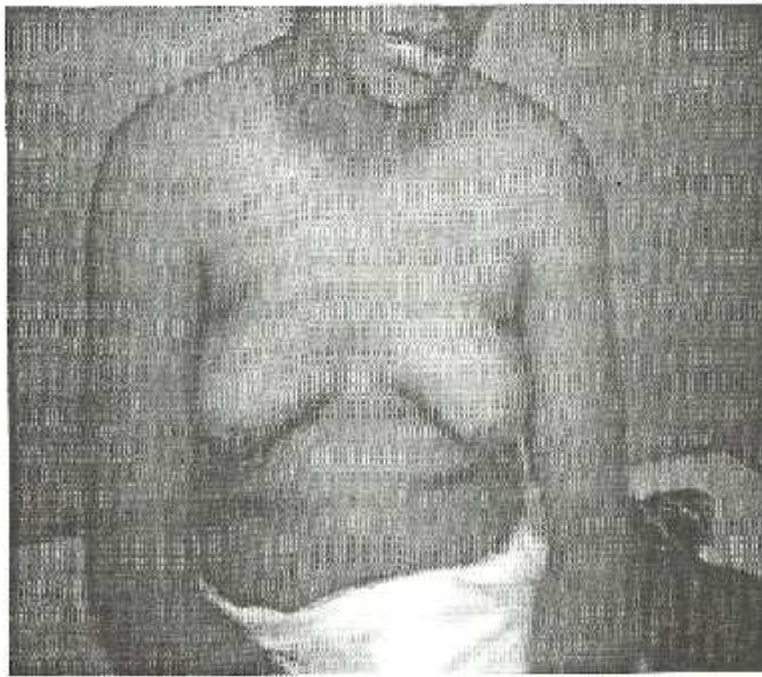


Fig. 1: Patient with breasts at Tanner stage 4

significant peripheral lymphadenopathy. He had bilateral breast enlargement, with the areolae and papillae forming a secondary mound (female Tanner stage 4). The left breast was bigger (14cm x 13cm) than the right (13cm x 12 cm). There was milky discharge from both breasts but they were not tender and had no palpable masses. He had pubic and axillary hair (Tanner stage 4), with normal male external genitalia, and well formed testes both measuring approximately 12ml in volume, using an orchidometer. The left testicle was hanging slightly lower than the right with diameters of 4.5cm and 4cm, respectively. The central nervous system and other systems were essentially normal.

A diagnosis of severe pubertal gynecomastia to exclude prolactinoma was made. Hormonal assays showed elevated serum levels of prolactin at 26.1ng/ml (6-24), progesterone at 68.8 (3-36ng/ml) and oestradiol at 516pg/ml (18-450). Follicle stimulating hormone (FSH) 15.5 (4-20miu/ml), luteinising hormone (LH) 16.8 (1-20miu/ml), and testosterone 5.6 (3-9ng/ml) levels were within normal limits. Liver function tests, renal function tests and thyroid function tests were also normal. Computed

tomography (CT) scan was unremarkable and showed normal brain and pituitary gland. Abdominal ultrasound scan was also normal.

Treatment options (medical and surgical) were discussed with the parents and medical treatment was chosen. He received Danazol 200mg daily for six months, and bromocriptine 12.5mg nocte for two months. He was also counselled on weight reduction. Repeat hormone assays showed that FSH, LH and testosterone levels were still within normal limits. Prolactin levels were also normal at 18.0ng/ml (6-24), but progesterone and oestradiol were still elevated at 60.8 ng/ml (3-36) and 497pg/ml (18-450), respectively.

There was no significant change in breast size but the discharge from the breasts ceased. His weight dropped from 75 to 69kg. He was again offered the option of surgery but his parents declined. Figure 1 shows a picture of the patient's breasts.

#### Discussion

Gynecomastia which may be true or pseudo, is a common occurrence in males and generally has three peaks, namely; in the neonatal period, puberty and

in middle-aged to older adult males.<sup>109</sup> Pubertal gynaecomastia usually starts at 10-12 years with a peak at 13-14 years and regresses within 18 months.<sup>110,11</sup> Breast development in our patient started at the peak age of 13 years and had persisted beyond two years.

True gynaecomastia results from an altered oestrogen androgen balance, in favour of oestrogen, or increased breast sensitivity to a normal circulating oestrogen level.<sup>4</sup> Oestrogen production in males is mainly from the peripheral conversion of androgens (testosterone and androstenedione) through the action of the enzyme aromatase, mainly in muscle, skin, and adipose tissue in the forms of oestrone and oestradiol.<sup>111</sup> During puberty, testosterone rises up to 30 times its pre-pubertal values in the male, while oestrogen only rises about three times its previous values. This rise in oestrogen stimulates the growth of breast tissue until the increased testosterone levels blunt this effect of oestrogen. Testosterone levels fluctuate widely until about the age of 15 years when it becomes steady enough to override oestrogen effects. However, some patients remain hypersensitive to the small amounts of circulating oestrogens. This hypersensitivity leads to more severe and persistent pubertal gynaecomastia in such patients.<sup>112,13</sup> Other hypotheses explaining the aetiology of gynaecomastia include lowered free testosterone levels, abnormal testosterone to oestrogen ratios, and lower dehydroepiandrosterone sulphate (DHEA-S) to oestrogen ratios.<sup>114,11</sup> Pseudogynaecomastia (fatty breast) is common in obese males and must be differentiated from true gynaecomastia.<sup>4,12</sup>

