Pain in the... PELVIS

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Educational Objectives

• To be familiar of the most common causes of female pelvic pain
• To understand the etiology of pelvic pain and how it progresses
• To diagnose the most common cause of pelvic pain: Endometriosis
• To know the best evidence-based treatment options and management for patients with documented Endometriosis
Possible causes of pelvic pain:

- Ectopic pregnancy
- Miscarriage
- Pelvic Inflammatory Disease
- Ovulation
- Menstrual cramps
- Ovarian cysts
- Fibroids
- **Endometriosis**
- Uterine cancer
- Cervical cancer

Determining cause of Pelvic Pain

- History and physical
- Blood and urine tests including Beta HCG
- Vaginal cultures
- Radiographic studies: abdominal and pelvic x-rays, **ULTRASOUND**, CT Scan of abdomen and pelvis
- Surgery
Description of Endometriosis

• Endometriosis is characterized by the presence of endometrial glands and stroma located outside of the uterus. Endometriotic tissue is most commonly found in the pelvis, although extrapelvic lesions also have been reported.
• There are three distinct forms of pelvic endometriotic lesions:
  — Endometriomas: ovarian endometriotic cysts (most common)
  — Peritoneal endometriosis: superficial endometriotic implants on the peritoneum described as classical (black powder-burn lesions) or nonclassical (red or white lesions)
  — Rectovaginal endometriotic nodules: masses of endometriotic tissue with adipose and fibromuscular tissue located between the vagina and rectum
• Adenomyosis or ‘endometriosis of the uterus’ is endometrial tissue within the muscle of the uterus and is not commonly included in a discussion of endometriosis.

Epidemiology

• Pelvic endometriosis has a prevalence of 6% to 10% in women of reproductive age.
• Approximately 35% to 50% of women presenting with pelvic pain and/or infertility are found to have endometriosis and 71% to 87% of women with chronic pelvic pain.
• Endometriosis accounts for up to 70% of adolescents undergoing laparoscopy for chronic pelvic pain unresponsive to oral contraceptives and nonsteroidal anti-inflammatory drugs (NSAIDs).
• In the U.S., endometriosis is the third most common inpatient gynecologic diagnosis among women aged 15 to 44 years.
Causes

No single theory explains all types and sites of endometriosis, but each of the following explains some findings in some patients:

• Retrograde menstruation and implantation theory (Sampson’s theory): reflux of endometrial tissue implants on the surfaces of the ovaries and peritoneum in women with a disordered immune system; supported by the association of obstructive anomalies of the female reproductive tract that enhance retrograde flow and endometriosis in adolescents
• Coelomic metaplasia (Meyer’s theory) and the induction theory: the endometrium, the ovarian surface, and the peritoneum share a common embryologic precursor, the coelomic cell; at puberty, increasing estrogen production induces the mature peritoneal or ovarian surface cells to undergo metaplasia into endometrial cells
• Vascular and lymphatic metastasis (Halban’s theory): viable endometrial cells spread via vascular or lymphatic channels, resulting in distant endometriosis; explains the occurrence of rare endometriotic lesions found in extrapelvic sites, such as the brain and lungs, but not the more common pelvic lesions occurring in gravity-dependent locations
• Endometrial disease theory: deep, infiltrating endometriosis and endometriotic cysts of the ovary are pathologic lesions resulting from somatic mutations of some cells

Risk Factors

• Family history: women with a mother or sister with endometriosis have a 5% to 8% risk of also developing the condition (compared to 1% in the general population); patients with a familial predisposition are also more likely to have severe endometriosis
• History of exposure to diethylstilbestrol in utero (1938-1971)
• Low birth weight and/or multiple gestation
Symptoms

• Some women with endometriosis have no symptoms. The most common symptom is pain in the pelvic area, especially with periods.
• **Pain** — Pelvic pain caused by endometriosis can occur:
  – Just before or during the menstrual period. In some women, painful periods get worse over time
  – Between menstrual periods, with worsened pain during the period
  – During or after sex
  – With bowel movements or while urinating, especially during the period
  Pelvic pain can also be caused by many other conditions, such as pelvic infections and irritable bowel syndrome.
• **Difficulty getting pregnant** — Endometriosis can make it more difficult to become pregnant. This might occur because endometriosis may cause scar tissue to develop, which can damage the ovaries or fallopian tubes. Even women with endometriosis who do not have scar tissue can have difficulty becoming pregnant.
• In women who become pregnant, endometriosis does not harm the pregnancy. Symptoms of endometriosis often improve after pregnancy.
• **Endometriomas (chocolate cysts)** — Endometriomas are sometimes seen during a pelvic ultrasound or felt during a pelvic exam.

