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Hormonal disturbances and etiology of gynecomastia in 17–30-year-old males

Zaburzenia hormonalne i etiologia ginekomastii u mężczyzn między 17. a 30. rokiem życia

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary **Background.** Gynecomastia (GM), usually a benign enlargement of male glandular breast tissue, may evolve both physiologically at some stages of man`s life or secondarily to various disorders. Hormonal investigations can help to establish the underlying cause of GM.
Objectives. The aim of the study was to assess hormonal disturbances in GM and to establish its etiology in 17–30-year-old patients.
Material and methods. 17 men (mean age 21.9 ± 4.2 years), hospitalized between 2003 and 2013 were included in the study. Detailed medical examination, breast and testes ultrasound and hormonal assays for T, E2, LH, FSH, and PRL were performed.
Results. In 9 (53%) patients idiopathic form of GM was diagnosed. In 1 patient GM was drug-induced. In another 3 (17%) it was a result of secondary hypogonadism caused by pituitary macroadenoma (2 pts) and puberty retardation (1). A big obesity was the cause of GM in 3 cases (17%). In the last case androgen imbalance caused by bilateral adrenalectomy propter Hippel-Lindau syndrome together with obesity were disclosed. In all patients with idiopathic GM the levels of LH, FSH, and PRL were normal. In 5 cases within this group the concentrations of estrogens were slightly elevated. Markedly decreased testosterone levels were found in patients with pituitary macroadenomas, as well as in cases of puberty retardation, big obesity, drug-induced GM and in one patient with idiopathic GM.
Conclusions. In this group of young men idiopathic GM was the most common and often coexisted with a variability of subtle hormonal disturbances. It may suggest that the breast glandular tissue is a very vulnerable sensor of sex hormones imbalance.
Key words: gynecomastia, etiology, hormonal disorders.

Streszczenie **Wstęp.** Ginekomastia (GM), łagodny zazwyczaj rozrost tkanki gruczołowej sutka, występuje u mężczyzn we wszystkich grupach wiekowych. Może mieć charakter fizjologiczny lub być objawem wielu chorób. W ustaleniu przyczyny GM może być pomocna ocena hormonalna.
Cel pracy. Ustalenie rodzaju zaburzeń hormonalnych towarzyszących GM oraz jej etiologii w grupie mężczyzn w wieku 17–30 lat.
Materiał i metody. 17 chorych (średnia wieku 21,9 ± 4,2), hospitalizowanych w latach 2003–2013. U każdego z pacjentów przeprowadzono dokładne badanie lekarskie, USG gruczołu piersiowego i jąder oraz ocenę stężeń T, E2, LH, FSH, PRL.
Wyniki. Idiopatyczną postać ginekomastii rozpoznano u 9 (53%) chorych. GM polekową stwierdzono u 1 chorego, u 3 następnych była ona rezultatem wtórnego hipogonadyzmu w przebiegu makrogruczolaka przysadki (2 chorych) i opóźnionego dojrzewania (1). Otyłość olbrzymia była powodem ginekomastii u 3 (17%) mężczyzn. U ostatniego chorego przyczyną zaburzenia równowagi hormonalnej była obustronna adrenalektomia z powodu zespołu Hippel-Lindau w połączeniu z olbrzymią otyłością. U wszystkich chorych z ginekomastią idiopatyczną stężenia LH, FSH i PRL były prawidłowe. U 5 chorych z tej grupy stwierdzono nieznacznie podwyższone stężenia E2. Wyraźnie obniżone stężenia T stwierdzono u 2 chorych z makrogruczolakiem przysadki oraz u pacjentów z opóźnionym dojrzewaniem, otyłością olbrzymią, GM polekową oraz u jednego chorego z idiopatyczną GM.
Wnioski. W badanej grupie młodych mężczyzn dominowała ginekomastia idiopatyczna, która często współistniała z różnorodnymi subtelnymi zaburzeniami hormonalnymi. Dane te sugerują, że tkanka gruczołowa sutków jest u mężczyzn bardzo wrażliwym czujnikiem zaburzenia równowagi hormonalnej.
Słowa kluczowe: ginekomastia, etiologia, zaburzenia hormonalne.

