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Serum AMH levels in the differential diagnosis of hyperandrogenemic conditions

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ABSTRACT

Objective: To investigate the diagnostic potential of anti-Müllerian hormone (AMH) in the differential diagnosis of various hyperandrogenemic conditions.
Study design: Among 2241 consecutive women of reproductive age who were seen at a tertiary care university hospital with complaints of acne, hirsutism, androgenetic alopecia, and menstrual dysfunction (oligomenorrhea and/or amenorrhea), 107 patients with serum 17α-hydroxyprogesterone (17α-OHP) levels higher than 2 ng/ml were recruited for this study. An ACTH stimulation test was performed, and basal serum hormonal parameters and AMH levels were measured for all patients.
Results: 25 patients were diagnosed with late-onset congenital adrenal hyperplasia (LOCAH), and 59 patients with polycystic ovary syndrome (PCOS) had significantly higher serum AMH levels than all other groups.
Conclusion: Among hyperandrogenemic patients with serum 17α-OHP levels >2 ng/ml, serum AMH levels might be introduced as a marker to be utilized clinically in the differential diagnosis of hyperandrogenemic patients, especially for identifying patients with PCOS.

Introduction

Polycystic ovary syndrome (PCOS), late-onset congenital adrenal hyperplasia (LOCAH), idiopathic hyperandrogenism (IHA) and idiopathic hirsutism (IH) are the most common diseases which result in hyperandrogenemia in women and all these disorders share common clinical features and laboratory findings [1]. In PCOS, most of the circulating androgens are produced in the ovaries but the adrenal gland also contributes to the hyperandrogenism in these patients [2,3]. Having similarities with PCOS, idiopathic hyperandrogenism is also characterized with an excess amount of ovarian androgens. In contrast to both these conditions, LOCAH is an adrenal gland disorder [4,5], and adrenal androgens constitute the majority of the circulating androgens. Idiopathic hirsutism, on the other hand, presents clinically with increased male-type hair growth, but circulating androgen levels are precisely between normal limits in this particular group of patients. One hypothesis on the pathophysiology of idiopathic hirsutism puts the emphasis on increased activity of the 5-α-reductase enzyme in the skin [6].

Anti-Müllerian hormone (AMH), a member of the transforming growth factor-β (TGF-β) superfamily, is secreted specifically from the granulosa cells of early developing pre-antral and antral follicles [7]. AMH is documented to have an inhibitory role in the ovary, and increased levels of serum AMH may contribute to diminished follicular development [8]. AMH is suggested to be a useful marker of ovarian reserve since it indicates the quantity of the ovarian follicle pool [9]. Serum [10] and follicular fluid [11] AMH levels are documented to be increased in women with PCOS compared to women with normal ovaries. In addition, the serum concentration of AMH correlates with the severity of symptoms [12].

Comparison of serum AMH levels between patients with different hyperandrogenemic diseases has never been investigated so far. Hyperandrogenism may be the symptom of ovarian or adrenal gland pathology, while in some cases both organs may contribute to the elevated levels of circulating androgens. In addition, in some patients the hyperandrogenism may be classified as idiopathic. As a well-known ovarian reserve marker, serum AMH levels may differ in various hyperandrogenemic diseases due to the

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varying extent of the ovarian contribution. Therefore we hypothesized that serum AMH levels might be a useful marker for the differential diagnosis of hyperandrogenemic conditions.

Materials and methods

The medical records of 2241 consecutive women of reproductive age who were seen at the Department of Gynecology and Obstetrics, Cerrahpasa School of Medicine, Istanbul, Turkey, between January 2009 and June 2012 with acne, hirsutism, androgenetic alopecia (hereafter termed alopecia) and menstrual dysfunction (oligomenorrhea and/or amenorrhea) complaints were reviewed retrospectively. Approval from the Human Ethics Committee of Istanbul University was obtained. Age, records of clinical examinations and sonographic evaluations, body mass index (BMI) values, serum levels of hormones measured on the third day of the menstrual cycle (AMH, follicle stimulating hormone (FSH), luteinizing hormone (LH) estradiol (E2), prolactin (PRL), thyroid stimulating hormone (TSH), 17-alpha-hyrdoxyprogesterone (17α-OHP), dehydroepiandrosterone sulphate (DHEAS), total testosterone, free testosterone, and 1–4 androstenedione) were recorded.