Diagnosis

• Endometriosis is diagnosed based on clinical symptoms of pelvic pain or painful menstrual periods. However, the only way to know for sure is to have surgery.
• Endometriosis is considered mild, moderate, or severe depending on what is found during surgery. Women with mild disease can have severe symptoms, and women with severe disease can have mild symptoms.
• Medical management can be offered as the first treatment for symptoms of endometriosis.
• If medical treatment does not improve symptoms within three to six months, surgery is a reasonable next step.
• In many cases, surgery is performed to diagnose and treat endometriosis before medical management.
Most common areas

Treatment

- There are several treatment options for women with endometriosis:
  - Nonsteroidal antiinflammatory drugs
  - Hormonal birth control
  - Other forms of hormone treatment (gonadotropin releasing hormone agonists)
  - Surgery

- The best treatment depends on future plans to become pregnant and what symptoms are most bothersome.
NSAIDS

- **Nonsteroidal antiinflammatory drugs** - works by stopping the release of prostaglandins, does not shrink or prevent the growth of endometriosis.
- Most NSAIDs are available without a prescription, including:
  - Ibuprofen (Advil, Motrin, and store brands) – most effective at 800 mg PO q 8 hrs at onset of menses
  - Naproxen sodium (sold as Aleve, Anaprox, Naprosyn, and store brands). 250 – 500 mg PO two times per day. Like ibuprofen, naproxen may be more effective if begun a day or two prior to the onset of typical menstrual pain.
- The disadvantage of NSAIDs is that they do not always relieve endometriosis-related pain. NSAIDs probably work better when combined with another treatment, like hormonal birth control. Serious side effects from NSAIDs, although uncommon, include stomach upset, kidney problems, and worsened high blood pressure.

Hormonal Birth Control

- **Hormonal birth control treatments** — Hormonal birth control, including the pill, patch, and the vaginal ring are often helpful in treating pain because they reduce heavy bleeding. Injectable and implantable long-acting progestins may be very effective in managing endometriosis-related pain. A progestin-containing intrauterine device can also be very effective in treating pain. Hormonal birth control works best in women who do not have severe pain unrelated to the period.
- Women with endometriosis are often advised to take hormonal birth control continuously (skipping the placebo pills) for three or more months. This allows you to have fewer periods and have less pain and bleeding during each period. The most common side effects of estrogen-containing hormonal birth control are:
  - Nausea
  - Breast tenderness
  - Irregular vaginal bleeding or spotting
- These side effects usually improve after using the treatment for several months. Serious side effects (eg, blood clots, stroke, heart attack) are rare in women who do not smoke
Progestins

- This treatment might be recommended for women who do not get pain relief from or who cannot take hormonal birth control that contains estrogen (such as smokers). Usually given as a pill or injection. Progestins are not used if you are trying to become pregnant. A progestin-containing intrauterine device delivers very low levels of progestin directly to the uterus and results in markedly lighter and less painful bleeding episodes with fewer systemic side effects.
- Side effects of progestins can be bothersome for some women. The most common side effects include: bloating, weight gain, irregular vaginal bleeding, and rarely, worsened depression.

Gonadotropin Releasing Hormone Agonists

- GnRH agonists work by causing a temporary menopause. The treatment causes the ovaries to stop producing estrogen, which causes the endometriosis implants to shrink.
- This treatment reduces pain in over 80 percent of women, including women with severe pain. GnRH agonists are not used if patient is trying to become pregnant.
  
