HORMONAL PROFILE AND ANDROGEN STATUS DURING THE MENSTRUAL CYCLE IN WOMEN WITH ACNE

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Summary: The androgen excess in women with acne can play an important role in gynecological endocrinology.

LH, FSH, PRL, Testoserone (T), Androstenedione (A), Deydroepiandrosterone sulphate (DHEA-S) and Progesterone (P) were investigated in 21 women with uncomplicated idiopathic acne during the menstrual cycle.

LF/FSH ratio >3 was found in 7 cases (36.8%).

Total T values were high in 90.4% of the whole group of women with acne (mean ± SD 618.6±253.6, normal range 92-352 pg/ml). An ovulatory pattern of P was found in 66.65% of women with acne. Hyperprolactinemia was found in 23.6% of cases. The common denominator for ovulatory dysfunction in these women seems to be elevated LH levels, rather than elevated T levels.

INTRODUCTION

Today many investigators are agreed in regarding acne vulgaris as a sign of androgen excess in women, sebaceous glands being dependent on androgen stimulation ([1, 2, 3, 4]); thus this condition can play an important role in gynecological endocrinology. The possibility that acne could be the result of an over production of androgens has been addressed by a number of investigators with different results. The presence of elevated levels of plasma androgens in women with acne vulgaris, with or without hirsutism has been reported by many authors ([5, 6, 7]).

Adrenals and ovaries are the main sources of androgens in women: it remains controversial whether the ovary or the adrenal is the primary source of the androgen excess in patients with acne. Ovarian androstenedione (A) and testosterone (T) release in the stroma and theca cells is under LH control ([8, 9]). ACTH stimulates adrenal zona reticularis to secrete androgens: but it has been hypothesised that there are other stimulating factors identified as prolactin (PRL) ([10, 11]) and Corticotrophin adrenal stimulating hormone (CASH) ([12]). The etiology of acne is often unclear: the sebaceous glands are target organ of androgen actions, mainly the intracellular conversion of T in Dihydrotestosterone (DHT) by the enzyme 5α-reductase. It is been reported that elevated Dihydroepiandrosterone sulphate (DHEA-S) levels are present in 81% of males with severe acne ([6]). Mild hyperprolactinemia has been demonstrated in women with acne, many of whom had associate androgen abnormalities ([13, 14]). On the other hand, acne and hirsutism may occur without elevated androgen serum levels ([15, 16]).

The present study was performed to characterize the hypophysal-adrenal-ovarian function and the androgen status in women with uncomplicated (not associated with hirsutism or evident ovarian disfunction) idiopathic acne during the menstrual cycle.

MATERIAL AND METHODS

No patients, 21 women with acne (aged 18-39 years, mean 25.5) had ever received glucocorticoid therapy and had taken no endocrinologically active drugs. They were all regularly menstruating, except 3 who had oligomenorrhoea.

Blood samples collected on 8, 12, 16, 20, 24 days of the cycle at 9 a.m. Plasma was frozen at −20 °C until the assay.

Hormone determinations

Plasma LH, FSH, PRL, Progesterone (P), T, A DHEA-S, were measured by RIA methods.

LH, FSH and PRL determination was performed by commercial available kits (Sorin, Saluggia, Italy) with a double-antibody.

T was measured by solid phase ^{125}I radioimmunoassay (Medical System Kit) in unextracted plasma, based on testosterone-specific antibody immobilized to the wall of a polyprophylene tube.

P and A plasma levels were assayed by RIA (Bio-Merieux Kit) after extraction with ether. Charcoal-dextran was used to separate bound from free-fractions.

DHEA-S was measured by RIA (Bio-Merieux Kit) after dilution with a buffer causing a normal Ag-Ab reaction, and separation with charcoal-dextran, as above.

All data are presented as the mean ± DS. Comparison was made using Student's t test.

RESULTS

Clinical and laboratory features of the acne group studied are shown in table 1.