A group of 107 patients with serum 17α-hydroxyprogesterone (17α-OHP) levels higher than 2 ng/ml were recruited in this study. All the patients presented with the features of clinical hyperandrogenism. Acne was described as the presence of comedones on the face, neck, upper chest, upper back, or upper arms. Hirsutism was considered when a woman had a score of ≥8 on the Ferriman-Gallwey scale [13]. Women with androgenetic alopecia who normally exhibited diffuse hair thinning over the top of the scalp were defined according to Ludwig classification system [14]. Oligomenorrhea and amenorrhea were described as menstrual cycles longer than 40 days and the absence of a menstrual period for three consecutive months, respectively. Body mass index (BMI) was calculated as kg/m^2. Criteria for inclusion were as follows: age between 15 and 40 years, BMI values of 18–30 kg/m^2, normal serum PRL and TSH values, normal gynecological sonographic examination and negative cervical smear test result.

All patients were examined by transvaginal ultrasonography with a 7-MHz transvaginal transducer (Sonoline Elegra; Siemens SAS, Saint-Denis, France) on the 3rd or 4th day of the menstrual cycle. Sonographic evaluations were performed by experienced sonographers. None of the patients had a history of any medication which could have influenced the hormonal parameters for the past six months. Patients with known systemic illnesses such as hypothalamic, pituitary and adrenal gland disorders were excluded from the study. Informed consent was obtained from all women who participated in the study.

As the first step of the evaluation process, an ACTH stimulation test was performed on all women in the fasting state and in the supine position between 08.00 and 09.00 am of the 3rd–5th day of their cycle. A heparin lock was placed in the forearm prior to any venous blood sampling. Venous blood samples were collected at baseline and at 60 min after the intravenous injection of 0.25 mg synthetic ACTH (Synacthen, Ciba-Geigy, Basel, Switzerland). Serum was separated afterwards and stored at −20 °C until it was assayed for 17α-OHP levels. An ACTH-stimulated 17-OHP level >10.0 ng/ml was considered as a criterion for non-classical or 'late-onset' CAH (LOCAH). Twenty-five patients out of 107 were diagnosed with LOCAH.

Fifty-nine of remaining 82 patients were diagnosed with PCOS according to the Rotterdam criteria, due to presence of at least two of the following features: oligo/anovulation, clinical or biochemical hyperandrogenism, and presence of polycystic ovarian morphology (PCOM) on ultrasonographic evaluation. PCOM was defined as the presence of ≥12 follicles of 2–9 mm in diameter and/or ovarian volume ≥10 ml in at least one ovary [15]. Ten patients were diagnosed with idiopathic hyperandrogenism (IHA), based on increased serum androgen levels (free $T > 4.2$ pg/ml, total $T > 5.82$ ng/ml, 1–4 androstenedione >3 ng/ml in follicular phase: the accepted normal range of DHEAS levels varied between ages) with the presence of normal ovulatory cycles, and normal ovaries on ultrasonographic evaluation [16]. Thirteen patients were diagnosed with idiopathic hirsutism (IH), with the presence of normal serum androgen levels (T, free T, 1,4-androstenedione and DHEAS), regular menstrual cycles and no signs of any ovarian abnormality on ultrasonographic evaluation [17].

Measurements of AMH were determined in duplicate using the AMH/MIS enzyme-linked immunosorbent assay kit (Diagnostic Systems Lab, Webster, TX, USA). The sensitivity of the assay was 0.017 ng/ml. The intra- and inter-assay variations were 5% and 8%, respectively. All samples were assayed for 17α-OHP in competitive immunoenzymatic colorimetric method (Dia Metra S.r.l., Milano, Italy). The sensitivity of the assay was 0.009 ng/mL. The intra- and inter-assay variations were <7.4% and <13%, respectively. Reference values are between 0.2 and 1.3 ng/ml in follicular phase in women. DHEAS, free testosterone and total testosterone values were assayed with competitive immunoenzymatic colorimetric method (Dia Metra S.r.l., Milano, Italy). Serum FSH, LH, TSH, E2 and PRL levels were measured by Chemiluminescent Microparticle Immunoassay (Architect Abbott Lab, IL, USA), and 1–4 androstenodione levels were measured by enzyme immunoassay with commercial kits (Biosource, Nivelles, Belgium).

