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Gestational Trophoblastic Disease and the Role of Ultrasound

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Objectives

- To understand the definition of Gestational Trophoblastic Disease (GTD).
- To recognize key diagnostic findings of complete and partial molar pregnancies on ultrasound.
- To review the differential diagnosis for ultrasound findings seen with GTD.
- To review the management of GTD and appropriate follow up for the patient.



Molar Pregnancy: Definitions

Gestational Trophoblastic Disease (GTD) is a proliferative disorder of trophoblastic cells. It can be benign, premalignant, or malignant.

Molar pregnancy, also known as Hydatidiform Mole, is a form of benign GTD.

-More specifically, it is an abnormal form of pregnancy in which a (usually) non-viable fertilized egg implants in the uterus and grows into a mass with swollen chorionic villi.

Molar Pregnancies occur in two forms:

- Complete mole
- Partial mole



Molar Pregnancy: Complete vs. Partial Mole

- Complete mole- either one (90%) or two (10%) sperm combine with an egg that has lost its DNA.
 - Genotype is typically 46XX (diploid) due to subsequent mitosis of the fertilizing sperm, but can also be 46XY (diploid).
 - Higher risk of developing into choriocarcinoma.
- Partial mole- an egg is fertilized by two sperm, or by one sperm which reduplicates itself.
 - Genotypes are either 69XXX (triploid), 69XXY (triploid) or 92XXXXY (tetraploid- rare).
 - Lower risk of developing into choriocarcinoma.
 - May have fetal parts.



Molar Pregnancy: Summary of Complete vs. Partial Moles

Complete Mole

Fertilization of an “empty” egg by a haploid sperm that then duplicates



46 XX

Partial Mole

Fertilization of an ovum by two sperm



69 XXX or 69 XXY



Features: Complete vs. Partial Mole

Feature	Complete	Partial
Incidence	1/1500 pregnancies	1/750 pregnancies
Karyotype	Diploid 46XX/46XY	Triploid 69XXX/69XXY
Embryonic/fetal tissue	Typically absent	Present
Villi	Diffusely hydropic	Focal, less prominently hydropic
Trophoblastic proliferation	Hyperplastic	Less trophoblastic hyperplasia
Uterine size	Often large for dates	Often small for dates
Persistent mole	15-20%	3-5%
Choriocarcinoma	3%	0.1%



Risk Factors and Clinical Presentation

- The two biggest risk factors for GTD are extremes of maternal age and previous GTD.
- Other risk factors may include current smoking (>15 cigarettes/day), maternal blood type AB, A, or B, history of infertility, nulliparity, and use of oral contraceptives, though increased risk with these factors has not been demonstrated consistently.

Clinical Presentation

Clinical presentation includes any of the following symptoms:

- Vaginal bleeding
- Enlarged uterus
- Pelvic pressure or pain
- Theca lutein cysts
- Anemia
- Hyperemesis gravidarum
- Hyperthyroidism
- Preeclampsia before 20 weeks of gestation
- Vaginal passage of hydropic vesicles



Diagnosis of Molar Pregnancy

- Preliminary diagnosis is made with elevated quantitative beta-hCG levels.
- Characteristic imaging findings on ultrasound strongly support the diagnosis.
- Diagnosis ultimately confirmed with histologic analysis of trophoblastic tissue after evacuation.
- Further accuracy of histologic diagnosis can be achieved using flow cytometry to establish karyotype.

Our Patient: Clinical Presentation

- 28 year old G1P0 at 14 weeks gestation who presents to her Obstetrician for a follow up appointment- at a prenatal screening appointment 2 weeks ago, her OB noted enlarged uterine size for dates, so she is here for further work-up.
- She reports only mild pelvic pressure and pain, but has no nausea/vomiting, no vaginal bleeding, and no passage of tissue.
- Her laboratory results from the previous visit came back within normal limits.
- At this appointment, she had a quantitative beta-HCG performed, which came back at 522,473 (ref 0-100,000).

