POLYCYSTIC OVARY SYNDROME: METABOLIC SYNDROME

Week 82

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SDH and .phrase slides by Chloé Altchek, MS4

Reading Assignment:
ACOG Practice Bulletin #194: Polycystic Ovary Syndrome, June 2018
LEARNING OBJECTIVES

• Understand the definitions and pathophysiology of PCOS
• Understand the basic work-up and evaluation of PCOS
• Understand the comorbidities associated with PCOS
• Understand appropriate management for patients with PCOS
CASE VIGNETTE

• Patient is a 33 y.o G0 woman who presents to your office for a new GYN visit. She reports a 10 year history of irregular cycles. Her LMP was 2 months ago.

• She complains of accelerating hair loss and persistent acne. She and her partner would like to have children; they have been attempting to conceive for 2 years.
FOCUSED HISTORY

What elements of the patient’s history are most relevant?

• **POB:** G0
• **PGYN:** Menarche 12 yo; **irregular cycles, q 3-4 months**
  No STI/cysts/fibroids
  No abnormal paps
• **PMH:** **Obesity**
• **PSH:** Laparoscopic ovarian cystectomy 4 years ago
• **FH:** None
• **Meds:** None
• **All:** NKDA
• **SH:** No T/E/D; works as manager at a Chipotle; married; denies IPV
PERTINENT OBJECTIVE FINDINGS

What elements of the patient’s physical exam are most relevant?

• P: 99  BP: 150/89  Wt: 99 kg  Ht: 170 cm  BMI: 34.3
• Gen:  NAD
• HEENT: No thyromegaly, no acanthosis nigricans; minimal alopecia noted in male distribution; some facial hair and minimal acne noted
• Chest: CTAB
• CVS: RRR, S1S2
• Abd: Soft, NT/ND; obese
• GU: NEFG; cervix WNL, no discharge/lesions; uterus 6 wk sized, retroverted, no adnexal masses
BACKGROUND

What is polycystic ovary syndrome?
• A disorder characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries
• The most common endocrine disorder in women

What is the prevalence of PCOS?
• Depends on diagnostic criteria used: 7% (NIH criteria), 15% (Rotterdam criteria)

What is the pathophysiology of PCOS?
• Unclear; likely multifactorial with multiple genetic and environmental factors
• Insulin resistance plays a key role in features of this disorder
  • Hyperinsulinemia causes decreased SHBG, leading to more available circulating androgens as well as increased secretion by the adrenals and the ovaries
• Hyperandrogenism has multiple etiologies; an underlying genetic predisposition is likely possible
• Ovarian folliculogenesis is abnormal with insufficient FSH stimulus or response to FSH
• Increased LH activity can lead to increased androgen secretion by thecal cells
  • Higher LH:FSH
• Obesity can worsen the effects of PCOS
  • Obesity is not a requirement for diagnosis**
CLINICAL ASSESSMENT

What is the differential for PCOS?

Box 3. Factors to Consider in the Differential Diagnosis of Polycystic Ovary Syndrome

- Androgen secreting tumor
- Exogenous androgens
- Cushing syndrome
- Nonclassical congenital adrenal hyperplasia
- Acromegaly
- Genetic defects in insulin action
- Primary hypothalamic amenorrhea
- Primary ovarian failure
- Thyroid disease
- Prolactin disorders

What are the diagnostic criteria for PCOS?

Table 1. Recommended Diagnostic Schemes for Polycystic Ovary Syndrome by Varying Expert Groups

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>National Institutes of Health Criteria(^1) 1990 (both are required for diagnosis)</th>
<th>Rotterdam Consensus Criteria 2003(^2) (two out of three are required for diagnosis)</th>
<th>Androgen Excess Society(^2) 2006 (hyperandrogenism plus one out of remaining two are required for diagnosis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperandrogenism(^1)</td>
<td>R</td>
<td>NR</td>
<td>R</td>
</tr>
<tr>
<td>Oligoamenorrhea or amenorrhea</td>
<td>R</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Polycystic ovaries by ultrasound diagnosis</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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</table>
CLINICAL ASSESSMENT

How do you assess patients for PCOS?

• History
  • Focus on menstrual history, onset and severity of the signs of androgen excess, medications, family history of DM and CV disease

• Physical exam
  • Full exam
  • Assess for signs of hyperandrogenism and insulin resistance, such as acne, hirsutism, androgenic alopecia, acanthosis nigricans
  • Consider assessing for signs of other etiologies of hyperandrogenism:
    - Cushing syndrome- moon facies, buffalo hump, abdominal striae, centripetal fat distribution, HTN, proximal myopathies, easy bruising
    - Clitoromegaly- more rarely seen in PCOS, more commonly seen in other conditions such as CAH or androgen-secreting tumors, or exogenous steroid use

• Lab evaluation
  • bHCG, PRL, TSH, free testosterone (or total testosterone + SHBG), 17-OH progesterone
  • 2 hr OGTT and lipid panel for confirmed PCOS

• Imaging
  • Ultrasonography can be considered, although not necessary for diagnosis
At what testosterone level and DHEAS level are you concerned about a tumor of ovarian/adrenal origin?

- Testosterone > 2 ng/mL
- DHEAS > 700 mcg/dL

What population should you consider screening for non-classical congenital adrenal hyperplasia?

