**Endometriosis & Andenomyosis**

* **Endometriosis** :
  + Presence of endometrial glands & stroma outside the endometrial cavity and uterine musculature .
  + Also called “ endometriosis externa “ , while Adenomyosis is called “endometriosis interna “ .
* Epidemiology :
  + Globally 90 million suffering with Endometriosis
  + Prevalence: 3-10% of reproductive age group & 25-35% of infertile women
  + Peak incidence: 30-45 yrs of age
  + Prevalence is similar in all races
* Sites :
  1. Ovaries , fallopian tubes , Uterosacral ligament and Pouch of douglas “most common sites”
  2. Omentum
  3. Bowel
  4. Pelvic peritoneum
  5. Ureters …. etc
* Pathogenesis :
  + Retrograde menstruation or Sampson theory “most accepted theory”, More common in young girls with genital outflow obstruction.
  + Some endometrial cells may behave like tumor cells and metastasize to distant organs like brain .
  + Mechanical : Endometriotic foci in surgical scars .
  + Lymphatic or Hematogenous .
  + Metaplasia theory “not accepted” it says that some cells in the body will go through metaplasia and become like endometrial cells .
* Genetic, Immunological & environmental factors
  + 7 times more common in 1°relatives
  + More common in Monozygotic twins than in Dizygotic twins
  + Decreased cellular immunity to endometriotic tissue
  + Dioxins : persistent environmental pollutants (POPs)
* Features on laparoscope :
  1. Puckered black lesions
  2. White scarring
  3. Red polyps
  4. Clear blebs
  5. Endometrioma :ovarian cyst filled with old blood, fluid & menstrual debris, Brown to black color due to Hemosiderin
* On Microscopy :
  + Endometrial glands & stroma ,Often contain fibrous tissue, blood & cysts
* Staging :
  + Staging is designed to predict the likelihood of future fertility (grade 4 worst fertility)
  + There is no correlation between the stage of disease & the degree of pain or the prognosis with treatment.
    - Stage 1 :Minimal endometriosis, characterized by isolated superficial implants and no significant adhesions.
    - Stage 2 :Mild endometriosis , characterized by superficial implants that measure less than 5 cm in diameter , no significant adhesions.
    - Stage 3 :Moderate endometriosis ,involves multiple deep implants, small cysts on one or both ovaries, and the presence of peritubal and periovarian adhesions.
    - stage 4 :Severe endometriosis , consists of multiple deep implants, large ovarian endometriomas on one or both ovaries, and thick adhesions.
* Endometriosis is one of the most common causes of pelvic adhesions , others are : PID and previous surgery .
* Endometriosis is characterized by **triad** of symptoms :
  + Dysmenorrhoea (congestive)
  + Deep dyspareunia
  + Heavy periods
* There are also other conditions that come with these symptoms : (ddx )
  + Chronic PID
  + Adenomyosis
  + Fibroid
  + IUCD
* Symptoms :
  + Urinary tract
    1. Cyclical hematuria
    2. Cyclical dysuria
    3. Ureteric obstruction
  + Lungs
    1. Cyclical hemoptysis
    2. Blood stained Pleural effusions
    3. Pneumothorax
    4. Haemothorax
    5. ascites
  + Umbilicus & Surgical scars
    1. Cyclical pain & swelling
  + Reproductive organs
    1. Dysmenorrhoea (congestive) 60-80%
    2. Deep dyspareunia 25-40%
    3. Lower abdominal, pelvic & low back pain 30-50%
    4. Menstrual irregularities (heavy periods) 10-20%
    5. Infertility 30-40%
  + GIT (symptoms similar to rectal cancer )
    1. Cyclical rectal bleeding
    2. Tenesmus
    3. Dyschesia
    4. Diarrhoea/ Cyclic constipation
* Signs :
  + Pelvic tenderness.
  + Fixed retroverted uterus (due to adhesions), other causes : chronic PID and pelvic surgery..
  + Nodularity of the Douglas pouch and uterosacral ligaments.
  + Ovaries may be enlarged and tender . Ovarian cyst may be detected.
* Risk of cancer : (there is risk but very low to transform into the following tumors)
  + Ovarian Clear cell & Endometrial cell carcinomas
  + Breast cancer, Melanoma
* Differential diagnosis :
  + Pelvic infection
  + Uterine Myomas
  + Ovarian malignant tumors with metastatic deposits in the pouch of Douglas
  + Acute abdomen (due to ruptured ovarian cyst )
  + Rectal carcinoma
* Investigations :
  + Laparoscopy ‘**Gold standard’** diagnostic test for endometriosis , It permits a “see & treat” approach, although its effectiveness may be limited by the nature of the disease and the surgeon's skill , we should take biopsy to confirm diagnosis .
