

Lec 11 Trophoblastic Diseases

- Trophoblasts are differentiated cells from fertilized ovum that form the placenta & nourish the developing embryo
- Hydatidiform mole (molar pregnancy) is abnormal fertilization leading to abnormal gestation w/ incidence of 1-1.5/2000
- higher incidence in Asian countries
- before maternal age 20, & after age 40

* diagnosis w/ ultrasound

Complete Hydatidiform Mole

- this is when an empty egg is fertilized by 2 sperm, or a diploid sperm leading to diploid karyotype w/ only paternal DNA (completely paternal DNA ... hence the name complete mole)

- Karyotype = 46 XX or 46 XY → uncommon (diploid)
- b/c maternal DNA is crucial for fetal development, this case has no fetus, & no embryogenesis

* Dispermy = 2 sperms ; Diandry = 2 sets of paternal DNA

- Diffuse & circumferential trophoblastic proliferation w/ atypia & edema in all villi
- huge HCG increase in serum & tissue

Prognosis

- 80-90% → no recurrence
- 10% → invasive mole into myometrium & can metastasize
- 2-3% → choriocarcinoma *

Partial Hydatidiform Mole

- when a normal egg fertilized by 2 sperm or diploid sperm, leading to triploid karyotype w/ predominance of paternal DNA

- early embryo formation w/ normal chorionic villi → 69 XXY → non-viable fetus

* outcomes are less severe than complete mole

↳ less elevated HCG than complete, some villi w/ edema,

no Atypia

- better prognosis than complete &

rarely give rise to choriocarcinoma

Mole vs. Normal Pregnancy

Feature	Complete Mole	Partial Mole
Karyotype	46,XX (46,XY)	Triploid (69,XXY)
Villous edema	All villi	Some villi
Trophoblast proliferation	Diffuse; circumferential	Focal; slight
Atypia	Often present	Absent
Serum hCG	Elevated	<u>Less elevated</u>
hCG in tissue	++++	+
Behavior Outcome	2% choriocarcinoma	Rare choriocarcinoma

- both pbs. present w/ amenorrhea, + urine / blood pregnancy test, & ↑ HCG ... but molar pregnancy has more elevated

HCG levels

- antenatal care ultrasound shows "snow storm" vesicles *
in molar; fetus in normal

Morphology of mole

- evacuation & Dilation should be done, & it shows abnormal swollen chorionic villi w/ abnormal trophoblast proliferation (grape-like structures) *, & atypical chorionic epithelium

Microscopically

- bigger sized villus in molar (look like vesicles)

- trophoblastic proliferation around villus

Choriocarcinoma

- rare aggressive malignant tumor from gestational chorionic epithelium or gonads
- higher incidence in Asian countries age before 20 or after 40
- 50% from complete mole, 25% from abortion, or could occur from normal pregnancy

Clinically

- bloody / brown discharge, ↑ HCG, hemorrhagic / necrotic mass in myometrium
- no chorionic villi, instead, it is made of anaplastic cytotrophoblasts & syncytiotrophoblast

Prognosis

- prognosis & survival rate is getting better due to chemotherapy
- spreads through the blood to lungs & other organs
- lymphatic invasion is uncommon

Lec 12 Breast Pathology

- Breast is a secretory gland made of epithelial structures (lobules → main secretory unit, & ducts) & non-epithelial stromal structures (stroma & fat)
- lobule is made up of acini

Clinical Presentation of Breast Disease

- Pain → 90% of painful mass is benign

- inflammation (edema, erythema, infections) → benign

- palpable masses → evaluated to rule out cancer

- nipple discharge

- gynecomastia → only in males

* all symptoms or only 1 symptom may be present,

90% of the time it is benign, & malignancy ↑ w/ ↑ age

- 1/2 pts. have symptoms, 1/2 are discovered incidentally

by mammogram → (↓ mortality & morbidity)

→ Successful screening test, detects early non-palpable asymptomatic breast cancer about 1 cm in size, & presents as whitish densities or micro calcifications

Fibroadenoma (non-epithelial)

- most common benign neoplasm of the stroma due to estrogen activity → enlargement during pregnancy & regression/ calcifications during menopause