  Examples of GnRH agonists include:
  - Nafarelin (Synarel) - 200 - 400 mcg nasally twice per day, duration 6 months
  - Leuprolide (Lupron) – 3.75 mg IM q month or 11.75 mg IM q 3 months, duration 6 months
  - Goserelin (Zoladex) – 3.6 mg implant SC q 28 days or 10.8 mg implant q 12 weeks x 6 months

  - Adult women can take the full dose of a GnRH agonist for up to 12 months. There are concerns about using GnRH agonists at full strength for more than 12 months. Women who use GnRH agonists lose bone density, and this can become serious over time. One way to minimize bone loss is to take hormonal “add-back” treatment (adding very small amounts of either estrogen or a synthetic progestin) in addition to the GnRH agonist.
  - Taking hormonal add-back can also help to treat the most common side effects of GnRH agonists, which are menopausal symptoms (hot flashes, vaginal dryness, decreased libido, insomnia).
Surgery

• Surgery might be an option to treat endometriosis if patient:
  
  – Has severe pain
  – Has tried medicines but still has bothersome pain (attributable to endometriosis)
  – Has a growth or mass in the pelvic area. Surgery may be necessary to remove the mass and ascertain if endometriosis, or another problem, is the cause.
  – Is having trouble getting pregnant and endometriosis might be the cause.

• The goal of surgery is to remove endometriosis implants and scar tissue. More than 80 percent of women who have surgery have less pain for several months after surgery. However, there is a good chance that the pain will come back unless some form of treatment is offered after surgery (like hormonal birth control).

Laparoscopy

• Minimally Invasive Laparoscopy — commonly used to diagnose and treat endometriosis.
  
  – Recurrence rate estimated at 21.5% at 2 years and 40-50% at 5 years.
  – Current research is needed to better understand the patterns of recurrence and risk factors and to develop biomarkers.
  – In women <=21 years of age, the 5 year recurrence was as high as 56% irrespective of site and stage
Hysterectomy

• Complete removal of uterus and /or ovaries can be considered if
  – Other treatments have been tried and exhausted but patient continues to have severe symptoms
  – Patient does not desire pregnancy in the future
  – Patient desires a permanent treatment
• It is not always necessary to remove the ovaries to treat endometriosis; this decision will depend on patient’s age and preferences.

Case Study

• 37 y/o female presents with irregular menstrual cycle lasting 5-6 days, passing large blood clots and pelvic pain. Symptoms had been present for over a year and gradually worsened.
  – PMH: HTN, Kidney Stones
  – PSH: C-Section x 2, Cholecystectomy, Lithotripsy
  – SocHX: 7 cigarettes/day, light alcohol and caffeine
  – OBHX: G2P2
Reason for Exam: Pelvic pain, menorrhagia.

TRANSVAGINAL PELVIC ULTRASOUND:
Ultrasound examination was interpreted with permanently recorded images.

FINDINGS: The uterus is retroverted and normal in appearance. The uterus measures a length of 7.5 cm. Endometrium measures normal thickness at 5.4 mm. No uterine parenchymal abnormality.

No pelvic free fluid. The ovaries are normal with physiologic-sized follicles within each ovary. Normal color flow is demonstrated in the ovaries. Right ovary measures 4.6 x 2.4 x 2.6 cm. Left ovary measures 4.2 x 2.6 x 2.6 cm.

IMPRESSION:
(1) Normal pelvic ultrasound. No abnormal endometrial thickening present.

Case Study: 37 Y/O

- Physical:
  - Ht: 5' 2"  Wt: 165 (lb) 2 (oz)  BMI: 30.2
  - BP: 154/90
  - Gen: moderately obese with central adiposity
  - Abd: subumbilical hair growth
  - Gyn: retroverted, retroflexed uterus of normal size, no significant tenderness, adnexae normal, no rectovaginal nodularity
Case Study: 37 Y/O

- **Test Name**
  - POLYCYST.OVARY SYND.CONF.PANEL
- **Prochloral, SERUM**
  - In Range: ng/mL
  - Out Range: See Below
  - Flag: F
  - Units: Bi

