Lec1

Vulvar Diseases

By : Noor Almomani

① Non-neoplastic (more common)

① Lichen sclerosus

* Post menopausal
* White plaques, thinned out skin

- Microscopically:
① Thinning of epidermis
② Disappearance of rete pegs
③ Hydropic degeneration of basal cells

- Pathogenesis: Autoimmune

* **Not Pre Malignant by itself !**

② Lichen simplex chronicus

* End result of many inflammatory diseases

* Clinically: (leukoplakia) ↪ whitish plaque
- Epithelial thickening.
- Hyperkeratosis
- Epithelium → No Atypia

* **No increase pre. to cancer, however, maybe present at margins of adjacent cancer.**

③ Condylomas

* Anogenital warts

* Infection by low risk HPV, mainly 6, 11

* **Koilocytosis**: Perinuclear cytoplasmic vacuolation & nuclear pleomorphism

* HPV types isolated from cancers differ from those found in Condylomas

* **Not preconcerous by itself.**

② Neoplastic

① Intraepithelial Neoplasia

* Dysplasia is graded depending on extent of epithelial involvement:
- VIN 1: mild dysplasia (< 1/3)
- VIN 2: moderate dysplasia 2/3
- VIN 3: severe, carcinoma in situ

* Dysplasia: increased N/C ratio, nuclear enlargement, hyperchromasia and abnormal nuclear membranes

② Invasive carcinoma SCC

* Two types:

① Basaloid (poor)
- most common 90%
- young women
- HPV related
- lesions also in vagina & cervix
- Poor diff. cells

② Well differentiated
- less common
- old women
- Non HPV related
- maybe found adjacent to lichen simplex or sclerosis
- well to moderately diff. cells

Cervical Diseases

* Pap cervical smear: screening test for detection of HPV related lesions of uterine cervix

* Cervical cancer types: SCC (75%), followed by adenocarcinoma and adenosquamous carcinoma (20%) and neuroendocrine (<5%)

* SCC now has peak incidence at 45 years, almost 10-15 years after detection of their precursors which are cervical intraepithelial neoplasms (CIN)

* CIN trx → laser or cone biopsy
* Invasive cancer trx → surgical excision
* 5 year survival drops with increased age

- Pre invasive (CIN) → 100%
- stage 1 → 90%
- stage 2 → 82%
- stage 3 → 35%
- stage 4 → 10%

* Radiotherapy & chemotherapy in advanced cases !

lec 2

إحذر... منطقة إنهيارات

* Uterine Diseases *

① Endometrium Diseases
② Myometrium Diseases.

Endometrium

① Endometritis

*inflammation of endometrium

*Causes :-

- Infections, Pelvic inf. disease (PID)
- miscarriage or delivery.
- Intrauterine device (IUCD)

* Could be acute or chronic

*Symptoms :

- fever, abdominal pain, menstrual abnormalities, infertility and ectopic pregnancy due to damage to the fallopian tubes.

*Treatment :

- Removal of cause
- Anti biotics
- D & C

② Adenomyosis

- endometrial stroma, glands or both embedded in myometrium.

- Thick uterine wall
- enlarged uterus.
- Derived from stratum basalis so no cyclical bleeding.

- Menorrhagia and dysmenorrhea due to enlarged uterus, uterine contractions are exaggerated.

③ Endometriosis

- endometrial stroma and glands outside the uterus (not cancer)
- 10% in reproductive years, ⬆ Infertility
- Dysmenorrhea, pelvic pain, pelvic mass filled with blood "chocolate cyst" 🍫🍫
- multifocal in pelvis (ovaries, pouch of Douglas, uterine ligaments, tubes & recto vaginal septum).
- Sometimes distal sites (LN, lungs, umbilicus)
- 4 theories for Pathogenesis :-

① Regurgitation theory (most accepted)
↳ Menstrual backflow through tubes & implantation.

② Metaplastic theory : Endometrial differentiation of coelomic epithelium.

③ Vascular or lymphatic dissemination theory
↳ explain extrapelvic or intranodal implants.