Table 1. –*Clinical and laboratory features of the acne group studied.*

Acne patients	No. cases (21)	%
LH/FSH ratio >3	7/19	36.8
Hyperprolactinaemia	5/19	26.3
High Testosterone	19/21	90.4
High Androstenedione	10/21	47.6
High DHEA-S	6/14	42.8
Ovulatories Cycles	14/21	66.6
Anovulatories Cycles	7/21	33.3

According to LH basal concentrations all subjects were subdivided into two groups; in the first group 7 cases with LH > 15 mU/ml and LH/FSH ratio > 3 (fig. 1); we found 6 cases with high T, one case with high A, two cases with high PRL (basal prolactin levels above 20 ng/ml), two cases with high DHEA-S and normal P pattern in the luteal phase in two cases (28.5%). The second group, 14 cases, was characterized by LH < 15 mU/ml and LH/FSH ratio < 3 (fig. 2). In this group high levels of T were found in 11 cases, high A levels in 8 cases, hyperprolactinemia in 3 cases, high DHEA-S levels in 4 cases and ovulatory pattern of P in 12 cases (85.7%). Ovulatory pattern of P was found in 66.6% of the entire group of the patients with acne. Therefore T values were high in 90.4% (19/21 cases) of the whole group of patients with acne (mean ± DS 618.6±253.6 normal range 92-352 pg/ml) (fig. 3).

High values of A were found in 47.6% (10/21 cases) (fig. 4) (mean ± DS 2543.3 ± 1769.9, normal range 590-1820 pg/ml) (fig. 4) and high DHEA-S in 42.8% (6/11 cases) (mean ± DS 213.3 ± 92 normal range 54-205 μg/ml) (fig. 5).

Hyperprolactinemia was found in 23.6% (5/19 cases) of cases.

DISCUSSION

The etiology of acne is often difficult to evaluate. The androgen action at the level of the target organ, the pilosebaceous glands, is mainly determined by the intracellular conversion of T in DHT by 5-α-reductase ([17, 18]); on the other hand in the sebaceous glands, DHEA-S can also be transformed in A([19]) by 3β-hydroxy steroid dehydrogenase. Hyperprolactinemia with high levels of T and DHEA-S was described in 40% of patients with acne and/or hirsutism ([13, 14, 20]). All the women with acne and elevated levels of PRL showed T levels above the upper limits of normal range, while A was over the upper limits of normal range in 3 cases of hyperprolactinemia. On the contrary DHEA-S was within the normal range in all except one patient with acne and hyperprolactinemia.

Several reports suggest a direct link between elevated PRL levels and adrenal androgen secretion ([21, 72, 23]).

A tropic effect of PRL on the adrenal cortex was suggested by Boyar *et al.* ([24]) in a case of hyperprolactinemia associated with adrenal hyperplasia.

El Tabbakh *et al.* ([23]) showed a significant drop of DHEA-S and PRL after bromocryptine in patients with PCOD. On the other hand, neither Parker ([25]) nor Metcalf ([26]) confirmed these findings: the

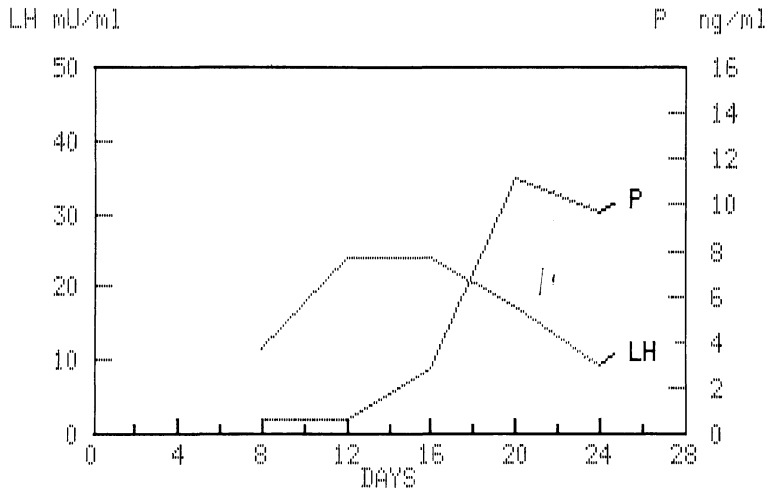

Fig. 1. — Pattern of progesterone during the menstrual cycle in 14 patients with acne and LH/FSH ratio <3.

first Author did not find significant differences of DHEA-S between a group of normal controls and patients with elevated PRL concentrations.

The second one, in 12 patients with hyperprolactinemia, showed no significant change in plasma DHEA-S after treatment with bromocryptine.

Therefore Scholl ([28]) observed in 34 women with acne low-normal PRL levels, suggested PRL may not be involved in hyperandrogenism of acne patients.