Background

Gynecomastia (GM) is usually a benign proliferation of male breast glandular tissue [1, 2]. Physiologic GM occurs in 60–90% of neonates, 50–60% of adolescents and up to 70% of men aged over 50 years [3].

Pathologic GM is a multifactorial disorder and so far at least 20 clinical conditions connected with its development have been discovered [1–3]. Drug-induced GM constitutes about 10–25% of all cases. It has been reported as an unwanted side effect of more than 300 pharmaceutical drugs [3].

The main cause of GM is an estrogen-androgen imbalance with estrogen predominance [1–4]. Hormonal investigations can help to establish the cause of GM and to classify the patient to physiologic or pathologic type.

Objectives

The aim of the study was to assess the prevalence of different causes of GM in young males and to evaluate the hormonal disturbances associated with this condition.

Material and methods

Seventeen 17–30-year-old men (mean 21.9 ± 4.2) hospitalized between 2003 and 2013 with gynecomastia as the main symptom were included in the study. The anamnesis, physical examination (BMI), breast and testes palpation and ultrasound, serum testosterone (T), estradiol (E2), LH, FSH and PRL measurements were performed. All hormonal studies were conducted with chemiluminescence method with the use of Centaur analyzer.

Results

The results are presented in Figure 1 and in Tables 1, 2, and 3. In patients with idiopathic GM persistent pubertal GM was diagnosed in 6 (67%).

Bilateral breast enlargement was present in 12 patients, unilateral in five: left-sided in 4 and right-sided in one case.

In all idiopathic GM patients the levels of LH, FSH and PRL were normal and in 5 the authors determined subtly elevated E2 concentrations (Tab. 2). Markedly decreased T levels (Tab. 3) were found in three patients: in two with obesity and in one with puberty retardation. In two obese patients low T coexisted with increased E2.

On the base of hormonal measurements, the patients were divided into three groups: group 1 – without hormonal disturbances (Tab. 1), group 2 – with isolated increase in E2 (Tab. 2) and group 3 – with miscellaneous hormonal disturbances (Tab. 3).

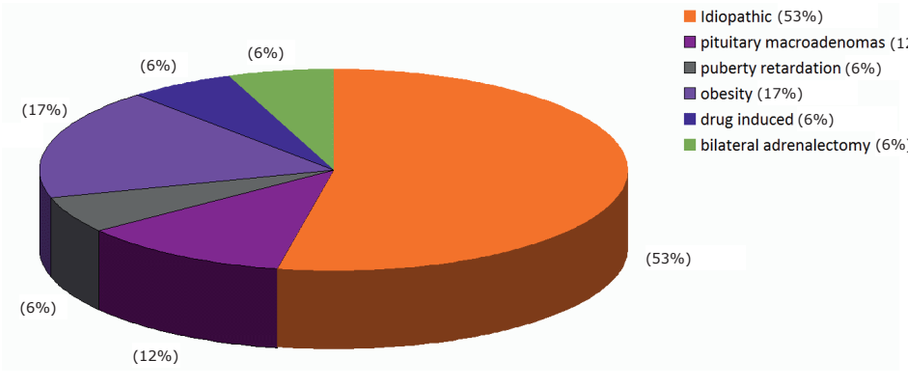

Figure 1. Causes of gynecomastia in 17–30-year-old males

Table 1. Group 1 – patients with GM and normal hormonal assays

Patient	Age years	Cause of GM	BMI kg/m^2	LH	FSH	PRL	E2	T
1.	17	IP*	27.4	5.2	2.1	7.3	33.0	274.9
2.	18	IP	27.0	5.9	2.3	19.5	38.0	497.9
3.	19	PBA**	34.0	3.9	1.8	15.2	36.0	464.6
4.	27	IP	19.1	3.0	1.7	9.9	40.0	472.5
5.	28	Drugs***	27.1	5.8	4.4	9.2	40.0	458.5

* Idiopathic, ** post bilateral adrenalectomy, *** antipsychotic drugs.

