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Case Report,

Irregular Menstruation, Acne, Hirsutism, and the Possibility with PCOS

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Abstract:
Background: PCOS was a common hormonal disorder caused by hyperandrogenism so the ovaries enlarged with many small follicles appear like cysts. The aetiology still unknown, but mounting evidence suggests that can be complex multigenic disorder with strong epigenetic and environmental influences. Therapeutic options include combined oral contraception, antiandrogens, etc.
Case Presentation: Ms. N, 17 years old, came to polyclinic of RSAL Mintohardjo evaluated for amenorrhea. Her parents didn't have comorbid conditions. The patient started Menarche at the age of 14, soon thereafter developed a secondary amenorrhea. On examination her BMI was 18.4kg/m², pulse-92/min and BP-115/80 mm of hg. She had a hirsute score (Ferriman-Gallway) of 8 and had no acanthosis nigricans. No abnormality on the other systemic examination and no laboratory tests were carried out. Patient given with combination hormonal pills. Hormonal birth control can help with PCOS symptoms, but it is not the only option. Lifestyle changes, such as losing weight and exercising more, may help.
Discussion: PCOS involves primary defects in hypothalamic–pituitary axis, insulin, and ovarian function. Excess LH levels lead to hyperandrogenism in PCOS.
Conclusion: All women with abnormal menstrual patterns should be evaluated for underlying PCOS, signs of hyperandrogenism, hormone profile, and pelvic ultrasonography to visualize the ovaries. Early diagnosis and treatment can avoid potential complications. Birth control pills (combined hormonal) can used for long-term treatment in women who didn't want to pregnant. The birth control pills may help regulate menstrual bleeding, reduce excessive hair growth and acne, and decrease the risk of endometrial cancer.

Keywords: Amenorrhea, Acne, Hirsutism, Menstruation, PCOS.

Introduction:

Polycystic ovary syndrome (PCOS) was originally introduced in 1935 by Leventhal and Stein. Even though PCOS is very common, it can still be confusing to many people, even doctors and it usually takes more than one visit or multiple doctors for it to get identified. [(1)] As stated by the Rotterdam consensus, PCOS diagnosis should be based on the presence of any two of the following three criteria: (a) irregular menstruation i.e. oligomenorrhea and/or anovulation, (b) clinical and/or biochemical evidence of hyperandrogenism, and (c) ultra-sonographic evidence of polycystic ovaries [(2)].

Symptoms include: irregular or no menstrual period, heavy periods, excess body and facial hair, acne, pelvic pain, trouble getting pregnant, patches of thick darker and velvety skin. Associated conditions include: type 2 diabetes, obesity, obstructive sleep apnoea, heart disease, mood disorders, and endometrial cancer. [(2)] PCOS occurs due to a combination of genetic and environmental factors. Risk factors include obesity, not enough physical exercise, poor lifestyle and diet and a family history of someone with the condition. [(2)] The exact cause of PCOS is

unknown. Most experts consider that several factors, including genetics, play a role like high androgen levels. Higher than usual androgen levels in women can prevent the ovaries from the release of the egg (ovulation) between each menstrual cycle and may cause extra hair growth and acne.[3]

The scientific symptoms of hyperandrogenism or biochemical hyperandrogenism are very vital diagnostic standards for PCOS. Cutaneous manifestations are probably the primary symptoms and symptoms of PCOS, so women presenting with pimples and/or hirsutism have to be evaluated in phrases of PCOS [4,14] Acne is a common manifestation of hyperandrogenemia. Therefore, acne may not pose only cosmetic concern, but may also be sign of underlying disease. In females, the most common cause of hyperandrogenemia is PCOS. [4]

Here, we report a case in adolescent with PCOS and acne.

Case Report:

Ms N, 17 years old, came to OPD RSAL Mintohardjo presented for evaluation of amenorrhea and acne. She had a history of irregular menstrual cycle since the previous year. The severity of acne was graded as mild. The patient was the fourth child in the family. Her parents were of normal weight, and they didn't have any conditions like hypertension, hypercholesterolemia, and impaired glucose tolerance. Her mother didn't have gestational diabetes mellitus during her pregnancies. The patient started Menarche at the age of 14, but she soon thereafter developed secondary amenorrhea. The patient was given OCP by the doctor and should come back every 3-6 months to be observed for adverse effects and responses to the treatment until her condition is stable and can be monitored annually.

