Endometriosis

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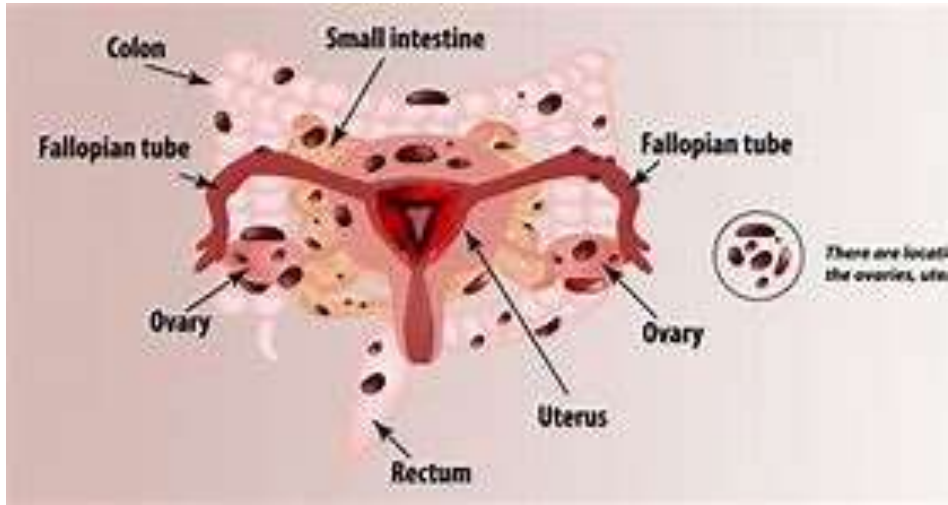

