النادي الطبي

GENITOURINARY SYSTEM

SUBJECT : Pathology

LEC NO. : 14

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GENITOURINARY SYSTEM

Germ cell tumor

most common type in testis tumors

- testicular epithelial tumors are very rare.
- benign cystic teratomas are never seen in the testis, while testicular malignant germ-cell tumors are the most common
- Teratomas constitute 20% of ovarian T.
- Majority of teratomas are Benign in ovaries.
- The immature malignant variant is rare (5-10%).

but in testis it is mostly malignant/ mature teratoma (because 37% metastasis)

Benign (Mature) Cystic Teratomas :

- All are marked by full **differentiation** from totipotential germ cells into mature tissues, representing all three germ cell layers: ectoderm, endoderm, & mesoderm.

SKIN + HAIR

GLANDULAR STRUCTURES

BONE + CARTILAGE

Ovary tumors > delayed symptoms [GI SYMPTOMS] >> (Nausea, vomiting, abdominal pain{discomfort}, floating)

At the time of the diagnosis > it could reach large size or metastasis

- Most are discovered in young women **(1-20 years)** as an ovarian **masses** or incidentally found by X-ray
- Grossly: cyst filled with sebaceous secretion and hair; bone and cartilage; epithelium, or teeth.
- 1% → malignant transformation.
- torsion (10% to 15% of cases).
- Most discovered incidentally.
- 90% unilateral.
- **Struma ovarii** composed entirely of **mature thyroid tissue** appearing as small or large solid, unilateral brown ovarian masses. Interestingly may hyper function & produce thyrotoxicosis.

Type of benign cystic teratoma

v.imp

v.imp

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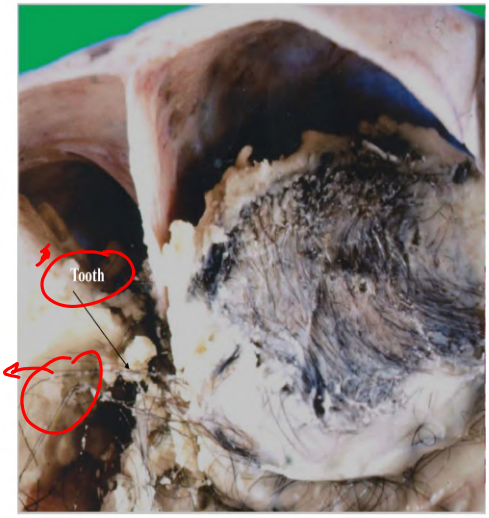
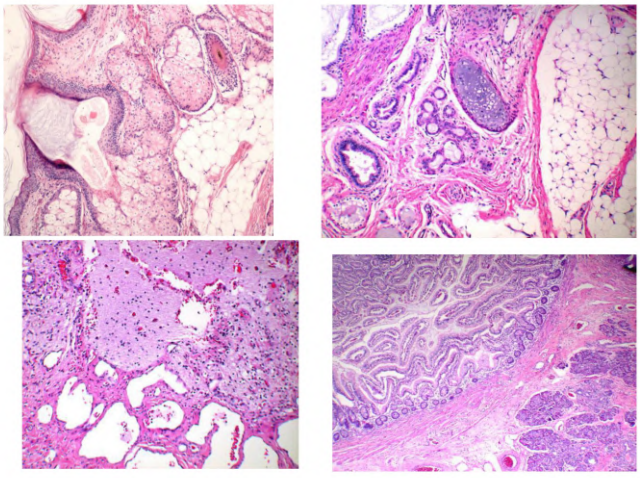
Benign (Mature) Cystic Teratomas

