OB/GYN

MEDICINE
KING SAUD UNIVERSITY

Polycystic Ovarian Syndrome

Done by: Haneen alsubki , Nora Almohideb , Anwar Alajmi , Nada Alsomali , Laila Mathkour

Revised by: Shatha Alghaihb, Shrooq Alsomali

References: 436 doctor's slides and notes , Kaplan

Color code: Notes | Important | Extra | Kaplan

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Objectives:

1. Understand the pathogenesis of PCOS
2. Identify the clinical picture of PCOS
3. The investigations required to diagnose PCOS
4. The health hazards associated with PCOS
5. The options of management

Polycystic Ovarian Syndrome (PCOS)

Definition

- It's primarily characterized by ovulatory dysfunction and hyperandrogenism symptoms that patient is having is secondary to hyperandrogenism.
- It's a set of symptoms due to elevated Androgens in women.
- It's due to a combination of genetic and environmental factors.
- It is one of the leading causes infertility.

Epidemiology

- It is the most common endocrine disorder amongst women between 18-44 years old, it affects 2%-20% of this age group and it's the most common cause of infertility.
- In the USA, prevalence is 4-12%. Up to 10% of women are diagnosed with PCO during gynecologic visits.
- Some European studies reported that prevalence of 6.5- 8%.
- In a study that assessed hirsutism in southern Chinese women, investigators found a prevalence of 10.5%.

Pathophysiology

- Women with PCOS have abnormalities in the metabolism of androgens and estrogen and in the control of androgen production. Androgens will not metabolize to estrogen :/! (this will give us the symptoms of high androgen levels), androgens can change to testosterone.
- Although the exact etiopathophysiology of PCOS is unclear! it can result from abnormal function of the hypothalamic-pituitary-ovarian (HPO) axis.

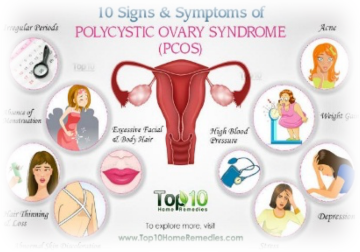
The biochemical features of PCOS:

- Raised androgen production such as testosterone, androstenedione, and dehydroepiandrosterone sulfate (DHEA-S) may be encountered in these patients. But only 50% of those patients have a change in testosterone or androgen level. However, individual variation is considerable, and a particular patient might have normal androgen levels.
- Peripheral insulin resistance and hyperinsulinemia (secondary to androgen affect), and obesity amplifies the degree of both abnormalities.
- Proposed mechanism for anovulation and elevated androgen level is due to increased level of luteinizing hormone (LH) secreted by the anterior pituitary gland

and thus simulations of the ovarian theca cells then increase androgen production (testosterone, androstenedione).

- Decreased level of FSH relative to LH.
- Lack of aromatization of androgens to estrogens → decreased estrogen levels and hence anovulation.
- PCOS is a genetically heterogeneous syndrome, however the genetic contributions remain incompletely described.
- Studies of family members with PCOS indicate that an autosomal dominant mode of inheritance occurs for many families with the disease. You see it between sisters, relatives and first degree cousins.

Signs and symptoms



- Menstrual dysfunction oligomenorrhea.
- Anovulation.
- Signs of hyperandrogenism (Hirsutism, acne, hair fall).
- Infertility.
- Obesity and metabolic syndrome. Insulin resistance cause fat deposition > break down of fat will not happen > gain weight.
- Obstructive sleep apnea.
- Typically, the onset is gradual, frequently with a positive family history. Menses and fertility are normal. This is the most common cause of androgen excess in women. Physical examination reveals hirsutism without virilization. Pelvic examination is normal.

On examination

- Virilizing signs hirsutism, acne, Acanthosis nigricans.
- Acanthosis nigricans sign of insulin resistance.
- Hypertension.
- Enlarged ovaries (may or may not be present) not palpable only seen by US.
- Polycystic ovaries are enlarged bilaterally- have smooth thickened capsule.
- On cut section, sub-capsular follicles in various stages of atresia are seen at the periphery with hyperplasia of theca stromal cells.
- On microscopic examinations, luteinized theca cells are seen.