Statistical analyses were performed using SPSS 18.0 for Windows (SPSS Inc., Chicago, IL, USA). For the statistical analyses,

Table 1
Comparison of demographical and clinical parameters in LOCAH, PCOS, IHA and IH patients.

	LOCAH *n*: 25	PCOS *n*: 59	IHA *n*: 10	IH *n*: 13
%	23.4	55.1	9.3	12.1
Age (years)	21.08 ± 3.62	21.49 ± 4.18	20.90 ± 2.23	21.56 ± 3.11
BMI (kg/m^2)	25.20 ± 4.16	26.02 ± 4.77	26.40 ± 3.86	24.49 ± 4.40
Cycle length (days)	47.12 ± 23.95[a]	72.12 ± 27.46[b]	30.50 ± 2.83	30.60 ± 3.30
Menstrual Irregularity n/N (%)	14/25(56%)[c,d]	52/59(88.1)[c]	0/10(0)	0/13(0)
Acne, n/N (%)	12/25(48)	27/59(45.7)	2/10(20)	4/13(30.7)
Hirsutism, n/N (%)	21/25(84)	47/59(79.6)	10/10(100)	13/13(100)
Alopecia, n/N (%)	4/25(16)	4/59(6.7)	1/10(10)	1/13(7.6)
PCO PCOM	12/25(48)	50/59(84.7)[e]	0/10(0)	0/13(0)

PCOS: polycystic ovary syndrome; LOCAH: late-onset congenital adrenal hyperplasia, IHA: idiopathic hyperandrogenism, IH: idiopathic hirsutism; BMI: body mass index; PCOM: polycystic ovarian morphology
[a] Tukey: compared to PCOS (*p*: 0.001).
[b] Tukey: compared to IHA, IH (*p*: 0.001).
[c] Chi-square test: compared to IHA, IH (*p*: 0.001).
[d] Chi-square test: compared to IHA, IH (*p*: 0.001).
[e] Chi-square test: compared to PCOS (*p*: 0.001).

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data were presented as mean ± SD or number as appropriate. Patients were distributed into four groups based on their diagnosis. Age, BMI, AMH, FSH, LH, E2, PRL, TSH, 17α-OHP, DHEAS, total testosterone, free testosterone and 1–4-androstenedione values of the patients in each group were compared using the ANOVA test. Chi-square test was performed for statistical significance of the nonparametric values and p values smaller than 0.05 were considered significant.

Results

Demographic and clinical parameters of the patients recruited for the study are presented in Table 1. There was no significant difference between the groups in terms of age and BMI values. Mean menstrual cycle length in the PCOS group was significantly longer and the prevalence of oligo/amenorrhea was significantly higher than in the LOCAH group (p: 0.001, p: 0.001; respectively). No statistically significant difference was found between the groups in terms of hyperandrogenemic features (acne, hirsutism, alopecia). PCOM was documented only in the LOCAH and PCOS groups (48% and 84.7%; respectively). None of the patients with IH and IHA had PCOM on ultrasonographic evaluation. The prevalence of PCOM was higher in patients with PCOS compared to the LOCAH group, but this difference was not statistically significant (Table 2).

No statistically significant difference was found between the groups in terms of FSH, E2, prolactin, TSH and 17α-OHP. Mean serum LH values of PCOS patients were higher than those of IH (p: 0.041) and LOCAH (p: 0.001) patients and these differences were statistically significant. However no significant difference was observed between the mean serum LH values of PCOS and IHA patients. The mean LH/FSH ratio in PCOS patients was significantly higher than both the LOCAH and IH groups (p values 0.001; 0.034). Mean serum AMH values of the PCOS patients were significantly higher than each of the LOCAH, IHA and IH groups (p values 0.013; 0.044; 0.039; respectively) (Fig. 1). No significant difference was observed in terms of mean total testosterone and 1–4 androstenedione values between the groups. The mean serum DHEAS values of IHA patients were significantly higher than those of the PCOS (p: 0.023) and IH (p: 0.013) patients. However, there was no significant difference in mean serum DHEAS values between the LOCAH and IHA patients. Mean serum free testosterone levels of IHA patients were significantly higher compared to each of the LOCAH, PCOS and IH groups (p values 0.044; 0.039; 0.043; respectively).