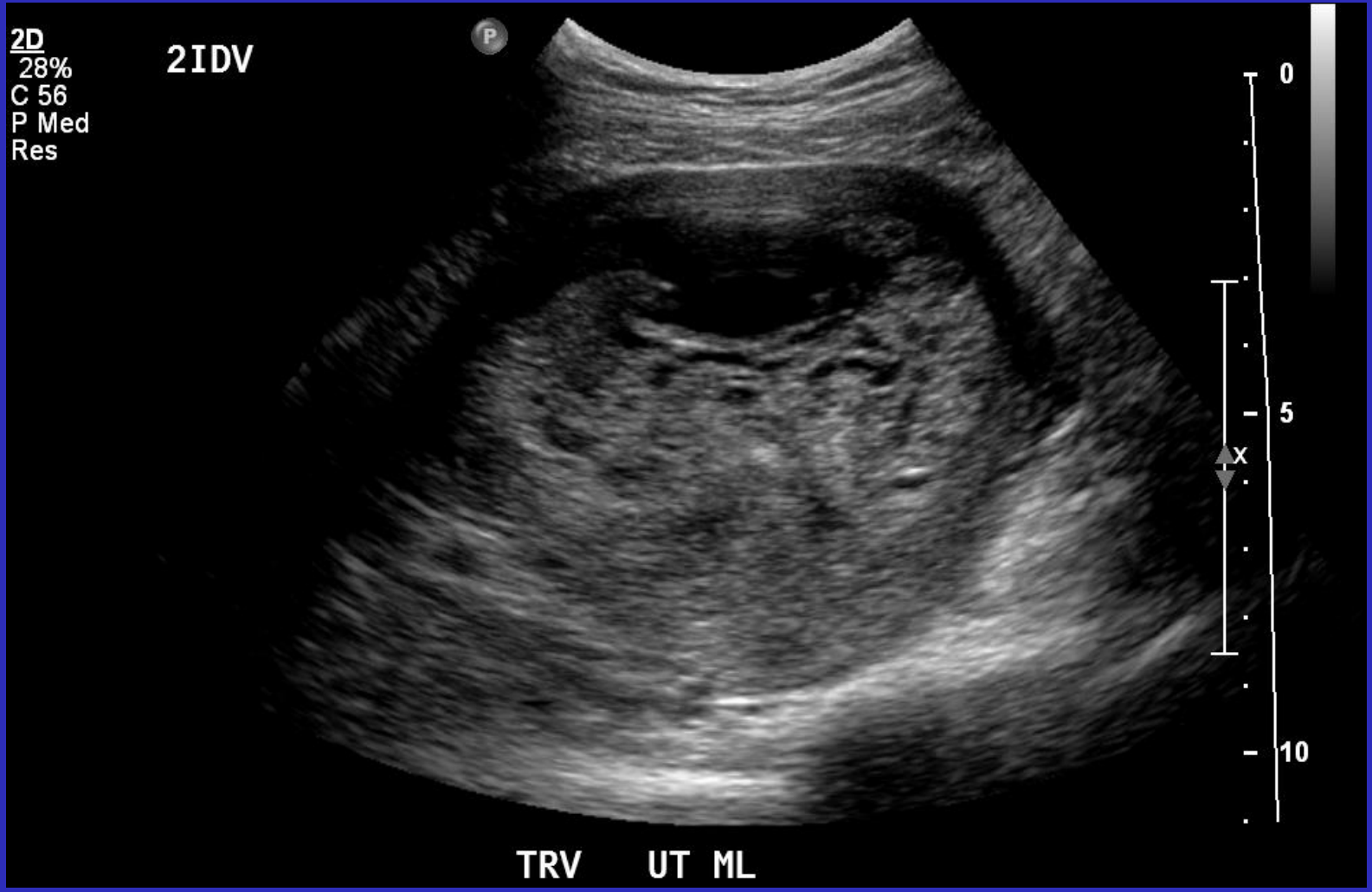
What imaging tests should we order for our patient?



Menu of Radiologic Tests

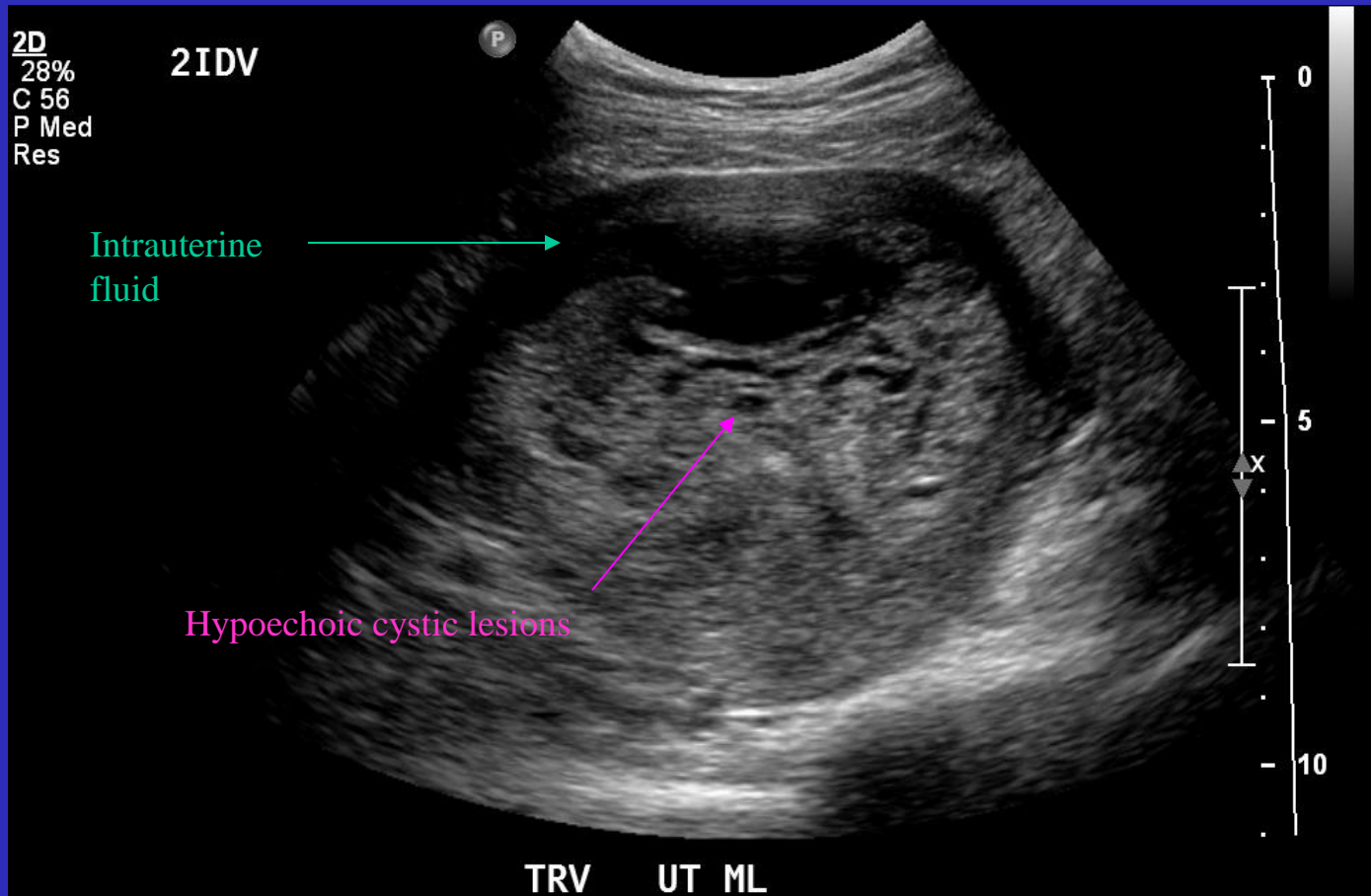
- **Ultrasound**- this is the gold standard for evaluating the presence of complete or partial mole with imaging.
- **MRI**-
 - Indications:
 - if suspecting a coexisting viable fetus- assessment of fetal CNS, fetal anomalies, placental anomalies (i.e. accreta)
 - Evaluate for possible local invasion
 - If ultrasound leads to inconclusive findings
 - Safety studies at 1.5T have shown minimal risk
 - Gadolinium is not recommended, as it crosses the placenta and remains in the amniotic fluid
- **Chest X-ray**- if a diagnosis of molar pregnancy is confirmed and malignant GTD is suspected, the lungs are the most common site of metastasis