## Prochloral Reference Ranges

- **Female Range (ng/mL)**
  - Non-Pregnant: 4.8 - 23.3
  - Pregnant 3rd Trimester: 95.0 - 473.0

## Insulin-Like Growth Factor 1

- **Value:** 162 ng/mL
  - Note: Pregnancy Range adapted from Tietz, 2006, 4th Ed.
- **Non-Pregnant Reference Range:** 109 - 307 F Bi

- **Dehydroepiandrosterone Sulfate (DHEA-SO4)**
  - Value: 258 ug/dL
  - Note: Pregnancy Range adapted from Tietz, 2006, 4th Ed.
- **DEHYDROEPIANDROSTERONE SULFATE**
  - Value: 109 - 307 F Bi

## DHEA-SO4 Ranges

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Female (ug/dL)</th>
<th>Male (ug/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-30</td>
<td>45-380</td>
<td>125-619</td>
</tr>
<tr>
<td>31-50</td>
<td>12-379</td>
<td>5-332</td>
</tr>
<tr>
<td>51-60</td>
<td>* 20-413</td>
<td>* 10-285</td>
</tr>
<tr>
<td>61-83</td>
<td>* 30-260</td>
<td>* 30-260</td>
</tr>
</tbody>
</table>

* Post-menopausal range 30-260 ug/dL

## Testosterone Free

- **Value:** 1.93 pg/mL
- **TESTOSTERONE FREE**
  - Value: 0.6 - 2.57 F Bi

## Testosterone

- **Value:** 62.5 ng/dL
  - Note: Above high normal
- **TESTOSTERONE**
  - Value: 8.4 - 48.1 F Bi

## Thyrotropin

- **Value:** 2.590 uiU/mL
  - Note: Pregnancy Range adapted from Tietz, 2006, 4th Ed.
- **THYROTROPIN**
  - Value: 0.270 - 4.200 F Bi

## Luteinizing Hormone (LH)

- **Value:** 30.4 mIU/mL
  - Note: Pregnancy Range adapted from Tietz, 2006, 4th Ed.
- **LUTROPIN**
  - Value: See Below F B

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Surgery 11/2013: 37 Y/O
Surgery 11/2013: 37 Y/O
Surgery 4/2014: 37 Y/O

Surgery 4/2014: 37 Y/O
Surgery 4/2014: 37 Y/O

Case Study: 23 Y/O

- 23 y/o female with chronic endometriosis diagnosed by laparoscopy at age 16 presents with recurrent pelvic pain getting progressively worse since last surgery.
  - PMH: Endometriosis
  - PSH: Dx Lap x 10, Appy, Vaginoplasty
  - SocHX: Negative
  - OBHX: G1P0
Case Study: 23 Y/O

• Physical:
  – Ht: 5’11” Wt: 130 (lb)
  – BP: 110/65
  – Gen: normal appearing slender female
  – Gyn: anteverted, anteflexed uterus of normal size, significant tenderness over suprapubic region and adnexae, no masses or rectovaginal nodularity

Surgery 12/2013: 23 Y/O
Surgery 12/2013: 23 Y/O
Key Points

- Endometriosis, which is defined as the presence of extrauterine endometrial tissue, is a common cause of pelvic pain in women.
- Symptoms include chronic pelvic pain, pain during intercourse and/or menstruation, and infertility, although most women with endometriosis are asymptomatic.
- The diagnosis is established by pathologic examination of tissue retrieved during laparoscopy or laparotomy, although symptoms are often treated empirically once other causes of pain and infertility have been eliminated.
- The goal of medical therapy is relief of pain using analgesics, combined oral contraceptives, progesterone (oral or injectable), testosterone derivatives, and gonadotropin-releasing hormone (GnRH) analogs.
- Surgical removal of endometriotic lesions is done with the goal of improving infertility; patients with intractable pain not responsive to medical therapy are managed with hysterectomy and bilateral salpingo-oophorectomy.
- The prognosis is good with treatment, although recurrence of pain after a course of hormonal therapy is common, and surgery does not result in improvement in all patients with infertility and/or pain.

References

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