Lec 8 Vulvar Diseases

- we will discuss non-neoplastic diseases (more common) & neoplastic (less common)

Non-Neoplastic

Lichen Sclerosus

- postmenopausal elderly women
- white plaques, thinned skin/epidermis, dissapearance of rete pegs, hydropic degeneration of basal cells
* so here we have THINNING or dissapearance
- unknown pathogenesis, maybe autoimmune
- does not lead to cancer

Lichen Simplex chronicus

- end result of inflamitory conditions
- white plaque (leukoplakia), thickening epithelium, hyperkeratosis, no atypia
- does not lead to cancer, but can be located next to cancers

Condylomas (STD)

- Anogenital warts from low risk HPV 6 & HPV 11
- hallmark: koilocytosis*
  - abnormal morphology of karatinocytes
- not premalignat

HPV & female genital Disease (some notes)

- low risk HPV → 6 & 11 → warts (condyloma) → same

presentation in all organs of genital tract

- High risk HPV -> 16, 18, 45, 31 -> cause intraepithelial dysplasia & invasive cancer in all lower genital tract organs, even in males
  - 16, 18 ↳ most important

how do HPV 16 & 18 cause dysplasia & cancer ?

- they create viral proteins E6 & E7 that block & inactivate tumor supressor genes P53 & RB -> causing mutations & malignancy

* HPV vaccine is effective in preventing warts, & HPV related cancers

Neoplastic Vulvar Disease

Intraepithelial neoplasm (IN)

- from high risk HPV
- peak age of IN is 30 -> here we have dysplasia & it is pre-malignant stage
- then we have latency period of about 15 years, & progresses to invasive cancer at 45 years
- pre malignant stage / Dysplasia has grading :
  - IN1 : mild dysplasia ($^1/_3$ of epithelium is thickened)
  - IN2 : moderate dysplasia ($^2/_3$ thickened)
  - IN3 : Severe dysplasia, full thickening = Carcinoma in Situ*
- IN is in all lower genital tract & named according

to location ... for example :

Vulvar dysplasia = VIN 1, 2, or 3

Vaginal dysplasia = VaIN 1, 2, or 3

Cervical dysplasia = CIN 1, 2 or 3

- Risk factors of malignancy include : genetic, immunologic or environmental (smoking, superinfection w/ HPV)

Vulvar Squamous Cell Carcinoma (invasive)

- 2 types :
  - Basaloid/poorly differentiated SCC - most common, younger age group; *from high risk HPV*, poorly differentiated
  - well differentiated SCC - less common, older women, *not related to HPV*, found next to lichen simplex or sclerosus, differentiated cells

Cervical Diseases

- most common cervical cancer is SCC w/ peak age of 45 years ... 10-15 years after its precursor (CIN 1, 2, 3)
- cervical cancer stage is the most important prognostic factor
- treatment for CIN = laser or cone biopsy
- Treatment for invasive = surgical excision (hystorectomy)
- 5 year survival rate drops as stage increases

but guess what ?!

- this used to be the most common cancer until ....

Papanicolau (PAP) smear test *

- Pap smear reduced incidence & mortality by 99 % !!
  ↳ one of the most sucessful screening tests
- a sample is taken from cervix transition/ transformation zone

Lec 9 Uterine pathology

Patho of endometrium

- endometrium is the most inner layer, contains glands & stroma, & is the functional part of uterus

Endometritis

- inflimation of endometrium by:
  - Infection (local or generalized) - pelvic inflamitory disease (PID) → generalized & can be associated w/ fillopian tube or ovarian infection
  - miscarage / abortion / delivery
  - Intrauterine device (IUCD)
- endometritis can be acute or chronic
- Symptoms: fever & abdominal pain (acute), menstrual abnormality, infertility, ectopic pregnancy
- treatment: removal of cause, antibiotics, Dilation & Curettage (D & C)

Adenomyosis

- Stroma or glands embedded in myometrium (this is benign & abnormal location of glands & stroma

- Thick & large uterus
- Derived from stratum basalis* (no cyclical bleeding)
- Symptoms: menorrhagia, dysmenorrhea, exaggerated uterine contractions

Endometriosis

- glands & stroma outside uterus (benign & abnormal)
  - most common location = ovaries

* can be in more distant sites (lungs, lymph nodes, umbilicus)

- usually during reproductive years = ↑ infertility rate
- presents w/ dysmenorrhea, peluic pain, & mass w/ blood (chocolate cyst)
- contains functionalis endometrium* (cyclic bleeding) → bleeding spots leading to fibrosis, sealing tubal fimbrated ends, distortion of ovaries, infertility & ectopic pregnancy
- need 2/3 to diagnose: endometrial glands, stroma, or hemosidren pigment
- 4 theories explaining endometriosis:
  1) Regurgitation Theory*: retrograde / backflow menstruation → most accepted theory
  2) metaplastic theory: endometrical differentiation of Coelomic epithelium
  3) vascular / lymphatic disemination
  4) extrauterine stem / progenitor cell theory