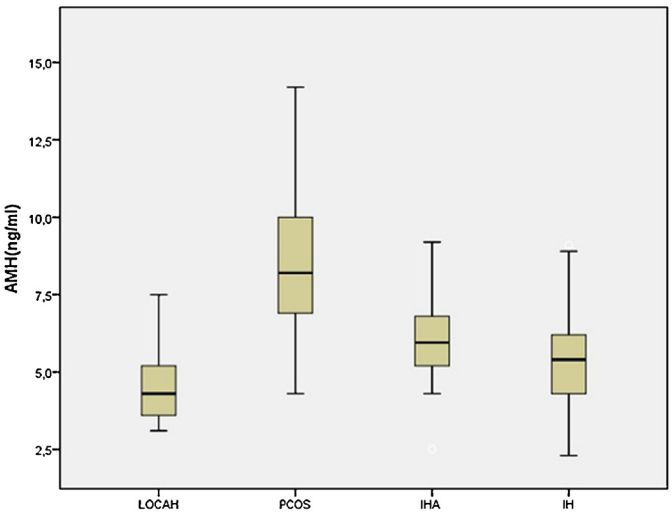

Fig. 1. Mean serum AMH levels of LOCAH, PCOS, IHA and IH patients.

Comment

The clinical features and laboratory findings of LOCAH, IH, IHA and PCOS in adolescents and adults share similarities. Therefore, differential diagnosis is essential and treatment options should be individualized for each patient. In this study we aimed to determine whether serum AMH levels could be utilized in the differential diagnosis of patients with hyperandrogenemia.

Our results demonstrated that oligo/amenorrhea and PCOM were significantly more prevalent among the PCOS patients compared to the patients with LOCAH (88.1% vs. 56%, 84.7% vs. 48%, respectively). In the IH and IHA groups, none of the patients had oligo/amenorrhea or PCOM on ultrasonographic evaluation, as expected. Earlier studies of non-classic adrenal hyperplasia reported a varying prevalence of menstrual irregularities (1.2–58%), which might be due to the diversity of the study populations

Table 2
Comparison of hormonal parameters in LOCAH, PCOS, IHA and IH patients.

	LOCAH (n: 25)	PCOS (n: 59)	IHA (n: 10)	IH (n: 13)
FSH (mIU/mL)	4.70 ± 1.62	4.81 ± 1.35	5.08 ± 1.63	5.74 ± 1.01
LH (mIU/mL)	3.81 ± 2.30	6.69 ± 3.48[a]	4.70 ± 2.66	4.23 ± 1.36
LH/FSH ratio	0.81 ± 1.02	1.39 ± 1.77[b]	0.98 ± 1.43	0.73 ± 0.89
E2 (pg/mL)	39.68 ± 22.69	39.90 ± 20.75	52.40 ± 37.59	31.85 ± 14.38
PRL (ng/mL)	19.64 ± 6.90	24.81 ± 18.71	24.60 ± 8.88	22.31 ± 8.10
TSH (mIU/L)	1.56 ± 0.56	1.93 ± 1.18	1.70 ± 0.82	2.00 ± 0.91
AMH(ng/ml)	4.56 ± 1.13	8.42 ± 2.28[c]	6.02 ± 1.95	5.58 ± 1.89
17α-OHP (ng/mL)	3.57 ± 1.48	3.00 ± 1.39	2.74 ± 0.61	3.21 ± 1.54
DHEA-S (nmol/l)	44.540 ± 15.076	39.966 ± 18.307	56.320 ± 152.06[d]	34.854 ± 87.59
Free Testosterone (pg/mL)	2.52 ± 1.24	2.73 ± 1.24	5.48 ± 2.23[e]	2.14 ± 1.03
Total Testosterone (ng/dL)	92.20 ± 33.14	10.371 ± 39.06	10.520 ± 23.43	76.92 ± 20.19
1-4Androstenodione (ng/mL)	2.81 ± 0.82	2.85 ± 0.76	2.80 ± 0.78	2.69 ± 0.63

