



POLYCYSTIC OVARIAN DISEASE: A DERMATOLOGIST'S VIEWPOINT

ZESPÓŁ POLICYSTYCZNYCH JAJNIKÓW: PUNKT WIDZENIA
DERMATOLOGA

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Abstract

Polycystic ovary syndrome (PCOS) is a common condition characterized by menstrual abnormalities and clinical or biochemical features of hyperandrogenism. Features of PCOS may manifest at any age, ranging from childhood (premature puberty), teenage years (hirsutism, menstrual irregularities), early adulthood and middle life (infertility, glucose intolerance) to later life (diabetes mellitus and cardiovascular disease). Cutaneous manifestations of PCOS are protean and include hirsutism, acne, androgenic alopecia and acanthosis nigricans. Treatment of cutaneous manifestations of PCOS requires a coordinated team approach. A combination of drug therapy, counseling and cosmetic procedures can maximize the results.

Streszczenie

Zespół policystycznych jajników (PCOS) jest częstym stanem charakteryzującym się zaburzeniem miesiączkowania oraz klinicznym i biochemicznym hiperandrogenizmem. Schorzenie PCOS może występować w każdym wieku, począwszy od dzieciństwa (przedwczesne pokwitanie), młodzieńczych lat (hirsutyzm, zaburzenia miesiączkowania), we wczesnej dorosłości i w połowie życia (niepłodność, nietolerancja glukozy) do późnych lat życia (cukrzyca i choroby układu krążenia). Skórnymi objawami PCOS są zmienne i to nadmierne owłosienie, trądzik, łysienie androgenowe i acanthosis nigricans. Leczenie skórnych objawów PCOS wymaga skoordynowanego podejścia zespołu. Połączenie leczenia farmakologicznego, poradnictwo i kosmetyczne zabiegi mogą zmaksymalizować wyniki.

Key words: Polycystic ovary syndrome, hyperandrogenism, hirsutism, androgenic alopecia

Słowa kluczowe: Zespół policystycznych jajników, hiperandrogenizm, hirsutyzm, androgenym łysienie

Introduction

As early as 1844, Chereau described sclerocystic changes in the human ovary [1]. In 1935, Stein & Levienthal reported seven women with amenorrhea, hirsutism, obesity, polycystic ovaries.....Stein-Levienthal Syndrome [2]. Polycystic ovary syndrome (PCOS) is the most commonly encountered endocrinopathy in women of reproductive age group. It has significant reproductive and non-reproductive consequences. Women of any ethnic background can present with PCOS [3]. Several studies have suggested a prevalence of PCOS of 5-10% in women of reproductive age group, using the diagnostic criteria proposed by the US National Institute of Health [4]. Because patients with PCOS can present with assortment of complaints such as menstrual disturbances, infertility, hirsutism, acne, their point of entry into the medical system may be by way of a primary care physician, gynecologist, endocrinologist, or a

dermatologist. Thus all the disciplines need to be familiar with this syndrome & its long term consequences.

Definition & Diagnosis:

Historically, there has been a lack of consensus regarding the features that define PCOS. A meeting convened by the National Institute of Health (NIH) in 1990 stressed three key features necessary for the diagnosis of PCOS [5]:

- Ovulatory dysfunction (oligo-ovulation or anovulation).
- Clinical hyperandrogenism or biochemical hyperandrogenemia.
- Exclusion of congenital adrenal hyperplasia (CAH), androgen secreting tumors, hyperprolactinemia or thyroid diseases.

Because 16-20% of normal population has polycystic-appearing ovaries on ultrasound, the presence of

polycystic ovaries was considered to be suggested but not diagnostic of PCOS [6].

Rotterdam Criteria (2 out of 3):

- Menstrual irregularity due to anovulation or oligo-ovulation.
- Evidence of clinical or biochemical hyperandrogenism.
- Polycystic ovaries (12 or more follicles in each ovary, measuring 2-9 mm in diameter and/or increased ovarian volume).

Pathogenesis:

The pathogenesis of PCOS is poorly understood, but the primary defect may be insulin resistance leading to hyperinsulinemia [7,8]. In the ovaries, the cardinal feature is functional hyperandrogenism. Circulating concentrations of insulin & LH are generally raised. The theca cells, which envelop the follicle and produce androgens for conversion in the ovary to oestrogens are over-responsive to this stimulation. They increase in size and produce androgens. This combination of raised levels of androgens, estrogens, insulin and LH explains the classic PCOS presentation of hirsutism, anovulation, dysfunctional bleeding, and dysfunction of glucose metabolism.