Endometrial Hyperplasia

- ↑ # of endometrial glands due to prolonged ↑ of exoginous or endogenous estrogen (more than progestin), & can progress to cancer
- Severity depends on atypia & architectural crowding:
    1) typical hyperplasia
    2) Atypical hyperplasia → ↑ risk of cancer by 20% *endometriod carcinoma
- Risk factors: obesity, Diabetes, hypertension, Infertility, estrogen replacement therapy, tumors that secrete estrogen

Tumors of Endometrium

Benign endometrial Polyps

- dilated glands w/ muscular arteries & fibrotic stroma, can be sessile or pedunculated
- no risk of Cancer

Endometrial Carcinoma

- most common cancer in female genital tract (50-60 years)
- type I: endometriod carcinoma associated w/ excess estrogen in perimenopausal women
- type II: Serous carcinoma associated w/ older women w/ endometrial Atrophy

Endometriod Carcinoma

- similar to normal endometrium
- same risk factors as endometrial hypersplasia
- mutations in DNA missmatch repair genes & PTEN *

- prognosis depends on stage
- precancerous lesion = Atypical endometrial hyperplasia

Serous Carcinoma

- no relation w/ estorgen or hyperplasia
- mutation in P53 *
- prognosis worse than endometriod & depends on staging

Tumors of Myometrium

- myometrium is 2nd layer, contains smooth muscle cells

Leiomyoma (fibroids)

- most common benign tumor of reproductive age
- tumor of smooth muscle cells → estrogen dependent, so it shrinks after menopause
- circumscribed firm gray/white mass w/ whorled cut surface *, tend to be multiple
- located intramural, submucosal, or subserosal
- asymptomatic or symptomatic: menorrhagia, dragging sensation, anemia

* never transform to sarcoma

Lieomyosarcoma

- malignant, not from preexisting lieomyoma
- * hemorrhagic, necrotic, infiltrative * borders, atypia, mitotic activity

- recurrence & metastasis

Lec 10 Ovarian & Fallopian Tube

Ovarian Neoplastic Diseases

- 5th most common cause of cancer & Death in women
- Primary origins : epethelium, germ cells, sex cord / stromal cells
- or can be Secondary
- Risk factors : Nulliparity, high estrogen, or family history

* pregnancy or oral contraceptive pills (OCP's) ↓ risk

Epithelial ovarian Neoplasm

- majority of ovarian tumors & 90% of ovarian cancer
- arise from fallopian tube or epithelial cyst in cortex of ovaries (they used to think it came from coelomic epithelium)
- Sporadic mutation : BRCA 1 & 2, P53, HER2/NEU overexpression, K-RAS over expression
- Familial : BRCA 1 & 2
- tumor types include : serous, mucinous, endometrioid, clear cell, Brenner
  - Can all be benign, borderline, malignant

Serous Tumors

- most* frequent ovarian* & epithelial* tumor

- * most common * malignant ovarian tumor

→ * so serous tumors are serious :)

* Psammoma bodies are seen in all serous tumors (benign, borderline, & malignant)

Benign Serous tumor (BRAF & K-Ras mutation)

- large * smooth unilobular cyst filled w/ serous fluid & can be bilateral

- single layer of ciliated columnar epithelium

Borderline Serous Tumor (BRAF & K-Ras mutation)

- complex archetecture, mild atypia, no stromal invasion, peritonial implants, solid papilla

- can recur & progress

Malignant Serous Tumor (2 types)

- low grade: from borderline lesion, progress slowly, Differentiated, KRAS mutation

- high grade: from fallopian tube, rapid progression, invasion of stroma w/ anaplasia, TP53 mutation

Mucinous ovarian Tumor

- large, multilocular mucin secreting tumor

* no psammoma bodies

- prognosis depends on stage (Benign, borderline, malignant)

* so mucinous & serous are of epithelial origin...

next...

Germ Cell Tumors

- Different types depending on differentiation (same as males)
- Dysgerminoma, embryonal carcinoma, yolk sac tumor, choriocarcinoma, Teratoma

Benign (mature) Cystic Teratoma

- most common germ cell tumor
- totipotent cells that create cysts w/ sebaceous secretion, hair, teeth, bone ..... anything
- unilateral, discovered incidentally & can cause torsion

Clinical Presentation of All Ovarian Tumors

- Abd. pain, GI complaints, urine frequency, torsion mimicking acute abdomen
- Ascites in fibroma & malignant serous
- Functioning ovarian tumors produce estrogen / androgens
- ovarian tumor outcome is unsatisfactory
- malignant tumors in advanced stage need debulking surgery

Fallopian Tube Patho

Ectopic Pregnancy

- implantation of fertilized ovum outside uterus, usually fallopian tubes, due to tubal obstruction, PID, IUCD, endometriosis, tumors
- embryo grows for a few weeks in tubes, then

burrows through tubal walls causing hematoma & hemorrhage

- Rupture causes Abd. pain (acute abdomen) & shock

* surgery is needed

* pregnancy not viable

Tubal Malignancies

- Serous carcinoma is most common

- Serous Tubal intraepithelial carcinoma (STIC) in fimbriated ends of fallopian tube & TP53 mutation

* BRCA mutation ↑ chance of STIC

* fallopian tube carcinomas can spread to omentum & peritonical cavity