Investigations

Exclude other disorders that result in menstrual irregularities and hyperandrogenism:

- Adrenal tumor, ovarian tumor increase of estrogen level.
- Granulosa cell tumor can cause high estrogen.
- Thyroid dysfunction can cause irregularity of cycle and weight gain.
- Congenital Adrenal hyperplasia
- Hyperprolactinemia
- Acromegaly

- Cushing syndrome

Screening labs studies for PCOS:

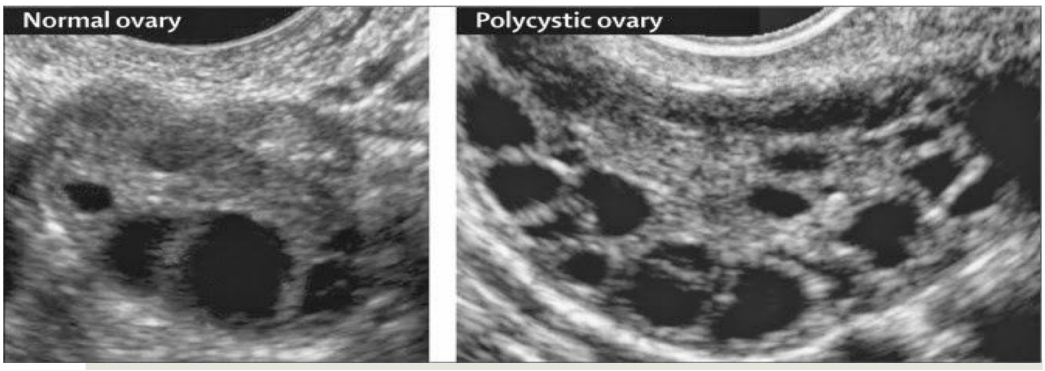
- free androgen index
- total and free testosterone level **free** testosterone reflect the androgen symptoms it will be higher than normal.
- serum prolactin level.
- Thyroid function test (TSH, free thyroxine).
- Serum hCG level.
- Cosyntropin stimulation test (The ACTH test).
- Serum 17-hydroxyprogesterone (17-OHPG) level.
- Urinary free cortisol and creatinine level.
- low dose dexamethasone suppression test.
- Serum insulin like growth factor.
- If the patient presented with amenorrhea or oligo the first thing we need to do in secondary amenorrhea is pregnancy test.
- Primary amenorrhea >>> FSH levels.

Other tests:

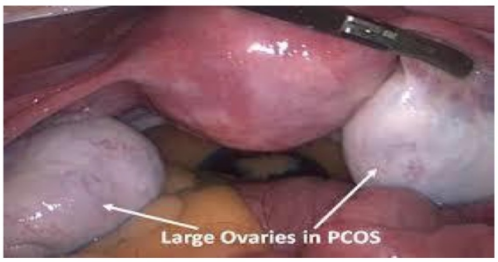
- Androstenedione level
- Insulin level.
- Lipid level they may develop dyslipidemia.
- Glucose level
- GnRH stimulation levels.
- FSH and LH levels is the most imp. But if it's normal it doesn't exclude PCO, usually the blood is not definitive diagnosis of PCO but it can give us a hint.

Imaging test:

- Ovarian ultrasonography, preferably using transvaginal approach.
- Pelvic CT scan or MRI to visualize the adrenals and ovaries.



- If we ONLY found PCO on US without any other symptoms we don't call it a disease or syndrome, we must have 2 of the criteria

