Pathology of the female genital tract

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Uterine Pathology

Quick recap of uterine histology:

The uterus has 2 layers:

1- **Endometrium**: is a special kind of mucosa [composed of glands/ epithelial cells and stroma in between]. It’s the inner layer lining the cavity of the uterus and this layer undergoes shedding during menstruation and the embryo implants in it in normal pregnancy.

2- **Myometrium**: Muscular layer/ muscles of the uterus. Smooth muscle fibers that cause contractions that are important for the menstrual cycle and delivery/ labor.

In this lecture, we are going to discuss diseases that affect the endometrium and myometrium.

**Endometrium Pathology:**

1- **Endometritis**:

As the name implies, it is inflammation of the endometrium because of [causes]: 1- pelvic inflammatory disease (PID) 2- miscarriage or delivery/ labor 3- intrauterine contraceptive device (IUCD).

We know that pelvic inflammatory disease (PID) is caused by infections in many cases. Also, miscarriage or delivery and usage of intrauterine contraceptive device can increase the risk of getting infections and therefore inflammation (endometritis).

Endometritis can be acute or chronic.

**Symptoms**: fever, lower abdominal pain, menstrual abnormalities. If endometritis is chronic, it may lead to [complications] infertility and ectopic pregnancy due to damage to the Fallopian tubes.

**Treatment**: removal of cause, antibiotics, D&C.

Dilation and curettage (D&C) is a procedure to remove tissue from inside uterus (endometrium).

2- **Endometriosis**: بطانة الرحم المهاجرة

Endometrial glands and stroma outside the uterus.

The endometrium leaves its normal place and goes outside the uterus.

Where does it go?

* it may go anywhere inside the peritoneal cavity (ovaries, pouch of Douglas, uterine ligaments, fallopian tubes, rectovaginal septum, and serosa of the organs inside the peritoneal cavity). these are the common locations because they are surrounding the uterus.
And in this case, they are usually **multifocal = present in multiple tissues in the pelvis.** The most common location ➔ ovaries

* sometimes it may reach **distant sites** not related to the female genital tract e.g., umbilicus, lymph nodes, lungs, skin wounds, fingers, brain, etc.

 ➔ it’s common (**10% of women in reproductive years**).

 ➔ it’s benign. It’s not cancerous because it doesn’t have monoclonal growth [consist of two types of tissue].

**Symptoms:** **dysmenorrhea, pelvic pain, pelvic mass filled with blood (chocolate cyst)**

**Dysmenorrhea:** pain with menstruation or menstrual cramps

Why does it cause symptoms? Endometrial tissue doesn’t get implanted outside the uterus without doing anything. It continues its own function. Glands will work as if they are inside the uterus and will be affected by the hormonal changes happening during menstrual cycle (hormonal dependent). So, in every menstrual period (bleeding), the endometrial tissue will experience shedding, break down and bleeding.

Let’s assume that endometriosis occurred above the **ovaries** in Douglas’ pouch, with time and recurrent bleeding, it will be converted to mass / cyst filled with blood from more than one menstrual cycle which will be thick and brown in color ➔ **chocolate cyst.**

 ➔ Endometriosis contains **functionalis endometrium** (one of the endometrial layers), so undergoes **cyclic bleeding.**

**Pathogenesis:**

**Three theories:**

A. **Regurgitation theory (most accepted):** menstrual blood backflow through tubes and implantation. This blood contains remnants of glands and stroma that contain viable cells. It explains a high percentage of endometriosis cases especially those in the ovaries, Fallopian tubes, and peritoneal surfaces.

B. **Metaplastic theory:** endometrial differentiation of coelomic epithelium.

Coelomic epithelium = peritoneal cavity and surfaces covered by peritoneum.

Metaplasia = normal mature tissue starts transforming into another **benign** mature tissue because of environmental changes.
vascular or lymphatic dissemination theory: may explain extra-pelvic or intranodal implants because it may enter inside the blood (most likely veins) or lymphatic vessels perhaps due tears that occur during menstruation.

Conceivably, all pathways are valid in individual instances.