Our Patient: Uterus on Ultrasound



Pause to evaluate, then continue to view findings

Our Patient: Complex Intrauterine Mass on Ultrasound- Labeled

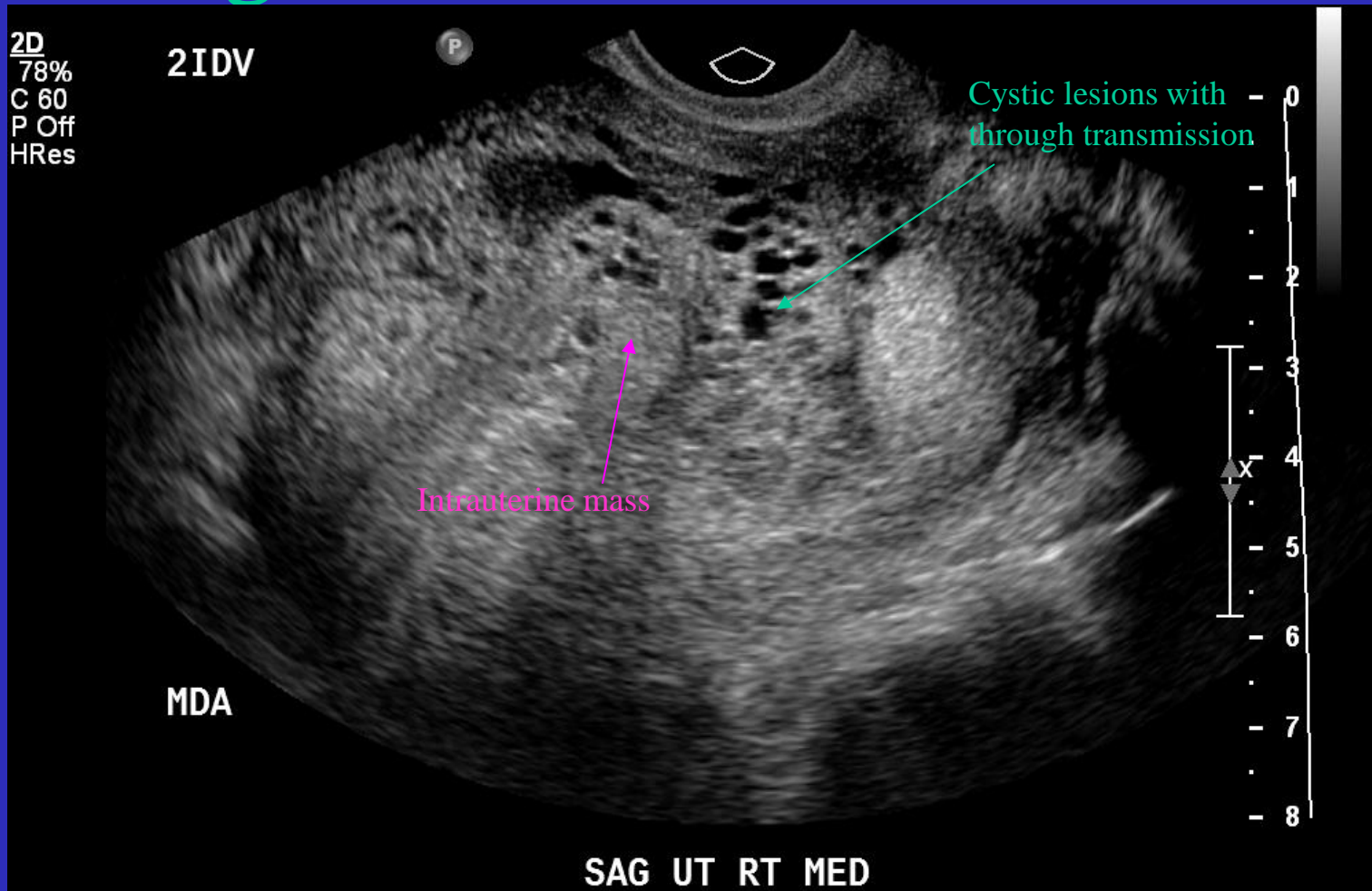


Our Patient: Sagittal Uterus



Pause to evaluate, then continue to view findings

Our Patient: Intrauterine Mass on Sagittal Ultrasound- Labeled





Typical Appearance of Molar Pregnancy on Ultrasound

- Snowstorm pattern representing hydropic chorionic villi
- Complex intrauterine mass containing many small cysts, resembling “clusters of grapes”
- In partial mole, fetal parts may be visualized



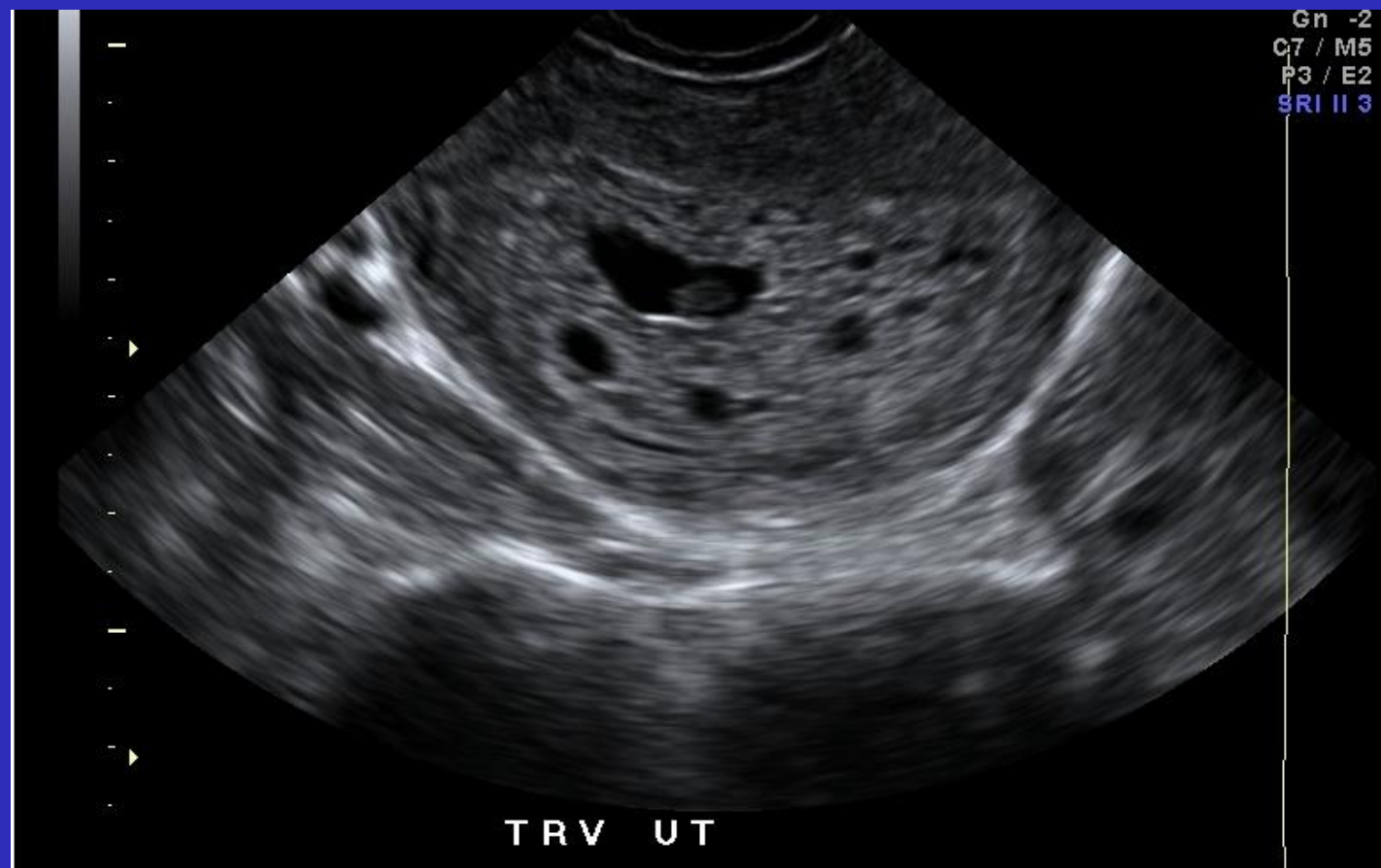
Differential Diagnosis of Ultrasound Findings

