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Causes and psychological impact of gynecomastia in boys and adolescents

Authors: Zdravka Petrova Todorova, Elissaveta Milkova Stefanova, Ivilin Plamenov Todorov

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The causes and psychological impact of gynaecomastia in boys and adolescents

Running head: Causes and psychological impact of gynaecomastia

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Zdravka P. Todorova (0000-0002-2969-5681)[1], Elissaveta M. Stefanova (0000-0003-4332-2619)[1], Ivilin P. Todorov (0000-0002-6556-4304)[2]

[1]*Department of Endocrinology, Specialized Hospital for Active Treatment of Paediatric Diseases, Faculty of Medicine, Medical University — Sofia, Sofia, Bulgaria*

[2]*Department of Cardiothoracic Surgery, Acibadem City Clinic Tokuda Hospital, Sofia, Bulgaria*

Corresponding author: Zdravka P. Todorova, Department of Endocrinology, Specialized Hospital for Active Treatment of Paediatric Diseases, Bulgaria, Sofia 1606, 11" Akad. I. Geshov" Blvd, +359885557359, Faculty of Medicine, Medical University —Sofia, Sofia, Bulgaria; todorova.zdr@gmail.com

Abstract

Introduction: Gynaecomastia (GM) is benign unilateral or bilateral proliferation of the glandular tissue of the breast in males. Its development during adolescence is usually considered a physiological phenomenon and is expected to resolve within months. Sometimes, however, it is due to pathological conditions or diseases, and it is not uncommon for these not to be recognized promptly. The present study aims to investigate the causes of prepubertal and pathological pubertal GM, its association with obesity, the age of appearance, and whether GM has a psychological impact on boys and adolescents admitted to the endocrine department.

Material and methods: A total of 157 boys and adolescents with GM were included in a cross-sectional retrospective study in a single tertiary centre for endocrine diseases. Patients were evaluated by anthropometric measurements, serum hormonal levels, and a questionnaire.

Results: In the period 2009-2018 a total of 157 boys and adolescents were diagnosed with GM (76.43% obese, 3.18% — overweight). Twelve (7.64 %, mean age of GM development 7.53 years) were prepubertal, 5.09% with primary or secondary testicular damage, 5.73% with hypogonadotropic hypogonadism, 11.48% with elevated prolactin level, and 110 boys (70.06%) with physiological pubertal GM. A statistically significant difference was found between the age of development of physiological GM — 11.85 years (9.35–16.92) and hypergonadotropic — 13.57 years (10-16.25) ($p=0.006$) and hypogonadotropic — 12.77 years (10.50–14.0) ($p = 0.028$) hypogonadism. Onset of pubertal GM in normal-weight boys was 13.13 years, and in obese/overweight it was 11.69 years ($p < 0.001$). Eighty-four patients (53.5%) expressed having a psychological burden of GM, 12.1% consulted because of its development, in 8.2% it led to cessation of sports, and 2.5 % changed their clothes.

Conclusions: Prepubertal and pubertal GM has a high association with obesity. Excess adipose tissue has an impact on the age of development in both groups. Nearly a quarter of pubertal cases are due to pathological conditions, and those are often diagnosed more than 18 months after the appearance of breasts. Hence, although a greater number of pubertal GMs are physiological, it may be reasonable for adolescents to be evaluated within the first 6 months of breast development so as not to delay the diagnosis of pathologic cases. Additionally, we found that GM has a complex influence on the psychological state of boys and adolescents.

Key words: prepubertal gynaecomastia, adolescent gynaecomastia, pathological gynaecomastia, psychological influence of gynaecomastia

Introduction

Gynaecomastia (GM) is a unilateral or bilateral benign proliferation of the glandular tissue of the breast in males [1]. During 3 periods of an individual's life GM is considered a physiological phenomenon — in the neonatal period, during adolescence, and in senile men. GM itself is not a disease but rather a condition or symptom of an underlying disease that has led to an altered balance, at the level of breast tissue, between the level and effect of oestrogens and androgens due to an absolute increase in oestrogen levels, absolute or relative decrease in androgen levels,

altered bioavailability, disorders of androgen receptors, or hypersensitivity of the glandular tissue [2, 3, 4]. Overweight and obesity among children and adolescents play an important role in the development of GM [5, 6]. The causes of pathological GM and its incidence in adult men are widely known. However, for children and adolescents there are almost no accurate data on the prevalence of different causes of pathological GM. The aim of the study is to investigate the causes of prepubertal and pathological pubertal GM, and its association with obesity among patients admitted to endocrinology clinic. In addition, analysis of its psychological impact was performed.

