MECHANISMS OF HUMAN DISEASE: LABORATORY SESSION
PATHOLOGY OF THE FEMALE GENITAL TRACT I
March 12, 2009

Faculty Copy

GOALS:

1. **Describe the basic morphologic and pathophysiologic changes in various conditions of the female genital tract.**

2. **Correlate the structural changes in the organs with clinical manifestations of the diseases.**

OBJECTIVES:

1. **Review the normal gross and histologic anatomy of the uterus, ovary and fallopian tube.**

2. **Describe the morpholic changes of endometriosis.**

3. **Describe the morpholic changes of infectious diseases of the female genital tract.**

4. **Describe the morphologic characteristics of benign neoplasms of the uterus.**

5. **Describe the morphologic characteristics of malignant neoplasms of the uterus.**

CASE 1

Review of normal proliferative endometrium

CASE 2

CHIEF COMPLAINT:
"My husband and I have been trying to have a baby for the past five years."

HISTORY:
The patient is a 27-year-old woman who presents with the inability to conceive a child during the past five years. She and her husband have regular sexual relations (1-2 times per week) and very much desire to have children. She describes her marriage as “loving and warm”.

Menstrual history:

- Menarche occurred at age 13.
- Menstrual cycles have been fairly regular since age 17.
- Average cycle is 29-30 days, with menses being 5 days in duration.
- Menstrual flow has been consistent, requiring 3 - 4 pads initially and gradually tapering off.
- She has had premenstrual cramping and cramping pain the first day of menses since her teen years.
- For the past year or two she has experienced a more diffuse pain throughout her lower pelvis and more severe menstrual pain.
- Sh has nausea and low back pain during menstruation.

She notes abdominal pain at times during intercourse and when she moves her bowels. Intermittent vaginal spotting occurs but no vaginal discharge. At age 24 she was involved in an automobile accident which required abdominal surgery to stop bleeding from "my intestines."

PHYSICAL EXAMINATION:
Patient is a thin, well nourished woman. She is alert and in no distress.
Vital signs: Blood pressure 116/82, Apical heart rate 76/minute and regular, respiratory rate 12/minute, temperature 98.2°F.
Abdomen – normal bowel sounds, no masses or tenderness . 3.5 cm long parasagital scar in the left lower quadrant represents a healed surgical incision. Several small nodules are felt below the scar (patient says her scar "hurts when I menstruate").
Pelvic exam reveals normal external genitalia. Speculum exam reveals normal vaginal and cervical mucosa. The external os is small and round.
Bimanual exam reveals slight tender nodularity in cul-de-sac, recto-vaginal septum and uterosacral ligaments. The uterus is retroverted and of normal size. The right adnexa is tender but the left is not.
The rectal exam produces pain when the anterior wall is palpated.

1. What is the major clinical problem? (As far as the patient is concerned)

   Infertility

2. What are the additional major clinical complaints?

   Pelvic pain; painful menstruation

3. Develop a differential diagnosis for pelvic pain in a woman.

   - **Ruptured ovarian cyst.**
   - **Twisted ovarian cyst.**
   - **Ovarian cancer.**
   - **Ectopic pregnancy**
   - **Pelvic inflammatory disease.**
   - **Adenomyosis**
   - **Endometriosis**
   - **GI tract conditions such as irritable bowel syndrome and Crohn's disease.**
   - **Cystitis/urethritis.**
   - **Chronic pelvic pain without obvious pathology.**
   - **Premenstrual syndrome.**

4. What helps differentiate the cause of pelvic pain? Describe some clinical distinguishing features of causes of pelvic pain.

   Although all these conditions may result in pain, most are associated with specific pathologic changes in organs and can be differentiated with a good history, physical exam and diagnostic procedures such as ultrasound or laparoscopy.

A twisted ovarian cyst or ruptured cyst is generally sudden in onset, severe and located to one side of the midline. Ovarian cancer pain may be more vague in description but associated with an adnexal mass.

The pain of ectopic pregnancy may be severe and located in the lower quadrant of the abdomen. Hypotension and peritoneal signs may be present. Historically, the patient likely missed her last period. PID often produces bilateral pain and may be associated with adnexal masses (tenderness) and vaginal discharge.

The pain of adenomyosis and endometriosis often occurs around menstruation. The pain may be associated with clinical findings reflecting other organ involvement, e.g., dyschezia. Infertility often accompanies endometriosis nodules in the parametrial structures and adnexal masses can be palpated.

Diseases primarily affecting other organ systems cause pain but should have unique historical and physical findings. For example, irritable bowel syndrome may cause crampy abdominal pain, constipation and may have some psychologic component.

For completeness sake, two additional conditions are included, chronic pelvic pain without obvious pathology and premenstrual syndrome. The purpose is to indicate to the students that chronic pelvic pain without structural changes in female organs is real and sometimes debilitating condition.