Gynaecomastia may occur as an acute unilateral or bilateral tender enlargement, or a progressive painless enlargement.<sup>11</sup> In about 75 percent of cases, gynaecomastia is bilateral, with the breasts enlarging concurrently or sequentially.<sup>116</sup> If the condition is bilateral, the breasts are commonly affected to different degrees as occurred in our patient.<sup>11,116</sup> He had severe gynaecomastia or macrogynaecomastia at Tanner stage 4.

There are several conditions including medical, and endocrine disorders associated with gynaecomastia.<sup>12</sup> Some are idiopathic<sup>4</sup> (25 percent), while others may be drug-induced (20 percent) e.g. anabolic steroids, anti-ulcer drugs like cimetidine, and digoxin, among others, or due to testicular tumours (three percent), hyperthyroidism, and chronic liver disease.<sup>12</sup> Our patient had elevated levels of prolactin and oestrogen, but the computed tomography scan of the brain did not suggest any prolactinoma. Some workers have demonstrated higher mean prolactin levels in boys with pubertal gynaecomastia than boys of similar pubertal development without

gynaecomastia.<sup>112,13</sup> However, Beck<sup>14</sup> reported that prolactin is not involved in the development of marked pubertal gynaecomastia, in spite of its elevated levels in some cases.

There is controversy about the association of gynaecomastia with body mass index (BMI).<sup>5,24</sup> Some workers have found pubertal gynaecomastia to be more common in adolescents who were heavier and taller than their peers.<sup>115,19</sup> Our patient was overweight with a body mass index of 27 kg/m<sup>2</sup>. On the contrary, Nydick *et al.*<sup>25</sup> did not find any significant difference in BMI between boys with gynaecomastia and their peers. Although, pseudogynaecomastia is seen more commonly in patients who are overweight (BMI > 25 kg/m<sup>2</sup>), mammography and ultrasonography can be used to distinguish it from true gynaecomastia.<sup>12,21</sup>

Pubertal gynaecomastia, especially when severe is known to have negative impact on the self-esteem of adolescent boys, and can lead to reduced participation in social activities, and depression.<sup>4,11,15</sup> This was already evident in our patient who would not undress in public places or participate in certain social activities.

Gynaecomastia of puberty has high rates of spontaneous regression.<sup>12</sup> Majority of patients require no treatment other than removal of the precipitating factor.<sup>12,17</sup> Specific treatment is indicated where gynaecomastia is severe, produces such negative effects as earlier mentioned, or causes significant pain.<sup>2</sup> Medical treatment is usually more effective in the early active phase. Historically, testosterone was the first drug used in the treatment of gynaecomastia but carried the risk of being aromatized to oestrogen which may stimulate further breast growth and worsen the problem.<sup>2</sup> Its non-aromatisable analogue, dihydrotestosterone, has also been used with good results.<sup>26</sup> Danazol is a weak androgen that inhibits pituitary secretion of LH and FSH and has been found to significantly reduce breast tenderness and size.<sup>12,27,28</sup> Our patient received danazol with no reduction in the size of the breast. Other medications which have been used with variable success include anti-oestrogens and aromatase inhibitors.<sup>12</sup> Anti-oestrogens like tamoxifen and toremifene block oestrogen receptors in target tissues.<sup>12</sup> Aromatase inhibitors such as testolactone, anastrozole, letrozole and exemestane prevent peripheral aromatization of circulating androgens to oestrogens.<sup>12,27,29</sup> Bromocriptine has been found to be useful in treating galactorrhea in boys with normal or elevated prolactin levels.<sup>21</sup>

Surgery is indicated when there is continued growth of the breasts despite medical treatment, or breast enlargement has persisted for more than 12

mentis as occurred in our patient. The general intent is aesthetic and to improve the psychosocial disturbances that arise from this feminine body characteristic. Surgical procedures include mastectomy, subcutaneous mastectomy, subcutaneous mastectomy, and reduction mammoplasty.<sup>16-17</sup> Liposuction is less effective in patients with true glandular gynecomastia but is used as an adjunct to the other surgical techniques.<sup>17,18</sup> More recently employed techniques include ultrasound assisted liposuction, endoscope assisted subcutaneous mastectomy and the use of vacuum assisted liposuction devices.<sup>19-21</sup> Complications of surgery include breast asymmetry, loss of nipple sensation, scars, pigment changes, haematoma, wound infection, and occasionally, skin desquamation.<sup>16-17</sup> Our patient could not benefit from surgery despite the severity of his gynecomastia because of fear of surgery expressed by parents who refused the option despite adequate counseling.

In conclusion, pubertal gynecomastia is a cause of psychosocial problems in adolescents. Severe and prolonged cases are unlikely to respond to medical treatment and should be treated surgically to alleviate the adverse psychological effects. There is a need for public enlightenment to improve acceptability of surgery for the condition.

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