Table 2. Group 2 – patients with GM and elevated estradiol concentrations only

Patient	Age	Cause of GM	BMI Kg/m^2	LH	FSH	PRL	E2	T
1.	18	IP	21.8	3.2	4.0	5.8	45.0	576.7
2.	18	IP	23.0	5.1	2.5	11.2	45.0	748.6
3.	20	OB	31.0	3.6	4.1	11.8	87.0	581.6
4.	20	IP	21.8	2.5	4.4	11.4	55.0	645.3
5.	20	PM*	25.0	4.1	5.4	10.7	44.0	405.0
6.	21	IP	24.9	5.9	2.4	11.0	49.0	332.1
7.	21	IP	24.2	2.5	3.8	4.0	50.0	628.0

* Pituitary macroadenoma.

Table 3. Group 3 – patients with GM and other or mixed hormonal disturbances

Patient	Age	Cause of GM	BMI	LH	FSH	PRL	E2	T
1	19	PR**	29.0	0.0	1.9	9.9	6.0	16.0
2.	23	IP	19.2	5.9	3.2	6.7	43.0	856.6
3.	24	OB*	40.0	1.8	1.7	10.2	44.0	202.0
4.	29	PM***	23.8	1.9	3.1	1838.0	27.0	286.0
5.	30	OB	30.1	2.6	3.7	11.2	19.2	194.0

* Obesity ** puberty retardation, *** pituitary macroadenoma.

Normal ranges in adult men were respectively: LH = 1.5–9.3 mIU/ml; FSH = 1.4–18.1 mIU/ml; prolactine (PRL) = 2.1-17.7 ng/ml; estradiol [E2] = 11.6–41.2 pg/ml; testosterone [T] = 242–827 ng/ml.

The highest average BMI (28.4 ± 1.8 kg/m^2) characterized the patients from group 3, while the lowest (24.5 ± 3.1 kg/m^2) the patients from group 2.

The highest E2 levels (mean 53.6 ± 15.2 pg/ml) and simultaneously the highest but within normal ranges mean T levels (559.6 ± 143.9 ng/ml) were detected in group 2.

LH concentrations did not differ significantly between groups 1 and 2, whereas FSH concentrations were higher in group 2.

Discussion

According to many reports [1–3] the etiology of GM is very miscellaneous and possible to establish in only about 50% of cases. It is common in adolescent and young men due to a pubertal transient relative imbalance between estrogens and testosterone [5–7].

Similarly, in presented material, the majority of idiopathic GM was induced by persistent pubertal GM. Secondary causes of this disease were heterogenic: obesity, primary and secondary hypogonadism, drugs and adrenalectomy.

Hormonal disturbances in these patients were also heterogenic: from normal hormone assays, through subtly elevated E2 concentrations to complex hormonal imbalance.

Czajka-Oraniec et al. [4] and Ersöz et al. [7] certified significantly higher BMI in patients with GM comparing with healthy controls. Those authors concluded that idiopathic GM is closely correlated with generalized obesity and with reduced LH and T levels as a result of increased conversion of T to E2 in increased adipose tissue mass. Other suggested causes of idiopathic GM are the mutations in aromatase and androgen receptor genes [2, 4].

The authors didn't observe significant differences in BMI between groups of patients with idiopathic GM. They certified two types of hormonal pictures in these males. In the first subgroup all hormonal studies were within normal ranges. In the second, they observed very subtly elevated E2 levels with normal titers of remaining hormones. The elevated E2 levels together with normal or decreased LH concentrations, after an exclusion of testes and adrenal diseases, can indicate the increased peripheral androgens aromatization, as it was suggested by Czajka-Oraniec et al. [4].

Conclusions

In young men idiopathic GM is the most common and often coexists with variability of subtle hormonal disturbances. It may suggest that the breast glandular tissue is a vulnerable sensor of sex hormones imbalance.

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