④ Extrauterine stem/progenitor cell theory
↳ circulating stem cells from BM differentiate into endometrial tissue.

*Contains functionalis stratum so cyclic bleeding occurs
↳ consequences: Fibrosis, sealing of tubal fimbriated ends and distortion of the ovaries.

* Diagnosis : 2 of 3 features : ① endometrial stroma ② Endometrial glands ③ Hemosiderin pigment.

④ Endometrial hyperplasia

- Prolonged or marked excess of estrogen relative to progestin causes exaggerated proliferation and may progress to cancer.

- Risk factors :-
* Obesity * DM * HTN
* infertility * prolonged estrogen replacement therapy * Estrogen secreting ovarian tumors.

- Severity is based on architectural crowding and cytologic atypia ranging from ① Typical hyperplasia ② Atypical hyperplasia. (20% risk of cancer).

⑤ Bening endo-polyps

- Sessile or pedunculated
- Endometrial dilated glands with small muscular arteries and fibrotic stroma
- no risk for cancer

⑥ Endometrial carcinoma

- The most common cancer in female genital tract.
- 50s & 60s.
- 2 clinical forms :

① Perimenopausal women with excess estrogen → Type 1 cancer → prototype is "endometrioid".

② Older women with endometrial atrophy → Type 2 cancer → prototype is "serous carcinoma"

* Endometrioid *
- similar to normal endometrium.
- Risk factors :
* Obesity * DM * HTN * infertility
* Prolonged estrogen replacement therapy
* Estrogen secreting ovarian tumors.
* Pre cancerous lesion is "Atypical endometrial hyperplasia"
*mutations in : ① PTEN ② DNA mismatch repair genes
* Prognosis depends on stage
5 year survival : stage 1: 90% ... stage 3&4: 40%

* Serous Carcinoma *
- no relation with endometrial hyperplasia
- not hormone dependent.
- mutations in P53 tumor supressor gene
* Prognosis depends on operative staging with peritoneal cytology.
- Worse than endometrioid !

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ONE MORE EPISODE

Myometrium

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tumors

① Lieomyoma = fibroids

ألياف الرحم

- Benign tumor of smooth muscle cells.
- most common bening tumor in females (30 - 50% in reproductive life)
- estrogen dependent, shrink after menopause
- circumscribed, firm gray-white masses with whorled cut surface
- location: intramural, submucosal or subserosal
- may develop hemorrhage, cystic change or calcification
- Clinically: asymptomatic or symptomatic, menorrhagia dragging sensation, anemia .... etc.
- Never transform to sarcoma.
- Presence of multiple lesions doesn't increase risk of malignancy.....

② Lieosarcoma

- malignant counterpart of lieomyoma
- NOT from preexisting lieomyomas
- hemorrhagic, necrotic, infiltrative
- Diagnosis: ① coagulative necrosis
② Cytologic Atypia
③ Mitotic activity
- Recurrence common & metastasize
- 5 Year survival rate = 40%

[cries, but in a cool way]

lec 3

Epithelial
Germ cells
sex cord / stromal

* Ovarian Neoplasms *

① Epithelial Neoplasms

- Spordic cases
  - BRCA 1 & 2
  - P53 most cases.
  - HER2 / NEU
  - KRAS
- Familial cases
  - BRCA 1 & 2.

Serous tumors

- most frequent ovarian tumors
- Bening, malignant, borderline
- most common malignant ovarian tumors.
- Genetics:
* BRAF & KRAS mutations → Borderline & low grade serous tumors.
- BRCA 1 & P53 → High grade serous tumors.

① Benign serous tumors.

- cystic, large
- May be bilateral
- Filled with clear serous fluid
- Single layer of columnar epithelium. Some cells are ciliated.
- Psammoma bodies (laminated calcified concretions) are common in tips of papillae of all serous tumors

② Borderline serous tumors.

