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Endometriosis

Objectives:

- Describe theories of the pathogenesis of endometriosis.
- List the most common sites of endometriosis
- Describe the symptoms and physical examination findings in a patient with endometriosis.
- Describe the diagnosis and management options of endometriosis.

References : 433 team, kaplan lecture notes 2018 and kaplan video notes , Hacker.

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Introduction

Endometriosis : is benign condition in which endometrial glands and stroma are present outside the uterine cavity and walls .

OCCURRENCE :

1- Endometriosis affect 7-10% of female in their productive age.

2- The prevalence of endometriosis in infertile women is 38%.

3- 71-87% of women with chronic pelvic pain have endometriosis. It's a very important cause of chronic pelvic pain.

4- alots of study shows association between it and immunologic diseases prevalence is higher in those with immunologic diseases may due hidden mechanism or cytokines role.

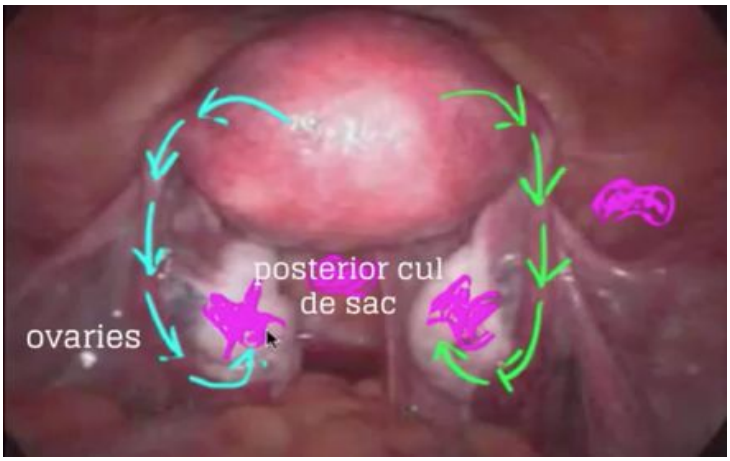
Pathogenesis:

The pathogenesis of endometriosis is not completely understood.

Theories:

1-**Retrograde flow** (Sampson theory) :

- Endometrial fragments of Endometrial tissue, which is normally shed at the time of menstruation transported through the fallopian tubes at the time of menstruation then implant and grow in various intra abdominal sites..



2-**Vascular-lymphatic dissemination** :

- Endometrial cells travel through vessels and lymph to distal places like: kidney, pleural cavity. Endometrial tissue has been found in pelvic lymphatics in up to 20% of patients with the disease.

3-**Coelomic metaplasia (also called mullerian metaplasia theory)** :

- Multipotent stem cells in peritoneal cavity that develop to functional endometrial tissue.
- This theory explains the presence of endometriosis in adolescence (before menarche).

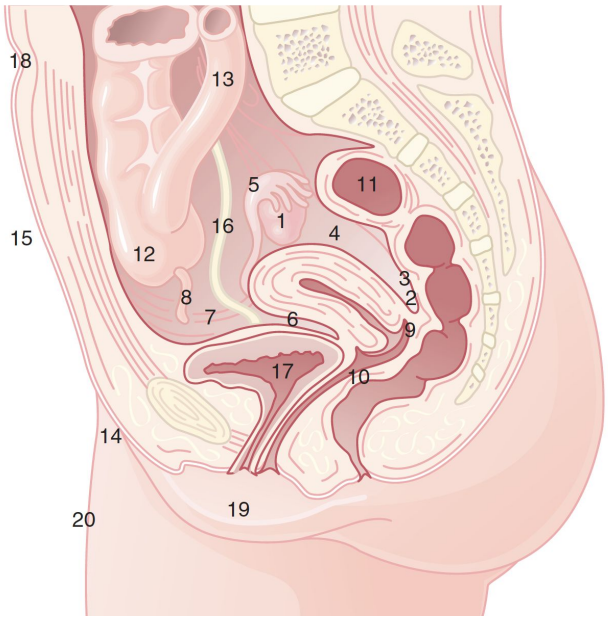
Sites of occurrence:

Common sites:

- **Ovaries** (**most common** site and its usually bilateral). Two of three women with endometriosis have ovarian involvement.
- **Pelvic peritoneum** :Posterior **cul-de-sac**[1] (uterosacral ligament and rectovaginal septum) Round ligament, fallopian tube. **2nd most common especially cul-de-sac**.

