Update on Endometriosis

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Disclosures

I have no disclosures relevant to this presentation.

Overview

Review objectives

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Basics of endometriosis

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Differential diagnosis, comorbidities, long-term risks

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Role of advanced practitioner in diagnosing/treating endometriosis

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New directions in endometriosis treatment

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New directions in endometriosis treatment

I will try to include pearls of clinical practice tangentially related to the talk when appropriate.

Learning objectives

Understand basic pathophysiology, prevalence, and clinical presentation of endometriosis

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Apply a basic algorithm for medically treating endometriosis, and have knowledge of some surgical options for management.

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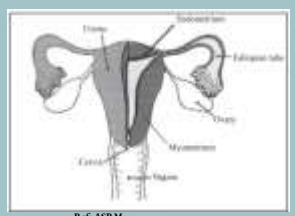
Apply a basic algorithm for medically treating endometriosis, and have knowledge of some surgical options for management.

Understand comorbid medical, psychiatric conditions and long-term cancer risk associated with endometriosis.

Brief pelvic anatomy overview



Ref: ASRM

CLINICAL CASE

25 year old G0P0 history of pelvic pain, very painful periods for five years.
Her periods keep her home for 3 days per month. Ibuprofen relieves some of the discomfort (diminishes pain from 9/10 to 7/10); heat packs also She also has occasional discomfort with urination. Pain with intercourse, especially with deeper penetration, in certain positions. Occasional painful bowel movements, no bleeding. Menarche age 13. Her periods are otherwise every 28-32 days, last 5-7 days. No intermenstrual bleeding. Sexually active with boyfriend, they use condoms.
PMH: depression and anxiety, currently on lexapro; sees a therapist.
PSH: history of laparoscopic appendectomy, age 16.
Meds: Ibuprofen as needed, lexapro
Allergies: none

CLINICAL CASE

Social: lives with roommate. IT manager for large healthcare practice. No tobacco. Social alcohol (3 drinks/week). Occasional marijuana on particularly painful days of month.
Review of systems: otherwise within normal limits.
Physical examination:
VS: normal blood pressure, pulse, temperature
Gen: no acute distress, pleasant and conversant
CV and Pulm: unremarkable
Abdomen: Non-distended abdomen, no rebound or guarding. Mild suprapubic tenderness to palpation.

CLINICAL CASE

Pelvic: normal external genitalia, normal hair distribution. Non-tender vulva/vestibule (always important to evaluate for vulvodynia!). Levators with normal tone. Vagina normal mucosa, physiological discharge. Cervix normal without friability, normal transformation zone and without lesions. On palpation, there is mild nodularity in the L uterosacral ligament. No cervical motion tenderness. Uterus fixed, mildly tender to palpation, retroverted. Rectovaginal exam confirms findings.

CLINICAL CASE

What laboratory evaluation would you perform?
What imaging studies might you consider?

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What imaging studies might you consider?

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What laboratory evaluation would you perform? Urine HCG, Wet mount, GC/CT nucleic acid amplification, Urine C&S and UA, CBC
What imaging studies might you consider? **Complete pelvic ultrasound (abdominal and transvaginal)**

CLINICAL CASE

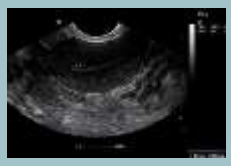
What is your differential diagnosis?

CLINICAL CASE

What is your differential diagnosis?

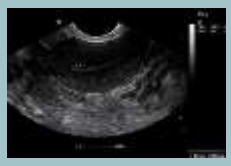
- Endometriosis
- Dysmenorrhea
- Adenomyosis
- Painful bladder syndrome
- Irritable bowel syndrome
- Vaginitis
- Cervicitis
- Inflammatory bowel disease
- Fibromyalgia
- Pelvic inflammatory disease
- Ovarian torsion

Ultrasound



What about this image is inconsistent with my exam findings?