Signs and symptoms:

PCOS symptoms have a gradual onset. Although the symptoms can exist at the time of menarche, most of the patients do not seek help until their early mid 20's.

- Menstrual irregularities and reproductive issues:- Abnormal vaginal bleeding is a typical complaint that ranges from amenorrhea to menorrhagia & metrorrhagia. Because these patients are anovulatory, they all present with infertility issues and have an increased incidence of pregnancy loss and pregnancy associated complication [9,10].
- Obesity and metabolic abnormalities:-Prevalence of obesity is high in patients with PCOS. The rate of obesity in the PCOS population ranges from 38-87% [11]. Because obesity is associated with insulin resistance, many women with PCOS have insulin resistance, but insulin resistance in PCOS is also independent of obesity.
- Metabolic syndrome:-PCOS patients are at a higher risk for the metabolic syndrome that includes dyslipidemias, type 2 DM, hypertension and obesity [12].

The cutaneous manifestations of PCOS vary depending on the ethnic background and include these are symptoms [13]:

- Hirsutism- 66%
- Acne- 35%
- Androgenic alopecia- 6%
- Acanthosis nigricans- 3%

Hirsutism is defined as excessive facial and/or body terminal hairs in a male pattern distribution. It results from an interaction between androgens and the sensitivity of hair follicle to androgens. It occurs at puberty in response to increasing levels of androgens. Under the influence of androgens, vellus hair develops into terminal hair. Ferriman – Gallwey scoring system is used to quantify the extent of hair growth at androgen sensitive sites [14]. A score of >8 is abnormal for adult Caucasian females. Limitations of this scoring system are that it is subjective and is effected by any previous or on going treatment.

Androgenic alopecia. There is progressive loss of terminal scalp hair in genetically susceptible women with diffuse thinning of hair diameter, length and density (hairs/cm). The pattern may embrace progressive thinning of the crown with preservation of hair-line or take on a male-pattern form with bitemporal recession. Various grading systems used for grading androgenic alopecia are Ludwig's scale (grade1 – grade3) and Olsen's scale [15,16].

Seborrhea and acne are also the results of increased androgen production and/or increased skin sensitivity to androgen [17].

Acne in PCOS has following important characters:

- Persistent.
- Refractory.
- Late onset.

Associated with irregular menstrual cycles, hirsutism, obesity and androgenic alopecia.

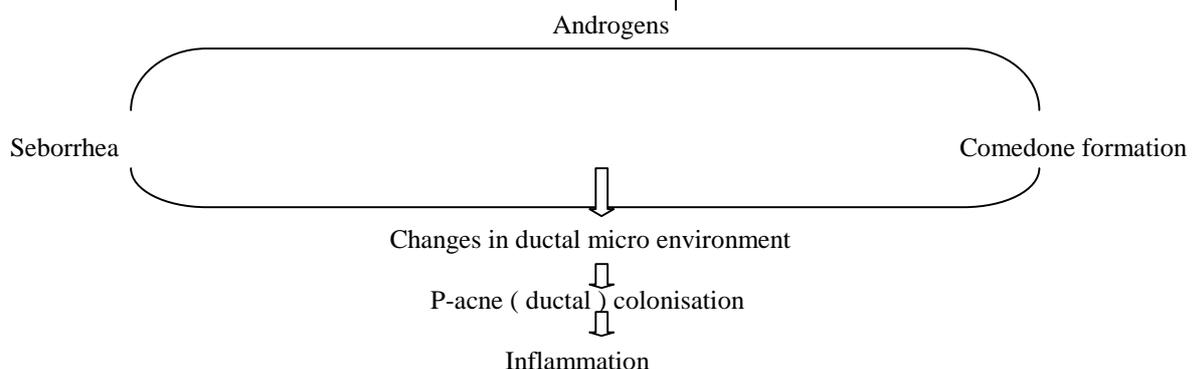


Figure 1.

Acanthosis Nigricans is characterized by hyperpigmentation and thickening of skin with papillomatous elevations. These velvety plaques are distributed bilaterally symmetrically in the neck, axillae, groins, antecubital and popliteal fossae, umbilicus and perianal areas. The exact mechanism of development of the skin lesions of acanthosis nigricans is not known, but may result from keratinocyte and dermal fibroblast proliferation stimulated by insulin and insulin like growth factors. Thus it is a Cutaneous marker of insulin resistance [18].