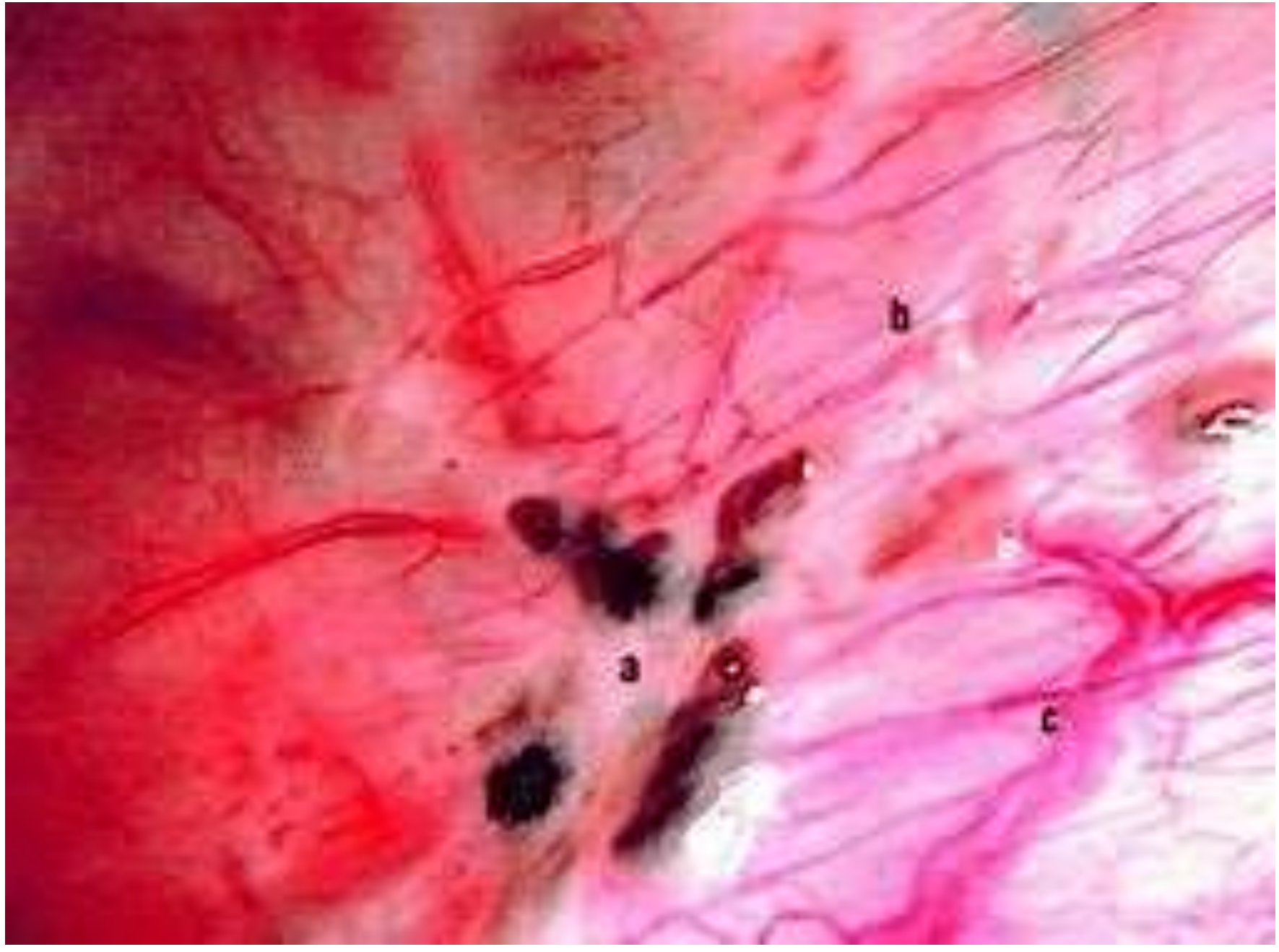
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