Polycystic Ovarian Syndrome in Adolescents: Keys to Diagnosis and Management

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ABSTRACT

Polycystic ovarian syndrome (PCOS) is the most common endocrine condition in women, affecting anywhere from 3% to 13% depending on the population being studied. PCOS often begins in adolescence, but diagnosis is difficult due to the overlap of symptoms with normal puberty. It is also necessary to rule out other potential causes of these symptoms before diagnosis. Once diagnostic criteria have been met, there are many treatment options to consider including lifestyle changes, combined oral contraceptive pills, metformin, and in some cases, antiandrogens. **[*Pediatr Ann*. 2021;50(7):e272-e275.]**

Polycystic ovarian syndrome (PCOS) can have a significant impact on many aspects of life and health for adolescent girls. Understanding the multitude of systems that are affected can help us better monitor and manage these patients to promote optimal health both physically and mentally.

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WHAT IS PCOS?

PCOS is the most common endocrine condition in women, and it affects between 3% and 13% of adolescent girls and women.[1-8] There is a higher frequency in women of Spanish, Native American, and Mexican descent.[1] Risk factors for developing PCOS include low birth weight, fetal exposure to androgens, rapid weight gain postnatally, premature adrenarche, early age of pubertal development, adult weight and lifestyle, and a family history of PCOS.[2,9,10] PCOS often manifests in adolescence when there is no establishment of regular menses and a gradual onset of hirsutism.[3,9] The syndrome consists of some combination of hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology.[2-5,11] The most commonly recommended criteria for diagnosis is the Rotterdam criteria, which requires two of the following: androgen excess (clinical or biochemical), ovulatory dysfunction, and polycystic ovaries on ultrasound.[5,6,11] In female adolescents, however, it is recommended that they have both androgen excess and persistent oligomenorrhea as anovulation and polycystic morphology on ultrasound are part of normal reproductive development in this age group.[6,7,11] About 60% to 80% of women with PCOS have hyperandrogenism and 90% are anovulatory.[9] It is also important to rule out other potential causes of these symptoms to prevent overtreatment and misdiagnosis.[3]

PCOS can manifest in many ways in female adolescents. Some signs and symptoms of PCOS overlap with normal pubertal development, which can make the diagnosis challenging. Many young women experience hirsutism (terminal hair growth), acne, alopecia, acanthosis nigricans, skin tags, abdominal adiposity, irregular periods, male pattern balding, and hoarse voice.[10,11] In adolescents, the most common clinical presentation includes irregular periods, hirsutism, acne, and signs of insulin resistance (obesity and acanthosis nigricans).[2,10]

PHYSIOLOGY OF PCOS

The hypothalamus stimulates more rapid release of gonadotropin-releasing hormone than normal, which stimulates the pituitary to release increased amounts of luteinizing hormone (LH) compared to follicle-stimulating hormone (FSH).[1,3,9] The lower FSH stimulates follicular growth but the process arrests before selection of a follicle for ovulation, resulting in anovulation.[9] The increased LH stimulates the theca cells in the ovary to produce excess androgen that then cannot be converted into estrogen, leading to hyperandrogenemia.[9] A third factor that contributes is insulin resistance, which leads to increased insulin

production that also stimulates the ovaries to produce androgen (**Figure 1**).[3,9]

DIAGNOSIS OF PCOS

Making the diagnosis of PCOS in adolescents can be difficult because many of the diagnostic criteria overlap with normal pubertal development.[4,5,11] To diagnose an adolescent, she must have both ovulatory dysfunction and signs of hyperandrogenism.[2,4] It is important to also exclude other conditions that can contribute to hyperandrogenism or ovulatory dysfunction such as pregnancy, thyroid disease, congenital adrenal hyperplasia, hyperprolactinemia, Cushing's disease, and androgen-producing tumors.[1-4,7,10] Diagnosis should be based on strict clinical and biochemical criteria to avoid overdiagnosis and unnecessary treatment.[2,10] For teenagers who have features of PCOS but do not meet diagnostic criteria, it should be noted that risk factors are present, and they should be rescreened as reproductive maturity approaches.[4,6]

Hyperandrogenism

To assess for hyperandrogenism there are two categories to consider: clinical signs and biochemical values.[3,4,7,9] The clinical signs of hyperandrogenism include severe acne, hirsutism, and androgenic alopecia (which is rare in adolescents).[4,7,9] There is no validated tool to score acne, but when associated with PCOS it tends to be more severe than average and does not respond well to typical treatments.[2,9] Because acne is so common in this age group, it should not be considered in isolation for diagnosis of hyperandrogenism.[11] Hirsutism is excessive growth of terminal hair that appears in a male pattern (upper lip, chin and neck, upper chest, upper abdomen, lower abdomen, thighs, upper back, lower back, and upper arms).[4,9] Hirsutism is scored with the Ferriman-Gallwey scale, taking into consideration a patient's ethnicity and previous treatments for hair removal.[3,4,9] It is notable that hirsutism develops slowly and may be less severe in adolescents.[11] The biochemical markers of hyperandrogenism include elevated testosterone (free, calculated free, or bioavailable), and elevated free androgen index.[4,6,7]