-The characteristic appearance of molar pregnancy on ultrasound can indicate the presence of all forms of Gestational Trophoblastic Disease (GTD), including:

- Hydatidiform mole- complete mole
- Hydatidiform mole- partial mole with non-viable fetus
- Hydatidiform mole- partial mole with viable fetus
- Persistent/invasive gestational trophoblastic neoplasia (GTN)
- Choriocarcinoma
- Placental site trophoblastic tumors (PSTTs)



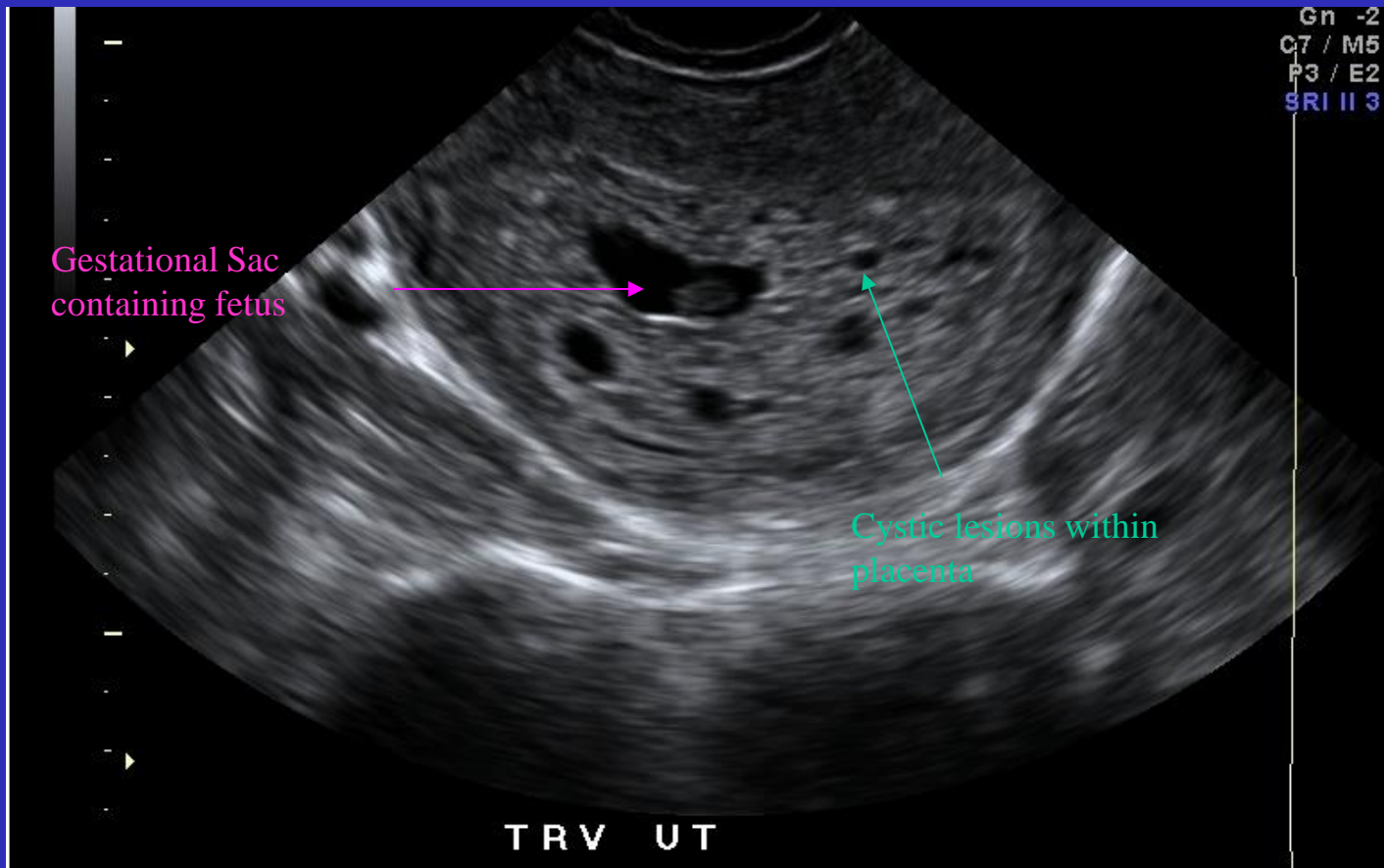
Companion Patient #1: Partial Molar Pregnancy on Ultrasound