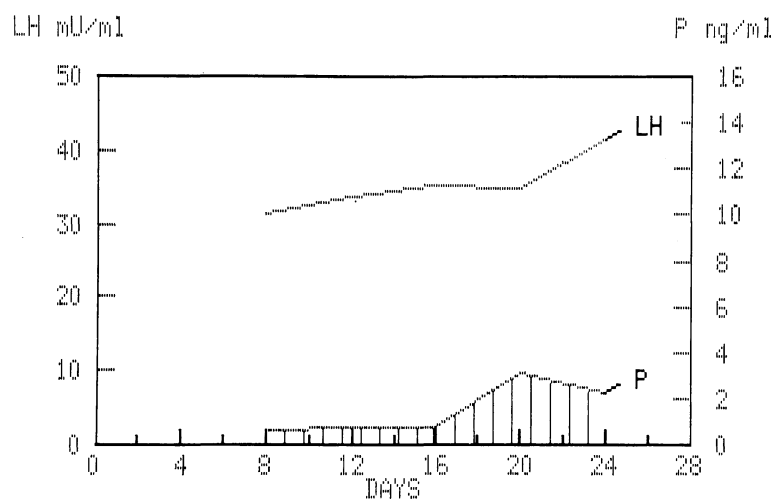

Fig. 2. — Pattern of progesterone during the menstrual cycle in 7 patients with acne and LH/FSH ratio <3.

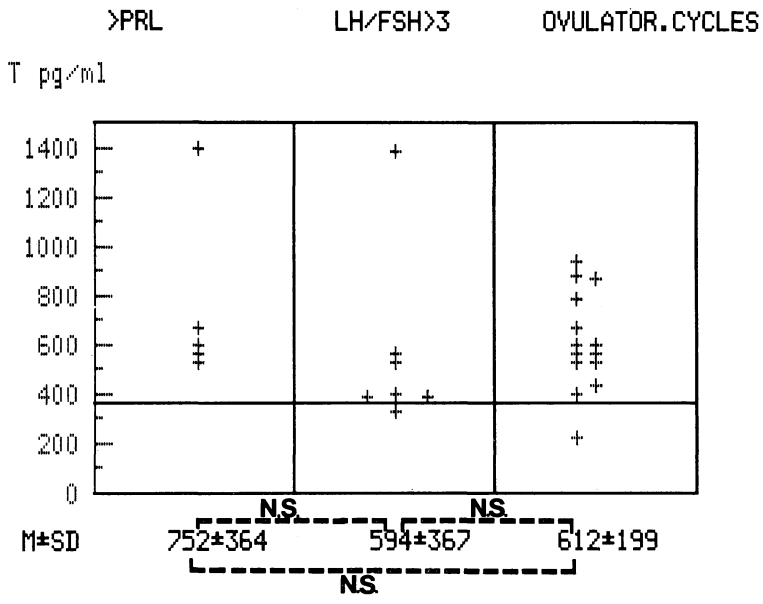

Fig. 3. — Basal serum testosterone concentrations in 21 women with acne: 5 showed hyperprolactinemia, 7 LH/FSH ratio >3 and 14 ovulatory patterns of progesterone. The upper limit of normal T (352 pg/ml) is indicated by the horizontal line.