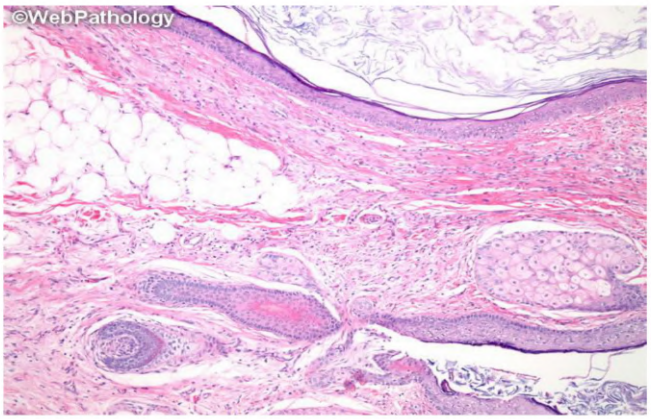


Opened mature cystic teratoma (dermoid cyst) of the ovary with a ball of hair

Benign (Mature) Cystic Teratomas



Mature Cystic Teratoma (Ovary) showing cystic spaces lined by stratified squamous epithelium containing sebaceous glands and hair follicles. Mature adipose tissue is also seen. Same case as the previous two images.



If we see neural elements : immature teratoma in ovary

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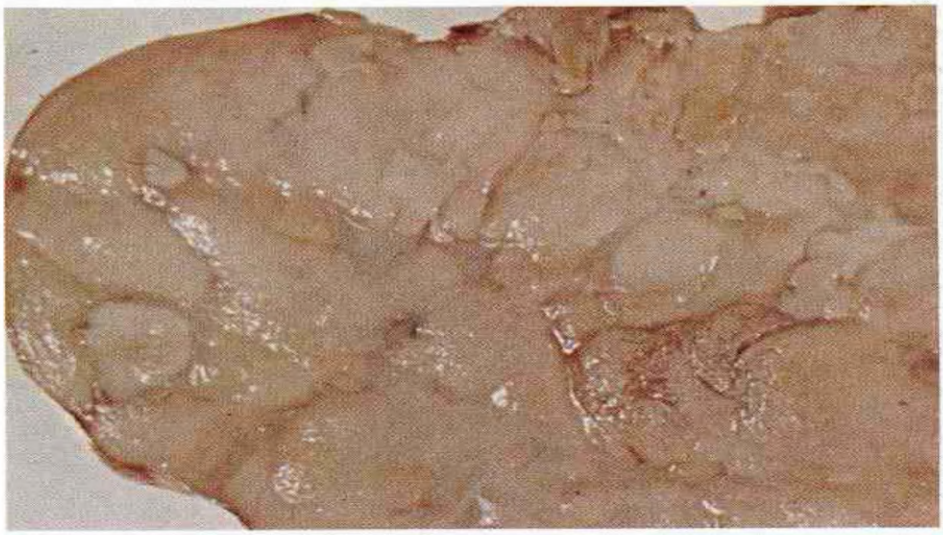
Dysgerminoma

- Counterpart of testicular seminoma
- 2nd to 3rd decades.
- occur with gonadal dysgenesis.
- All are malignant, but only one-third aggressive & spread;
- All radiosensitive with 80% cure.
- Mostly unilateral, solid, small to large potato-like gray masses

Dysgerminoma: ovary =counterpart of testicular **seminoma**. The C/S is **potato**-like, solid, lobulated, pinkish-grey with foci of whitish necrosis.



12.63 Dysgerminoma: ovary

Sex Cord Tumors; mostly benign

(I) Granulosa-thecal cell:

- (5-10% of all ovarian T).
- Mostly postmenopausal, but may occur at any age.
- Unilateral, small to large, gray to yellow with cystic spaces.
- Morphology:composed of mixture of: (1) cuboidal granulosa cells (may recapitulate ovarian follicle as Call-Exner bodies arrange in cords, sheets, or strands, Mostly benign, but malignant granulosa cell T are seen in 5% to 25% of cases, & (2) spindled/plump lipid-laden thecal cells which elaborate large amounts of estrogen promoting endometrial or breast ca.