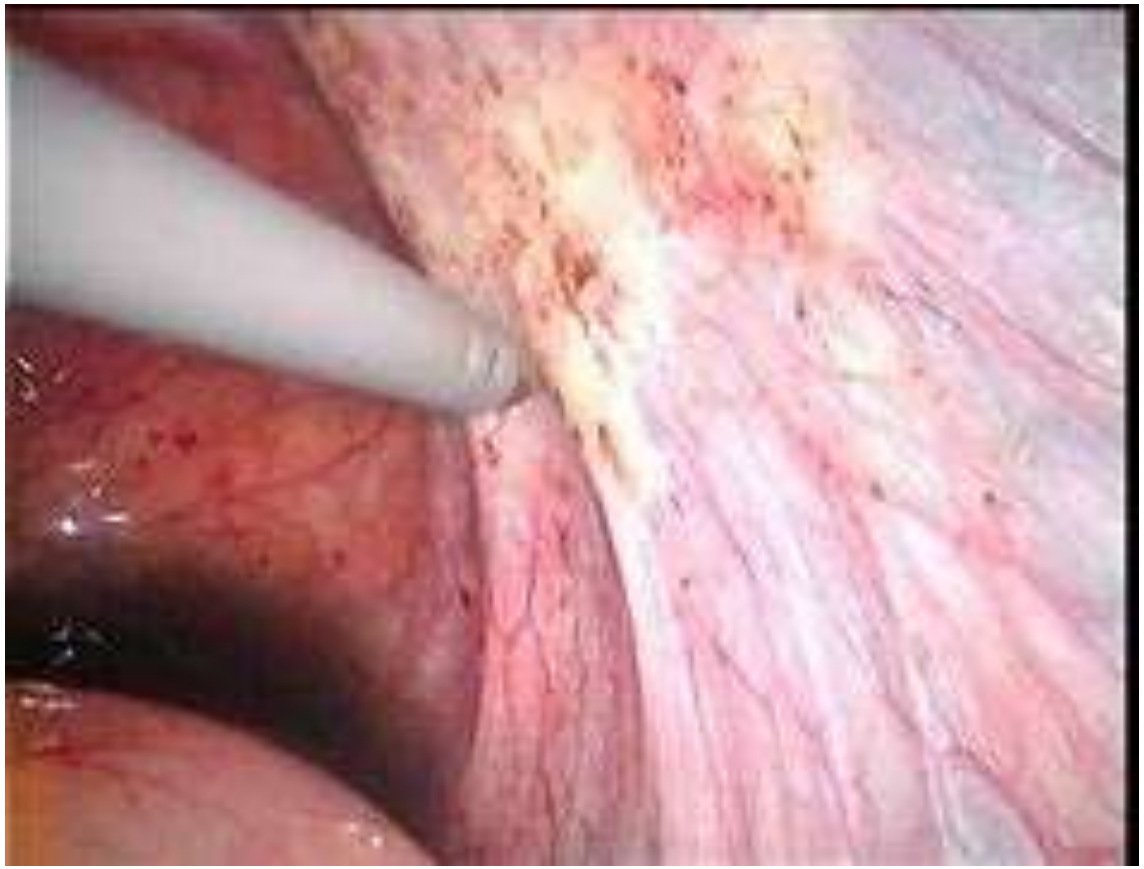
