



437 Team: Obstetrics and Gynecology

Gestational Trophoblastic Tumors

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:

- Kaplan USMLE step 2 CK - Obstetrics and Gynecology
- Online Meded videos
- Team 435
- Dr.khalid slides

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GTD & GTN

- **Gestational trophoblastic disease (GTD):** It's an abnormal proliferation of trophoblasts (cytotrophoblast and/or syncytiotrophoblast) from the placenta.
- (GTD) include: hydatidiform moles (both complete and partial) and gestational Trophoblastic Neoplasia.

GTD non invasive localized(benign)

- They typically arise from abnormal fertilization events that result in proliferation of trophoblastic tissue they are classified as partial or complete molar pregnancy. Both types manage similarly.



Complete hydatidiform mole
The whole uterus is full of hydropic implants

Partial hydatidiform mole

Coexistent mole and live fetus

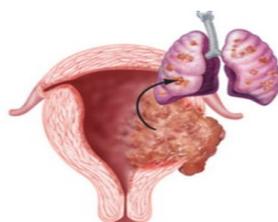
Complete mole	Incomplete(partial) mole
Fertilization of EMPTY ovum with 2 sperms or 1 sperm that will divide later on	Fertilization of normal ovum (haploid) with 2 sperms or 1 sperm that will divide later on
No fetal components	fetal components present
5-15% risk of malignancy	<1% risk of malignancy
Most common genetic 46 XX - followed by 46 XY	Most common genetic 69 XXY - followed By 69XXX
<p>COMPLETE MOLE Two sperm (XX or XY) + Egg (No Maternal DNA) → 46XX or 46XY (Paternal chromosomes only (Androgenetic mole)) Most Common → X sperm + Egg (No Maternal DNA)</p>	<p>PARTIAL MOLE Most Common → 23X sperm + 23X egg → 69XXY or 69XXX (Maternal and paternal chromosomes (Triploid)) One of two sperm (23X or 23Y) + Egg (23X)</p>

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



Invasive mole

Edematous chorionic villi with trophoblastic proliferation that invade into the endometrium (localised to the uterus) (most common)



Choriocarcinoma

(from normal or molar) neoplastic syncytiotrophoblast and cytotrophoblast without chorionic villi
Invade distant structures (not localised to the uterus)



Placental site trophoblastic tumor
absence of villi with proliferation of intermediate trophoblast cells (rare)

A post-term patient who is still bleeding with: High HPL, β -hCG elevated a little bit (500,700), empty US.
Lesion invading the uterus on MRI. It's chemo-resistant and radio-resistant, so **the only treatment is surgical.**
We do hysterectomy unless she's para 1 and we want to reserve the uterus we do wedge resection and reconstruction of the uterus.

Risk factors for molar pregnancy :

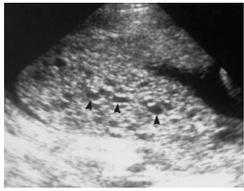
Previous GTD, maternal age (upper and lower extremes) (<20 & >40), dietary factors (Vit. A deficiency, low intake of carotene), ethnicity (higher incidence in Asia), and family history

Signs and Symptoms:

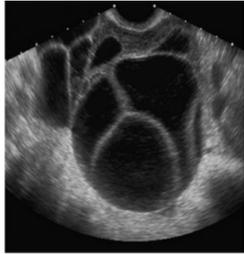
- **Complete mole:**
 - **Vaginal bleeding** (most common symptom)
 - Endocrine symptoms (due to \uparrow β -hCG level) : Hyperemesis gravidarum, preeclampsia, Hyperthyroidism, and large cystic ovaries
 - No fetal heart tone
 - Excessive uterine size
- **Partial mole:**
 - **Vaginal bleeding**
 - No fetal heart tone
- **Malignant** : Vaginal bleeding >6 weeks

Diagnosis :