- Adult women w/ anovulation and hirsutism and are from specific ethnic groups (Ashkenazi Jews, Hispanics, Yugoslavs, Native American Inuits, Italians)

*—Patient has both hyperandrogenism (excessive acne, androgenic alopecia, or hirsutism) and ovulatory dysfunction.
†—Measurements to be taken in the morning, preferably during the follicular phase.
‡—Screen for hypertension, type 2 diabetes mellitus, dyslipidemia, depression, and obstructive sleep apnea, given their association with PCOS.

Williams 2016, p 108
COUNSELING AND MANAGEMENT

What are **reproductive health risks** in women with PCOS?
- Infertility, menstrual disorders
- Increased risk of ovarian hyperstimulation in those undergoing ovulation induction
- Increased risk for pregnancy complications (GDM, hypertensive disorders)

What are the **long-term health risks** of PCOS?
- Increased risk of diabetes and cardiovascular disease
- Increased risk of metabolic syndrome, NAFLD, obesity-related morbidities (including OSA)
- Increased risk of endometrial cancer (especially in women with multiple risk factors-centripetal obesity, diabetes, chronic anovulation)
- Possible increased risk of mood disturbances and depression

How do you define **metabolic syndrome**?
- Elevated BP (>/= 130/85)
- Increased waist circumference (>/= 35 in.)
- Elevated fasting glucose levels (>/= 100 mg/dL)
- Reduced HDL (</= 50 mg/dL)
- Elevated triglyceride levels (>/= 150 mg/dL)
Diagnosis of PCOS

**COUNSELING AND MANAGEMENT**

**General management**
- Screen for T2DM (2hr OGTT)
- Screen for CV disease (lipid panel)

**Lifestyle modifications**
- Assess reproduction goals
- Referral to other providers for appropriate management of long-term health issues

**Obesity**
- Weight loss of at least 5% total body weight

**Diet & exercise**

**Medications:**
- sibutramine, orlistat

**Surgical management**
- Reduce CV risk
- Lifestyle modifications (exercise, diet)

**Insulin-sensitizing agents (metformin)** in high risk cases (i.e. impaired glucose tolerance + metabolic syndrome)

**Statins** as indicated for dyslipidemia (referral to PCP)

**Menstrual regulation**
- Combined hormonal contraception,
- progestin-only contraception

**Insulin sensitizing agents (metformin, pioglitazone, rosiglitazone)**
- Add contraception if pregnancy not desired as these agents may normalize ovulation

**Ovulation induction**
- 1st line: Letrozole
- 2nd line: Exogenous gonadotropins or laparoscopic ovarian drilling

**Hirsutism**
- Eflornithine (FDA approved) & laser therapy

**CHCs:** not FDA approved, better in combination with antiandrogen

**Antiandrogens:** not FDA approved
- spironolactone
- flutamide
- finasteride

**Letrozole** has increased live birth rate compared to clomid for PCOS; Both have equal risk of twin gestation
### Social Determinants of Health

#### Racial and ethnic differences in insulin resistance, metabolic syndrome, and hyperandrogenemia in women with PCOS

<table>
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<tr>
<th>Hispanic women have the most severe PCOS phenotype compared to Black and White women</th>
<th>Black women have an overall milder PCOS phenotype than Hispanics and White women</th>
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<tr>
<td>- Higher prevalence of hyperandrogenemia, insulin resistance, systolic hypertension, and hyperglycemia</td>
<td>- Lower prevalence of metabolic syndrome than Hispanic women</td>
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<tr>
<td>- Higher prevalence of hyperandrogenemia may be related to the higher prevalence of hyperinsulinemia, insulin resistance, and consequently low serum sex hormone binding globulin</td>
<td>- Lower prevalence of hypertriglyceridemia than both Hispanics and White women</td>
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</table>
Pt with new diagnosis of PCOS was counseled on characteristics/symptoms of the syndrome including hyperandrogenism, ovulatory dysfunction, and polycystic ovaries. The lack of known pathophysiology of PCOS was discussed, but the patient was advised that the etiology is likely multifactorial with multiple genetic and environmental factors. The patient was counseled on associated reproductive health risks including infertility, menstrual disorders, ovarian hyperstimulation in those undergoing ovulation induction, and pregnancy complications (GDM, hypertensive disorders). Long-term health risks of PCOS were also discussed including increased risk of diabetes, cardiovascular disease, metabolic syndrome, NAFLD, obesity-related morbidities (including OSA), endometrial cancer (especially in women with multiple risk factors-centripetal obesity, diabetes, chronic anovulation), mood disturbances and depression. All questions were answered.

Pt was counseled on initial management and treatment options. It was explained that the goals of therapy will be restoration of ovulatory cycles, improvement of metabolic/cardiovascular risks and reduction of hyperandrogenic features. Initial lab work will include 2hr OGTT and lipid panel. ***If overweight, life style modifications including diet and exercise were discussed for a goal of 5% weight reduction. Options for initial medical management of menstrual irregularities, metabolic abnormalities and endometrial protection were outlined and the patient will be started on ***[OCPs/progestin-only contraception/metformin]. The patient’s reproductive goals were elicited and options for future ovulation induction were discussed.
CODING AND BILLING

• ICD-10
  • E28.0 - Polycystic ovary syndrome
  • E88.1 - Metabolic syndrome

• CPT
  • 99213 - Established outpatient visit (99214 if attending sees patient with you)
EVIDENCE