Material and methods

The medical records of boys and adolescents referred to the tertiary department of endocrinology because of GM or diagnosed with GM during clinical evaluation between 2009 and 2018 were selected (n = 157) for inclusion in the presented retrospective cross-sectional study. GM was assessed by means of palpation, and in cases suspicious for pseudo gynaecomastia ultrasound was used. Data about age of development of GM, anthropometric (height, weight) characteristics, degree of puberty according to Tanner stages, as well as hormonal values [testosterone (T), luteinizing hormone (LH), follicle-stimulating hormone (FSH), oestradiol (E2), thyroid-stimulating hormone (TSH), and prolactin (Prl)] were collected retrospectively. To evaluate the psychological impact of GM a questionnaire was used. The hormonal parameters were measured by means of a chemiluminescent immunoassay (Siemens, Immulite 2000, USA). Descriptive statistics and frequency analysis were used where appropriate. Comparisons between groups were made through independent samples t-test. p values of ≤ 0.05 were accepted as statistically significant. Data were analysed by SPSS (Statistical Package for Social Sciences) version 13.0.

Results

For the aforementioned period, from a total of 2039 boys and adolescents referred to the Department of Endocrinology, 157 (7.7%) were diagnosed with GM. From them 76.43% were diagnosed also with obesity, 3.18% were overweight (n = 125), and 20.39 % (n = 32) were normal weight. Twelve (7.64 %) were below the age of 9 years without pubertal development and hence were considered as prepubertal. Of the studies performed, the most common cause was elevated E_2 (n = 6), five patient were obese. From the group with elevated E_2 one boy had also elevated prolactin due to therapy with risperidone and sodium valproate, and in another boy

advanced bone maturation (by 2.5 years) was registered. In 3 more boys, with obesity but without increased E_2, advanced bone age was registered (12–13 years).

Primary or secondary testicular damage and development of hypergonadotropic hypogonadism were diagnosed in 8 (5.09%) of the boys. This group included 4 boys with Klinefelter syndrome (46, XXY), one with a disorder of sexual differentiation (karyotype with two lines 46, XX (25)/47, XXY (5), one boy with testicular regression syndrome, one with acquired testicular damage due to acute lymphoblastic leukaemia, and one patient had congenital unilateral cryptorchidism with his only testicle surgically removed at 4 years of age.

The third group comprised those with hypogonadotropic hypogonadism — a total of 9 boys (5.73%). In this group 2 boys (1.27%) were diagnosed with Kallmann syndrome, and one boy with a normal sense of smell. Another 5 boys (3,18%) were with constitutional delay in growth and pubertal development (CDGPD) and low T with elevated E_2 in 4 of them. One boy was diagnosed with hypopituitarism.

Elevated Prl levels were found in 20 boys (1 boy in the prepubertal group and 1 with CDGPD, and increased E_2 and Prl). In this group, 2 more boys (1.28%) were treated with drugs leading to hyperprolactinaemia (paliperidone, quetiapine, haloperidol). In one boy, elevated prolactin was found along with elevated TSH due to undiagnosed Hashimoto's thyroiditis. In 3 boys (1.91%) hyperprolactinaemia led to decreased levels of gonadotropic hormones and delayed puberty. In the remaining 14 boys, prolactin was elevated at varying degrees but without abnormalities in gonadotropic hormones or adenohypophyseal hyperplasia (in 6 of them combined with increased E_2).

In 110 boys (70.06%), no other cause of GM was identified, and so they were considered as physiologically pubertal. No boys with GM due to tumours, hyperthyroidism, chronic liver failure, or chronic kidney disease were identified (Tab. 1).

A statistically significant difference was found between the mean age of development of physiologic pubertal GM and those due to hypergonadotropic ($p = 0.006$) and hypogonadotropic ($p = 0.028$) hypogonadism. The onset of pubertal GM in boys with a normal weight was found at 13.13 years, and in boys with overweight and obesity it was 11.69 years. ($p < 0.001$).

Breast development is a sign typical for females, and when GM occurs in adolescents this happens at an age associated with the development of identity and establishment of self-esteem. The appearance of breast tissue may lead to anxiety, a sense of difference from one’s peers, as well as limiting social contact and participation in sport, especially group sports. That is why patients were asked several questions. Eighty-four patients (53.5%) confessed a psychological

burden of GM (feeling of shame, embarrassment, reduced well-being, anxiety), 12.1% consulted because of its development, in 8.2% GM led to cessation of sports, and 2.5% changed their clothes.