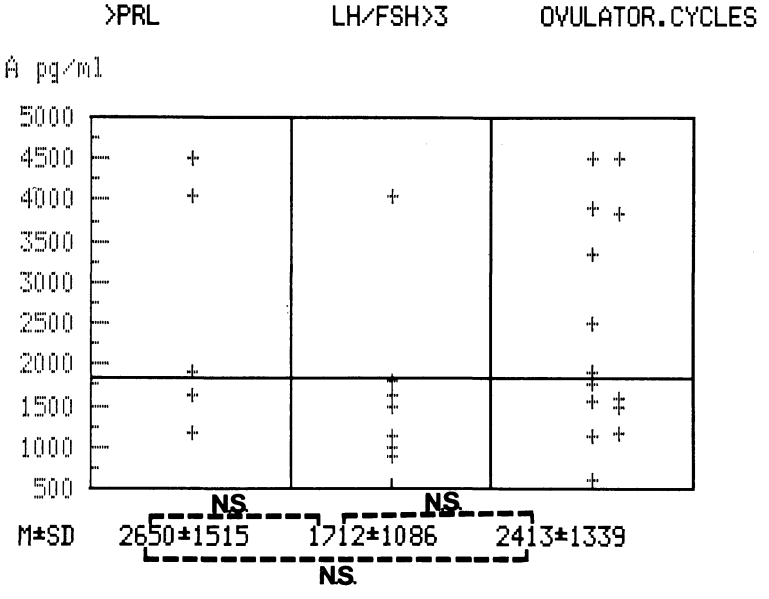

Fig. 4. — Basal serum. A concentrations in 21 women with acne: 5 women showed hyperprolactinemia, 7 LH/FSH ratio >3 and 14 ovulatory patterns of progesterone. The upper limit of normal of A (1820 pg/ml) is indicated by the horizontal line.

We think, in agreement with Steinberger ([27]), active acne could be considered a suitable model of hyperandrogenism: in fact acne related to hyperandrogenism becomes inactive once the androgen levels return to normal.

In the present study 90.4% of acne patients has shown total T levels above the normal levels in accordance with other investigators ([28]).

with acne and LH/FSH ratio >3 the high values of LH and the anovulatory pattern of P in the same cases confirm the association between ovarian dysfunction and LH levels. In the second group normal LH plasma levels are related with ovulatory pattern of P in the luteal phase: it seems, thus, that the common denominator for ovulatory dysfunction in these women is elevated LH levels, rather than elevated

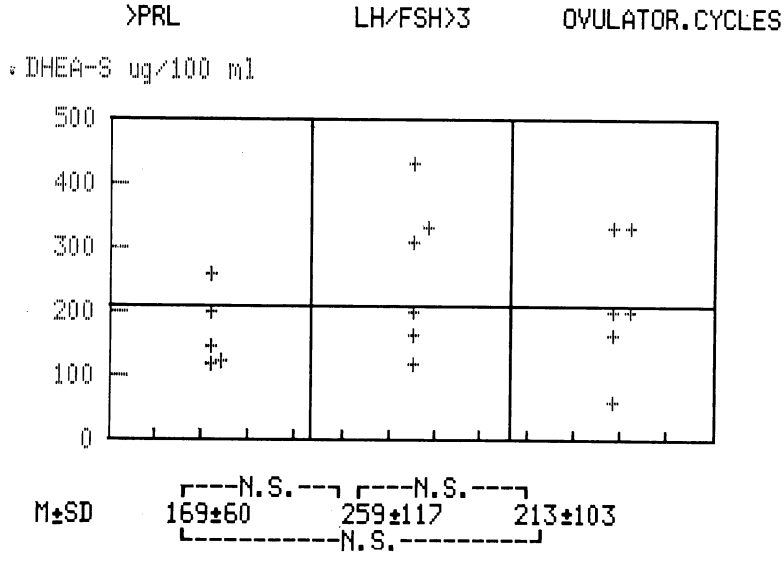

Fig. 5. — Basal serum DHEA-S concentrations in 21 women with acne: 5 women showed hyperprolactinemia, 7 LH/FSH ratio >3 and 6 ovulatory patterns of progesterone. The upper limit of normal of DEAS-S (205 μg/100 ml) is indicated by the horizontal line.

On the other hand, Chrouson *et al.* ([19]) found that plasma T values were similar in patients with acne and in normal controls.

Gynecologic disorders are frequently associated with high circulating androgen levels and acne as a related consequence of hyperandrogenism. Circulating levels of LH or LH/FSH ratio have frequently been found to be deviated in patients with polycystic ovarian diseases ([30, 31]) and it is hypothesised that the inappropriate LH secretion may be the etiologic factor in PCOD ([32]). In our first group of women

T levels. Typical features of PCOD are oligo- or amenorrhea, hirsutism, chronic anovulatory cycles, overweight. In our study, in spite of elevated plasma levels of T, the women with acne had an incidence of ovulatory cycles of 66.6%. May be that the degree of androgen excess necessary to interfere with ovarian function is more than that required to stimulate acne. There are many reports finding normal T values ([33, 34]) in women with acne and others showing elevated T values ([5, 6, 35]). The evaluation of androgen

skin receptors with increased androgen sensitivity may be an explanation for acne, also in patients with androgen within the normal range ([36]).

These observations led us to the conclusion that other factors, as well increased sensitivity of the sebaceous glands to androgens must be evaluated in the pathogenesis of acne.

Further studies are needed to verify our findings and their application to all acne patients.

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