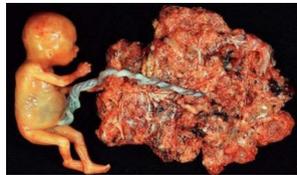
- **Physical exam:**
 - ABCs, Vital signs, **general examination**
 - Eyes: **pallor** (anemia), **exophthalmos** (thyroid)
 - Neck: goiter
 - Cardiovascular and respiratory examination
 - Abdominal examination: inspection (previous scars), size of uterus, tenderness, peritoneal signs, ascites, **you can find theca-lutein cyst (huge ovarian cyst due to stimulation from β -hCG).**
 - **Fundal height** (in complete molar pregnancy the gestational age isn't consistent with the fundal height, the uterus will be larger than the gestational age).
 - Pelvic examination: speculum (to assess bleeding, tissue), to determine cervical dilatation & tenderness, **to take swab.**
- **Investigations:**
 - β -hCG (quantitative)
 - The expected β -hCG at 10 weeks is 100,000. so if a 10 weeks pregnant lady has β -hCG of 175,000 it's considered high and gives you a hint that it may be molar.
 - CBC (anemia, bleeding disorders)
 - Coagulation profile
 - Type and screen
 - possibility of transfusion because of the bleeding.
 - important to know the RH group, if the mother is -ve you have to give her RhoGAM in case of partial where there's a fetal component.
 - If ectopic or molar is suspected add LFTs, renal function tests.
 - because in ectopic we use methotrexate which is hepatotoxic and nephrotoxic, so we can't start it in patients with impaired liver or renal function.
 - Pelvic US
 - It will tell us if it's a normal pregnancy or not, if there's a fetal heart or not, intrauterine or ectopic.
 - Thyroid function test as it's commonly affected with the molar pregnancy.



An intrauterine pregnancy with a *characteristic snowstorm or vesicular pattern* and no identifiable fetal parts. *this goes with molar pregnancy!*



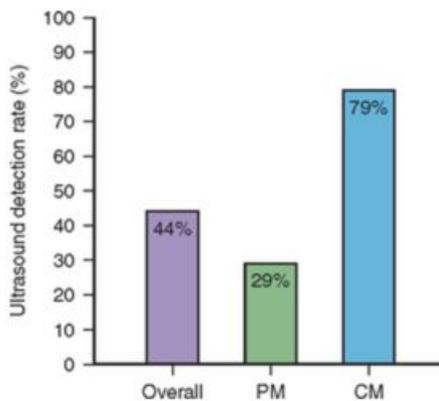
Theca Lutein Cysts
diagnosis → *molar pregnancy*



Partial mole is when there's a baby or parts of a fetus with a hydropic placenta. Differential diagnosis of partial mole is missed abortion, the β -hCG is higher in partial mole but you can't differentiate until you do surgery!

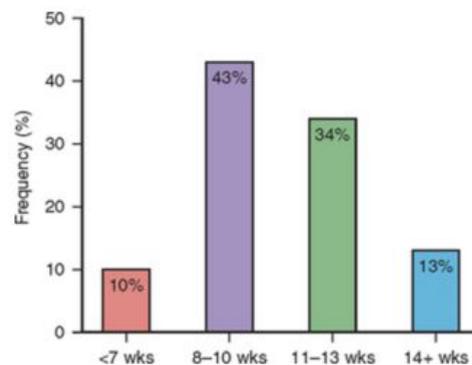
How good US is in diagnosing molar pregnancy?

In complete molar 80% because of the snowstorm appearance.



At what gestational age diagnosis of molar pregnancy is made?

The majority of the cases are diagnosed before 13 weeks.



Q: mention 2 confirmatory tests for molar pregnancy?

1. Quantitative β -hCG (high)
2. US (snowstorm appearance)

Risk of recurrence of a molar pregnancy

- 1 molar pregnancy: 1% recurrence risk
- 2 molar pregnancies: 23% recurrence risk
- If a patient had a molar pregnancy we ask her to come immediately when she's amenorrheic, and do a β -hCG and US, because if it's molar we need to detect it early and treat it early.

