The HAIR-AN syndrome : a case report

Therapeutic response, and Acanthosis nigricans as a guide

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The HAIR-AN Syndrome affects about 5% of hirsute women and characterized by insulin resistance, elevated insulin levels, acanthosis nigricans(AN) and hyperandrogenism. The patient presented here is a 21 year-old woman who has secondary amenorrhea, hirsutism, and hyperpigmented skin changes. The patient was given oral contraceptive and spironolactone. After nine months, the patient was observed for significant clinical and hormonal improvement. *[Journal of Turgut Özal Medical Center 2(2):204-205,1995]*
Key Words : Acantosis nigricans, hirsutismus, insulin resistance ,oral contraceptive, spironolactone

HAIR-AN sendromu : bir vaka takdimi

HAIR-AN sendromu hirsut kadınların yaklaşık %5'ini etkiler ve insülin rezistansı, yüksek insülin seviyeleri, akantosis nigrikans (AN) ve hiperandrojenizm ile karakterizedir. Burada sunulan hasta 21 yaşında bir kadın olup sekonder amenore, hirsutism ve hiperpigmente deri değişiklikleri vardı. Hastaya kontraseptif ve spironolakton verildi. Dokuz ay sonra, hastada anlamlı klinik ve hormonal iyileşme gözlendi. [Turgut Özal Tıp Merkezi Dergisi 2(2):204-205,1995]
Anahtar Kelimeler *: Acantosis nigricans, hirsutismus, insulin resistansı ,oral kontraseptif, spironolactone*

The hyperandrogenic-insulin resistant- acanthosis nigricans syndrome affects about 5% of hirsute women and is characterized by insulin resistance (IR), elevated insulin levels (INS), acanthosis nigricans (AN), and hyperandrogenism (HA)[1]. In the HAIR-AN syndrome the insulin resistance is typically due to a decreased number of insulin receptors and decreased functional activity of circulating anti-insulin receptor antibodies. It is also reported that some women with the HAIR-AN syndrome have point mutations in the insulin reseptor gene[1-3]. Clinically, AN presents as a velvety, mossy, verrucous, hyperpigmented skin changes that usually develops over the nape of the neck, in the axillae, beneath the breasts and occasionally in other folds[1,2]. There is no unique therapeutic model.Oral contraceptives and antiandrogens are given by some autors[4-6]. In this report, the diagnostic importance of AN, and therapeutic response in the HAIR-AN syndrome is reviewed.

CASE REPORT

A twenty-one year old woman presented with secondary amenorrhea, hirsutism and hyperpigmented skin changes. Her menarche was at age 15, and she had irregular periods to date. She had menstrual bleeding between 3-6 months range, and had no periods for the last 8 months. Physical examination revealed hyperpigmented skin changes that developed over the nape of the neck and beneath the breasts. She had abnormal hair growth all over her body. Pelvic examination was unremarkable. We consulted the case with dermatologist and a biopsy was recomended for hyperpigmented skin lesions. But the patient refused the biopsy and declined to have the lesions photographed. Blood chemistries were unremarkable. Pregnancy test was negative, gestagen test was positive. Pelvic ultrasound revealed several bilateral 5-6 mm follicle cysts and normal uterus. Basal characteristics of the patient are shown

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in Table I.

Table 1. Basal characteristics of the patient

Parameter	Result
Age	21.0
Body Mass Index (Kg/m^2)	34.3
F-G score*	13.0
Total T (ng/dl)	88.0
Free T (ng/dl)	5.6
SHBG (nmol/L)	142.0
DHEAS (ng/ml)	680.0
FSH (mIU/ml)	6.6
LH (mIU/ml)	5.8
Prolactin (ng/ml)	10.2
E2 (pg/ml)	86
17-OHP (ng/ml)	1.2
Basal INS (uU/ml)	94.0
Peak INS (uU/ml)	965.0

*F-G score, the scoring of hirsutism according to the method of Ferriman and Galloway

All the hormones were measured by RIA, using Gambyt 10 gamma counter (Diagnostic Product Corporation, USA).We started oral contraceptive agent called "Diane" (0.035 mg ethinylestradiol and 2 mg cyproterone acetate, Diane 35; Schering AG, Germany) and peroral 100 mg twice daily spironolactone (SPA) (Aldactone; Searle, Chicago, IL).

The patient has recieved this therapy for 9 months.These therapy significantly supressed Total T (88 versus 37 ng/dl), free T (5,6 versus 4,6 ng/dl), and increased SHBG (142 versus 178 nmol/L), also decreased F-G score (13 versus 11). No change in acanthosis nigricans and the other parameters was observed. She is currently on this therapy.

DISCUSSION

Although acanthosis nigricans is a epiphenomenon of the hyperandrogenism, only 5% of hyperandrogenic women have AN. Acanthosis nigricans can occur in the setting of benign or malignant diseases[1]. The tendency for severe hyperinsulinemia to be associated with stromal hyperthecosis, rather than polycystic ovaries, is further evidence that the HAIR-AN syndrome is a unique subclasification of hyperandrogenism. In the HAIR-AN syndrome, the primary pathologic derangement is the IR and compansatory hyperinsulinemia. The hyperinsulinemia together with LH, stimulates ovarian stromal and thecal androgen production. The AN is a dermatologic manifestation of severe hyperinsulinemia and hyperandrogenism[1,2]. If AN is present in a young woman who does not have an associated malignancy, marked IR can be demonstrated to be present in more than 90% of cases. Although the finding of AN is relatively specific for the presence of IR, it is not a sensitive marker of IR[1,2]. As it is known, there is little data about the treatment of this syndrome.Anecdotal reports have noted an improvement in hyperandrogenemia after estrogen-progestin administration alone[4,5], oraccompanied by antiandrogen[6]. Furthermore, Corneblum and Boylin[7] successfully used the long acting GnRH-analogue (GnRH-a) leuprolid acetate as primary therapy.

The results of our study revealed that in the patient suffering from the HAIR-AN syndrome, the hyperandrogenemia and hirsutism can be effectively treated an OC and SPA combination therapy.We discussed the oral contraceptive and spironolacton as therapeutic agents, and hyperpigmented skin changes as a guide to diagnose the HAIR-AN syndrome.

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