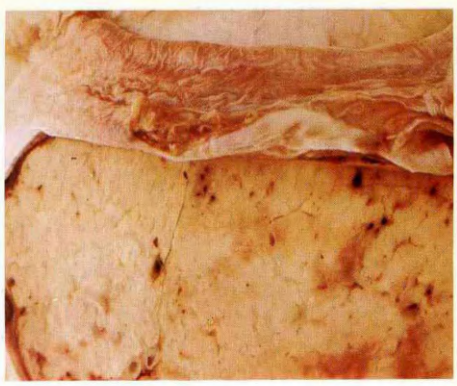
cause hyperplasia
associated with vaginal bleeding

(II) Thecoma-fibroma:

- Any age, Benign, unilateral, Solid, & gray
- Morphology: fibrocytes, to yellow (lipid-laden) plump thecal cells.
- Most are hormonally inactive; few elaborate estrogens.
- **For obscure reasons, about 40% produce ascites + hydrothorax = (Meig's syndrome).**

(1)

Granulosa cell tumor: ovary. Unilateral, solid encapsulated, C/S is yellow with foci of hemorrhage.



12.67 Granulosa cell tumour: ovary

(2)

Fibroma: ovary. Spherical, firm & smooth-surfaced, O/S whorled with fibrous trabeculae.

12.66 Fibroma: ovary

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(III) Sertoli-Leydig cell:All ages, Unilateral,
★Usually small, gray to yellow-brown, & solid. ★Recaps (simulate) testis development, with tubules or cords & plump pink Sertoli cells;
★Many masculinizing or defeminizing.
★ Rarely malignant. (secondary sex character of the male)

➔**Metastases to Ovary = Krukenberg tumors**
- ★Older ages, Mostly **bilateral**
- ★Solid gray-white masses up to 20 cm in Ø(1 Kg)
- Anaplastic T cells in cords, glands, dispersed through fibrous background.
- Cells may be "signet-ring" mucin-secreting.
- ★Primaries are GIT, breast, & lung.

Clinical Correlation of all Ovarian Tumors

- clinical presentation of all is similar:
  - 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 often come to attention because of hormonal production (Estrogens or androgens).
- **Most** ovarian T are asymptomatic until they are well advanced.
- **30%** of all ovarian T are discovered incidentally on routine gynecologic examination!

Pathology of Fallopian Tube

الحمل خارج الرحم Ectopic pregnancy

- implantation of the fertilized ovum outside uterus
- Incidence: 1%
- 90% of cases → 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.

Intrauterine Contraceptive Device

Pelvic inflammatory disease

Ectopic Pregnancy

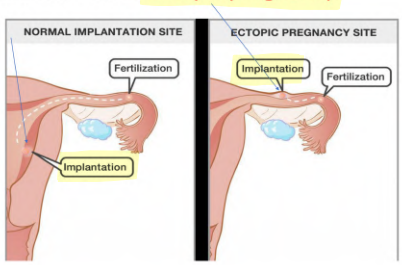
- Early: Grossly, EP in all sites is characterized by fairly normal early development of the embryo, with the formation of placental tissue, decidual changes & the amniotic sac.
- Later: the placenta burrows (hole) through tubal wall causing intratubal **hematoma (hematosalpinx) and intraperitoneal hemorrhage.**
- Rupture of an ectopic pregnancy: intense abdominal pain **(acute abdomen)**, often followed by shock.(EMERGENCY)
- **Prompt surgical intervention is necessary.**
- **Histological diagnosis & confirmation** depends on the visualization of the ® **placental villi or, rarely, of the embryo.**

imp

any married female with lower abdominal pain/ right iliac fossa pain/ left iliac fossa pain >> we have to consider the diagnosis of ectopic pregnancy till we exclude it

we do pregnancy test

Normal Versus ectopic pregnancy.



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- **Until rupture occurs**, **EP** may be indistinguishable from a normal pregnancy, with amenorrhea & elevation of serum & urinary hCG (Positive pregnancy test).

- Under the influence of hCG, the **endometrium** undergoes characteristic hypersecretory & decidual changes called ® **Arias Stella Reaction** (in 50% of cases); But, as expected, there are **NO chorionic villi in the uterus**.
- However, the **absence** of elevated hCG levels & positive pregnancy test **does not exclude** the diagnosis of EP because poor attachment with necrosis of the placenta is common.

