ENDOMETRIOSIS PRESENTATION & PATHOGENESIS

FLAME 179

NGUYEN/SISTO 11.25.17

LEARNING OBJECTIVES

- To define endometriosis
- To describe the pathogenesis of endometriosis
- To list risk factors for endometriosis
- To describe the presentation and physiology of endometriosis
- Prerequisites:
  - None
- Closely related topics:
  - FLAME 180: MEDICAL MANAGEMENT OF ENDOMETRIOSIS
  - FLAME 181: ENDOMETRIOSIS IN PREGNANCY

DEFINITIONS

- Endometriosis: is a chronic disease marked by the presence of endometrial tissue (*glands and stroma*) outside the endometrial cavity
  - Able to invade anywhere in the body, but most common sites include the ovary and pelvic peritoneum
- Endometrioma: endometriosis in the ovary that appears as a cystic collection

PREVALENCE

- Almost exclusively in women of reproductive age
- Prevalence: 6-10%[1]
- Higher in certain populations:
  - Up to 50% in women w/ infertility
  - Up to 70% in women w/ pelvic pain

Yates J, Endometriosis and Infertility: Experts answers to 6 questions to help pinpoint the best route to pregnancy, OBG Management, June 2015, Vol 27, No 6, 30-35.

PATHOGENESIS
MULTIFACTORIAL

- Halban theory: ectopic growth of endometrial tissue transported via lymphatic drainage
  - Lung (catameric hemoptysis), Brain (catameric seizures)
- Meyer theory: multi-potential cells in peritoneal tissue undergo metaplastic transformation into functional endometrial tissue
- Sampson theory: endometrial tissue transported through fallopian tubes during retrograde menstruation
    - Caveat! 90% of women have retrograde menstruation, but 90% of all women do **NOT** have endometriosis!
- Current prevailing theory suggests that women who develop endometriosis may have an altered immune system that is less likely to recognize and attack ectopic endometrial implants

PATHOGENESIS

MOLECULAR ROLES OF SEX HORMONES

- Estrogen:
  - Activates cell cycle
  - Epithelial & stromal mitogenesis
  - Angiogenesis
    - Endometriosis surgeries can be sticky & bloody!
- Progesterone:
  - Epithelial secretion
  - Stromal edema & decidualization
  - Preparation for apoptosis

Progesterone is needed for apoptosis.
Progesterone resistance in endometriotic implants leads to proliferation.

Slide adapted from Dr. Joy Brotheron, Endometriosis

RISK FACTORS[1]

- Nulliparity
- Low BMI
- Prolonged estrogen exposure: early menarche, late menopause, short cycle, HMB
- Familial aggregation
  - 7X increased risk if 1st degree relative w/ endo
- Obstruction of menstrual flow (i.e. some Müllerian anomalies)

Vercellini P, Viganò P, Somigliana E, Fedele L. Endometriosis: pathogenesis and treatment. Nat Rev Endocrinol. 2014 May;10(5):261-75. doi: 10.1038/nrendo.2013.255. Epub 2013 Dec 24.

PROTECTIVE FACTORS[1]

- Multiparity
- Late menarche
- Extended intervals of lactation
- Race:
  - Lower prevalence in African American & Hispanic women

Schenken. Endometriosis: Pathogenesis, clinical features, and diagnosis. Uptodate, Sep 2017.

SYMPTOMS / SEQUELAE

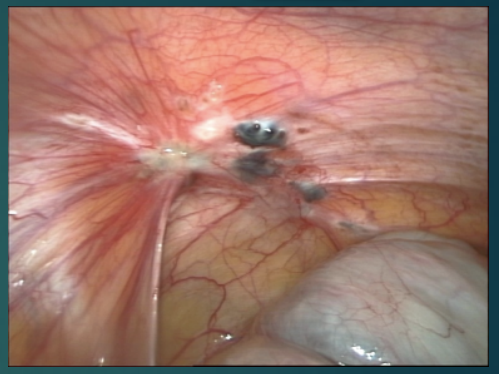
- Mechanism: implants disrupt normal tissue via formation of adhesions and fibrosis → inflammation
- [1] Dysmenorrhea
  - Common (~80% in symptomatic pts)
  - Occurs 1-2 wks before menses
  - Peaks 1-2 days onset of menses
  - Can last for many days
- [2] Deep dyspareunia (30%)
  - Often assoc. w/peritoneal or uterosacral involvement
- [3] Abnormal bleeding
- [4] Bowel and bladder symptoms
  - Dyschezia
- [5] Urinary complaints
- [6] Subfertility, which can lead to…
  - Infertility: 2/2 buildup of dense adhesions which distort pelvic architecture, interfere with tubal mobility, impair oocyte release, and cause tubal obstruction
- Note: the severity of symptoms does not necessarily correlate with severity of disease

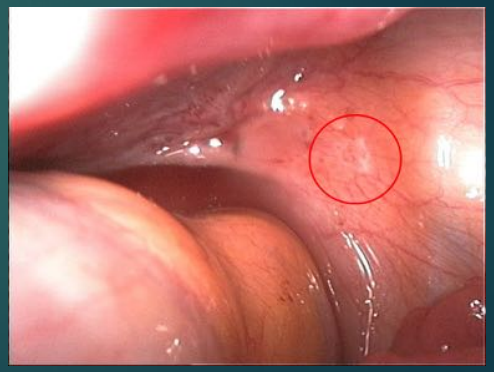
CLINICAL PRESENTATION

- Pain often elicited by movement of the uterus
- Physical examination:
  - May be subtle or non-existent
  - Tender uterus during early menses
  - If disseminated endometriosis…
    - Rectovaginal examination may reveal uterosacral nodularity and tenderness
  - If there is ovarian involvement…
    - Bimanual examination or pelvic U/S may reveal a tender, fixed adnexal mass

VISUALIZATION DURING SURGERY

- Definitively diagnosed via direct visualization
  - Via laparoscopy or laparotomy
- May appear as:
  - Rust-colored to dark brown powder burns
  - Raised, blue-colored raspberry or mulberry lesions
  - Large cysts filled with thick, dark, old blood and debris (known as endometriomas or chocolate cysts)
- Older lesions may appear white/normal, may be difficult to visualize
- Occult endometriosis
  - "Normal appearing" peritoneum can actually contain endometriosis.





STAGING OF ENDOMETRIOSIS

- Stage I: Minimal disease
  - Isolated implants; no significant adhesions
- Stage II: Mild disease
  - Superficial implants <5 cm in aggregate, scattered on peritoneum and ovaries; no significant adhesions
- Stage III: Moderate disease
  - Multiple implants, superficial and deeply invasive; Peritubal and periovarian adhesions may be present
- Stage IV: Severe disease
  - Multiple superficial and deep implants
  - Includes large ovarian endometriomas

Stage of disease does NOT correlate with severity of symptoms.
Advanced stages more likely to need ART for patients with infertility.

Revised American Society for Reproductive Medicine classification of endometriosis: 1996.

REFERENCES

- Callahan, T., Caughey, A. 2013. Blueprints Obstetrics and Gynecology, 6th ed. Baltimore (MD): Lippincott Williams & Wilkins. Chapter 15, Endometriosis and Adenomyosis; p. 204-208.
- Schenken, RS, Barbieri, RL, Eckler, KE. Resnik, R., Silver, RM. Endometriosis: Pathogenesis, clinical features, and diagnosis. Post TW (Ed), UpToDate, Waltham, MA. Accessed: October 24, 2016.
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