CLINICAL CHARACTERISTICS OF A BATCH OF WOMEN WITH HYPERANDROGENISM BROUGHT ABOUT THE CONGENITAL ADRENAL HYPERPLASIA WITH DELAYED DEBUT

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Abstract: *Congenital adrenal hyperplasia (CAH), non-classic form (with delayed debut) is the second cause of hyperandrogenism with a prevalence of 1,4-4%. The aim of the study was to establish the frequency of main hyperandrogenic manifestation in a group of women diagnosed with non-classic form of CAH. The study was performed on 41 patients diagnosed with non-classic form of CAH through the measurement of 17-hydroxyprogesterone and ACTH test. The following frequency was observed: hirsutism 85%, ovulatory dysfunction 56%, seborrheic syndrome 53%, alopecia 27%, and obesity 46%.*

Keywords: *congenital adrenal hyperplasia, hyperandrogenic manifestation.*

Rezumat: *Hiperplazia adrenală congenitală (HAC), forma neclasică (cu debut tardiv) este considerată a doua cauză de hiperandrogenism, cu o prevalenţă de 1,4-4%. Scopul studiului a fost determinarea frecvenţei principalelor manifestări hiperandrogenice la un lot de femei diagnosticate cu forma neclasică a HAC. Studiul a fost realizat pe un număr de 41 de cazuri diagnosticate cu forma neclasică a HAC, prin dozarea 17-hidroxiprogesteronului şi a testului la ACTH. A fost întâlnită următoarea frecvenţă: hirsutismul 85%, disfuncţia ovulatorie 56%, sindromul seboreic 53%, alopecia 27%, supraponderea şi obezitatea 46%.*

Cuvinte cheie: *hiperplazia adrenală congenitală, manifestări hiperandrogenice*

INTRODUCTION

The main hyperandrogenic manifestations (hirsutism, alopecia, ovulatory dysfunction, acne) are important criteria of addressability, both in the medical specialities (endocrinology, dermatology, plastic surgery, gynecology), as well in paramedical manifestations (cosmetology, beauty centres etc.). Thus, acne is encountered in around 85% of the subjects of the second decade of life (1,4,6), androgenetic alopecia may affect up to 50% of the women below 50 years old, while hirsutism will affect 5-15% of the total of the women (2,10) and more than 40% of those at menopause (4).

Being considered as the second cause of hyperandrogenism, the congenital adrenal hyperplasia (CAH) with delayed debut has a prevalence of 1,4-4%(11). 21-hidroxilasis deficit is the most frequent cause of CAH (90-95%)(8,9). Hyperandrogenism changes may consist in premature pubarche, bone age advancement, acne (33%), hirsutism (60%), oligomenorrhea (54%), infertility, final small weight and psychical disorders (9).

PURPOSE OF THE STUDY

The purpose of the study was to establish the frequency of the main hyperandrogenic manifestations (hirsutism, acne, alopecia, ovulatory dysfunction) in a group of women with neoclassic form of CAH.

MATERIAL AND METHOD

The study was performed on a number of 41 cases, recruited out of a total of 1132 women with hyperandrogenic symptomathology, based on the following criteria:

Inclusion criteria:

1. hyperandrogenic symptomathology: hirsutism, seborrheic syndrome (acne seborrhoea), alopecia, ovulatory dysfunction (menstrual disorders, sterility).
2. ACTH positive stimulation test (17-OHP>3,2ng/ml) or basal 17-OHP above 4ng/ml.

Exclusion criteria:

1. Other causes of hyperandrogenism: polycystic ovary syndrome, Cushing's syndrome, tumours (ovary, suprarenal, hypophysis) iatrogenic hyperandrogenism
2. ACTH negative test (17-OHP<3,2ng/ml)

The main signs of hyperandrogenism were quantified taking into account different classifications:

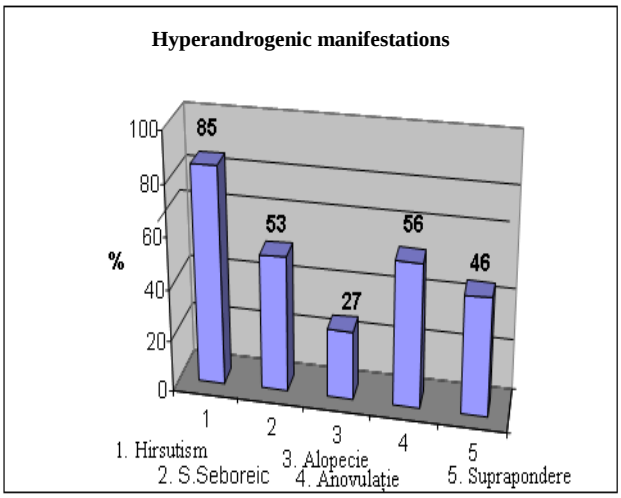
1. **Hirsutism** was classified according to Ferriman-Gallwey scale, through pilosity assessment on nine areas (5). Pilosity was classified from 0 (without pilosity) to 4 (franc virile). Between 10 and 14, hirsutism was considered an easy form, between 15 and 19, it was considered mild and above 19, it was severe.
2. **Acne** was classified in: simple, papulo-pustular, conglobated and severe (6).
3. **Alopecia** was classified according to Ludwig's scale, in three classes (7).
4. **Ovulatory dysfunction** was recorded in the case of menstrual disorders (tahy or brady-spaniomenorrhea) and in case of sterility and/or ovarian cysts.

RESULTS AND DISCUSSIONS

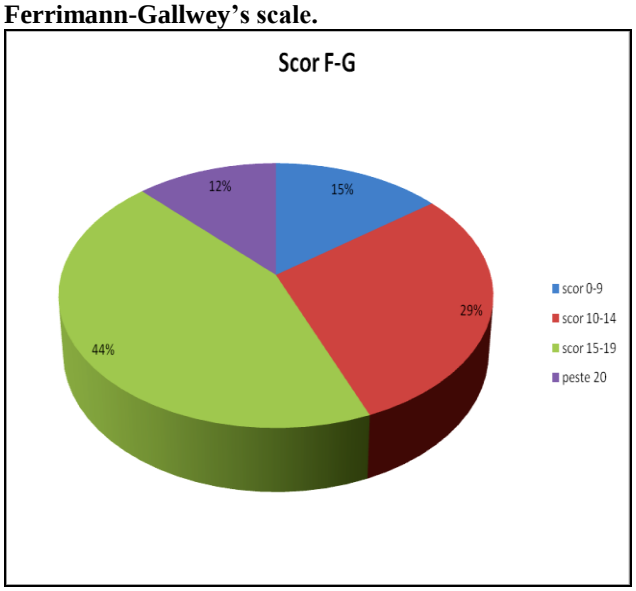
The percentage of the main hyperandrogenic manifestations within the studied batch is emphasized in picture 1.

1. **Hirsutism score** on Ferriman-Gallwey's scale is placed between 5 and 24, with an average of 14,63. Hirsutim scales repartition is given in picture 2.
2. Proportion of acne types is given in picture 3.
3. The association of seborrheic syndrome to **alopecia** is given in picture 4.
4. The main maifestations of the ovulatory dysfunctions, *menstrual disorder* and *sterility* in the patients within the studied batch were ecountered in a percentage of 48,78%, respectively 19,5%.
5. **Hirsutism** is considered the most sensitive marker of androgen hormones, followed by acne, seborrhoea, menstrual disorders, increased libido, clitomegaly and finally, virilization (1).

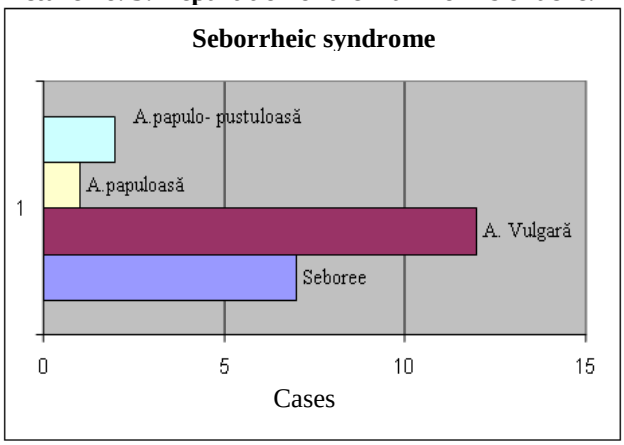
Picture no. 1: Frequency of the main hyperandrogenic manifestations