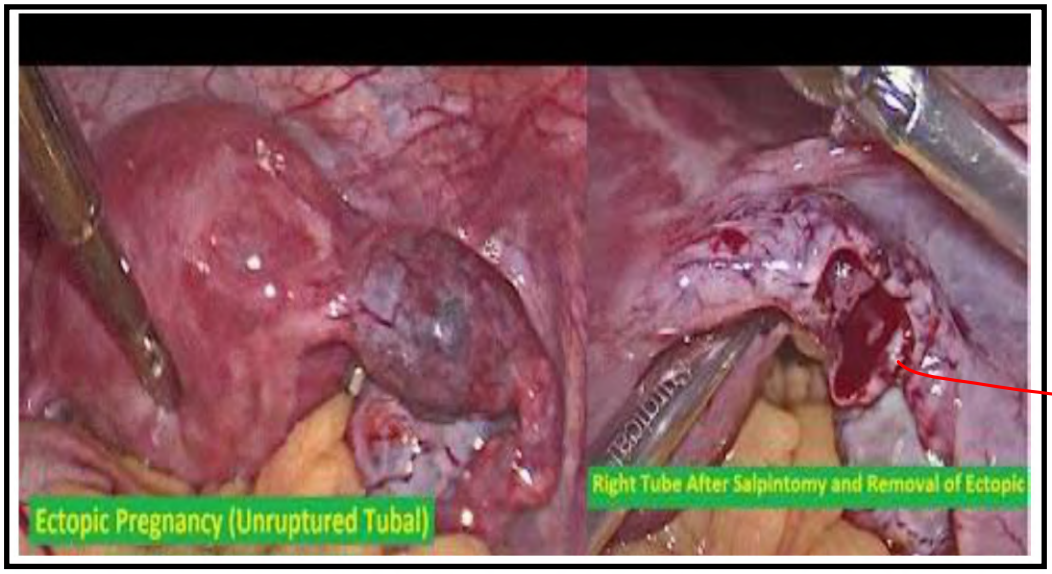
- **Rupture of an EP may be catastrophic, with** sudden onset of intense abdominal pain & signs of an **acute abdomen**, often followed by sever hemorrhage & hypovolemic shock. Prompt surgical intervention is **life-saving**

Tubal malignancy

- considered rare.
- **most common histo. type is serous carcinoma.**

- increased in women with **BRCA mutations** (In studies of prophylactic oophorectomies: 10% → occult foci of malignancy in fimbria).

- Because **of access to peritoneal cavity**, fallopian tube carcinomas frequently spread to omentum and peritoneal cavity at time of presentation (advanced).



Salpintomy

GESTATIONAL TROPHOBLASTIC DISEASE

- Gestational trophoblastic T are divided into 3 categories, ranging in their aggressiveness from the:
- (I) Benign, Complete & Partial Hydatidiform moles (HM),
- (II) Invasive mole. → presence of villi
- (III) highly malignant Choriocarcinomas (Chorio ca). → no villi
- All trophoblastic T elaborate human chorionic gonadotropin (hCG), which can be detected in the circulating blood & urine (used for the diagnosis of pregnancy) at titers considerably higher than those found during normal pregnancy ;the titers progressively rising from HM, to invasive mole, to Choriocarcinoma.

increased level >> recurrence or metastasis

- The fall or the rise in the hCG level in the blood or urine can be used also to monitor the effectiveness of treatment.
- Clinicians therefore prefer the term gestational trophoblastic disease, because the response to therapy as judged by the HCG titers is significantly more important than the anatomic segregation of one lesion from another.

1 Hydatidiform Mole (HM): Complete & Partial

- Typical HM appears grossly as grape like structure, is a voluminous mass of swollen, cystically dilated chorionic villi.
- The swollen villi are covered by varying amounts of normal to highly atypical chorionic epithelium. cytotrophoblast +syncytotrophoblast
- HM is due to an abnormal contribution of paternal chromosomes in gestation.

- Two distinctives subtypes of HM, complete& partial have been characterized & the 2 patterns result from abnormal fertilization, in which a:

- **Complete HM,** an empty egg is fertilized by 2 spermatozoa(or a diploid sperm),yielding a diploid karyotype (46, XX or, uncommonly, 46, XY) composed entirely paternal genes. all from father (empty egg)

- The complete HM does not permit embryogenesis & therefore never contains fetal parts. All of the chorionic villi are abnormal, & the chorionic epithelial cells are diploid & all chromosomes are paternal.