**Consequences**: inflammation --> fibrosis, sealing of tubal fimbriated ends and distortion of the shape and function of the ovaries → increase the risk of infertility

**Diagnosis**: (histopathological conformation) 2 of 3 features: endometrial glands, endometrial stroma, or hemosiderin pigment.

3- **Endometrial hyperplasia**

Prolonged or marked excess of **estrogen** (exogenous/endogenous) relative to progestin → exaggerated proliferation of endometrial glands → may progress to cancer.

Severity is based on architectural crowding and cytologic atypia, ranging from:

1- simple hyperplasia

2- complex hyperplasia

3- atypical hyperplasia (20% risk of cancer)

**Tumors of the Endometrium:**

4- benign endometrial polyps:

Sessile or pedunculated.

Endometrial dilated glands, with small muscular arteries and fibrotic stroma.

No risk of endometrial cancer.
5- endometrial carcinoma:

The most common cancer in female genital tract

50s and 60s.

Two clinical settings correlated with differences in histology:

A) **Perimenopausal women with estrogen excess → endometrioid carcinoma:**

Precancerous lesion is atypical endometrial hyperplasia.

Termed so because it is similar to normal endometrium (-oid) with much more glands.

Mutations in **DNA mismatch repair genes** and **PTEN**

**risk factors:** (same as the risk factors for endometrial hyperplasia)

- **obesity** [true risk factor because morbid obesity increases estrogen]
- **diabetes** and **hypertension** [mostly an association and not a true risk factor]
- **infertility**
- **prolonged estrogen replacement therapy** [exogenous]

**Estrogen-secreting ovarian tumors**

**Prognosis:** depends on stage. 5-year survival in stage 1= 90%; drops to 20% in stages 3 and 4

B) **Older women with endometrial atrophy → serous carcinoma**

No relation with endometrial hyperplasia (no relation with estrogen)

Not hormone-dependent

**Mutations in p53 tumor suppressor gene.**

Prognosis: depends on operative staging with peritoneal cytology. Generally worse than endometrioid carcinoma. (more aggressive, less common)
Myometrium pathology:

1- Adenomyosis:

Adeno = glands, myo = muscles. That indicates the presence of glands inside the muscles and of course it is abnormal because the myometrium is a muscular layer that shouldn’t contain glands.

As we said previously, the endometrium is the layer that contain glands, and in this disease these glands are leaving the endometrium invading the myometrium.

Adenomyosis: endometrial stroma, glands, or both embedded in myometrium.

These glands are derived from stratum basalis (one of the endometrial layers).

Glands derived from stratum basalis don’t normally undergo cyclical bleeding but their abnormal presence in the myometrium will cause irritation of the surrounding muscles + muscular hypertrophy => thickening of the uterine wall and enlargement of the uterus which will be globular in shape. => Symptoms: menorrhagia, dysmenorrhea (due to enlarged uterus, uterine contractions are exaggerated).

Menorrhagia: heavy or prolonged bleeding. Dysmenorrhea: pain with menstruation or menstrual cramps

Tumors of myometrium:

2- Leiomyoma: (Fibroids)

Leio = smooth, myo = muscles, oma = benign

Benign tumor of smooth muscle cells

Most common benign tumor in females (30 – 50% in reproductive life)

Estrogen-dependent; enlarge during reproductive years and shrink after menopause.

Circumscribed, firm gray-white masses with whorled cut surface.

 Might be single or multiple.

Location: intramural => inside the wall of the uterus, submucosal => under the endometrium or subserosal => under the serosa

May develop hemorrhage, cystic change, or calcification.
Clinically: (depend on the size and location of the tumor) **asymptomatic** or **symptomatic**; menorrhagia; a dragging sensation, anemia, etc.

Leiomyomas almost **never** transform into sarcomas, and the presence of multiple lesions **does not** increase the risk of malignancy.

3- **Leiomyosarcoma**:

Malignant counterpart of leiomyoma.

**Not** derived from preexisting leiomyomas.

**Macroscopically**: Hemorrhagic, necrotic, infiltrative borders.

**Diagnosis**: (under microscope) **coagulative necrosis**, **cytologic atypia**, and **mitotic activity**.

Recurrence common, and metastasize, 5-year survival rate 40%.