PCOS: Polycystic Ovary Syndrome; LOCAH: Late-Onset Congenital Adrenal Hyperplasia, IHA: Idiopathic Hyperandrogenism, IH: Idiopathic Hirsutism; BMI: Body Mass Index; PCOM: Polycystic Ovarian Morphology; AMH: Anti-Müllerian Hormone; FSH: Follicle Stimulating Hormone; LH: Luteinizing Hormone; E2: Estradiol; PRL: Prolactin; TSH: Thyroid Stimulating Hormone; 17α-OHP: 17-alpha-hydroxyprogesterone; DHEAS: Dehydroepiandrosterone Sulphate. CONDENSATION Serum AMH levels may be introduced as a marker to be utilized clinically in differential diagnosis of hyperandrogenemic patients, especially for identifying patients with PCOS.

[a] Tukey test: compared to LOCAH group (p: 0.001) and idiopathic hirsutism (p: 0.041).
[b] Tukey test: compared to LOCAH group (p: 0.001) and idiopathic hirsutism group (p: 0.034).
[c] Tukey test: compared to LOCAH group (p: 0.001), idiopathic hyperandrogenism (p: 0.004), idiopathic hirsutism (p: 0.001).
[d] Tukey test: compared to PCOS (p: 0.023), idiopathic hirsutism (p: 0.013).
[e] Tukey teest: compared to LOCAH (p: 0.044), PCOS (p: 0.039), idiopathic hirsutism (p: 0.043).

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[18–21], but up to 95% of women with PCOS were reported to have oligomenorrhea or amenorrhea [22]. Patients with LOCAH can present with PCOM, but the prevalence of PCOM on ultrasonographic evaluation was significantly higher in PCOS patients and this finding was compatible with the data available [23].

No significant difference was observed between the groups in terms of serum TSH, FSH, E2, 17α-OHP, total testosterone, 1–4-androstenedione levels. LH levels and the LH/FSH ratio in PCOS patients were higher than in the LOCAH and IH groups, but LH levels in both groups were in the normal ranges. Alterations in the secretion of gonadotropin-releasing hormone (GnRH) by inadequately described mechanisms have been suggested in PCOS. As supported by the study of Waldstreicher et al. [24] the increase in GnRH secretion enhances the LH pulse frequency and release, while not affecting or slightly decreasing the secretion of FSH and ultimately leading to an increase in the serum LH/FSH ratio. The results of our study are compatible with the data available [24,25].

DHEAS levels were significantly higher in patients with IHA compared with the PCOS and IH groups (p values 0.023 and 0.013; respectively). However, no significant difference was found in terms of DHEAS compared with the LOCAH group as expected, since DHEAS is associated with adrenal hyperandrogenemia. Free testosterone levels were found to be significantly increased in the IHA group as well, compared to the PCOS, LOCAH and IH groups (p values 0.039; 0.044; 0.043, respectively).

In this study, the patients diagnosed with PCOS had significantly higher serum AMH levels than all groups. The cause of the increased AMH production in PCOS is unknown, but increased concentrations may be the consequence of other factors altered in PCOS. Evaluation of serum from PCOS patients revealed two to three-fold higher AMH levels, compared to those of women without PCOS [26]. Increased serum AMH levels presumably have a stronger association with the increased production of AMH by each follicle individually, compared with the increased number of follicles as suggested in recent studies [27]. On the other hand, elevation in serum AMH levels are suggested to be correlated with the severity of the symptoms such as oligo/amenorrhoea (OA) and hyperandrogenism [28,29]. Insulin is also another candidate suggested as the cause of the increase in AMH in PCOS. Conway et al. documented the association between hyperinsulinemia and anovulatory cycles [30]. In addition, La Marca et al. found no correlation between serum AMH and androgen levels, but observed a positive correlation between serum AMH levels and insulin insensitivity [31].