❖ **While Partial HM,a** normal egg (23 chromosome) is fertilized by 2 spermatozoa (or a diploid sperm),resulting in a triploid karyotype (69, XXY) with a preponderance of paternal genes. **23 from mother (normal egg) , 46 from father (diploid sperm)**

❖ The partial HM is compatible with early embryo formation & therefore contains fetal parts, has some normal chorionic villi, & is always triploid & having 2 sets of paternal chromosomes.

Complete HM: empty ovum (0) fertilized by two sperm (46); karyotype 46xx ,46xy (all from father)
grape like, no normal villi, no fetal parts

Partial HM: normal ovum (23) fertilized by two sperm (46); karyotype 69xxx ,69xxy (23 from mother, 46 from father)
grape like, mixed normal+abnormal villi, fetal parts

Table showing Features of Complete & Partial HM:		
Karyotype: 46, XX (46, XY)		Triploid (69, XXY)
Villous edema: All villi		All villi
Trophoblast Proliferation: Diffuse & circumferential		Focal & slight
Atypia: Often present		Absent
Serum hCG: Elevated		Less elevated
hCG in tissue: ++++		+
Progress to choriocarcinoma: 2%	v.imP	Rare

❑ Complete HM incidence is about 1/1000 pregnancies in the US & other Western countries. For unknown reasons there is a much higher incidence in Asian countries.

❑ HM are most common before age 20 years & after age 40 years, & a history of HM increase the risk in subsequent pregnancies.

❑ HM is traditionally discovered at 12 to 14 weeks of pregnancy because of a gestation that was("too large for dates,")however;...

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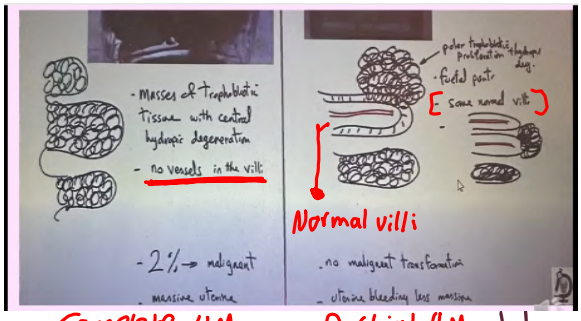
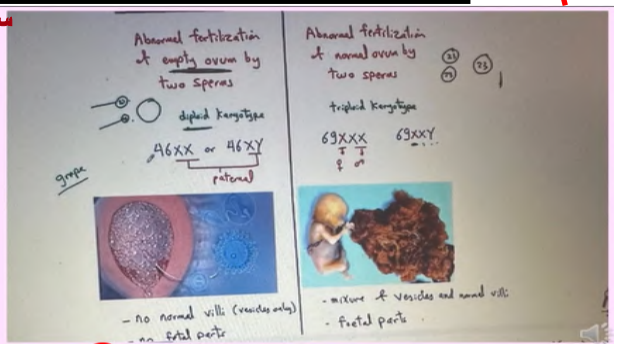


Complete HM
massive uterine bleeding

Partial HM
less uterine bleeding



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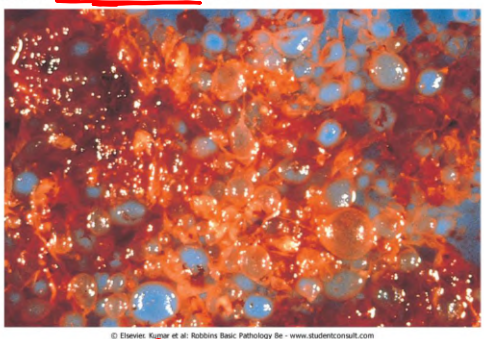
- An **early diagnosis** of HM can be done by
  - (1) early monitoring of pregnancies by ultrasound **(U/S)** which reveal **typical absence of fetal parts, or fetal heart sounds,**
  - **(2) by detecting elevations of hCG** in the maternal blood .