Less common sites:

- In rare cases can occur in brain, lung, upper ureter, sites of surgical scars The only site that endometriosis has not been found is the spleen.



Numbered by common site of occurrence.

Risk factor:

- Female in their productive age
- **First degree family history.**

Complication:

- cause inflammatory reaction which lead to the formation of (adhesion + scarring)[2].
- Not malignant but associated with higher risk of ovarian carcinoma mechanism unclear

Gross appearance:

1- clear white lesions as result from scarring

2- powder burn lesions

3- dark \ red blue domes

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[1] **Cul-de-sac** can can be palpated or tender in DRE main Sx in this place Dyspareunia and may pain with bowel movement due to adhesion with rectal side.

[2] The implants proliferate under estrogenic stimulation and slough when support from estrogen and progesterone is removed with involution of the corpus luteum. The sloughed material induces a profound inflammatory response, resulting in pain immediately and fibrosis in the longer term.

Sign and symptoms

Symptoms:

cyclical pelvic pain 1 to 2 weeks before menstruation and peaks 1 to 2 days before menstruation pain end with menstruation also abnormal bleeding is common.
There is no clear relationship between the size or stage of endometriosis and the frequency and severity of pain.
Pain is usually dull ache not colicky
Symptoms triad:
1- **Dysmenorrhea.**
2- **Dyspareunia**.[3]
3- **Dyschezia**.
4- Infertility (The association between mild to moderate endometriosis and infertility is not clear. When more advanced stages of endometriosis distort the pelvic structures, the role of endometriosis in infertility is more predictable)
5- Hematochezia. Less common.

Signs:

Sometimes there is no signs Because either small or not clear. but we may see:
1- fixed non-Mobile uterus. Secondary to adhesions.
2- **ovarian endometriosis (chocolate cyst)** tender but not palpable.
3-uterosacral nodularity (classic sign).

In PEx:

Pelvic tenderness is common. A fixed, retroverted uterus is often caused by cul-de-sac adhesions. Uterosacral ligament nodularity is characteristic. Enlarged adnexa may be found if an endometrioma is present.
In more than half the patients who are noted to develop endometriosis during childhood and adolescence, varying degrees of genital tract obstruction may be found .

Diagnosis

- The definitive diagnosis is generally made on the basis of the characteristic **gross** and **histologic** findings obtained at laparoscopy or laparotomy.
Finding: 2 out of 4

1- endometrial stroma
2- endometrial gland
3- endometrial epithelium
4- hemosiderin-laden macrophages.

laparoscopy or laparotomy identification of endometriotic nodules or endometriomas is the definitive diagnosis.

[3] occurs mainly 1- when the cul-de-sac, uterosacral ligaments, and portions of the posterior vaginal fornix are involved. 2- from uterine immobility caused by significant internal scarring caused by endometriosis.

Management goals:

1- decrease pelvic pain.
2- decrease surgical intervention
3- preserve fertility.

Medical therapy:

ETHER **PREGNANCY** IF WANTED OR **PSEUDOPREGNANCY** OR **PSEUDOMENOPAUSE**

PSEUDOPREGNANCY (preventing Progesterone withdrawal)
1- **First line therapy:** oral contraceptive. Easy to use and inhibit functional endometriosis.
2- Progesterone therapy: implants, oral or injection, inhibit GnRh which suppress endometriosis.

pseudomenopause
3- GnRh agonist : down regulate pituitary gland. can cause menopause like symptoms. It can't be used as a long term therapy in young patients bc of low estrogen.
4-Danazol[4]: suppresses LH\FSH secretion. menopause like symptoms. it have androgenic properties. so, women may have hirsutism, acne and breast atrophy.

Surgical therapy:

Large endometriomas (>3 cm) are usually amenable only to surgical resection
1- Conservative (Fertility-preserving treatment):

- Excision.
- Cauterization or ablation of vestal endometriosis.
- Lysis of adhesion.

2- Extirpative or aggressive: if medical and conservative is **not feasible or severe pain** and the patient is **not desire future fertility.**

- Hysterectomy and Bilateral salpingo-oophorectomy

Follow up :

As we said before it is Not malignant but associated with higher risk of ovarian carcinoma by mechanism which is not clear.

