



Polycystic Ovarian Disease and Endometriosis

Lecture 9

430 Pathology Team

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Red: Doctors' and important notes.
Green: Team notes.

Polycystic Ovarian Disease:

- Other names for this syndrome include polycystic ovarian syndrome and **Stein-Leventhal syndrome**
- Polycystic ovaries are characterized by **bilaterally enlarged polycystic ovaries**, chronic anovulation and clinical manifestations secondary to **excessive production of estrogens and androgens**, mainly androgens **such as hirsutism, virilization**.
- The initial abnormality resulting in the syndrome is not known but is believed to be related to hypothalamus-pituitary dysfunction leading to **over secretion of luteinizing hormone (LH)**.
- LH in turn stimulates the ovary to produce excess androgens. **Secretion of follicle stimulating hormone (FSH) is inhibited** resulting in repression of ovulation with follicle cyst formation = **no progesterone**.
- High level of LH, estrogen and androgen and low FSH

Clinical appearances:

The usual clinical presentation is a young woman (between 15 and 30 years) with:

1. secondary amenorrhea with anovulation
2. oligomenorrhea or irregular menses
3. Infertility due to the anovulation.
4. hirsutism
5. virilism due to excessive amounts or effects of androgenic (masculinizing) hormones
6. obese
7. acne

Grossly:

Both ovaries are markedly enlarged usually twice normal in size and have a thickened, fibrotic gray white capsule with smooth pearl-white outer surface, studded (**covered**) with sub cortical cysts 0.5 to 1.5 cm in diameter.

Histology:

- Microscopically, the outer portion of the **cortex is thickened and fibrotic**.
- Many **follicle cysts lined by granulosa cells** are present in the subcapsular cortex. The cysts have prominent outer theca interna layer, which is often luteinized.
- **Corpora lutea are frequently absent** due to the anovulation and occasional focal stromal luteinization is present.
- Cortical stromal fibrosis
- The chronic anovulation **results in unopposed estrogenic stimulation (absence of negative feedback)** of the endometrium leading to a variety of appearances ranging from mild atypical hyperplasia to well-differentiated endometrial adenocarcinoma

Clinical behavior:

- Treatment with drugs that either **induce ovulation (resolve most of the problems)**(clomiphene or hCG) or regulate the menstrual cycle restores fertility. And asking the patient to lose weight will improve the condition.
- Reduction of ovarian volume by wedge resection is also successful in initiating ovulation and restoring fertility.
- The endometrial changes usually regress once ovulation is achieved.

First case:

A **30 years** old female with atypical complex hyperplasia +/- endometrial adenocarcinoma and infertility. The physician should check for polycystic ovarian syndrome because it may be the cause of this tumor. In this case the preferable treatment is giving progesterone to oppose estrogen ACTION.

Second case :

A **56 female** having atypical complex hyperplasia +/- adenocarcinoma with previous polycystic ovarian syndrome, the treatment in this case is bilateral ovariectomy and hysterectomy

Women with PCOS are at risk for the following:

1. **Endometrial hyperplasia and endometrial cancer (due to high estrogen levels)**
2. Insulin resistance/Type II diabetes **(due to obesity)**
3. High blood pressure **(due to obesity)**
4. Depression/Anxiety
5. Dyslipidemia
6. Cardiovascular disease
7. Strokes
8. Weight gain
9. Miscarriage
10. Acanthosis nigricans (patches of darkened skin under the arms, in the groin area, on the back of the neck)
11. Autoimmune thyroiditis

Endometriosis:

- This is the presence of ectopic **endometrial tissue that is both glands and stroma outside the uterus.**
N.B: presence of endometrial glands only somewhere else indicates metastatic carcinoma.
- The lesions are usually found on the peritoneal surfaces of the reproductive organs and adjacent pelvic organs.
- The **most frequent location is the ovary** (approx. 50%) **followed by the pouch of Douglas**, uterine ligaments. Occasional sites include the cervix, vagina, perineum, bladder, large bowel and the umbilicus. Rare lesions are seen as far as small bowel, kidneys, **lungs and brain.**
- **It has been reported in men.** The sites involved have been the bladder, scrotum and prostate
- **How males are affected with the absent of uterus?**
- **It is developed during the embryo developments at the differentiation phase.**
- **Non-neoplastic.**
- Like the uterine endometrium it is responsive to the hormonal variations of the menstrual cycle. **Whatever physiological changes happen to the uterus under the control of hormones it reaches these ectopic endometrial foci through the circulation.**
- It is characterized by menstrual type bleeding at the site of the ectopic endometrium, resulting in blood filled areas (e.g. chocolate cysts).