- **Grossly**, in early HM, the uterus may be normal in size; but in fully developed HM the uterine cavity is **larger** than the expected date, **filled** with a delicate, friable mass of thin-walled, translucent cystic structures .Fetal parts are not seen in complete HM but are common in partial HM.
- H, the **complete mole** shows:
- (I) **Hydropic swelling** of chorionic villi, with loose, edematous & myxomatous stroma.
- (II) Virtual **absence of vascularization** of villi.
- (III) **Proliferation** of both cytotrophoblast & syncytiotrophoblast of the chorionic epithelium which may be mild, or striking circumferential hyperplasia.

Complete hydatidiform mole suspended in saline showing numerous swollen (hydropic) villi.



(No fetal parts)

12.49 Hydatidiform mole

Hydatidiform mole.
Mass of grape-like, discrete, rounded translucent vesicles which consist of hydropic & cystic chorionic villi.

Complete HM showing (1) distended hydropic villi, (2)absence of BV & (2) proliferation of the chorionic epithelium (above).

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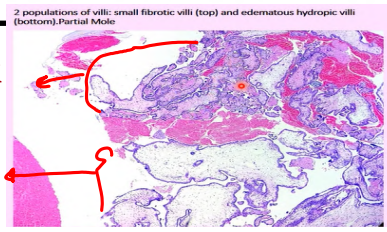
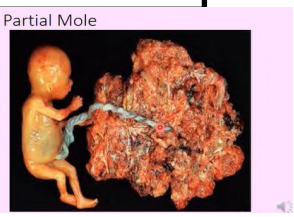
- **Microscopically** : in **partial moles** the
- (1) villous edema involves only **some** of the villi &
- (2) the trophoblastic proliferation is **focal & slight**.
- (3) the villi have a characteristic irregular **scalloped** margin,
- (4) in most cases of partial HM there is evidence of an **embryo** or fetus, which may be in the form of fetal RBCs in placental villi or, in some cases, a fully formed fetus that, despite a triploid karyotype, is morphologically nearly normal in appearance.
- **Prognosis**: Overall, 80% to 90% of HM do not recur after thorough curettage; **10%** of complete HMs are invasive, & **2% to 3% give rise to chorio ca**.
- Partial HM rarely give rise to choriocarcinomas.
- With complete HM, monitoring the post-curettage blood & urinary β-subunit of hCG concentrations, permits detection of incomplete removal or a more ominous complication which can be treated by **chemotherapy, which is almost always curative.**





Invasive Mole

- **Invasive moles are complete HM that are more invasive locally but do not metastasize.**
- An invasive mole retains hydropic villi (which are absent in choriocarcinoma),
- Microscopically : the villi epithelium shows
- (1) **atypical** hyperplastic cytotrophoblast & syncytiotrophoblasts proliferation &
- (2) **penetration of the uterine wall deeply, possibly causing rupture** & sometimes serous **hemorrhage**.
- Local spread to the broad ligament & vagina may also occur.
- **Although they are invasive, metastases do not occur.**

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it doesn't metastasis but

- Hydropic villi may embolize to distant organs, such as lungs or brain, but these emboli do not constitute true metastases & may actually regress spontaneously. Invasive mole is **difficult to remove completely by curettage**, because of the greater depth of myometrium invasion.
- So, serum hCG may remain elevated & required further treatment by **chemotherapy** which is fortunately **curative** in most cases.

Choriocarcinoma (Chorio ca)

- Very aggressive malignant T, **arises either from gestational chorionic epithelium** or, less frequently, from **totipotential cells within the gonads (testis or ovary) or elsewhere.**

- Chorio ca are **rare** in the West, & in the US but are much more common (X15 fold) in Asian & African countries.
- The risk is more before age 20 & is significantly elevated after age 40.
- **50%** of chorio ca arise in complete HM;
- **25%** arise after an abortion,
- **25%** occurs during what had been a normal pregnancy.

Most chorio ca are discovered by the appearance of

- (1) **bloody uterine discharge** accompanied by
- (2) a **rising titer of β-hCG** in blood & urine (much higher than those associated with a HM),
- (3) the **absence of marked uterine enlargement**, such as would be anticipated with a HM.

foul smell

12.50 Hydatidiform mole: uterus

Invasive hydatidifrom mole.