Treatment

- Evacuation via suction dilation and curettage
- Hysterectomy (if patient desires surgical sterilization)

Follow Up

- β -hCG. follow with weekly β -hCG until 3 negatives, then for another 6 months for both complete and partial.
- Contraception x 6 months – OCP, depo-provera or barrier methods (not IUD). we can use IUD when β -hCG goes back to normal or zero.
- Risk of malignant sequelae (complete = 5-15%, partial = <1%). we follow them because of this risk of transformation to malignancy.

Metastasis

- The most common sites of metastasis: **IMP!**
 - Lung (80%) (stage III) most common site
 - Vagina (30%) 2nd most common
 - Pelvis (20%)
 - Liver (10%)
 - Brain (10%)

- Prognostic scoring:

Scores	0	1	2	4
Age	<40	>40	—	—
Antecedent pregnancy	Mole	Miscarriage	Term	—
Interval months from index pregnancy	<4	4-6	7-12	>12
Pretreatment serum β hCG (IU/L)	<10 ³	10 ³ -10 ⁴	10 ⁴ -10 ⁵	>10 ⁵
Largest tumour size (including uterus) (cm)	<3	3-4	≥5	—
Site of metastases	Lung	Spleen/kidney	Gastrointestinal	Liver/brain
Number of metastases	—	1-4	5-8	>8
Previous failed chemotherapy	—	—	Single drug	≥2 drugs

- Low risk score ≤6
 - Treat with single agent chemotherapy (methotrexate or dactinomycin)
 - Follow up with β -hCG for 1 year + give contraception for 1 year
- High risk score ≥7
 - Multiple agents chemotherapy (EMA-CO)
 - Follow up with β -hCG for 2 years + give contraception for 2 years

	Complete moles	Incomplete moles	Choriocarcinoma
Path	<ul style="list-style-type: none"> - Completely molar= no fetal parts - Completely chromosomal= 46 chromosomes - Completely spermal= product of good fertilization and a bad egg (broken egg +single sperm à sperm doubles its chromosomes) 	<ul style="list-style-type: none"> - Incompletely molar= fetal parts are present - Incompletely chromosomal= 69 chromosomes - Incompletely spermal= product of good egg and a bad fertilization (good egg + 2 sperms) 	malignant product of gestational content
Pt	Size-date discrepancy, very elevated β -hCG, hyperthyroidism, hyperemesis gravidarum, vaginal bleeding (non-specific), grape like mass that protrudes from the cervix on vaginal exam, adnexal mass		An elevated B-HCG after molar, aborted or normal pregnancy (worst prognosis)
Dx	initial: transvaginal U/S à snowstorm pattern		initial: transvaginal U/S à snowstorm pattern Best: biopsy obtained by a curettage Then stage with CT (lungs/brain)
Tx	Suction curettage (most accurate method of diagnosis and treatment and the same time)		Surgical: TAH for stage 1 (localized disease to the uterus) or debulking surgery for stage 3 Medical: Methotrexate+ Actinomycin D +/- Cyclophomide or aggressive chemo
F/U	serial B-HCG while on OCP x12 months ;if there is a rise in B-HCG while on OCP = invasive gestational disease: invasive molar disease and choriocarcinoma.		



Teaching case (video 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 so-called molar appearance. No fetus is noted. Ultrasound also showed enlarged multiloculated ovarian cysts bilaterally.

Questions

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.

تم بحمد الله

كل الشكر و التقدير لكل من ساهم في إنجاز هذا العمل
إن أصبنا فمن الله وإن أخطأنا فمن أنفسنا ومن الشيطان

شكر خاص وامتنان كبير للجندري المجهول:
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مها بركة
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منيرة المسعد
منيرة الهدلق
ميعاد النفيعي
نورة القاضي
رهف الثنيان
رزان الزهراني
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والقائدة الأكاديمية: سندس الحوامدة

عهد القرين ورهف الشمري