

Diseases of Pregnancy

- Diseases of pregnancy and pathologic conditions of the placenta are important causes to morbidity and mortality for both mother and child. These include:
 - Spontaneous abortion
 - Ectopic pregnancy
 - Placental inflammations and infections
 - Abnormalities of Placental Implantation
 - Preeclampsia /eclampsia
 - Gestational trophoblastic diseases.

❖ Gestational trophoblastic diseases

- **Definition:** spectrum of tumors and tumorlike conditions characterized by abnormal proliferation of placental tissue, either villous or trophoblastic
- They are divided into **three** overlapping morphologic categories:
 - 1-Hydatidiform mole (non invasive mole); which is of two types: Complete and Partial
 - 2- Invasive mole; Penetrates the uterine wall, produce hemorrhage but does not metastasize.
 - 3- Choriocarcinoma: highly malignant metastasize into distant organs.
- **Age incidence:** the risk greater **before 20 & after 40 yr.**
- All these disorders elaborate human chorionic gonadotropins (hCG), which is detected in the blood and urine at levels considerably higher than those found during normal pregnancy, the titers progressively rising from hydatidiform mole to invasive mole to choriocarcinoma.
- This elevation in hCG important in :1-Diagnosis of these diseases 2- it can be used to monitor treatment efficacy.

❖ Hydatidiform mole (H- mole):

Voluminous mass of swollen sometimes cystically dilated chorionic villi and variable trophoblastic proliferation, appear grossly as grape like structure.

- It is of 2 subtypes: A. Complete mole B. Partial Mole

Clinically: painless vaginal bleeding 12-14 week after conception,

Diagnosis: In both complete and partial moles, elevation of hCG in the maternal blood & urine. and absence of fetal heart sounds are typical.

Follow up after curetting the uterus is done by ultrasound examination and the serial measurement of hCG hormone monitored for 6 months to 1 year to ensure that hCG levels decrease to nonpregnant levels.

Continuous elevation of hCG may be indicative of persistent or invasive mole.

A. The complete H. mole is characterized by:

- Results from fertilization of an empty egg (that has lost its female chromosome), and as a result the genetic material is completely paternally derived. (In **90%** of cases:

duplication of the genetic material of one sperm, 10% result from the fertilization of an empty egg by two sperm).

- **karyotype:** The chorionic epithelial cells are diploid
- All chorionic villi are abnormal (hydropic changes--- cystic dilated).
- Patients have 10 % risk of invasive mole and 2-3 % risk of subsequent choriocarcinoma.
- **Gross:** uterine cavity filled with **delicate friable masses** of thin wall translucent cystic grapelike structures without fetal parts.
- **Mic.:** almost all villi are enlarged and hydropic with a loose, myxomatous, edematous stroma and circumferential abnormal proliferation of both cytotrophoblasts and syncytiotrophoblasts.

B. Partial H. mole is characterized by:

- Result from fertilization of normal egg with two sperm. the **karyotype** is triploid (e.g., 69,XXY)
- The villous edema involve only some villi & trophoblastic proliferation is focal & slight.
- In partial mole, there are parts of fetus (in complete mole no fetal parts).
- Partial moles have an increased risk of invasive molar disease but are rarely associated with choriocarcinoma.
- **Gross:** hydropic change involving **only some villi. Fetal tissue may be present.**
- **Mic.:** only some of the villi is enlarged and edematous, and the trophoblastic proliferation is focal and slight.

❖ **Invasive mole**

- Invasive moles are complete moles that are locally invasive but lack the metastatic potential of choriocarcinoma.
- An invasive mole **retains hydropic villi, which penetrate the uterine wall deeply, possibly causing rupture and sometimes life-threatening hemorrhage.**
- **Clinically** vaginal bleeding and irregular uterine enlargement, persistently elevated serum HCG.
- **Treatment:** Because invasive mole is difficult to remove completely by curettage, therefore if serum β -hCG remains elevated, further treatment is required. Fortunately, in most cases cure is possible with chemotherapy.
- **Gross:**
Erosive and hemorrhagic lesion caused by hydropic villi, which penetrate uterine wall deeply
- **Mic.:** There is invasion of the myometrium by hydropic chorionic villi, accompanied by proliferation of both cytotrophoblasts and syncytiotrophoblasts.

❖ **Choriocarcinoma:**

- Very aggressive malignant tumor.
- **Origin: arise either** from gestational chorionic (trophoblastic) epithelium (gestational choriocarcinoma) **Or**, less frequently from totipotential cells (germ cells) within gonads (non gestational choriocarcinoma in ovaries or testes) (as a germ cell tumor).
- 50% follow complete mole & rarely follow partial mole, 25% after abortion while the remainder manifest following an apparently normal pregnancy.
- **Clinical presentation:**
 1. Irregular vaginal spotting of bloody brown fluid, which may appear in the course of normal pregnancy, after a miscarriage or after curettage (possibly months after).
 2. **Increase titer of β -hCG** in blood & urine (much higher than with mole).
- **Gross:** soft, fleshy, hemorrhagic, necrotic uterine masses. Sometimes the necrosis is so extensive that little viable tumor remains.
- **Mic.:** In contrast to H. mole & invasive mole, **villi are not formed** instead, the tumor is composed of anaplastic cuboidal cytotrophoblasts and multinucleate syncytiotrophoblasts
- **Disease course and prognosis:**
 - By the time of diagnosis of choriocarcinoma, there is vascular spread usually has occurred to the lungs (50%), vagina (30%– 40%), brain, liver, or kidneys. Lymphatic invasion is uncommon.
 - **Treatment:** depends on tumor **stage**. Usually evacuation of uterus contents and chemotherapy.
 - Despite aggressiveness, **chemotherapy achieve 100% cure** even with tumor that spread beyond pelvis, vagina & into the lung.
 - There is relatively poor response to chemotherapy in choriocarcinoma that arise in gonads (ovary & testis) due to **presence of paternal Ag on placental choriocarcinoma but not on gonadal lesion**, so maternal immune response against foreign (paternal Ag) help by acting as an adjuvant to chemotherapy.