Discussion

GM among hospitalized boys and adolescents is found in 7.7%. This value is close to the prevalence of 4% of 10–19-year-old Bulgarian boys found by Kumanov et al. [7] but it is 3-times lower than the incidence of 23% found among Danish boys [8, 9]. So, it is possible that only a small number of patients with GM are examined and evaluated, and this may be a reason for underestimation of the condition, omission of pathologic GM and delay in diagnosis. In accordance with this is also the fact that even in prepubertal boys, GM, which is always a pathological condition that should be evaluated, the average time before first endocrine evaluation is 18 months (between 0.12 and 5.33 years) (Tab. 1). The sample also shows the high-grade association of GM and obesity, and illustrates the importance of excess adipose tissue on the pathogenesis and age of development of prepubertal and pubertal GM. This confirms the increased incidence of GM in obese individuals found in other studies [10]. In our group, the percentage of association is even higher, possibly because it was conducted in the last decade.

The current analysis focuses on the pathological cases of GM and finds that nearly 1/3 of them are due to some hormonal disturbance or disease, and that GM evaluation was the reason for diagnosis. Therefore, it may be reasonable to recommend a structured and early evaluation of boys and adolescents with breast development. We suppose this percentage is to some extent due to the fact that this study was in a tertiary paediatric endocrine unit. Around 25% of children with GM do not convey importance to breast development, but the majority of patients admit that it creates a psychological burden, and some gave more than one answer, so the influence of breast development on the psycho-emotional state is complex. A similar study was conducted by a team from Turkey [5]. The results obtained in our study show a higher percentage of boys in whom GM led to emotional discomfort.

We are aware of the limitations that a monocentric retrospective study carries. As a single centre, the number of patients was limited. This may lead to underestimation of the actual size of the affected population and omission of rare conditions.

Conclusions

In conclusion, in our study nearly a quarter of pubertal cases are due to pathological conditions, which are often diagnosed more than 18 months after the appearance of breasts. Hence, although

a greater number of pubertal GMs are physiological, it may be reasonable for adolescents to be evaluated within the first 6 months of breast development so as not to omit pathological causes and delay the diagnosis. Additionally, we found that GM has a complex influence on the psychological state of boys and adolescents. Perhaps early establishment of the patient's condition may have a positive impact on his psychological state, behaviour, and habits, especially in obese boys with pubertal GM.

Conflict of interest

None to declare.

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None to declare.

Data statement

Datasets are available from the corresponding author on reasonable request after permission from the local authorities.

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Table 1. Causes and age of development of gynaecomastia in different patients and hormonal characteristics in the investigated group. Data are presented as median (*n*), min–max. All groups include boys and adolescents at different stages of pubertal development. Hormonal values of every patient were compared with reference values for the specific pubertal stage or age.

Causes of gynaecomastia	**N**	**%**	**Age of development**	**Time before 1st medical consultation [years]**	**Testosterone, [nmol/L]**	**Oestradiol [pmol/L]**	**FSH, [mIU/mL]**	**LH, [mIU/mL]**	**Prolactin [mIU/L]**
Prepubertal development	12	7.64	7.53 (12), 0.69–9.0	1.91 (0.12–5.33)	0.693 (10), 0.37–1.77	96.2 (10), 41–189	0.91(9), 0.149–3.31	0.30(9), 0.104–0.67	181.75(9), 110–267
Hypergonado	8	5.0	13.57	1.65	1.21 (8),	139.86	49.8	20.82	222.5

tropic hypogonadism		9	(8), 10–16.25	(0.25–3.83)	0.3–7.04	(8), 18.35–164.87	(8), 1.8–59.15	(8), 1.88–29.96	(8), 109.8–441
Hypogonadotropic hypogonadism	9	5.73	12.77 (9), 10.5–14	2.94 (1.42–4.83)	0.693 (9), 0.15–5.51	119 (9), 62.5–164	1.18 (9), 0.114–8.96	0.573 (9), 0.1–3.91	267.8 (9), 135–413
Hyperprolactinaemia	18	11.46	12.06 (18), 9.33–15.25	1.46 (0.25–3.92)	7.44 (17) 0.34–15.6	97.6(18), 36.7–211	3.27 (17) 1.37–6.77	4.97 (17), 0.605–7.45	438.5 (18), 354–755
Pubertal gynaecomastia	110	70.08	11.84 (104), 9.33–16.92	1.66 (0.04–5)	4.47 (92) 0.693–28.9	122 (93) 73.4–470	2.77 (92) 0.121–15.7	2.83 (93), 0.1–13.4	(93), 49–359
	157	100							