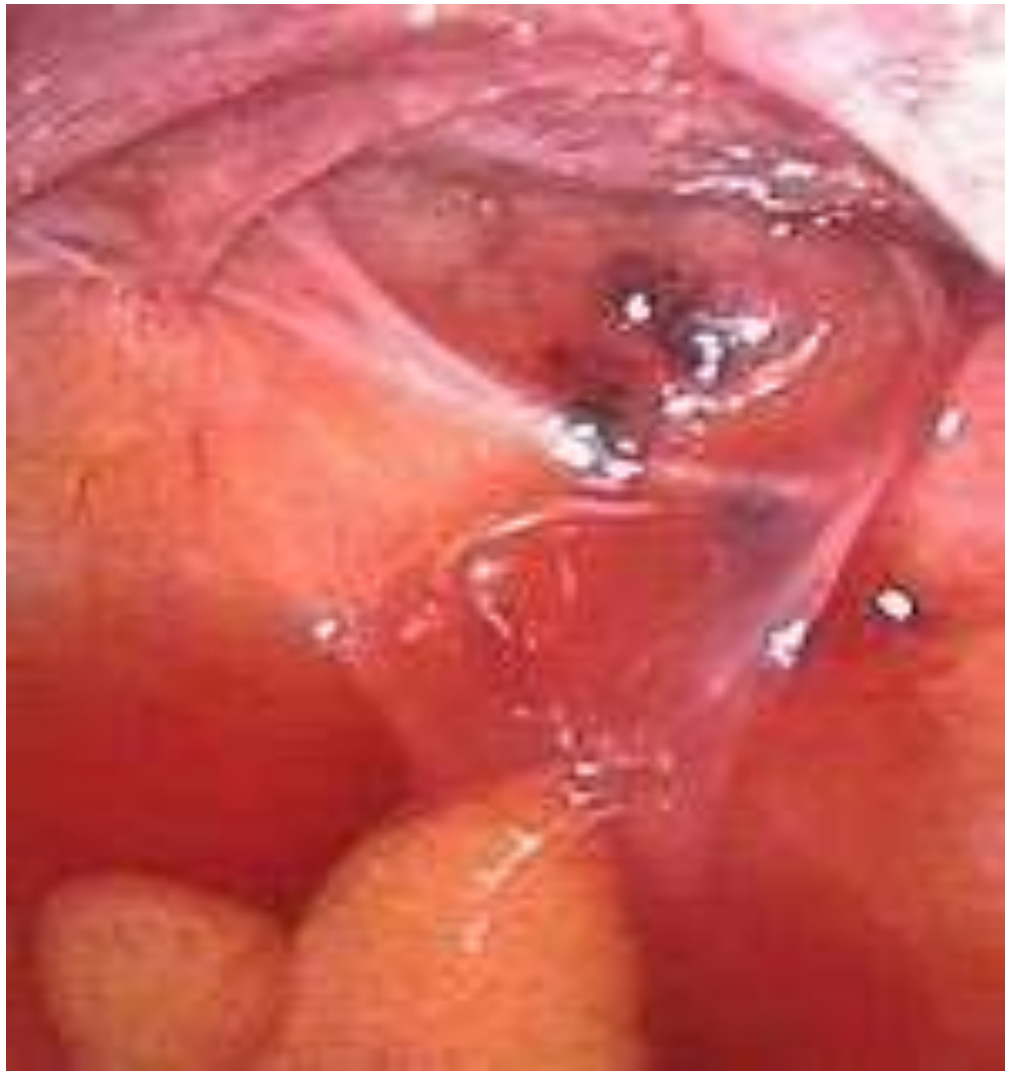
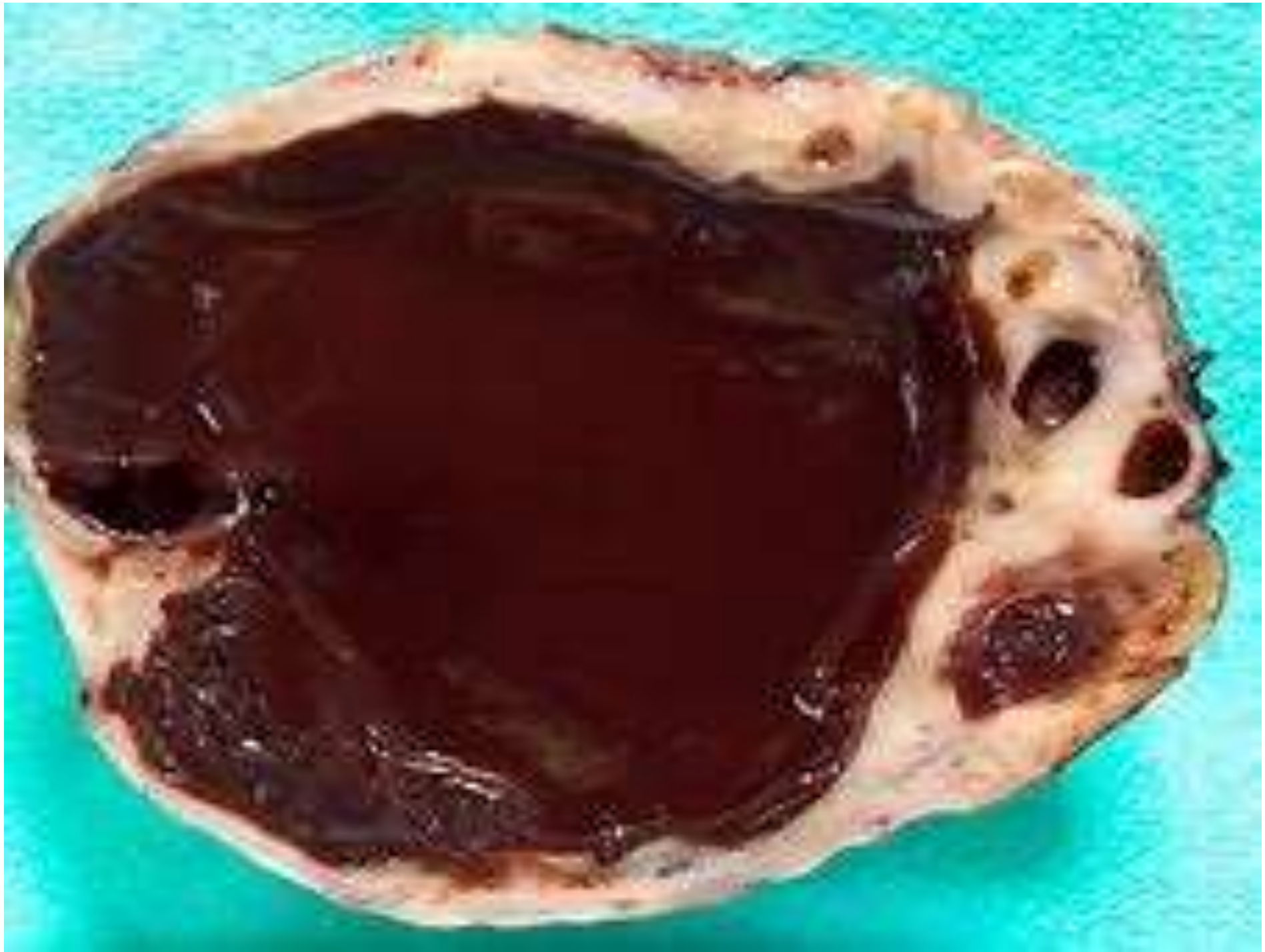