★Uterus sagittal section, showing grape-like vesicles in the cavity, extensively invading the myometrial muscular wall locally (as a result of proliferating trophoblastic activity). The lesion sometimes may **cause (1) hemorrhage, (2) uterine wall perforation**.

❖Grossly:

❖ Chorio ca is very hemorrhagic, necrotic T mass within the uterus, so much so that, sometimes, the histologic diagnosis is difficult. Indeed, the primary lesion may self-destruct, & only the metastases "mets" tell the story.

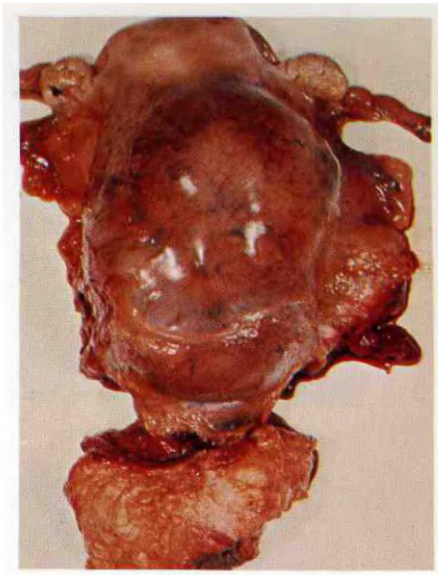
❖ Very early, the T invades into the myometrium & into BV.

❖ Microscopically:, in contrast to HM & invasive moles, the chorionic villi are not formed & are never seen; instead, the T is purely epithelial, composed of anaplastic cytotrophoblast & syncytiotrophoblast .

❖ When discovered, most chorioca are widely disseminated via the blood, most often to the lungs (50%), vagina (30% to 40%) brain, liver, & kidneys

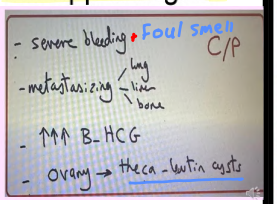
❖ Lymphatic invasion is uncommon

GENITOURINARY SYSTEM



12.51 Choriocarcinoma: uterus

Choriocarcinoma: uterus.
The tumor forms a large mass which has expanded the lower part of the body of the uterus & invaded the cervix & the upper vagina

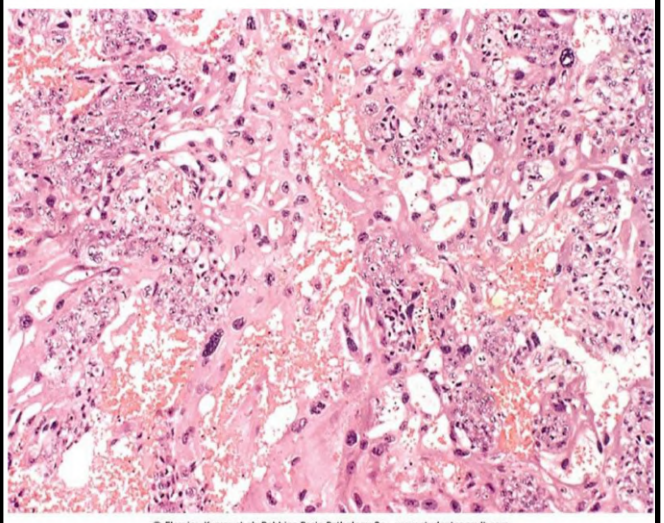


clinical picture

multinuclear
like giant cells

uninuclear

Choriocarcinoma showing: both (1) Neoplastic cytotrophoblasts & syncytiotrophoblasts; & (2) Complete **absence** of chorionic villi.



- Despite the extreme aggressiveness of chorio ca, which made them uniformly fatal in the past, **chemotherapy** has achieved remarkable results with nearly 100% cure, even with T that have spread beyond the pelvis & vagina & into the lungs.
- Equally remarkable are reports of healthy infants born later to these survivors!
- By contrast, there is poor response to chemotherapy in chorio ca that arise in the gonads (ovary or testis).
- This striking difference in prognosis may be related to the presence of paternal antigens on placental chorio ca but not on gonadal lesions. Conceivably (Possibly), a maternal immune response against the foreign (paternal) antigens helps by acting as an adjunct to chemotherapy.

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