Ultrasound

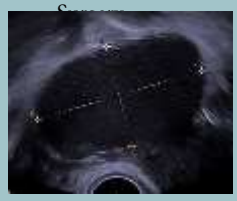


What about this image is inconsistent with my exam findings? **This uterus is ANTEverted**.

Endometriosis - overview

- Chronic condition
- Estrogen-dependent, chronic pain, dysmenorrhea
- 6-10% prevalence in women of reproductive age
- In 38% of women with infertility
- In up to 90% of women with chronic pelvic pain
- In 2002 dollars, estimated annual cost of $22B

Ultrasound



Source: wikipedia

Endometriosis - pathophysiology

- Complex gene expression/predisposition interaction
- Local prostaglandins, local estrogen
- Progesterone resistance?
- Retrograde menses, gland implantation;
- Hematological, lymphatic transport
- Coelomic metaplasia
- A little of everything

Endometriosis - risk factors

- Early menarche
- Shorter cycles
- Prolonged and heavy cycles

Endometriosis - mitigating factors

- Increased parity
- Increased duration of lactation
- Regular exercise >4 hrs/week

→ More children, more breastfeeding, more exercise

What causes the pain?

- Inflammatory factors (intraperitoneal cytokines)
- Adhesion formation
- Cystic structures
- Nerve growth factors within lesions
  - This is especially true for rectovaginal fibers

Ref: ASRM

Comorbid conditions

- Irritable bowel syndrome
- Painful bladder syndrome
- Chronic PID, endometritis
- Chronic abdominal pain/back pain, not otherwise specified
- History of sexual and physical abuse

Comorbid conditions, continued

- Immunological conditions: rheumatoid arthritis, systemic lupus erythematosus, hypo- and hyperthyroidism, multiple sclerosis.
- Stress incontinence
- Ovarian cysts
- Diabetes, hypertension, hyperlipidemia
- Depression
- Fibromyalgia

Endometriosis and pain

- Degree of disease does NOT correspond to amount of pain
- Brain chemistry is altered - aberrant neurochemistry implicated in other pain syndromes
- Greater brain activity in regions associated with depression, anxiety
- Greater activity in regions correlated with perception of pain

Endometriosis and pain

"Are you saying this pain is *all in my head*?"

How do we explain and rationalize this with and to our patients?

Cancer risk

- Baseline population risk of ovarian cancer is 1.3%
- Study of Swedish patients demonstrates increased risk
- Overall relative risk of ovarian cancer 1.3-1.9-fold
  - Serous cancer only mildly increast (1.4-fold)
  - Clear cell = 5-fold
  - Endometrioid = 3-fold
- Overall risk is 2 additional cases per 1,000 patients in a 10 year period

Advanced practitioner - diagnosing endometriosis

- Common clinical manifestations of endometriosis:
  - Dysmenorrhea (OR = 8.1)
  - Chronic pelvic pain
  - Dyspareunia (OR = 6)
  - Menorrhagia (OR =4)
  - Uterosacral ligament nodularity
  - Adnexal mass
  - Abdominopelvic pain (OR = 5.2)
  - diarrhea/constipation, tenesmus, dyschezia
  - **Painful defecation in menses and severe dyspareunia most predictable symptoms of deeply infiltrating endometriosis.**

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- **Ultrasound, MRI, CT can help only in diagnosing endometriomas or other cystic lesions or co-morbid pelvic pathology such as adenomyosis**

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- Definitive diagnosis = SURGERY, HISTOLOGY
- Even visual inspection at surgery can result in false positives
- Ultrasound, MRI, CT can help only in diagnosing endometriomas or other cystic lesions or co-morbid pelvic pathology such as adenomyosis
- **In the absence of surgery, the presumptive diagnosis of the advanced practitioner must be clinical and based on index of suspicion.**

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Advanced practitioner - diagnosing endometriosis

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- **Entertain the diagnosis, and initiate preliminary treatment, and refer the patient to a gynecologist for evaluation and management.**

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- Consider dysmenorrhea more than cramps managed by NSAIDs alone.
- If a woman does not get relief with NSAIDs (e.g. Ibuprofen), her dysmenorrhea is NOT NORMAL
- Entertain the diagnosis, and initiate preliminary treatment, and refer the patient to a gynecologist for evaluation and management.
- **Avoid narcotic pain medication!**