[4] Breast atrophy and hirsutism

BOX 25-1

OPTIONS FOR TREATING ENDOMETRIOSIS

Watchful Waiting

There is a limited role for expectant management without any medical or surgical intervention. Women who are attempting pregnancy with little or no symptoms may consider this option. In addition, women who are approaching menopause and have minimal symptoms may choose to wait for the cessation of cyclic ovarian function, at which stage endometriosis is usually far less active.

Medical Treatment

First-line therapy: Nonsteroidal antiinflammatory drugs, low-dose oral contraceptives, or progestins (e.g., medroxyprogesterone acetate). ***Note:*** This treatment should be given an adequate trial of 3 to 6 months before initiating second-line therapy.

Second-line therapy: Higher-dose progestins (e.g., medroxyprogesterone acetate or megestrol acetate [Megace]), danazol, or gonadotropin-releasing hormone analogues appear to be equally effective. ***Note:*** Laparoscopic confirmation of the diagnosis of endometriosis before initiation of second-line treatment is usually performed, but it is not required according to some guidelines. Biopsy of visualized lesions, however, is the only definitive way to diagnose endometriosis.

Surgical Treatment

Most definitive therapy: Total abdominal hysterectomy with bilateral salpingo-oopherectomy with destruction and/or removal of all peritoneal endometriotic implants and adhesions. ***Note:*** There is always a risk of recurrence, even with "definitive" treatment.

Fertility-preserving treatment: Laparoscopic or open surgery (laparotomy) with destruction and/or removal of all peritoneal endometriotic implants and adhesions. ***Note:*** Removal of endometriomas may decrease fertility potential, especially in women with already-reduced ovarian reserve (see Chapter 34). Large endometriomas >3 cm in diameter should be removed surgically. Preoperative suppressive treatment for 3 to 6 months may improve surgical success.

CLINICAL KEYS FOR THIS CHAPTER

- *Endometriosis* is defined as the presence of endometrial glands and stroma in extrauterine locations. An accurate prevalence for endometriosis is not known, but it is estimated that about 10% of women of reproductive age have the disease. Most women are without symptoms, but some have severe pain often manifested by dysmenorrhea, dyspareunia, and, less often, dyschezia. Infertility is often the initial sign of endometriosis.
- Retrograde menstruation, metaplastic transformation of peritoneal mesothelium, and lymphatic spread are the three most often cited hypotheses for the origins and locations of endometriosis. An immunologic factor is presumed to explain why some women who have risk factors similar to those that are affected do not develop the disease. Genetic predisposition is highly likely, based on polygenetic, multifactorial inheritance.
- The staging of endometriosis is based upon the location, extent, and appearance of the lesions. Implants of glands and stroma may be dark red, brown, bluish gray, or even white. The lesions are frequently surrounded by fibrosis, which results in puckering. Ovarian cysts filled with hemosiderin-laden, "chocolate"-colored fluid may form metaplastic endometriomas.
- The amount of endometriosis does not always correlate with the severity of symptoms. Women with minimal or no symptoms may be managed expectantly. Medical treatments consist of initial trials of nonsteroidal antiinflammatory drugs (NSAIDs) and low-dose progestins, including oral contraceptives (OCs). More advanced medical therapy includes the androgenic danazol and gonadotropin-releasing hormone (GnRH) analogues. When fertility is desired but is not occurring spontaneously and medical therapy has failed, conservative laparoscopic surgery to reduce the amount of endometriosis and reactive adhesions is indicated. More definitive extirpative surgery involves removal of all endometriosis and adhesions, along with the uterus and adnexal tissues. One or both ovaries may be preserved if they are completely free of endometriosis.
- Adenomyosis is the extension of endometrial glands and stroma into the uterine musculature more than 2.5 mm beneath the basalis layer. The uterus is homogeneously enlarged. Although many women with adenomyosis are without symptoms, some have severe dysmenorrhea, and the disorder may adversely affect fertility. Medical therapy with NSAIDs is indicated initially for the pain and uterine bleeding. Endometrial ablation may be performed for heavy bleeding, and hysterectomy is sometimes indicated when more conservative treatment has failed.