To the best of our knowledge, this is the first study to evaluate the serum AMH levels in patients with LOCAH. LOCAH is an adrenal gland disease and there is no information that AMH is secreted anywhere other than from granulosa cells in the antral and preantral follicles of ovary. Therefore, serum AMH levels of LOCAH patients are expected to be significantly lower compared with those of the patients with PCOS. In the patients with IHA, the source of the excess androgens generally has a mixed etiology (ovary and adrenal gland) similar to PCOS. However, elevated serum AMH levels are not encountered in these patients, potentially as a result of the absence of oligo/anovulation and PCOM. Serum AMH levels in IH are also found to be normal, which is an expected result since IH is primarily characterized as a skin-related disease.

The partially retrospective design and the relatively small study population contributed to the limitations of this study. Future prospectively designed studies with larger populations are needed in order to obtain an elaborate definition of the association between AMH and hyperandrogenism. Nevertheless, our results suggest that AMH can be introduced as a marker to be utilized in the differential diagnosis of hyperandrogenism among patients with serum 17α-OHP levels >2 ng/ml, especially for identifying patients with PCOS.

Condensation

Serum AMH levels may be introduced as a marker to be utilized clinically in differential diagnosis of hyperandrogenemic patients, especially for identifying patients with PCOS.

Conflict of interests

None.

Acknowledgement

None.

References

[1] Bode D, Seehusen DA, Baird D. Hirsutism in women. Am Fam Physician 2012;85:373–80.
[2] Barnes RB, Rosenfield RL, Burstein S, Ehrmann DA. Pituitary-ovarian responses to nafarelin testing in the polycystic ovary syndrome. N Engl J Med 1989;320:559–65.
[3] Carmina E, Gonzalez F, Chang L, Lobo RA. Reassessment of adrenal androgen secretion in women with polycystic ovary syndrome. Obstet Gynecol 1995;85:971–6.
[4] Azziz R, Dewailly D, Owerbach D. Clinical review 56: nonclassic adrenal hyperplasia: current concepts. J Clin Endocrinol Metab 1994;78:810–5.
[5] Levin JH, Carmina E, Lobo RA. Is the inappropriate gonadotropin secretion of patients with polycystic ovary syndrome similar to that of patients with adult-onset congenital adrenal hyperplasia. Fertil Steril 1991;56:635–40.
[6] Parks JS, Brown MR. Transcription factors regulating pituitary development. Growth Horm IGF Res 1999;9(Suppl B):2–8. discussion-11.
[7] La Marca A, Broekmans FJ, Volpe A, Fauser BC, Macklon NS. Anti-Mullerian hormone (AMH): what do we still need to know. Hum Reprod 2009;24:2264–75.
[8] Broekmans FJ, Visser JA, Laven JS, Broer SL, Themmen AP, Fauser BC. Anti-Mullerian hormone and ovarian dysfunction. Trends Endocrinol Metab 2008;19:340–7.
[9] Kwee J, Schats R, McDonnell J, Themmen A, de Jong F, Lambalk C. Evaluation of anti-Mullerian hormone as a test for the prediction of ovarian reserve. Fertil Steril 2008;90:737–43.
[10] Pigny P, Merlen E, Robert Y, et al. Elevated serum level of anti-Mullerian hormone in patients with polycystic ovary syndrome: relationship to the ovarian follicle excess and to the follicular arrest. J Clin Endocrinol Metab 2003;88:5957–62.
[11] Das M, Gillott DJ, Saridogan E, Djahanbakhch O. Anti-Mullerian hormone is increased in follicular fluid from unstimulated ovaries in women with polycystic ovary syndrome. Hum Reprod 2008;23:2122–6.
[12] Piouka A, Farmakiotis D, Katsikis I, Macut D, Gerou S, Panidis D. Anti-Mullerian hormone levels reflect severity of PCOS but are negatively influenced by obesity: relationship with increased luteinizing hormone levels. Am J Physiol Endocrinol Metab 2009;296:E238–43.
[13] Hatch R, Rosenfield RL, Kim MH, Tredway D. Hirsutism: implications, etiology, and management. Am J Obstet Gynecol 1981;140:815–30.
[14] Ludwig E. Classification of the types of androgenetic alopecia (common baldness) occurring in the female sex. Br J Dermatol 1977;97:247–54.
[15] Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81:19–25.
[16] Carmina E, Lobo RA. Prevalence and metabolic characteristics of adrenal androgen excess in hyperandrogenic women with different phenotypes. J Endocrinol Invest 2007;30:111–6.
[17] Azziz R, Carmina E, Sawaya ME. Idiopathic hirsutism. Endocr Rev 2000;21:347–62.
[18] Lobo RA, Goebelsmann U. Adult manifestation of congenital adrenal hyperplasia due to incomplete 21-hydroxylase deficiency mimicking polycystic ovarian disease. Am J Obstet Gynecol 1980;138:720–6.
[19] Azziz R, Zacur HA. 21-Hydroxylase deficiency in female hyperandrogenism: screening and diagnosis. J Clin Endocrinol Metab 1989;69:577–84.
[20] Feldman S, Billaud L, Thalabard JC, et al. Fertility in women with late-onset adrenal hyperplasia due to 21-hydroxylase deficiency. J Clin Endocrinol Metab 1992;74:635–9.
[21] Moran C, Azziz R, Carmina E, et al. 21-Hydroxylase-deficient nonclassic adrenal hyperplasia is a progressive disorder: a multicenter study. Am J Obstet Gynecol 2000;183:1468–74.
[22] Kumarapeli V, Seneviratne Rde A, Wijeyaratne CN, Yapa RM, Dodampahala SH. A simple screening approach for assessing community prevalence and phenotype of polycystic ovary syndrome in a semi-urban population in Sri Lanka. Am J Epidemiol 2008;168:321–8.