Patient Assessment

On examination her height was 160 cm, weight 47 kg, BMI 18.4kg/m², pulse-92/min and BP-115/80 mm of hg. Her hirsute score (Ferriman-Gallway) was 8 and had no acanthosis nigricans. Her acne is moderate and the location around the cheeks and chin for the quality are mixed (comedonal, inflammatory with papules and pustules. Other systemic examination revealed no abnormality. The patient had a habit of eating junk and fast food with sedentary lifestyle which helps to aggravate the disease. The patient skin was dry, had mild acne, dry mouth. abdominal USG showed uterus anteflex 41x20x19 cm, thin endometrium, both ovaries are PCO

Figure 1. USG Transrectal in a patient with PCOS

Figure 2. Ferriman and Gallwey described a visual scoring method to clinically assess the degree of hirsutism known as the Ferriman-Gallwey (FG) score. According to the FG score, hair is scored in nine parts of the body, with a score of 0 representing a complete absence of terminal hair and a score of 4 represents extensive hair growth.. Women with an FG score of 8 or higher are regarded as hirsute

Discussion:

Patophysiology

The pathophysiology of PCOS involves primary defects in the hypothalamic–pituitary axis, insulin secretion and action, and ovarian function. [5] Although the cause of PCOS is unknown, PCOS has been linked to insulin resistance and obesity. The association with insulin function is expected insulin helps to regulate ovarian function, and the ovaries respond to excess insulin by producing androgens, which can lead to anovulation. [6] Clinical signs of PCOS include elevated luteinizing hormone (LH) and gonadotropin–releasing hormone (GnRH) levels, whereas follicular stimulating hormone (FSH) levels are muted or unchanged. Excess LH stimulates ovarian androgen production, whereas a relative deficit in FSH impairs follicular development. The imbalance in LH: FSH causes proliferation of ovarian theca cells leading to increased steroid genesis, and ultimately leading to hyperandrogenism in PCOS women. [6]

Therapeutic interventions are designed to reduce insulin levels and ovarian androgen production, ultimately correcting sex hormone–binding globulin (SHBG) levels. This increased SHBG levels can be used to effectively manage the symptoms of PCOS. [7]

Hyperandrogenism can be based on clinical symptoms or measurement of serum androgens. In females, androgens originate from three primary sources: (1) the ovarian theca, (2) the adrenal cortex, and (3) within end organs by peripheral conversion. The major androgens include dehydroepiandrosterone, dehydroepiandrosterone sulfate (DHEAS), androstenedione, testosterone, and dihydrotestosterone, with the latter two having the highest affinity for the androgen receptor and the greatest potency. In healthy women, testosterone is largely bound by sex hormone binding globulin and albumin, leaving only approximately 1% freely circulating as bioactive “free testosterone” [8].

The pilosebaceous unit expresses 5a-reductase, which converts testosterone to the highly potent dihydrotestosterone. Varying expression of enzyme activity within the pilosebaceous unit leads to a lack of clear correlation between serum androgens and the presence or severity of acne and hirsutism[9]

Signs and Symptoms

PCOS is a hormonal disorder with a potential to lead to various diseases. It also continues to be a common cause of infertility among women. Although signs and symptoms vary. The three most common factors associated with PCOS include ovulation irregularities, increased androgen levels, and cystic ovaries. [9] Problems with ovulation and elevated androgen levels occur in the majority of women with PCOS. Moreover, hirsutism, acne, and alopecia are directly associated with elevated androgen levels. [9]

If PCOS is suspected, a complete medical history, physical examination, blood tests, and a pelvic ultrasound should be performed. A medical history and physical examination provide the physician with information about unexplained weight gain, menstrual cycle abnormalities, male-pattern hair growth, skin changes, and elevated blood pressure (BP). Blood is drawn to assess hormone, glucose, and lipid levels, and a pelvic ultrasound is performed to scan for ovarian cysts. During the assessment period, other potential causes associated with reproductive, endocrine, and metabolic dysfunction should be excluded. Physicians should rule out adrenal hyperplasia, Cushing's syndrome, and hyperprolactinemia before a PCOS diagnosis is confirmed. After PCOS is diagnosed, studies show that more than 50% of patients develop prediabetes or diabetes, and there is an increased risk of myocardial infarction (MI), dyslipidemia, hypertension, anxiety, depression, endometrial cancer, and sleep apnea. Moreover, pregnant women with PCOS should be informed of the increased rates of miscarriage, gestational diabetes, pre-eclampsia, and premature delivery. [(10)]