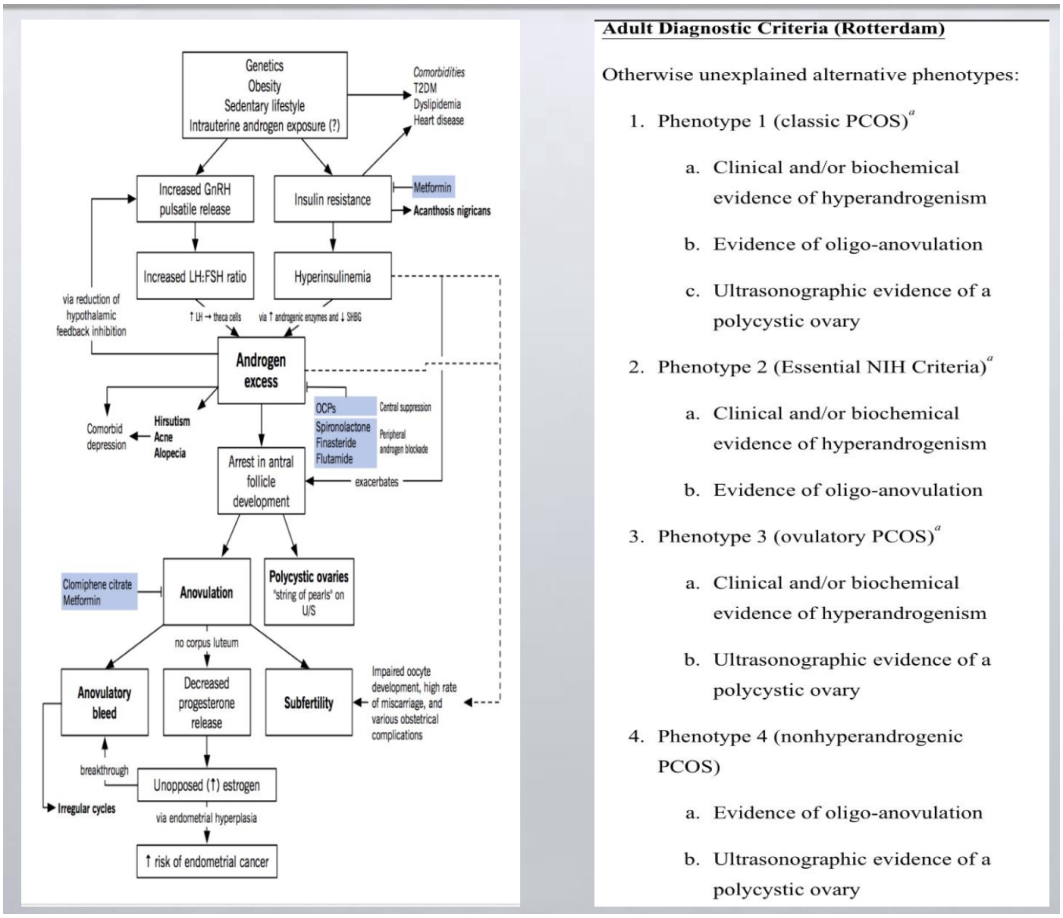


This is laparoscopic image; you can see a huge ovary

Procedures:

- Ovarian biopsy for histological confirmation of PCOS.
- US diagnostic for PCOS.
- Endometrial biopsy to evaluate for endometrial disease (malignancy) some androgens may change to estrogen because those patients don't have ovulatory cycle, long exposure of estrogen in endometrium can cause hyperplasia >>> with time will change to cancer and use the hormones to reduce the risk of having endometrial cancer.

criteria of diagnosing (V.imp)



Adult Diagnostic Criteria (Rotterdam)

Otherwise unexplained alternative phenotypes:

1. Phenotype 1 (classic PCOS)[a]
   a. Clinical and/or biochemical evidence of hyperandrogenism
   b. Evidence of oligo-anovulation
   c. Ultrasonographic evidence of a polycystic ovary
2. Phenotype 2 (Essential NIH Criteria)[a]
   a. Clinical and/or biochemical evidence of hyperandrogenism
   b. Evidence of oligo-anovulation
3. Phenotype 3 (ovulatory PCOS)[a]
   a. Clinical and/or biochemical evidence of hyperandrogenism
   b. Ultrasonographic evidence of a polycystic ovary
4. Phenotype 4 (nonhyperandrogenic PCOS)
   a. Evidence of oligo-anovulation
   b. Ultrasonographic evidence of a polycystic ovary

- Diagnosis by exclusion
  Exclude:
  - Hyperprolactinemia
  - Hypothyroidism
  - Cushing's syndrome
  - Congenital adrenal hyperplasia
  - External estrogen

- After excluding other diseases, we have to find 2 criteria from the 3 which is:
  - anovulatory cycle (change in menstrual pattern).
  - Hyperandrogenism (hirsutism, acne, Acanthosis nigricans, hair loss).
  - US shows polycystic.

Prognosis

- Approx. 40% of patients with PCOS have insulin resistance hence increased risk of type 2 diabetes and cardiovascular complications.
- Increased risk for endometrial hyperplasia and carcinoma (chronic anovulation in PCOS leads to constant endometrial stimulation with estrogen without progesterone, and this increases the risk of endometrial hyperplasia and carcinoma.

Management

In PCOS we are treating the symptoms because the disease will not disappear, our aim is to fix the hormonal disturbance in the body

❖ **Lifestyle modification** is the **first line of treatment**: Diet because they have risk to develop DM, Exercise, Weight loss might regulate the cycle.

❖ **Medical management:** Treat metabolic disorders- (Anovulation, hirsutism, and menstrual irregularities).