Clinical appearances:

- Clinical presentation depends on the **site of endometriosis.**

- Dysmenorrhea, cyclic abdominal pain and dyspareunia (painful sexual intercourse) are common symptoms. Usually there is severe menstrual-related pain. Sometimes it might present with abdominal mass that is mistakenly diagnosed as metastatic carcinoma.
- Often results in infertility.
- Endometriosis usually appears as multiple red or brown (due to hemosiderin) 1mm to 5mm nodules (some may form larger masses or cysts). Dense fibrous adhesions may surround the foci.
- Repeated hemorrhage into foci in the ovary with each menstrual cycle produces cysts, which contain inspissated (thick), chocolate-brown material, called "chocolate cysts".

Clinical behavior:

Benign with no malignant potential. May recur after surgical excision but the risk is low.

Histology:

- Microscopic diagnosis of endometriosis is made by the presence of two out of three elements: ectopic endometrial glands, stroma, macrophages containing hemosiderin (siderophages) may be present in lesions with previous hemorrhage.
- When endometriosis develops in a muscular viscus (internal organ), the smooth muscle around it is often hyperplastic.

Adenomyosis:

- This is defined as the presence of endometrial glands and stroma in the myometrium. The condition involves the posterior wall more often than the anterior wall but it may affect both walls in the same uterus.
- The disease is primarily a disorder of parous women and occurs infrequently in the nullipara. It is associated with menorrhagia and severe dysmenorrhea. In about a third of patients there are no symptoms and the lesions are discovered accidentally.
- When extensive the lesions produce myometrial thickening with small yellow or brown cystic spaces containing fluid or blood.
- Occasionally, a proliferation of smooth muscle around a focus of adenomyosis produces a tumor called adenomyoma, which resembles uterine leiomyoma except the presence of the glands in the adenomyosis.

Clinical behavior:

This is a benign condition with no known malignant potential that regresses after the menopause

Summary

Polycystic Ovarian Disease: also known as Stein-Leventhal syndrome. It is characterized by high level of LH, estrogen and androgen and low FSH. It is also characterized by bilaterally enlarged polycystic ovaries, chronic anovulation. The initial abnormality resulting in the syndrome is not known. Secretion of follicle stimulating hormone (FSH) is inhibited resulting in repression of ovulation with follicle cyst formation = no progesterone. **Clinical appearances:** secondary amenorrhea with anovulation, oligomenorrhea or irregular menses, infertility, hirsutism, virilism due to excessive amounts or effects of androgenic (masculinizing) hormones, obese, acne. **Grossly:** both ovaries are markedly enlarged usually twice normal in size and have a thickened, fibrotic gray white capsule with smooth pearl-white outer surface. **Histology:** the cortex is thickened and fibrotic, many follicle cysts lined by granulosa cells, corpora lutea are frequently absent.

- ✧ **Endometriosis:** this is the presence of ectopic endometrial glands and stroma outside the uterus. The most frequent location is the ovary (approx. 50%) followed by the pouch of Douglas pouch. It has been reported in men. Like the uterine endometrium it is responsive to the hormonal variations of the menstrual cycle. It is characterized by menstrual type bleeding at the site of the ectopic endometrium, resulting in blood filled areas (e.g. chocolate cysts). Benign with no malignant potential. May recur after surgical excision but the risk is low. Microscopic diagnosis of endometriosis is made by the presence of two out of three elements: ectopic endometrial glands, stroma, macrophages containing hemosiderin (siderophages) may be present in lesions with previous hemorrhage.
- ✧ **Adenomyosis:** this is defined as the presence of endometrial glands and stroma in the myometrium. The condition involves the posterior wall more often than the anterior wall but it may affect both walls in the same uterus. Occasionally, a proliferation of smooth muscle around a focus of adenomyosis produces a tumor called adenomyoma, which resembles uterine leiomyoma except the presence of the glands in the adenomyosis. **Clinical behavior:** this is a benign condition with no known malignant potential that regresses after the menopause