- 20-30 yrs

↳ discrete, sharp borders, solitary, free moving nodule

↳ easily shelled out during surgery

- entrapped ducts due to growing stroma

Benign Epithelial lesions (3 groups)

- 3 classifications to estimate risk of breast cancer

Nonproliferative changes (Fibrocystic)

- Common

- cyclical pain & tenderness w/ menstruation

- Cystic apocrine metaplasia (most common), Fibrosis, & Adenosis

* no ↑ risk of breast cancer

Proliferative lesion w/out Atypia

- 1.5 - 2 fold ↑ risk of cancer
- prominent glands & ↑ # of lobules, but normal structures
- epithelial hyperplasia, sclerosing adenosis, complex sclerosing lesion, papilloma

* not clonal, no genetic changes

Proliferative w/ Atypia

- 4.5 fold ↑ risk of cancer
- Atypical lobular hyperplasia (ALH) → resembles LCIS
- Atypical Ductal hyperplasia (ADH) → resembles DCIS
- clonal, w/ some histologic features required for in situ diagnosis

Breast Cancer

- most common malignancy & cancer related deaths in women
- ↓ mortality rate due to improved screening, chemo/radio/immuno/hormonal therapy
- >95% are adenocarcinomas

Risk factors

- ↑ after age 30; only 1% of men compared to women
- first degree relatives w/ early onset = ↑ risk

Pathogenesis

- mutations in : BRCA 1/2 , TP53 , PTEN loss , HER2 amplification

- associated w/ estrogen & estrogen agonists , but progesterone is protective

- environmental : smoking , obesity , lifestyle

- Reproductive history : nulliparity , no breastfeeding , old age pregnancies

morphology

- most common location is upper outer quadrant (50%)

* Breast carcinoma separated depending on histologic type : noninvasive & invasive

Noninvasive (IN SITU)

- confined malignant glands in ducts or lobules that do not invade stroma or lymphovascular channels

Lobular Carcinoma in SITU (LCIS)

- malignant clonal proliferation in Lobule

Ductal Carcinoma in SITU (DCIS)

- malignant clonal proliferation in Ducts w/ wide variety of histologic features depending on what is produced inside the duct from necrosis : Solid , Comedo , papillary , & micro-papillary

- can range from low - high grade

Management of both LCIS & DCIS

- after seeing white irregularities on mammogram , do biopsy

using true cut procedure

- wide local excision surgery, irradiation, tamoxifen
- excellent prognosis but can become invasive if left untreated

* associated w/ adjacent invasive carcinoma

Invasive

- classification depends on hormonal receptor profile:

estrogen receptor (ER) → positive in 60% of cases → use

estrogen antagonist in treatment; progesterone receptor (PR);

human epidermal growth factor receptor 2 (HER2/neu) →

positive 20%

- triple negative (ER, PR, & HER2) → 10% of cases →

Agressive

* the point is, w/ each type, they use different treatment method

Invasive Ductal Carcinoma (not otherwise specified carcinoma)

- 70% of cases * most common

- precancerous lesion = DCIS

- ER+, PR+, HER2-

Invasive lobular carcinoma

- 10%

- precancerous = LCIS

- multicentric / bilateral masses

- ER+, PR+, HER2+ → rare or absent

Carcinoma w/ medullary features

- 5%.
- triple negative & precancer is absent
- large anaplastic cells w/ lymphocytic infiltrate
- * ↑ risk w/ BRCA1 mutation

Colloid (Mucinous) Carcinoma

- rare < 5%.
- ER+, HER2-
- soft gelatinous mass w/ extracellular mucin

Tubular Carcinoma

- < 5% (least common)
- ER+, HER2-
- irregular mammogram densities, well-formed tubules, low grade nuclei, rare lymph metastasis, great prognosis

Spread of Breast Cancer

- lymphatic → Axillary lymph nodes
- hematogenous
- mostly to bones, lungs, liver, Adrenals
- pts. need follow up after treatment, b/c metastasis can happen many years after treatment

Prognosis

- depends on: tumor stage, Lymph invasion, molecular subtype, histologic types & grade, ER/PR/HER2 expression