Ovulatory Dysfunction

There are several definitions of ovulatory dysfunction, including cycles that last more than 35 days but less than 6 months (oligomenorrhea) or absence of menstruation for at least 6 months after a previous cyclic pattern (secondary amenorrhea).[7] It can also present as unpredictable menses with cycles less than 21 days or greater than 35 days.[3] Lack of menarche by age 15 years or more than 2 to 3 years post-thelarche is also indicative of possible PCOS.[10] Ovulatory dysfunction is difficult to diagnose in adolescent girls as anovulation is common after menarche, particularly in the first 2 years.[6,7] It may be necessary to delay testing for 2 years post-menarche to truly be able to diagnose oligomenorrhea.[6,7]

Ultrasound

Ultrasound to evaluate for polycystic ovaries is not recommended in adolescence due to high incidence of multifollicular ovaries during this developmental stage.[4] Pelvic ultrasound for diagnosis is not recommended until at least 8 years post-menarche.[4,10] When ultrasound is used as part of the diagnostic testing, it should be done transvaginally as transabdominal ultrasound is limited in evaluating for cysts, especially in the setting of obesity.[11] An ovary is considered polycystic when it contains 12 or more follicles that measure from 2- to 9-mm in diameter or when its total volume is greater than 10 mL on ultrasound.[7]

LABORATORY TESTING

Laboratory testing should include free and total testosterone to evaluate for biochemical hyperandrogenism.[4,6,7,10] It may also be helpful to obtain a DHEAS (dehydroepiandrosterone sulfate) test and 17-OHP (17-hydroxyprogesterone) test to rule out congenital adrenal hyperplasia.[2,4,7,10] Thyroid-stimulating hormone, prolactin, and LH/FSH can help rule out other causes of ovulatory dysfunction.[4,7] A pregnancy test is important to rule out pregnancy as a cause for absence of menses.[4,10] Finally, a glucose tolerance test or hemoglobin A1c and a lipid panel can help diagnose comorbidities commonly associated with PCOS.[4,7,10]

Other Symptoms Associated with PCOS

Although not part of the diagnostic criteria, there are many symptoms that are associated with PCOS. The metabolic abnormalities caused by the hormonal changes of PCOS contribute to higher rates of type 2 diabetes mellitus in this population.[3,7,11] It is recommended that adolescent and adult women diagnosed with PCOS undergo an oral glucose tolerance test (or a hemoglobin A1C test if they cannot tolerate the oral test) at diagnosis.[3,7,11] Women should be rescreened every 1 to 5 years dependening on their individual risk factors.[3,11] Other metabolic abnormalities are also more common in women with PCOS, including metabolic syndrome.[7] Women should be screened for dyslipidemia (elevated triglycerides and low-density lipoprotein and lower high-density lipoprotein) and hypertension.[1,3,7] There is a higher rate of central adiposity with PCOS as well, so it is important to monitor and manage waist circumference and body mass index in this population.[11] Keeping these within healthy ranges can improve symptoms and lower cardiovascular