Pause to evaluate, then continue to view findings

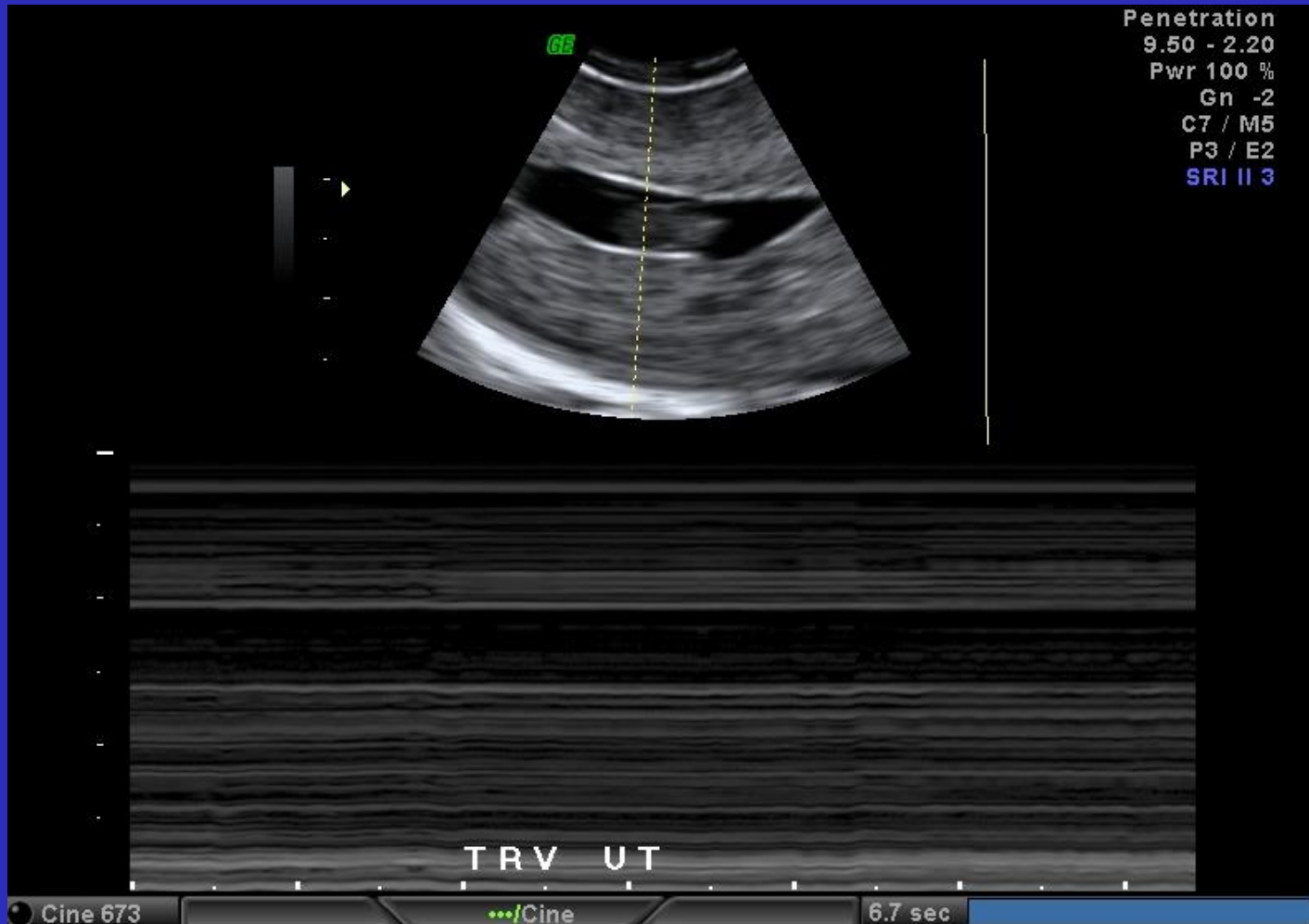


Companion Patient #1: Partial Molar Pregnancy with Gestational Sac on Ultrasound- Labeled