Acne occurs in 12–14 % of women with PCOS. Acne consists of comedones, due to accumulation of sebum and epithelial cell debris, which is colonised by the bacterium Propionibacterium acnes. Inflammation of the comedones leads to the formation of papules, pustules and nodules. Androgens may exacerbate this process, increasing sebum production by pilosebaceous units. About 50 % of women with acne have no clinical or biochemical evidence of hyperandrogenism. Moreover, many hirsute women with PCOS do not have acne. These differences may be due to the different peripheral sensitivity of androgen receptors. Hirsutism in PCOS women is attributed to increased circulatory levels of free testosterone and more active form of testosterone, formed by the activity of 5α reductase on testosterone in the pilosebaceous gland. Hirsutism is the most consistent and reliable symptom used for evaluating clinical hyperandrogenism. [(10)] In healthy women, testosterone is largely bound by sex hormone binding globulin and albumin, leaving only approximately 1% freely circulating as bioactive "free testosterone".

The pilosebaceous unit expresses 5α-reductase, which converts testosterone to the highly potent dihydrotestosterone. Varying expression of enzyme activity within the pilosebaceous unit leads to a lack of clear correlation between serum androgens and the presence or severity of acne and hirsutism[(10)]

Treatment

The most important part of managing PCOS in an adolescent is improving their long-term health and quality of life. When it comes to medical care, treatment depends on the symptoms. Nonpharmacological treatments are needed, and because the essential cause of PCOS is uncertain, treatment is done to remove the side effects. [(10)]

Treatment objectives ought to incorporate correcting anovulation, restraining the activity of androgens on target tissues, and diminishing resistance. Healthy lifestyle is beneficial to diminish androgen, and luteinizing hormone (LH). It moreover makes a difference to regulate ovulation, subsequently increasing the potential for pregnancy. [(11)]

Importantly, some adolescents are not bothered by their symptoms of hyperandrogenism. Because treatment is indicated only when symptoms are distressing to the patient, the degree to which acne or hirsutism bothers the patient should be assessed. All patients who present with clinical hyperandrogenism should be counseled on a healthy lifestyle.[(12)] Weight loss and increased physical exercise are generally recommended as the first-line therapy in overweight or obese girls. In overweight PCOS girls have shown that the combination of weight loss and intensified exercise decreases testosterone levels and the free androgen index, increases SHBG concentrations, and normalizes menstrual regularity comparably to drug therapy, and is devoid of side effects. The combination of lifestyle intervention with medications normalized more androgen levels and menses in one of these studies.

Dietary interventions as a first-line treatment for patients with polycystic ovary syndrome (PCOS).Proper diet and the maintenance of adequate nutritional status are of great importance in the prevention of this disorder, and therapeutics and dietary habits play an important role in the recovery of patients with PCOS. [(12)]

The most favorable dietary macronutrient composition with other dietary approaches, including low glycemic Index, low glycemic load, high-protein, low-carbohydrate, high monounsaturated fatty acids (MUFA) diet or modified fatty acids diets to improve the insulin

resistance and obesity.[13]

In the general population, recommendations for macro-nutrients is high-carbohydrate (approximately 50 – 60%), moderate-protein (approximately 15%), moderate-fat (approximately 30% of energy, saturated fat approximately 10% of total fat, < 300 mg cholesterol daily) and with increased consumption of fiber, fruits and vegetables, and whole-grain breads and cereals, along with regular exercise.[13]

A comprehensive lifestyle intervention program including moderate energy restriction based on basic healthy eating principles, atleast 30 minutes moderate physical activity 3 – 5 days a week and behavior modification.