Advanced practitioner - initial treatment of endometriosis

- **NSAIDs have not been proven effective in treatment, although they are a reasonable component of therapy**

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- **Hormonal suppression is the hallmark:**
  - **Combined estrogen/progesterone birth control pills - consider CONTINUOUS**
    - **Progesterone component - consider levonorgestrel**

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  - **Progesterone only birth control (high dose)**
    - **Norethindrone 5 mg daily**
    - **Depo-medroxyprogesterone acetate**
    - **Etonogestrel subcutaneous implant**

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    - **Levonorgestrel IUD shown to decrease dysmenorrhea and pelvic pain**

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  - **GnRH agonist therapy - leuprolide acetate**
    - **Long-term leuprolide acetate associated with antiestrogenic effects (lower bone mineral density, unfavorable lipid profile changes, menopausal symptoms).**

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  - **Aromatase inhibitors - Danazol**

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  - GnRH agonist therapy - leuprolide acetate (IM injection)
  - Aromatase inhibitors - Danazol
  - **Surgery often necessary to treat and assess the physical burden of disease.**

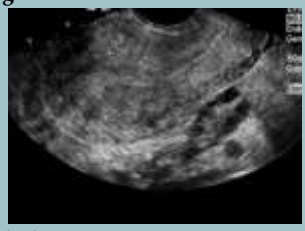
Advanced practitioner - initial treatment of endometriosis

- If patient has questions about possible surgery:
  - Diagnostic - look, +/- tissue sample
  - Ablate tissue (burn and destroy)
  - Excise tissue (can be very extensive surgery)
  - Remove the cause of problem (hysterectomy, BSO, resection of all affected tissue)
  - Cystectomy to remove endometriomas
  - May do some of a fertility evaluation
  - Also survey abdomen for other causes of pain (look at liver, appendix), look for scar tissue.

New therapeutic directions

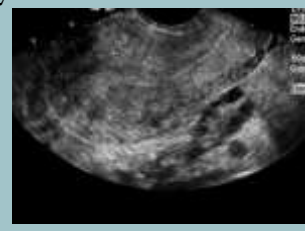
Elagolix - oral GnRH **ANTAGONIST**
Studied in Elaris Endometriosis trials I and II (Elaris EM-I, II)
Reductions of dysmenorrhea 50-70% (compared with ~20-25%)
Similar anti-estrogenic effects
Not on KP formulary, should not be prescribed as first-line in any case :)

Don't forget about the close cousin - Adenomyosis



Glandular tissue within the myometrium
A common pathology found when hysterectomy performed for pelvic pain.
Still yet to be consensus about optimal diagnostic criteria for adenomyosis

Adenomyosis



The good news: treatment is largely similar - hormonal suppression, local and/or systemic
Hysterectomy often the treatment for patients after completion of childbearing.

CLINICAL CASE

25 year old G0P0 history of pelvic pain, very painful periods for five years.
Presumptive diagnosis of endometriosis
Could also be:
- Primary dysmenorrhea - why or why not?
- Adenomyosis - would this change treatment management?

Treatment plan
Referral - general gynecologist.
Plan for follow up - how should you manage this patient if she has lapses in care/coverage and then returns for care? (this gets at how disease can progress, how to manage and encourage long-term care; can restart methods of birth control provided you know what their reproductive life plans are, e.g. if patient is going to initiate IVF and you give depo that could be counterproductive).

ENDOMETRIOSIS FOLLOW UP

When in doubt, reach out
- Contact primary gynecologist managing the patient
- Hold off on significant medication changes unless done in conjunction with specialist (particularly in patients which may be headed to surgery)
- Avoid narcotics (may be appropriate for acute exacerbations of pain in order to avoid the ED)
- Treat comorbid conditions - nausea, diarrhea, constipation, urinary complaints; refer to physical therapy if chronic musculoskeletal pains.

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