5. What is this patient's likely diagnosis?

Endometriosis

6. Correlate the pathology with the clinical findings in this case.

Nodules palpated beneath the patient's healed surgical scar and tender nodularity palpated on bimanual exam and may all represent endometrial deposits.

On the virtual microsocopy section, endometrial tissue is present in a healed scar.

A histologic diagnosis of endometriosis can be made if 2 of the following 3 features are identified: endometrial glands, stroma, hemosiderin pigment.

CASE 3

CHIEF COMPLAINT: "I'm bleeding from my vagina."

HISTORY:
The patient is a 69 year-old woman who presents with intermittent vaginal bleeding of 9 months duration. Initially she noted spotting of bright red blood which seemed to occur several times each month. No particular activity precipitates the bleeding and she experiences no other symptoms. She states, "I just thought my period came back." She is twelve years post-menopause. She has never been pregnant.
After three months of spotting, she sought care from a physician who placed her on "estrogen pills to control my bleeding." He also gave her "iron pills".
The vaginal bleeding continued and contained small clots. The bleeding was always irregular
She sought a second opinion because the bleeding progressed.
She has been treated for diabetes mellitus, type 2 since age 52.

PHYSICAL EXAMINATION:
The patient is obese, alert and in no distress.
Vital signs: Blood pressure 146/90, pulse 90/minute, respiratory rate 18/minute, temperature 98° F.
Abdomen is soft and round. Organomegaly and masses are not palpable.
Pelvic exam reveals external genitalia consistent with the age of the patient. The vaginal introitus is narrowed and only admits two fingers.
A small speculum allows visualization of the cervix. The ectocervix is smooth. Blood is noted in the os.
Bimanual exam reveals a symmetrically enlarged, non-tender uterus. The adnexae are not palpable. A rectocele or cystocele are not present.

LAB TESTS:
Hemoglobin 9.8 grams/dl
Hematocrit 30%
MCV 79 fl

1. What is the major clinical problem? (As far as the patient is concerned)

   Vaginal bleeding (Abnormal uterine bleeding)

2. Develop a differential diagnosis for this problem.

   - **Endometrial polyp**
   - **Endometrial hyperplasia**
   - **Endometrial carcinoma**
   - **Leiomyoma (submucosal)**
   - **Ectopic pregnancy**
   - **Abnormalities of pregnancy: spontaneous abortion, gestational trophoblastic disease, third trimester hemorrhage (abruptio placenta, placenta previa)**
   - **Endocervical polyp**
   - **Cervical carcinoma**
   - **Dysfunctional uterine bleeding**

   Abnormal uterine bleeding is a common gynecologic problem. Many of these cases during the reproductive years represent a condition known as dysfunctional uterine bleeding. This condition will be discussed by the gynecologists but must be included in the differential diagnosis. There are generally no pathologic changes.

3. What factors may help differentiate the cause of bleeding?

Various historical and physical examination findings will help differentiate causes of uterine bleeding: age, reproductive years, obvious pregnancy, timing in cycle, associated findings such as pain, palpable mass or visible lesion on cervix, PAP smear findings.

4. What are the common causes of abnormal uterine bleeding in post-menopausal women?

- **Exogenous estrogens (30%)**
- **Atrophic endometritis/vaginitis (30%)**
- **Endometrial cancer (15%)**
- **Endometrial/ endocervical polyps (10%)**
- **Endometrial hyperplasia (5%)**

5. What condition must be ruled out in a postmenopausal woman? How?

Endometrial cancer; endometrial biopsy

6. A biopsy was peformed on this patient and is found on the virtual microscopy slide. What is your diagnosis? Compare to normal uterus/endometrium (case 1)

Endometrial carcinoma (Confluent glands lined by malignant stratified columnar epithelial cells without intervening stroma)

7. List the risk factors for this disease in this patient.
   - **Late menopause**
   - **Nulligravida**
   - **Diabetes**
   - **Obesity**
   - **Hypertension**

8. From this patient's history, explain what was wrong with her initial treatment. Why?

The initial physician placed the patient on hormone therapy without determining the exact cause of the uterine bleeding. Delay in diagnosis could lead to tumor invasion and metastases.

9. Define the following terms:

   A. Menorrhagia: **cyclic menstrual bleeding that is excessive in amount or duration.**

   B. Hypomenorrhea: **decreased menstrual flow; menstrual flow that is less than the norm of 3 to 7 days in duration**

   C. Hypermenorrhea: **increased menstrual flow; menstrual flow that is longer than the norm of 3 to 7 days in duration**

   D. Polymenorrhea: **regular bleedng that occurs at an interval less than 21 days**

E. Oligomenorrhea: **bleeding that occurs at an interval greater than 35 days**.

F. Metrorrhagia: **uterine bleeding between periods**.

G. Menometrorrhagia: **uterine bleeding that is irregular in frequency and excessive in amount**.

H. Postmenopausal bleeding: **bleeding occurring more than one year following menopause**.

CASE 4

CHIEF COMPLAINT: None

HISTORY: A 38-year-old woman undergoes a routine, annual gynecologic examination. Her gestational history is as follows: gravida 4, para 3 with one spontaneous abortion. She menstruates every 28-31 days for 2-4 days.