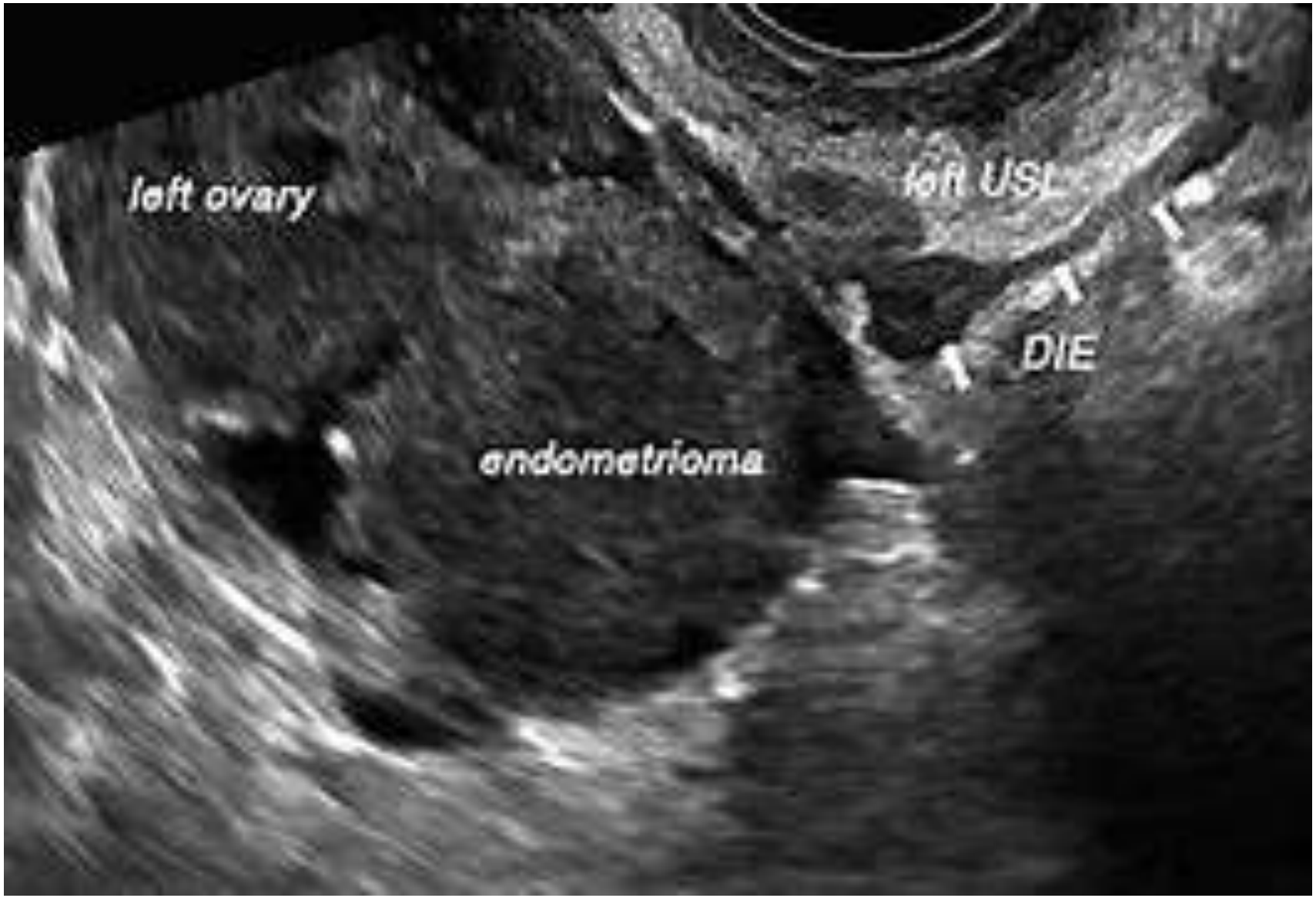
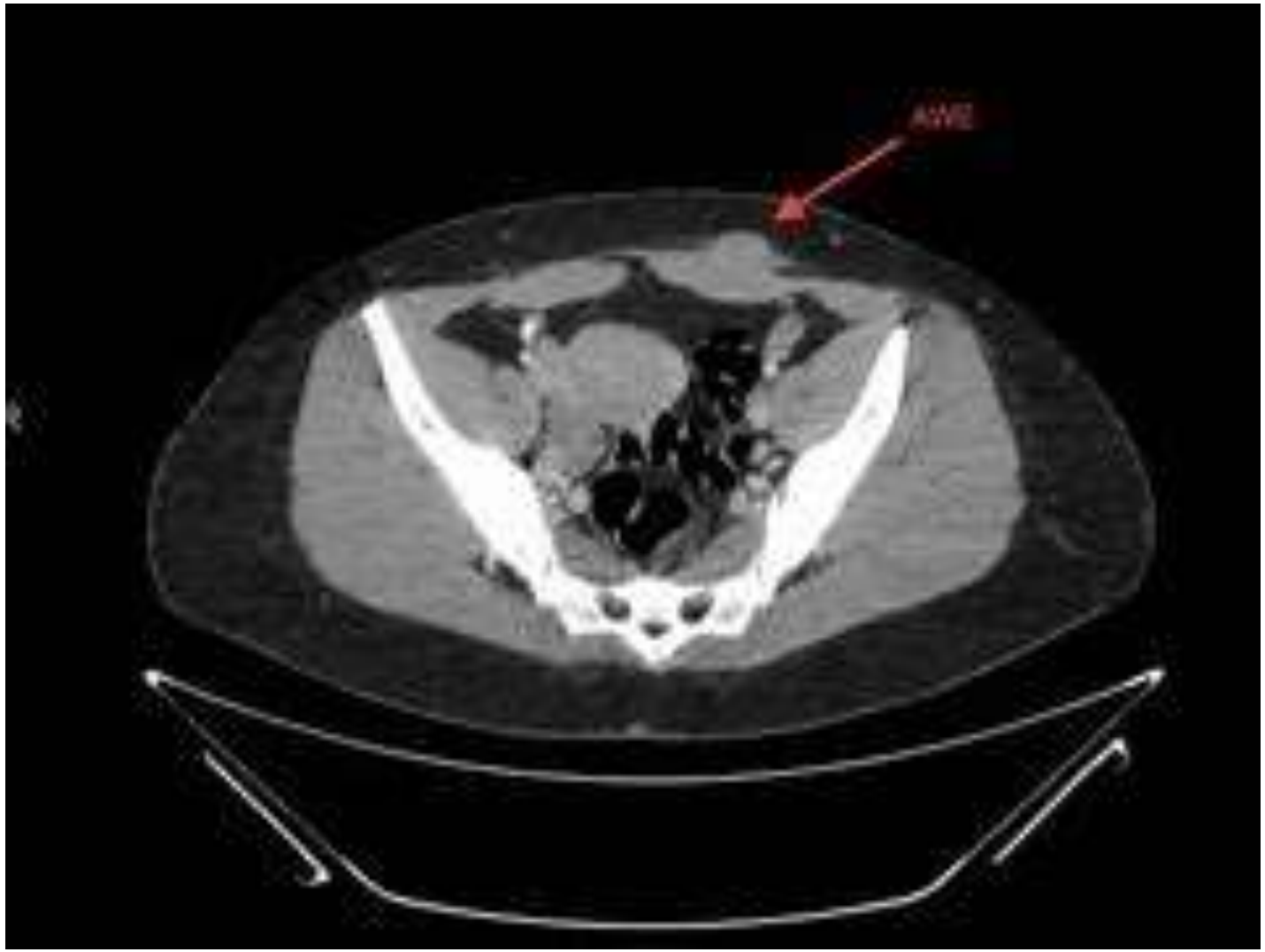