Companion Patient #1: Fetal Heart Rate

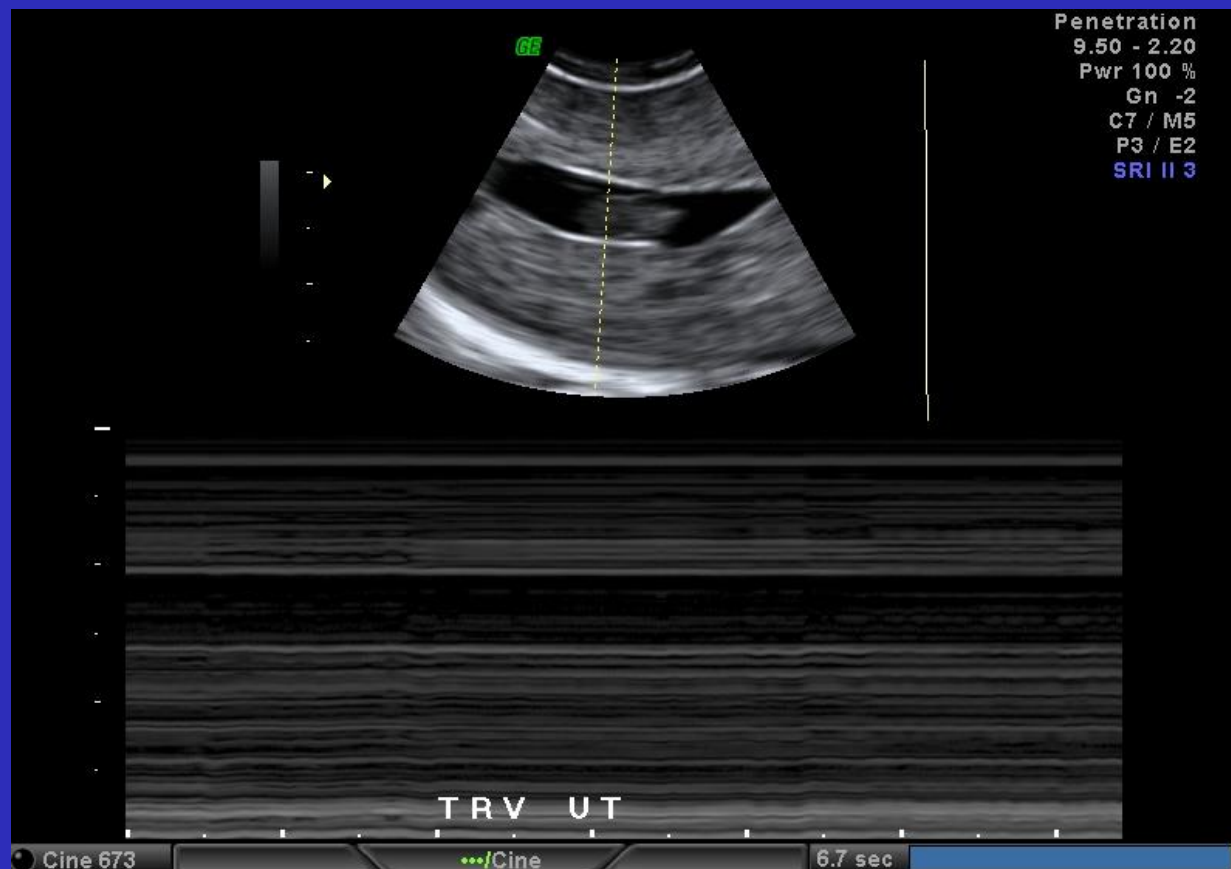


Investigating the presence or absence of a fetal heart rate can help determine whether or not the fetus is viable in a partial molar pregnancy.

Pause to evaluate, then continue to view findings.



Companion Patient #1: Absence of Fetal Heart Rate- Labeled



No motion detected in cross section of the gestational sac contents means there is no evidence of a fetal heart rate. This indicates a non-viable fetus.

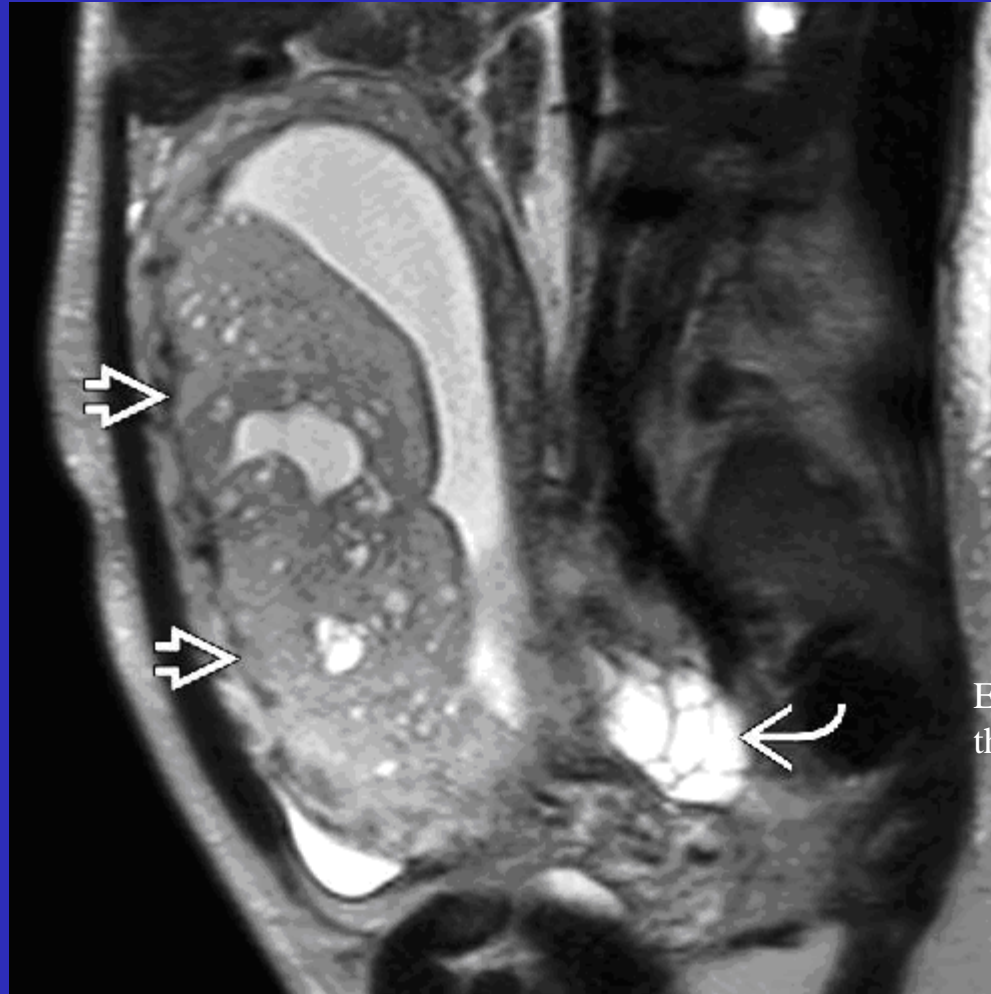


Molar Pregnancy with a Fetus

- While our Companion Patient demonstrated a non-viable fetus in a partial molar pregnancy, molar pregnancy may coexist with a viable fetus.
 - If allowed to proceed, these pregnancies often experience complications (e.g., hemorrhage, preeclampsia, preterm delivery).
 - Patients are also at elevated risk of persistent gestational trophoblastic neoplasia.