Case

A 28-year-old woman G0P0 woman is seen because of the inability to conceive for the past two years. She has never used oral contraceptives and she and her husband have not used any form of birth control for over two years. Her menarche occurred at the age of 12 and her menses became very painful in her late teens. She has had chronic cyclical pelvic pain, which has progressively worsened over the years.

This pain is incapacitating at times. She describes the location of the pain to be in the lower abdomen and pelvis that radiates into the lower back. In addition to the pain, her menstrual periods have become increasingly frequent and heavy. She experiences deep dyspareunia that began with her first sexual partner and has continued with her husband. She denies any non-cyclical vaginal bleeding, discharge and weight loss. She states that her 22-year-old younger sister has always had very painful menses.

On physical examination the patient looks her age. She is 138 lbs and is 5'6". Her BP is 110/76 mm Hg with a heart rate of 85 bpm. Her head and neck examination is negative. Cardiac and respiratory systems are also normal. Examination of the abdomen reveals that it is flat with no scars. On palpation she has generalized tenderness of the lower abdomen. There are no signs suggesting evidence of a surgical abdomen and she has no costovertebral angle tenderness. The pelvic exam showed a fixed, retroverted uterus. The uterosacral ligaments on both sides are nodular. A 5 cm right adnexal mass is palpated and tender.

Transvaginal ultrasound of the pelvis showed a 5.5 cm cystic mass with low-level echoes in the right ovary. The left ovary was reported as normal. The uterus is retroverted and is of normal size and contour. There is no evidence of fibroids and the endometrial lining is normal.

1. What symptoms does this patient present with that would lead to a suspicion of endometriosis?

Infertility
Dysmenorrhea
Cyclic lower abdominal and pelvic radiate to lower back
Dyspareunia
Possible family history
Key Learning Point: Endometriosis can manifest in many ways. Patients may have no symptoms to significant symptoms.

2. Describe the physical findings for this patient that helps confirm a possible diagnosis of endometriosis?

- Tender nodular uterosacral ligaments on pelvic exam.
- Fixed, retroflexed uterus.
- Palpable and tender right adnexal mass

3. After discussing the possibility of endometriosis, the patient asks, "How did I get this disease?" How do you answer the patient?

1. Attachment and implantation of endometrial glands and stroma to peritoneal tissue from retrograde menstrual flow.
2. Hematogenous and lymphatic spread.
3. stem cells in peritoneal cavity that develop to functional endometrial tissue (celiomic).

4. What alternative diagnoses would you consider in this patient (DDx)?

- chronic pelvic pain: chronic pelvic inflammatory disease, adhesions, gastrointestinal conditions, interstitial cystitis and benign or malignant ovarian neoplasm.
- Dysmenorrhea: causes of primary and secondary dysmenorrhea
- Dyspareunia: chronic pelvic inflammatory disease, or ovarian cysts.

5. How is the diagnosis of endometriosis made?

- **First steps:** History and physical examination.
- Direct visualization is needed for establishing a diagnosis.
- **Definitive diagnosis**: tissue biopsy.
- Pelvic sonogram cannot make diagnosis, but can exclude other conditions.

6. What protocols are used to stage endometriosis?

1- **The revised American Fertility Society (AFS)** staging system is generally used to stage endometriosis in the infer.le pa.ent. In the AFS system, points are assigned for size and depth of implants and for the severity of adhesions in various loca.ons. Stages I through IV are assigned on the basis of points. Management of endometriosis can be guided by the stage of disease and the desire for fertility.

1- **The American Society of Reproductive Medicine (ASRM)** protocol correlates fertility potential with a quantified stage of disease. The staging includes the color of lesions, the percentage of surface involved and a detailed descrip.on of endometriomas.

7. What are the treatment options for a patient with a diagnosis of endometriosis?

- **Depends** on presenting symptoms and severity, location and severity, desire for future childbearing, age, and possible gastrointestinal or urinary tract involvement.
- Conservative management may be considered for patients with minimal symptoms and disease and/or patients who are trying to conceive.
- Medical therapy includes:
    1. NSAIDs.
    2. combined estrogen and progestin contraceptives.
    3. progestins alone.
    4. danazol.
    5. gonadotropin- releasing hormone (GnRH).

- Surgical management
    1. Conservative options such as removal of endometriomas and destruction of endometriotic implants
    2. definitive approaches such as Hysterectomy and Bilateral salpingo-oophorectomy