  + Serum CA 125 : Not useful for diagnosis , because of poor sensitivity , but help in prognosis and follow up .
  + Ultrasound: Sensitivity for focal endometrial implants is poor , very good for diagnosing Endometriomas “chocolate cyst” >> (appearance of turbid fluid ) .
  + CT scan : Endometriomas may appear solid, cystic or mixed, Because of poor specificity & high radiation, CT has been replaced by MRI .
  + MRI : Role is limited in visualizing small endometriotic implants and adhesions, More useful for lesions in extraperitoneal locations & the contents of pelvic mass ,More frequently used in staging & treatment response monitoring .
* Treatment :
  + - Consider : Age ,Symptoms ,Stage and Infertility .
  + Expectant management :
    - Young , asymptomatic infertile patient with mild endometriosis.
    - If pregnancy is not achieved within 12 - 18 months of observation, hormonal or surgical treatment is indicated .
  + Medical Treatment : (Symptomatic pts with minimal or mild lesions )
    - NSAIDs ,Opioids.
    - The aim of medical treatment is to induce a period of amenorrhea for 6-9 months .
    - Best way to treat endometriosis is to” get pregnant” , but if she is infertile like most of cases we can induce pseudo pregnancy or pseudo menopause state by hormonal therapy .
  + Hormonal Treatment : (Produces pseudo pregnancy or pseudo menopause )
    - Indications
      * Small & superficial lesions
      * Recurrence after conservative surgery
      * Preoperative for 6-12 wks to decrease size
      * Postoperative for residual lesions
      * When surgery is contraindicated or refused by the patient.
      * Enometriosis in Rectovaginal septum & laparotomy scars doesn’t respond to Hormonal therapy
    - Danazol : (androgen)
      * Isoxazole derivative of 17 – alpha ethinyl testosterone
      * Causes anovulation by :
        + Attenuating the mid cycle surge of LH
        + Inhibiting multiple enzymes in steroidogenic pathway
        + ↑ Testosterone levels
      * Dose: 400 – 800 mg/ day for 6 months , not expensive
      * Adverse effects: Androgenic effects (signs of virilism : excessive facial hair , deepening of the voice , smaller-than-normal breasts , enlarged clitoris , male-pattern baldness >> all are reversible except deepening of voice) , effects on serum lipids, ￼ Bone mineral density & Liver damage
      * You should tell the Patient to come to the doctor if she notices changes in voice , and stop drug immediately .
    - Progestins :
      * Causes endometrial deciduali zation & atrophy
      * Medroxyprogesterone (Provera) is commonly used
      * Dose: 20-30 mg/ day for 6 -9 months
      * Adverse effects: Abnormal uterine bleeding, nausea, breast tenderness, fluid retention & depression
    - Gestrinone (Ethylnorgestrienone) :
      * Androgen and Antiprogestational steroid causes ↓ estrogen & progesterone receptors
      * Dose: 5-10 mg/ wk - dly or twice a wk or 3 times a wk, for 6-9 months
      * Adverse effects: deepening of voice, hirsuitism & Clitorial hypertrophy
    - Combined oestrogen-progestogen Pills :
      * Well tolerated & can be continued for long term
      * 1 pill/ day either continuously “best method” or cyclically
      * Continuous regimen is superior in patients with dysmenorrhea
      * Adverse effects: weight gain, abnormal bleeding & HTN
    - GnRH agonists : (induce psuedomenopause state)
      * ↓ FSH & LH & results in endometrial atrophy & amenorrhea
      * Intranasally or SC or IM with a frequency of twice dly to once in 3 months up to 3 - 6 months
      * Adverse effects: transient vaginal bleeding, hot flushes, vaginal dryness, ↓ libido, breast tenderness, insomnia, depression, irritability, fatigue, headache, osteoporosis, ↓ elasticity of skin , heart diseases
      * GnRH agonists + Add-back therapy (estrogens & progestogen) – less side-effects but with same efficacy, can be continued beyond 6 months
  + Mirena (LNG-IUS) :The LNG-IUS is a real option for endometriosis pelvic pain treatment
    - Leads to: Glandular atrophy .