- **Menstrual irregularity**
  First-line medical therapy is oral contraceptive pills induce regular menses (e.g. ethinyl estradiol, medroxyprogesterone) combined of estrogen and progesterone. The progesterone is better to be antiandrogen so the effectiveness of the medication will be much better. The result will appear after 3 months of using the contraception regarding the hirsutism, hair loss and irregularity of the cycle.

- **Hyperandrogenism (hirsutism and Acne vulgaris)**
  The first 2 are the most common
  - Reducing androgen production.
  - Reducing serum free androgen levels by increasing androgen binding to plasma-binding proteins.
  - Blocking androgen action at the level of target organs (e.g. hair follicle).
  - Androgen blocking agent (e.g. spironolactone, leuprolide, finasteride).

- **Anovulation**
  Clomiphene citrate or letrozole (selective estrogen receptor modulators) for ovulation induction, first- line treatment.

- **Hypoglycemic agents**
  Metformin commonly used (it increases the sensitivity of insulin and help to reduce the absorption of glucose so it helps to lose weight), insulin.
- **Topical hair removal agent**
  eflornithine (if they're not responding, the best treatment is Laser).
- **Topical acne agent**
  benzoyl peroxide, tretinoin topical cream (0.02-0.1%)/gel (0.01-0.1%)/ solution (0.05%).

❖ **Surgical management**[1]**:** aim to restore ovulation

- Laparoscopically:
  - Electrocutare.
  - Laser drilling.
  - Multiple biopsy.

- Patients who underwent induction ovulation for pregnancy and they develop ovarian hyperstimulation had pulmonary edema, abdominal ascites, huge bilateral ovary and hypokalemia. To prevent this, the next cycle we can do the drilling. (we have to stop the cycle if the patient developed the ovarian hyperstimulation).

[1] **we don't go a lot for surgical management.**

Summary

PCOS	
biochemical features	• Decreased level of FSH relative to LH, anovulation • Raised androgen production • Peripheral insulin resistance, hyperinsulinemia.
Diagnosis	Rotterdam criteria: two of the following 1. clinical or biochemical hyperandrogenism. 2. evidence of oligo/anovulation. 3. polycystic ovaries.
Signs and symptoms	1. Menstrual dysfunction 2. Anovulation 3. Signs of hyperandrogenism (Hirsutism, acne) 4. Infertility 5. Obesity 6. metabolic syndrome
Investigations	• Ovarian ultrasonography • FSH and LH levels • GnRH stimulation levels • Pelvic CT scan or MRI • Exclude other disorders that can result in menstrual irregularities and hyperandrogenism
Prognosis	• increased risk of type 2 diabetes • Increased risk for endometrial hyperplasia, carcinoma
Management	• Lifestyle modifications. • oral contraceptive (eg ethinyl estradiol,medroxyprogesterone) induce regular menses • Clomiphene citrate or letrozole (selective estrogen receptor modulators) for ovulation induction • Hypoglycemic agents (metformin, insulin) • Hyperandrogenism: Reducing androgen production ,Increasing androgen binding to plasma-binding proteins, Blocking androgen action at the level of target organs, Androgen blocking agent (e.g. spironolactone, leuprolide, finasteride)

MCQs

Q1: A 26-year-old G0P0 comes to your office with a chief complaint of being too hairy. She reports that her menses started at age 13 and have always been very irregular. She has menses every 2 to 6 months. She also complains of acne and is currently seeing a dermatologist for the skin condition. She denies any medical problems. Her height is 165cm, her weight is 81kg, and her blood pressure is 100/60 mm Hg. On physical examination, there is sparse hair around the nipples, chin, and upper lip. Pelvic examination is normal. Which of the following is the most likely explanation for this patient's problem?

A- Idiopathic hirsutism

B- Polycystic ovarian syndrome

C- Late-onset congenital adrenal hyperplasia

D- Adrenal tumor

Q2: What is the best management in Q1?

A- OCPs.

B- Life style modification.

C- Metformin.

D-Spironolactone

Q3: in the Treatment of Hirsutism in PCOS, drugs used are:

A- Menopausal Gonadotropin

B- GnRH

C- Spironolactone

D- Hcg

Q4: which of the following is not True about PCOS:

A- High FSH/LH ratio

B- Increased risk of DM

C- Hirsutism

D- OCP is given for treatment

Q5: Which of the following is the most likely diagnosis in a 27-year-old obese woman presenting with Oligomenorrhea, infertility and hirsutism?

A- Polycystic ovaries

B- Endometriosis

C-Pelvic inflammatory disease

D- Turner's syndrome

Answers: 1- B. 2-B. 3-C. 4-A. 5-A.