left ovary
left USL
DIE
endometrioma


AWE

Endometriosis (abstract)

- Definition: endometrial glands and stroma that occur outside the uterus cavity
- An estrogen-dependent, inflammatory, benign disease
- Affects women during their premenstrual, reproductive, and postmenopausal stages
- Pelvis, bowel, diaphragm, pleural cavity
- Inflammation can cause: dysmenorrhea, dyspareunia, chronic pain, and infertility
- Symptoms can range from minimal to severely debilitating

Endometriosis

- Lesions in the pelvis categorized:

✓ superficial peritoneal

✓ ovarian (endometrioma) (1/3: both ovaries), typically have surface adhesions, chocolate colored material, epithelial abnormalities (complex hyperplasia or atypia)

✓ deeply infiltrating (DIE), more than 5 mm deep to the peritoneum, generally found in the retro vaginal septum, rectum, retro sigmoid colon, bladder, ureter, uterine ligaments, vagina, …

Anatomical sites

- Anatomic sights: ovaries, anterior and posterior cul-de-sac, posterior broad ligaments, …
- In anterior abdominal wall: usually in surgical incision, with no history of surgery or endometriosis
- Most women have multiple areas of involvement

Epidemiology

- 10 % of reproductive age women, in premenstrual girls, in 2 to 5 % of post menopausal women
- 40 % of adolescents with general tract anomalies
- 50 % of women with infertility
- 70 % of adolescents and women with pelvic pain

risk factors

- Nulliparity
- Prolonged exposure to endogenous estrogen
- Shorter menstrual cycles < 27 days
- HMB
- Obstruction of menstrual outflow
- Exposure to DES in utero
- Higher greater than 170 cm
- Lower BMI
- Exposure to sexual abuse in child hood or adolescence
- High consumption of trans unsaturated fat
- White and Asian women
- In women with peritoneal endometriosis, ovarian endometriosis was less common who had used oral OCP