- complex architecture.
- mild cytological atypia
- No stromal invasion
- May have peritoneal implants
- Can recurs some can progress to carcinoma
- Prognosis: intermediate between benign & malignant
- Survival with peritoneal metastases = 75%)

③ Malignant serous tumors:

- Two types:-

① low grade

- arise from borderline lesions
- Progress slowly to become invasive
- Differentiated morphology
- Mutations in KRAS.

high grade

- develop rapidly.
- many rise from fallopian tube via serous tubal intraepithelial carcinoma, rather than ovarian coelomic epithelium
- Mutations in TP53.
- Anaplasia of cells & invasion of the stroma
- Prognosis Poor, depends on stage at time of diagnosis.

Mucinous tumors.

- Mucin secreting cells.
- 80% bening, 10% borderline
  10% malignant.
- usually large & multilocular
- Psammoma bodies NOT found.
- Stage is major determinant of prognosis

Clinical Correlations for All Ovarian Tumors (epithelial, germ cells, stromal)

Clinical presentation of all is similar:

- Abd. pain, gastrointestinal complaints, urinary frequency; rarely torsion producing severe abdominal pain mimicking an "acute abdomen."
- Ascites (in Fibromas and malignant serous tumors).
- Functioning ovarian tumors : Estrogens or androgens.
- Treatment: surgery + chemotherapy + radiotherapy
- Outcome of ovarian cancers remains unsatisfactory
- Malignant tumors are usually discovered in advanced stages
- survival minimally improved since 1970s.
- No early Screening methods are yet available

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② Germ cell Tumors

By : Noor Almomani

- Types according to differentiation :

* Dysgerminoma , embryonal carcinoma , yolk sac tumor , choriocarcinoma , Teratoma *

⇒ Benign (mature) cystic teratoma
- Totipotential germ cells form mature tissues of all three germ cell layers.
- 15 - 20 % of ovarian tumors
- many discovered incidentally
- 90% unilateral
- cyst filled with sebaceous secretion of hair, bone and cartilage ; epithelium, or teeth
- 790 % are benign mature cystic teratoma... immature is rare.
- Torsion (10% to 15% of cases)

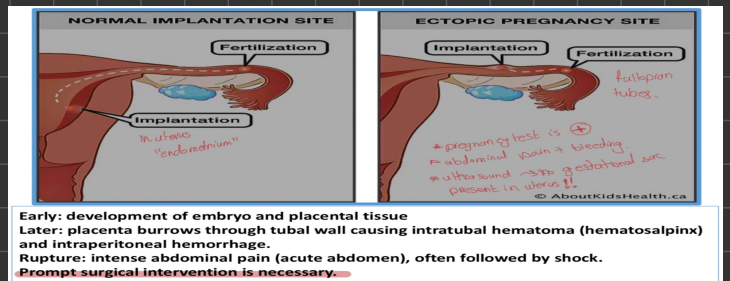
Germ cell and sex cord–stromal cell tumors
- less frequent
- constitute 20% to 30% of ovarian tumors
- collectively responsible for less than 10% of malignant tumors of the ovary (so many pf them are benign)

* Pathology of fallopian tubes *

① Ectopic Pregnancy

- implantation of the fertilized ovum outside uterus
- Incidence 1%
- 90% of cases occur in fallopian tubes
- Other sites: ovaries , abdominal cavity

- Predisposing factors: Tubal obstruction (50%) , PID Tumors, endometriosis , IUCD.
- In 50% : no anatomic cause can be demonstrated



Early: development of embryo and placental tissue
Later: placenta burrows through tubal wall causing intratubal hematoma (hematosalpinx) and intraperitoneal hemorrhage.
Rupture: intense abdominal pain (acute abdomen), often followed by shock.
Prompt surgical intervention is necessary.

② Tubal malignancies

- most common histologic type is serous carcinoma
- maybe the origin for many ovarian high grade serous carcinomas.
- Serous Tubal Intraepithelial carcinoma (STIC) in fimbriated ends of fallopian tubes

- Increased in women with BRCA muta

- Fallopian tube carcinomas frequently spread to omentum and peritoneal cavity at time of presentation (advanced) because of their access to peritoneal cavity