She experienced three or four episodes of metrorrhagia in the previous year, but no hypermenorrhea. She has a persistent, mild leukorrhea.

PHYSICAL EXAMINATION: The patient is a moderately obese woman who is alert and in no distress. Vital signs are as follows: blood pressure 136/84, apical heart rate 80/minute and regular, respiratory rate 14/minute, temperature 97.9°F. Examination of the abdomen: It is soft and slightly round; no organomegaly.
Pelvic examination reveals normal external genitalia. Speculum exam reveals normal vaginal and cervical mucosa. Bimanual exam reveals an asymmetrically enlarged uterus. The uterus is the size of a 2-3 month gestation and is freely movable. The uterus contains multiple nodules of varying size which are not tender. The adnexae are not palpable.

1. What is the clinical problem?

   Enlarged, nodular uterus

2. Describe the gross pathology.

   Uterus with sharply circumscrbied, discrete, round, firm gray-white tumors. They are usually found in the myometrium of the corpus. They can occur in the myometrium (intramural) just beneath the endometrium (submucosal), and beneath the serosa (submucosal).

3. Describe the histologic findings on the virtual microscopy slide.

   Whorled pattern of smooth muscle bundles

4. What is the diagnosis?

   Leiomyoma

5. What are potential symptoms of this condition?

   Abnormal bleeding (submucosal leiomyomas)
   Pain if blood supply to a leiomyoma is disrupted
   If large, leiomyomas can compress adjacent organs (such as the bladder resulting in urinary frequency)
   Impaired fertility

CASE 5 (no virtual micoscopy images)

HISTORY:

The patient is a 25 year-old woman who presents with bilateral lower abdominal pain of 3 days duration. The pain is sometimes sharp but more often dull; it is moderate in intensity and continuous. Movement accentuates the pain which remains localized to the right and left lower quadrants of the abdomen. In addition to the abdominal pain,

the patient has noticed a yellow-white vaginal discharge for two weeks. She also has mild dysuria but no urgency or frequency. The patient relates that she had similar health problems in the past for which she had been treated. Treatment did not require hospitalization. Her gestational history is gravida 0. She is sexually active and does not regularly use condoms. Her last menstrual period was 12 days ago.

PHYSICAL EXAMINATION:

The abdomen is scaphoid and soft. Palpation reveals mild point tenderness in the right and left lower quadrants but no rebound tenderness. No organomegaly. The bowel sounds are normoactive. Pelvic exam reveals normal external genitalia. The vaginal mucosa is hyperemic and covered by a thin, yellow-white exudate. The same exudate flows from the cervical os. Bimanual examination of the corpus/cervix uteri demonstrates normal size but adnexal pain on motion of the cervix. The adnexae are tender by palpation.

1. Develop a differential diagnosis.

Pelvic Inflammatory Disease
Cervicitis
Endometriosis
Ectopic Pregnancy
Urinary tract infection
Appendicitis

LABORATORY DATA:
WBC 13,700/mm3 (reference rage 4,500- 11,000/mm3).
Urine HCG - negative

Gram stain of the vaginal discharge reveals numerous polymorophuclear cells and intracellular, Gram negative diplococci.

2. What is the clinical diagnosis?

- **Pelvic Inflammatory Disease – an acute infection of the upper genital tract structures in women involving any or all of the uterus, fallopian tubes, and ovaries**
  Findings may include endometritis, salpingitis, oophoritis, peritonitis, perihepatitis and tubo-ovarian abscess.

3. What microorganism is the most likely etiologic agent in this case? What are other etiologic agents?

- ***Neisseria gonorrhoeae***
- ***Chlamydia trachomatis***
- **Genital *mycoplasma***
- **Enterobacteriaceae**
- **Mixed-polymicrobial**

4. Describe the pathology.

There is marked acute inflammation of the fallopian tube.
Grossly, the fimbriated ends of the fallopian tubes are distended with purulent material and adherent to adjacent structures. The serosa is hyperemic and covered with a fibrinous exudate. The inflammation extends to the ovaries. This acute inflammation is superimposed on chronic inflammatory changes.

5. What is the diagnosis?

Acute salpingitis

6. What are potential complications of this disease process?

Peritonitis
Bacteremia
Adhesions between pelvic organs and bowel resulting in bowel obstruction
Infertility – a consequence of chronic PID