The Mediterranean diet (MedDiet) is recognized as the healthiest dietary model and has been included in international guidelines among recommended healthy dietary patterns because of its unique characteristics, including regular consumption of unsaturated fat, fiber, low-glycemic index (low-GI) carbohydrates, antioxidants, and vitamins, as well as appropriate amounts of animal-derived protein . Numerous studies over several decades have shown that the adoption of the MedDiet pattern can protect against IR-related diseases, such as obesity, cardiovascular disease, type 2 diabetes (T2D), nonalcoholic fatty liver disease (NAFLD), cognitive impairment, breast cancer, and chronic kidney disease. The beneficial mechanisms of the MedDiet involve reducing inflammatory and oxidative stress markers and improving lipid profiles, insulin sensitivity, and endothelial function, as well as antiatherosclerotic and antithrombotic properties.[14] In addition, the MedDiet pattern is also regarded as the primary prevention of metabolic syndrome. In a recent study showed that women with PCOS had low consumption of extra-virgin olive oil, legumes, fish, and nuts compared to controls consumed more simple carbohydrates, saturated fatty acids, total fat, polyunsaturated fatty acids (PUFAs), and n-6 PUFAs and consumed fewer complex carbohydrates, fiber, n-3 PUFAs, and monounsaturated fatty acids than a control group. Meanwhile, testosterone levels showed significant correlations with the dietary nutrients mentioned above: there were positive associations with C-reactive protein levels, simple carbohydrates, saturated fatty acids, PUFAs, and n-6 PUFAs, and negative correlations with consumption of protein, complex carbohydrates, fiber, n-3 PUFAs and monounsaturated fatty acids. Among them, n-3 PUFAs supplementation has been proven to improve insulin sensitivity and is beneficial to metabolic management In consideration of the tight relationship between PCOS and obesity, low-grade chronic inflammation and IR, it appears likely that the MedDiet is one of the optimal nonpharmacological strategies for the treatment of PCOS.[14,16]

Combined contraceptives, including oral contraceptive pills, are commonly prescribed for adults and adolescents with PCOS to the clinical symptoms and associated hormonal disturbances. The effects of OCPs on menstrual cycle, hirsutism, weight loss, waist/hip ratio, testosterone concentrations, lipid profile and blood sugar levels are variably reported and depend on type of COCP used, duration of use, severity of presentation/phenotype, adherence to the regimen, among other factors. Different combinations of OCPs are available with heterogeneous estrogen and progestin preparations with varying pharmacological and clinical properties. Thus, the efficacy and consequences of OCPs in PCOS may vary. Some preparations also comprise natural estrogen instead of synthetic ethinyloestradiol (EE) with benefits and contraindications considered similar.

OCPs are estrogen- and progestin-containing preparations. Their mechanism of action is the estrogen component is almost always ethinyl estradiol (EE) in doses ranging from 0,03μg. The progestin component is of variable potency and androgen city. Newer OCPs contain less androgenic progestins such as norgestimate, desogestrel and drospirenone. Certain OCPs, according to their progestin content, may also have antagonizing effects on the androgen receptor or may inhibit 5α reductase activity.[12]

OCPs are commonly used in the management of patients with PCOS. They induce predictable cyclic menses, reduce luteinizing hormone secretion and thus lower ovarian androgen production; the estrogen component increases sex hormone-binding globulin, thus reducing free androgens. The progestin component protects the endometrium from hyperplasia, and OCPs also provide contraception while allowing the use of other drugs, such as anti-androgens, in this patient population. Within 3−6 months of treatment, inflammatory acne counts are reduced by 30–60% and the menstruation are getting better with improvement in 50–90% of patients. ([16]

Conclusion:

PCOS is one of the most common disorders affecting women of reproductive age. As a syndrome, it has multiple components, including reproductive, metabolic, and cardiovascular, with long-term health concerns that cross the life span. Treatment of this disorder should focus on reduction of androgen-associated symptoms, the protection of the endometrium, and reduction of the long-term risks of diabetes and cardiovascular complications. For many women with this syndrome, improving infertility is a primary goal of therapy.

All women with acne should be considered for underlying PCOS and asked about their menstrual patterns and examined for other sign of hyperandrogenism. Those who have menstrual disturbances should have hormonal profile determination as well as pelvic ultrasonography for ovarian visualization. Early diagnoses and treatment can avoid the possible complications.

OCPs are used as first-line therapy until in any other case found. Anti-androgens can be introduced to enhance the medical outcome. Not all oral contraceptives are equally able to treat acne caused by PCOS. Two types of progesterone called cyproterone acetate and drospirenone block the effect of androgens and work particularly well for this purpose

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