Companion Patient #2: Molar Pregnancy on MRI- Labeled

Enlarged, thickened placenta with innumerable tiny cystic structures



MRI's are often done in GTD to evaluate for malignant spread outside the uterus- in this patient, there is no evidence of local invasion.

Enlarged ovary with theca lutein cysts



Back to our Patient: Summary of Ultrasound Report

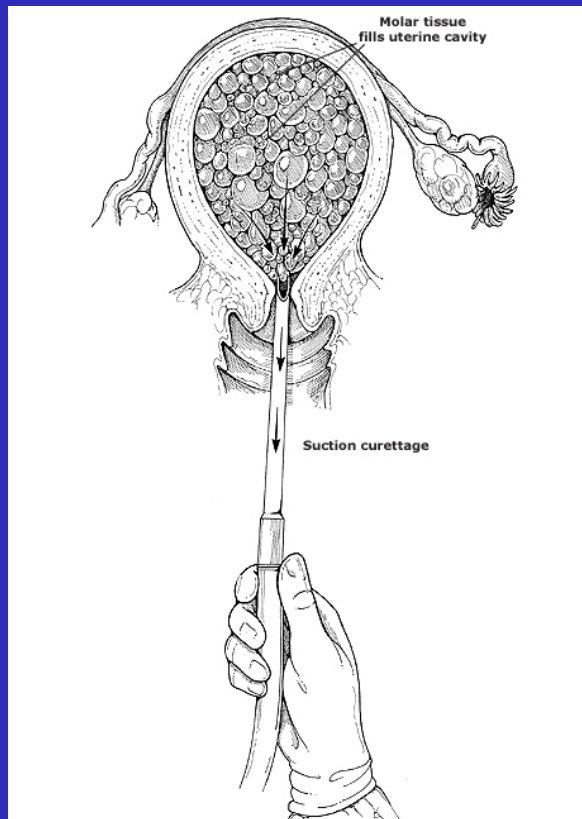
Ultrasound report noted “heterogeneous content with fluid and echogenic material with cystic spaces” within the endometrial cavity, consistent with the classic imaging findings of molar pregnancy.

What should be done next?



Management of Molar Pregnancy

- The standard treatment is surgical evacuation of uterine contents via suction curettage.



- Tissue is required for pathologic confirmation of the diagnosis.
- If a woman does not desire preservation of fertility, hysterectomy is also a possibility.
- Depending on the risk of persistent (malignant) disease, prophylactic chemotherapy may be recommended
- hCG levels must be monitored post-op to ensure resolution of disease.



Complications of Molar Pregnancy

- Increased risk of future GTD
- Respiratory distress from trophoblastic emboli
- Persistent GTD or malignant transformation



Persistent GTD

The presence of persistent (malignant) GTD after evacuation of a complete or partial molar pregnancy should be suspected if any of the following apply:

- A serum hCG concentration that plateaus (defined as a decline of less than 10 percent for at least four values over three weeks).
- A serum hCG concentration that rises (defined as an increase of more than 10 percent of three values over two consecutive weeks).
- Persistence of detectable serum hCG for more than six months after molar evacuation.

Approximately 90 percent of these cases represent invasive mole, and <10 percent are choriocarcinomas; PSTTs are rare. Patients should be referred to a Gynecologic Oncologist for management.



Summary

- Molar pregnancy is a form of Gestational Trophoblastic Disease in which a (usually) non-viable fertilized egg implants into the uterus and grows into a mass with swollen chorionic villi.
- Ultrasound is the imaging modality of choice to visualize molar pregnancy, as well as to work up any abnormalities initially in early pregnancy (according to ACR Appropriateness Criteria).
- The differential diagnosis for ultrasound findings with hypo-echoic cystic lesions within the uterus that have a snowstorm appearance or resemble clusters of grapes includes all forms of GTD (complete mole, partial mole, gestational trophoblastic neoplasia, choriocarcinoma, and placental site trophoblastic tumors).



Summary cont' d

- While ultrasound findings are classic and an important part of the work-up in a patient with suspected molar pregnancy, pathologic examination of trophoblastic tissue is necessary to confirm the diagnosis.
- Partial moles can contain fetal parts, which may be visualized on ultrasound. Imaging can be used to evaluate whether or not the fetus is viable.
- Management involves surgical evacuation of the intrauterine mass via suction curettage, and subsequent monitoring of hCG levels to ensure there is no malignant transformation.
- Complications of molar pregnancy include increased risk of future GTD, respiratory distress from trophoblastic emboli, and persistent GTD or malignant transformation.



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Acknowledgements

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