Clinical manifestations

- Pelvic pain (dysmenorrhea and dyspareunia), 80 %

❑ dysmenorrhea: begins 1 to 2 days before menses, throughout menses, several days afterward

❑ dyspareunia (introital or superficial: lesions in cervix, hymen, perineum, episiotomy scars)

❑ pelvic pain is typically chronic

- Infertility, 25 %
- Ovarian mass, 20 %, associated with pelvic pain or pressure
- Bowel (diarrhea, constipation, dyschezia, bowel cramping, painful defecation), bladder dysfunction (frequency, urgency, pain at micturition), ureteral endometriosis (asymptomatic or colicky flank pain or gross hematuria)

Clinical manifestations

- AUB
- Low back pain
- Chronic fatigue
- Peak prevalence: women 25 to 35 years of age
- Vulvar endometriosis: cyclic bleeding
- Endometriosis of abdominal wall mass: cyclic with menses or continuous
- Thoracic endometriosis: chest pain, pneumothorax, hemoptysis, scapular or neck pain

Physical examination

- Variable, depend to location and size of implants, can be normal
- Tenderness on vaginal examination
- Nodules in the posterior fornix
- Adnexal masses
- Immobility or lateral placement of the cervix or uterus
- Visible on the cervix or vaginal mucosa

Laboratory and imaging

- No pathognomonic lab finding
- CA125 (> 35 units/ mL)

➢ role in primary diagnosis is undefined

Imaging findings:

➢ endometriomas (TVS and MRI)

➢Nodules in vaginal septum an bladder (TVS and MRI)

➢ abdominal wall endometriosis (sonography)

➢ thoracic (CT scan, MRI)

Diagnosis

- Definitive diagnosis: histologic evaluation of the lesion
- Role of presumptive diagnosis: combination of symptoms, signs and imaging findings

➢ clinical diagnosis can be sufficient to initiate therapy

➢ presence or absence to empiric treatment cannot be construed as definitive confirmation or exclusion of the diagnosis

Diagnosis: non surgical diagnosis

- Examination findings of rectovaginal endometriosis
- Imaging findings
- Serum diagnosis using microRNA markers
- Visual inspection of the posterior vaginal fornix and biopsy of rectovaginal lesions
- Cystoscopic evaluation and biopsy of detrusor lesions

Surgical exploration indications

- Diagnosis of persistent pelvic pain that does not respond to medical therapy
- Evaluation of symptoms that limit function
- Treatment of anatomic abnormalities such as bladder lesions

Surgical staging of disease

- Stage 1: minimal disease, isolated implants and no significant adhesions
- Stage 2: mild endometriosis, superficial implants less than 5 cm in aggregate on peritoneum and ovaries, no significant adhesions
- Stage 3: moderate disease, multiple implants both superficial and deep. Peri tubal and periovarian adhesions may be evident
- Stage 4: severe disease, multiple superficial and deep implants, including large endometriomas. Filmy and dense adhesions are usually present.

Natural history

- The number of peritoneal areas affected by endometriosis appears to increase during adolescence until to early 20s
- Course during pregnancy: endometriosis lesions and symptoms often disappear or improve
- Complications during pregnancy: intestinal perforation, hemoperitoneum, uroperitoneum, acute appendicitis, ruptured or infected endometioma
- Possible mechanisms: traction by growing uterus on adhesions, increased friability on inflamed tissues, alteration of vessel walls by decidualized lesions

Obstetric outcomes increased risk of

- Preterm labor
- Preeclampsia
- Cesarean delivery
- Miscarriage
- EP
- Previa
- Unexplained antepartum hemorrhage
- LBW

Link to cancer

- Associated with some epithelial ovarian cancers
- Overall risk is low and prophylactic removal &screening is not recommended
- 1%for premenopausal women, 1 to 2.5 % for postmenopausal woman
- For women with endometriomas, probably not for women with peritoneal or deep infiltrating endometriosis

Atherosclerosis and cardiovascular disease

- Systemic chronic inflammation and oxidative stress are present in the pathogenesis of both atherosclerosis and endometriosis

- More data are needed on the risk of CHD in women with endometriosis and potential benefits of CHD screening for these women.

