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## Gestational Trophoblastic Neoplasia (GTN)

### Objectives:

- Describe the symptoms and physical examination findings of a patient with GTN including molar pregnancy
- Describe the diagnostic methods, treatment options and follow-up for GTN including molar pregnancy.
- Recognize the difference between molar pregnancy and malignant GTN

**References:** 433 team, kablán

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## Introduction

**Gestational trophoblastic disease (GTD):** It's an abnormal proliferation of trophoblasts (cytotrophoblast and/or syncytiotrophoblast) from the placenta.

**Gestational trophoblastic neoplasia (GTN):** malignant GTD. include choriocarcinoma , placental site trophoblastic tumor and invasive mole these may follow a normal pregnancy or hydatidiform mole.

In the past the majority of patients with GTN localized to the uterus were cured with hysterectomy, but metastatic disease was associated with high mortality.

But Now with ability to measure beta HCG level and highly effective chemotherapy most GTN can be cured and reproductive function preserved.

## Hydatidiform mole\molar pregnancy

Are non invasive localized (benign) tumors that result from abnormal fertilization events that result in proliferation of trophoblastic tissue they are classified as partial or complete molar pregnancy. Both types manage similarly.

Category	Partial	Complete
Eggs	Normal (haploid)	empty
X's	Paternal & maternal X's	Only paternal X's
Karyotype	69XXX or 69XXY	46XX or 46XY
Fetus	Present but Non-viable	absent
Malignancy chance	<5%	6-32%

## GTN or malignant GTD can develop from

- 1- **invasive mole:** Edematous chorionic villi with trophoblastic proliferation that invade into the endometrium
- 2- **choriocarcinoma:** (from normal or molar ) neoplastic syncytiotrophoblast and cytotrophoblast without chorionic villi
- 3- **placental site trophoblastic tumor (rare):** absence of villi with proliferation of intermediate trophoblast cells

-GTN can be characterized as either localized or metastatic as well as classified into either Good Prognosis or Poor Prognosis

Category	nonmetastatic	Good prognosis metastatic	Poor prognosis metastatic
site	Uterus only	Pelvic or lung	Brain or liver
Cure rate	100%	>95%	65%
Number of agents	Single agent chemotherapy		Multiple agent chemotherapy

## Signs and Symptom

Most patients with hydatidiform moles present with irregular or heavy vaginal bleeding during the first or early second trimester of pregnancy. The bleeding is usually painless, while some patients experience pre-eclampsia. Patients may occasionally exhibit symptoms related to hyperthyroidism, such as nervousness, anorexia, and tremors.

### CMP (complete molar pregnancy)

- Hyperemesis gravidarum
- Large uterus for gestational age
- large cystic ovaries
- no fetal heart tone
- Abnormal high B-HCG

### PMP (similar for miscarriage) (partial molar pregnancy)

- No fetal heart tone
- Vaginal bleeding

### Malignant

- Vaginal bleeding >6 weeks

## Risk factor

- Advanced maternal age
- History of GTN
- Asian, Native American or African ancestry
- The incidence of molar pregnancy has been noted to be higher in geographic areas where people consume less  $\beta$ -carotene (a retinoid) and folic acid.

## Diagnosis

**CMP:** with ultrasound

- Diffuse heterogeneous echogenic pattern known as **snowstorm pattern**
- large cystic ovaries can support the diagnosis of complete molar pregnancy

**Malignant:**

- Postmolar GTN Diagnosed by increasing or plateauing of Beta hCG after evacuation of a mole
- Postnormal pregnancy with elevated B-HCG level + excluding the pregnancy

## Management

### Treatment:

- 1- suction dilation and curettage (evacuation)
- 2- hysterectomy (for patients don't wish to preserve childbearing).

The most striking difference between partial and complete moles is related to the malignant potential of the two lesions. **Partial moles rarely metastasize, and only rarely is there the need for chemotherapy**

### For follow up:

check Beta hCG level at 48 hours post-evacuation then every 1-2 weeks while elevated and then monthly for 6 months. (during this time the patient should use a reliable contraceptive method)

All patients should have weekly  $\beta$ -hCG level measurements until three normal levels have been measured.