  + Surgical management CAN BE BY LAPARASCOPY OR LAPARATOMY :
    - Conservative – Excision, Cauterization & Evaporation , devide adhesions
    - Surgeries for pain - Uterosacral Nerve Ablation , Presacral Neurectomy
    - Radical surgeries - Hysterectomy +/- BSO (to stop estrogen effect on ectopic endometrial tissue )
    - Surgeries for Endometrioma “must be removed” , Cystectomy, Drainage & coagulation, Fenestration
* **Andenomyosis :**
* Is a benign disease of the uterus characterizedby ectopic endometrial glands and stroma within the myometrium , It is associated with myometrial hypertrophy andmay be either diffuse “most common” or focal.
* The gland tissue grows during the menstrual cycle and then at menses tries to slough, the old tissue and blood cannot escape, This trapping of the blood and tissue causes uterine mass and pain in the form of monthly menstrual cramps.
* It also produces abnormal uterine bleeding.
* Risk factors :
  + Multiparity
  + Old age 40-50 years
* Symptoms :
  + Pelvic pain,
  + Dysmenorrhea,
  + menorrhagia unresponsive to hormonal therapy or uterine curettage.
  + Subfertility , And pregnancy termination.
  + Cyclic, cramping uterine pain beginning later in reproductive life (generally after age 35) and often associated with prolonged and heavy menses
* Diagnosis :
  + A good gynecologist may suspect adenomyosis based on the clinical factors, but the final diagnosis usually has to wait until hysterectomy is performed (The diagnosis can only be proven by the pathologists ).
  + pelvic exam :
    - there may be uterine enlargement from about 6-10 weeks pregnancy size
    - The uterus can feel soft and boggy on pelvic exam.
    - Sometimes adenomyosis is associated with uterine fibroids (leiomyomata) >> because both are estrogen dependant lesions (estrogen also may cause increase endometrial thickness , or endometrial CA in old cases )
  + CA 125 :
    - adenomyosis is associated with increased numbers of myometrial macrophages, elevated antiphospolipid auto-antibodies and CA 125 levels in peripheral blood.
    - Not helpful in diagnosis , but helpful to know progress of treatment .
  + TVUS :
    - Good method but it is strongly operator dependent .
    - ill defined hypoechoic areas
    - indistinct endometrial-myometrial border
    - increases myometrial thickness ( posterior uterine wall is thicker than anterior uterine wall )
    - decreased uterine echogenicity ( anterior myometrium is less echogenic than posterior myometrium )
    - effective, noninvasive, and relatively inexpensive procedure for the preoperative differential diagnosis of adenomyoma versus leiomyoma .
  + MRI :
    - MRI is better than TVS for the diagnosis of adenomyosis.
    - MRI had a higher specificity than TVS, but their sensitivities were in line.
* Treatment :
  + The only definitive treatment for adenomyosis is total hysterectomy, with or without ovarian conservation.
  + GnRH agonists : (induce psuedomenopause state)
    - GnRH- agonist is efficient in reducing the adenomyotic uterine size, and may facilitate fertility.
    - For ademyomata associated with infertility, GnRH-alpha therapy may avoid the risk of rupture of uterus which may occur after adenomyomectomy pregnancy.
    - For infertility, GnRH-alpha treatment before laparoscopic surgery greatly decreases surgical difficulties and blood loss in certain cases.
  + Mirena IUD :
    - Recently the Mirena IUD has also been shown to improve symptoms from adenomyosis. The progesterone hormone the IUD continually releases shrinks the tissue lining the uterus and through this mechanism decreases symptoms from adenomyosis.
  + conservative surgery :
    - The conservative surgery for adenomyoma can reduce symptom and raise pregnancy rate significantly, it can be accepted by young women who want to preserve their reproductive capacity.
    - Though the pregnancy rate of conservative surgery for diffused adenomyosis was low, it still has therapeutic value
  + Uterine arterial embolization : (also used in fibroid )
    - UAE is an effective and safe method in the treatment of adenomyosis. BUT the recurrence rate is not yet evaluated.
    - Used for focal adenomyosis
* Notes :
  + Dysmenorrhea could be either : congestive or spasmodic
  + Decidua : it is the endometrium of a pregnant uterus
  + Normal uterus is anteverted anteflexed (80%) , but in 20% it is retroverted but not fixed and this is normal , if it is retroverted and fixed this is abnormal and there is problem .
  + CA 125 is tumor marker for epithelial ovarian tumor .
  + **Krukenberg tumor** refers to a malignancy in the ovary that metastasized from a primary site, classically the gastrointestinal tract, although it can arise in other tissues such as the breast , it has a “signet cell” appearance on microscope .
  + Endometriosis may present with ovarian mass , while adenomyosis present with uterine mass .

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Check pictures in the slide