Treatment

- Treatment of endometriosis requires a lifelong management plan.
- Treatment are individualized and consider clinical presentation (pain, infertility, mass), symptom severity, disease extent and location, reproductive desires, patient age, medical side effects, surgical complication rates, and cost.
- Maximizing the use of medical treatment and avoiding repeated surgical procedures

Treatment of pain

- Mild to moderate pain: do not cause regular absence from school or work and no endometrioma- NSAIDs & continuous hormonal contraceptives (pill, patch, or vaginal ring), desire pregnancy can use NSAIDs, although we avoid selective celecoxib because it can prevent or delay ovulation
- Progestin-only contraceptive pills (norethindrone 0.35 mg) with an NSAID
- DEPO 150 mg IM every 3 months
- GnRh analog is an alternative

Treatment of pain

- severe pain: regular missing school or work

  do not respond to above therapies

GnRH analog with add-back hormonal therapy

Laparoscopy for diagnosis and treatment. Excision of endometrial implants, endometriomas and adhesions and hormonal suppression to prevent recurrence of symptoms

treatment

- Medical interventions do not improve fertility, diminish endometriosis, or treat complications of deep endometriosis such as ureteral obstruction

OCP

- Typically begin with OCP containing 20 mcg ethinyl estradiol
- Continuous or cyclic
- Mechanism: decidualization and subsequent atrophy of endometrial tissue
- OCP may slow progression of disease

progestins

- MPA
- Norethindrone acetate 5 mg
- Dienogest 2 mg daily
- Depot MPA 150 mg IM Q 3 months
- Mechanism: inhibit endometrial tissue growth by decidualization and then atrophy
- Levonorgestrel IUD
- Etonogestrel implant

GnRH analogs

- Agonist analogs: naferelin, busereline, ….
- Antagonists: elagolix

treatment

- Danazol: 400- 800 mg daily
- Aromatase inhibitors: letrozole 2.5 mg daily, ….
- Neuropathic pain: gabapentin, antidepressants, antiepileptic drugs

Surgical treatment options

- Offered to women who do not respond to medical therapy or who do not respond to medical therapy or who have recurrent symptoms.
- Disadvantages: risk of injury, possible reduction of ovarian reserve, adhesion formation, common surgical risks
- Ablation or resection
- Definitive (TAH + or - BSO) and resection of endometriosis
- Radical: removal of all visible implants
- Nerve transection: presacral neurectomy, uterosacral nerve ablation

Treatment of special populations

- Infertility- are not candidates for the hormone suppression therapies because prevents pregnancy and does not improve fertility
- Treatment of fertility: combination of surgery and ART
- Endometriomas- goals of treatment:

➢ relieve symptoms (pain, mass)

➢ prevent complications (rupture, torsion)

➢ exclude malignancy

➢ improve sub infertility

➢ preserve ovarian function

Endometriomas

- Medical therapy does not resolve endometriomas
- Symptomatic or expanding endometriomas are removed
- Surgical removal can diminish ovarian reserve
- Asymptomatic and small omas $\leq$ 5 cm can be left in place

Deep endometriosis

- Infiltrative forms of the disease that involve the uterosacral ligaments, rectovaginal septum, bowel, ureters, or bladder
- Medical treatment with hormonal suppression for patients with urinary urgency or frequency, dyspareunia, dysmenorrhea or dyschezia
- Surgery is indicated for women with ureteral or bowel obstruction or for women whose symptoms do not improve with medical management

Complementary therapies

- Acupuncture
- Diet (beef, ham, other red meat)

Treatment of endometrioma, chocolate cyst

- Densely adherent to surrounding structures

- Enlarging cysts are removed
- Exclusion of malignancy
- Treatment of sub infertility (spontaneous pregnancy rate, IVF & ICSI)
- Preservation of ovarian function

- Surgical options
- observation

approach

- For women with known endometriosis and a symptomatic or expanding suspected endometrioma, we suggest cystectomy- after surgery we recommend treatment with OCP
- For women with less than 5 cm and asymptomatic endometriomas we suggest observation every 6 months for 1 to 2 years, followed by annual examination and ultrasound