Treatment of hirsutism

- Direct hair removal: shaving, plucking, threading, waxing, epilators.
- Electrical depilation: it includes galvanic depilation and diathermic depilation.
- Lasers: Laser light (694-1064 nm) passes through the skin surface and is absorbed by melanin (chromophore), converted to heat energy which destroys the hair follicle. The largest is the stem cell population where pigmented cells are populated. Patients with fair skin are ideal for this procedure because darker skin carries the risk of epidermal damage as it requires higher energy pulses leading to pigmentary changes and scarring [19].
- Eflornithine 11.5% cream: It inhibits the enzyme ornithine decarboxylase responsible for catalyzing ornithine to polyamine critical to regulation of cell growth and differentiation. It slows down hair growth and reduces hair visibility and coarse nature of hair.
- Antiandrogens: Antiandrogens interfere with androgen action at the target organ either by blocking enzyme reactions or by blocking the androgen receptors [20]. A male fetus in utero is at risk of developing feminization if his mother is having treatment with an antiandrogen. So, concurrent use of adequate contraception is an essential component of any treatment regimen using an antiandrogen. Antiandrogens mostly used in hirsutism are cyproterone acetate, spironolactone flutamide, biclutamide.
- Combined oral contraceptive pills: These suppress ovarian androgen production and thus should be the treatment of choice for mild hirsutism of PCOS [21]. But some of the progestrogens in oral contraceptives have androgenic properties. It is therefore of utmost importance to choose a combination that does not have any androgenic activity. Besides being useful in hirsutism, these also cause a marked improvement in acne and seborrhea as well as a good control of menstrual cycle.
- Finasteride: It is a competitive 5- α - reductase inhibitor and blocks the conversion of testosterone to more potent dihydrotestosterone [22]. Comparative randomized trials have shown that finasteride (5 mg daily) has a clinical effect on hirsutism similar to that of spironolactone and flutamide. It might be also useful in women with androgenic alopecia [23].
- GnRH agonists: GnRH agonists such as Nafarelin, Buserelin, Leuprorelin decrease ovarian steroid production by suppressing LH and FSH secretion. Over a period of six months therapy, hair growth reduces in majority of patients and there is a marked reduction of seborrhea also [24].

- Ketoconazole: Its principle inhibitory role involves inhibition of the 17, 20-desmolase and 11- β - hydroxylase steps in steroidogenesis. Because of its significant ovarian suppressive effects, its use has also been suggested for ovarian androgen suppression in hirsutism [25]. Improvement has been noted with 400mg per day in PCOS.

Other treatment options for hirsutism

- Metformin: Metformin (500mg thrice a day) is being increasingly used in PCOS. It significantly reduces hyperinsulinemia and hyperandrogenism. It causes a significant reduction in serum androgens, improvement in menstrual irregularities and resumption of ovulation, but only a mild improvement in hirsutism [26].
- Weight reduction: It is well recognized that obesity worsens hirsutism. Failure to respond to antiandrogen therapy is much more common in obese than in slim patients. Weight reduction decreases hyperinsulinemia, insulin resistance and hyperandrogenism and has thus beneficial effects on menstrual abnormalities and hirsutism [27]. Therefore low-energy diet and exercise should be encouraged as a form of first line therapy.
- Psychotherapy: It is very important to address the sociopsychological aspects of this disorder in some women. Hirsute women have increased levels of anxiety and depression. So, psychotherapy in the form of group therapy is very beneficial.

Treatment of Androgenic alopecia

- Minoxidil: Used as 2% and 5% topical solution, it increases duration of anagen and enlarges miniaturized and suboptimal follicle. About 1 ml is applied to scalp twice daily for a minimum period of four months. About 5% cases improve over a period of 48 weeks.
- Hormonal therapy: Antiandrogens and Finasteride may also be beneficial in severe cases [28].

Treatment of Acne [29-31]

- Topical Retinoids: Topical retinoids including Tretinoin, Adapalene and Isotretinoin normalizes desquamation and also decreases the inflammatory response.
- Benzoyl peroxide: It kills the microorganisms and prevents the development of severe acne scarring.
- Antibiotics: Antibiotics such as tetracycline, doxycycline, minocycline, erythromycin, azithromycin are the mainstay of therapy for acne.
- Oral Isotretinoin: It reduces sebum production, normalizes desquamation and decreases the inflammatory response.
- Hormonal therapy: In severe unresponsive cases, antiandrogens or OCP'S may be administered either alone or in combination with topical or systemic antibiotics.

Treatment of Acanthosis nigricans

Treatment is only symptomatic and consists of topical application of mild keratolytics like salicylic acid ointment or retinoic acid cream. Oral Isotretinoin has also been used in some cases [32].

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