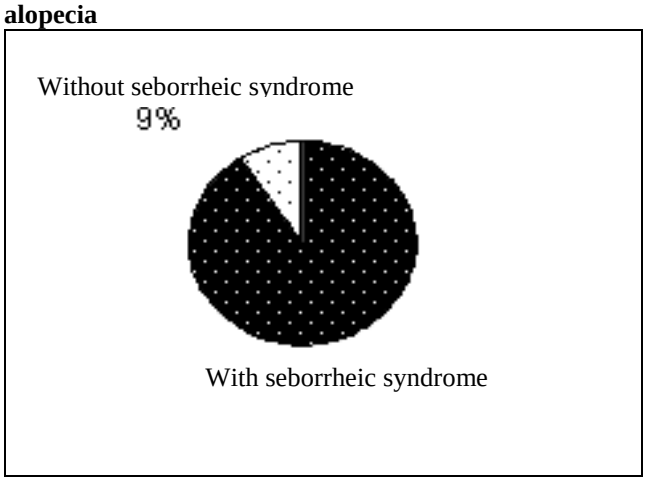
Picture no. 2: Distribution of hirsutism score on Ferrimann-Gallwey's scale.



Picture no. 3: Repartition of the main forms of acne.



Picture no. 4. Association of seborrheic syndrome in alopecia



Regarding our study (picture 1), 85% of the patients have hirsutism (score over 9 on Ferriman-Gallway's scale), as against the general population where this affection is detected in 5-15% cases (2,10). The percentage of the hirsute women is larger than that mentioned in different studies dealing with the neoclassical form of CAH, where there are percentages between 39%(8) and 60% (9). Picture no. 2 reveals that the majority of the studied patients have an easy and mild form of hirsutism. The average of the Ferriman-Gallway's scoring is of 14,63, that is at the mild hirsutism level.

1. **Seborrheic syndrome** includes tegumentary clinical aspects relative to sebaceous hypersecretion: seborrhoea, acne, seborrheic eczema and seborrheic alopecia (4).

Within our study, this syndrome is encountered in 22 patients, that is in 53% of cases (picture no. 1). It is a larger proportion than in other studies, where a prevalence up to 33% is mentioned, regarding acne in CAH with late debut. (9).

Generally, the seborrheic syndrome is considered rather a physiological factor in puberty, when the androgen hormones occur, which are secreted by the suprarenal glands within adrenarche and encountered in 85% of the subjects of the second decade of age. Its persistence after this age, its occurrence in adult women

or, on the contrary, before puberty, just like severe acne in adolescent girls, should alert the doctor about the possibility of hyperandrogenism. (1).

Regarding our study, half of the patients with seborrheic syndrome are between 21 and 30 years old, followed by the age group between 31 and 40 (27%) and on the last place, there are the young girls below 20 (23%). So, more than three fourths of the patients with seborrheic syndrome within the studied batch are outside the age considered as physiological for this syndrome.

The picture no. 3 reveals that the most frequent manifestation of the seborrheic syndrome is the simple or vulgar acne (54,5%), followed by seborrhoea (32%), papulo-pustular acne (9%) and papulous acne (4,5%).

If the age criterion when the seborrheic syndrome occurs is abnormally increased within the batch in comparison with the general population, it may be said that the type of manifestation does not represent a gravity criterion, seborrhoea and the simple acne being more frequent.

2. Alopecia is the rarest sign detected in the patients of the studied batch: 27% of the cases (Picture no. 1).

Androgenetic alopecia is considered the most common form of alopecia, both in women and in men. Due to the fact that suprarenal androgens are in general less potent and taking into consideration that the women have ovarian androgens with peripheral antiandrogenic role, it is understandable why alopecia is not a frequent symptom in women with CAH.

In our study, the majority of the alopecia cases are simple forms, characterised by scalp hair injuries in the conditions of intense seborrhoea. Less than a tenth of the cases are advanced alopecias, where seborrhoea is no longer present (picture no. 4).

3. Ovulatory dysfunction includes different ovarian functional disorders that may also be induced by hyperandrogenism: oligomenorrhea, amenorrhea, menorrhagia, metrorrhagia, pelvin pain, premenstrual syndrome, infertility (1). Oligomenorrhea is quoted as a CAH symptom with delayed debut in percentages between 39% (8) and 54% of the cases (9).

In our study, the ovarian dysfunction is encountered under different manifestations in 56% of the cases (picture 1), being the second major syndrome, in terms of frequency, after hirsutism.

The most frequent manifestation of this syndrome is the menstrual disorder under the form of brady-spaniomenorrhea**,** tahimenorrhea or the alternance both of them and rhythmic menstruations. Regarding the patients of our studied batch, menstrual disorder is encountered in 20 cases, representing 48.78%, while sterility can be found in a percentage of 19,5%. Other studies consider that infertility is a symptom of presentation in 13% of the women with this affection (9). Another study quotes a French statistic, according to which, half of the patients with 21-hidroxilasis deficit get pregnant before being diagnosticated with this deficit (8).

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