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[23] Pall M, Azziz R, Beires J, Pignatelli D. The phenotype of hirsute women: a comparison of polycystic ovary syndrome and 21-hydroxylase-deficient non-classic adrenal hyperplasia. Fertil Steril 2010;94:684–9.
[24] Waldstreicher J, Santoro NF, Hall JE, Filicori M, Crowley Jr WF. Hyperfunction of the hypothalamic–pituitary axis in women with polycystic ovarian disease: indirect evidence for partial gonadotroph desensitization. J Clin Endocrinol Metab 1988;66:165–72.
[25] Rebar R, Judd HL, Yen SS, Rakoff J, Vandenberg G, Naftolin F. Characterization of the inappropriate gonadotropin secretion in polycystic ovary syndrome. J Clin Invest 1976;57:1320–9.
[26] Fallat ME, Siow Y, Marra M, Cook C, Carrillo A. Mullerian-inhibiting substance in follicular fluid and serum: a comparison of patients with tubal factor infertility, polycystic ovary syndrome, and endometriosis. Fertil Steril 1997;67:962–5.
[27] Pellatt L, Rice S, Brincat M, Galea R, Mason H. Anti-Müllerian hormone (AMH) inhibits aromatase expression in granulosa cells from human ovaries. In: Proceedings of the Endocrine Society USA, 89th Annual Meeting; 2007. 48-4.
[28] Laven JS, Mulders AG, Visser JA, Themmen AP, De Jong FH, Fauser BC. Anti-Mullerian hormone serum concentrations in normoovulatory and anovulatory women of reproductive age. J Clin Endocrinol Metab 2004;89:318–23.
[29] Carlsen SM, Vanky E, Fleming R. Anti-Mullerian hormone concentrations in androgen-suppressed women with polycystic ovary syndrome. Hum Reprod 2009;24:1732–8.
[30] Conway GS, Jacobs HS. Clinical implications of hyperinsulinaemia in women. Clin Endocrinol (Oxf) 1993;39:623–32.
[31] La Marca A, Orvieto R, Giulini S, Jasonni VM, Volpe A, De Leo V. Mullerian-inhibiting substance in women with polycystic ovary syndrome: relationship with hormonal and metabolic characteristics. Fertil Steril 2004;82:970–2.

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