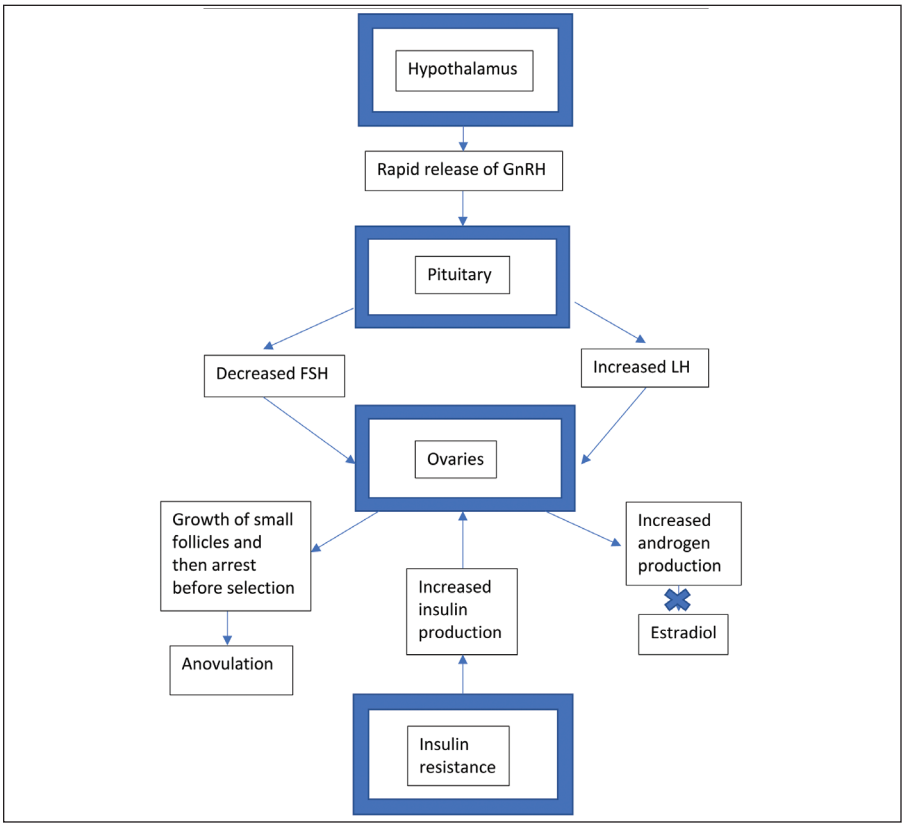

Figure 1. Abnormal hormone changes in polycystic ovarian syndrome (PCOS). Hormonal release in PCOS is abnormal, leading to increased androgen production and anovulation. GnRH, gonadotropin-releasing hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone. Adapted from McCartney and Marshall[3] and Ibanez et al.[9]

risk.[11] Women with PCOS are also at higher risk for sleep apnea, nonalcoholic fatty liver disease, and cardiovascular disease.[3,7,11] Along with physical symptoms, many women and adolescents with PCOS experience higher levels of anxiety and depression.[2-4,7,11] Adolescents report a lower quality of life related to the clinical manifestations of PCOS such as acne, hirsutism, and obesity.[1,8] Mental health should be monitored closely in this population.

Although less of an issue during the teenage years, those with PCOS have an increased risk of endometrial cancer (2.7 times higher than the general population) due to endometrial hyperplasia that occurs with anovulation.[1,3,5,11] Infertility is also higher in those with PCOS, although studies show that there is not a decreased risk of pregnancy in teenagers with PCOS.[9]

TREATMENT OF PCOS

There are three main categories of treatment for adolescents with PCOS: lifestyle changes, hormonal contraception, and metformin.[1,5,10,11] It should be noted, however, that there are no pharmacologic treatments for PCOS in adolescents approved by the US Food and Drug Administration.[9] There are no data to suggest that one pharmacologic intervention is better than another.[8] Often a combination of two or even all three categories is necessary to manage symptoms. A combination of all three is indicated in patients whose body mass index is greater than 25 kg/m^2, and lifestyle changes with combined oral contraceptive pills (COCPs) alone have not achieved adequate outcomes.[4] A multidisciplinary approach including a primary care provider, endocrinologist, nutritionist, and health psychologist is ideal when caring for patients with PCOS.[4] Decisions regarding which types of treatments to pursue should be based on patient priorities and which symptoms are most bothersome to them.[2,3]

Lifestyle Management

Lifestyle management consists of dietary changes with a focus on calorie restriction in people with obesity, increased exercise, decreased sedentary behaviors, and behavioral strategies to maintain a healthy lifestyle.[2,4,7,9,11] This can lead to weight loss, improved insulin resistance, and a reduction in cardiovascular risk factors as well as improved menstrual function and fertility.[3,7,9,11] Although lifestyle changes and weight management are helpful, they are often insufficient on their own to manage the symptoms of PCOS.[11] When that is the case, oral contraceptives and metformin are commonly used in addition to lifestyle changes.

Combined Oral Contraceptive Pills

COCPs are one of two recommended pharmacologic treatments for adolescents and adults with PCOS who are not trying to become pregnant.[4,5] COCPs are the first-line treatment for the adolescent age group in addition to lifestyle changes.[6,11] COCPs are helpful in managing irregular menstrual cycles and clinical signs of hyperandrogenism including acne and hirsutism.[1,3,4,7,9,11] Regular menstrual cycles are important for the prevention of endometrial hyperplasia, which can increase risk for endometrial cancer.[1,3] There is no current recommendation on which combination of hor-

mones should be used, so general population guidelines should be followed for selection.[4,7] Some data have suggested that COCPs containing progesterone, cyproterone acetate, or drospirenone are better for managing hirsutism.[5]

Metformin

Metformin is the other recommended pharmacologic treatment for adolescents with PCOS. Metformin can be helpful for metabolic comorbidities that often go along with PCOS.[4,6,11] It can also improve the cutaneous abnormalities such as acanthosis nigricans and enhance diabetes management as it lowers hyperinsulinemia.[3,8,11] Metformin can also improve cycle regulation, ovulation, and testosterone levels.[9]

Antiandrogens

One additional category of pharmacologic intervention can be considered in select patients.[4] Antiandrogens may be used in conjunction with COCPs to assist with hirsutism that has been refractory to other treatment.[4] These medications are teratogenic so extra care must be taken to ensure appropriate contraception.[4]

SUMMARY

PCOS is a common and complicated endocrine disease that often begins during adolescence. It is important to monitor teenagers who have risk factors and make the diagnosis when appropriate criteria are met. Due to the overlap of symptoms with normal pubertal development, this can sometimes be challenging and necessitate a delay in diagnosis. Once the diagnosis has been made, treatment should be tailored to the individual patient's priorities and symptoms. Treatment should be managed by a multidisciplinary team and could include lifestyle changes, COCPs, metformin, and in certain cases antiandrogens. Special attention should be given to anxiety and depression in adolescents with PCOS. Optimal management can improve metabolic, cardiovascular, and fertility outcomes for these young women in the future.

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