Patients with a hydatidiform mole should then have monthly level measurements until six normal levels have been measured.

For patients with GTN who have a good prognosis, monthly measurements should be done until 12 normal levels have been recorded.

Patients with GTN who have a poor prognosis should have monthly levels until 24 normal measurements have been recorded.

Patients should use effective contraception during follow-up, following which they may attempt pregnancy.

### Malignant management:

referral and evaluation of metastases and its risk factors.

## Evaluation of metastases

### Blood analysis like

- CBC
- coags
- Renal, Liver function test
- Blood type and antibody screen
- pretherapy B-HCG

### Imaging

- CXR
- CT for head, chest, abdomen and pelvis
- Pelvic USN

**If there is no metastases** >> weekly chemotherapy (methotrexate) + \- hysterectomy almost 100% cure rate

**If there is metastases** >> referral, chemo + possible radiation

(during this time the patient should use a reliable contraceptive method)

# Case



A 15-year-old primigravida presents for routine prenatal care. She is 14 weeks pregnant by last menstrual period. She has some nausea but otherwise feels well. The pregnancy to date has been unremarkable. She has support from her parents and the father of the baby. The uterus is enlarged, measuring 20 cm from the pubic symphysis. Fetal heart tones are not auscultated by Doppler. She denies vaginal bleeding or passage of tissue from the vagina. Vaginal exam is unremarkable. Routine prenatal labs were unremarkable. She is Rh-positive. Quantitative beta hCG levels were markedly elevated at 112,320 mIU/ml. TSH was low and further thyroid testing revealed the patient to be mildly hyperthyroid. Ultrasound showed the uterus to be enlarged, with multiple internal echoes and a snowstorm appearance. No fetus is noted. Ultrasound also showed enlarged multiloculated ovarian cysts bilaterally.

## 1- What is the differential diagnosis prior to receiving your ultrasound result?

- Poor dates, most likely if the patient's menses are irregular
- Multiple gestation
- Molar pregnancy (complete or partial)

## 2- What aspects of the ultrasound guide the diagnosis?

- Ultrasound will evaluate the abnormal placental appearance of molar pregnancy and the presence (partial molar pregnancy) or absence of an associated fetus (complete molar pregnancy)
- Ultrasound will also reveal any associated ovarian enlargement.

## 3- What evaluation do you need to make a final diagnosis?

- Although ultrasound can diagnose gestational trophoblastic neoplasia; pathology is needed to confirm the diagnosis with or without malignant change.
- A chest x-ray is recommended prior to uterine evacuation to diagnose the likelihood of metastatic disease.
- In this context ultrasound is diagnostic of bilateral theca lutein cysts (no ovarian tissue is needed for this diagnosis).

#### 4- What is the epidemiology and clinical course of this condition?

- Gestational trophoblastic neoplasia is the most curable gynecological malignancy.
- Although patients with hydatidiform mole are classically described as having a uterus that is large for dates, this only occurs in approximately half of the patients.
- Molar pregnancies are more likely to occur in women 15-years-old or less, or 40-years-old and greater.
- Ethnicity: Asian women are almost twice as likely to develop GTN as women of other ethnic groups.
- Gestational trophoblastic neoplasia is frequently associated with hyperthyroidism due to the release of a thyrotropin-like compound by the molar tissue.
- Patients with molar pregnancy have increased risk of trophoblastic disease in later pregnancies (recurrence rate is 1%) and should have early ultrasound in every subsequent pregnancy.

#### 5- What is your management plan?

- Primary treatment is suction evacuation of the uterus.
- Beta hCG's should be followed regularly until negative, i.e. weekly until negative and then monthly for six months to a year.
- As patients with gestational trophoblastic neoplasia should not attempt subsequent pregnancy until after this time period, reliable contraception use needs to be discussed and implemented.
- If beta hCG does not rapidly decrease, consideration of post molar GTN must be considered. - Methotrexate would be appropriate as secondary treatment.
- Thyroid function should also be followed until normalized.
- Chest x-ray and pelvic examination for uterine enlargement should be followed to rule out choriocarcinoma and to document the resolution of the ovarian cysts.

