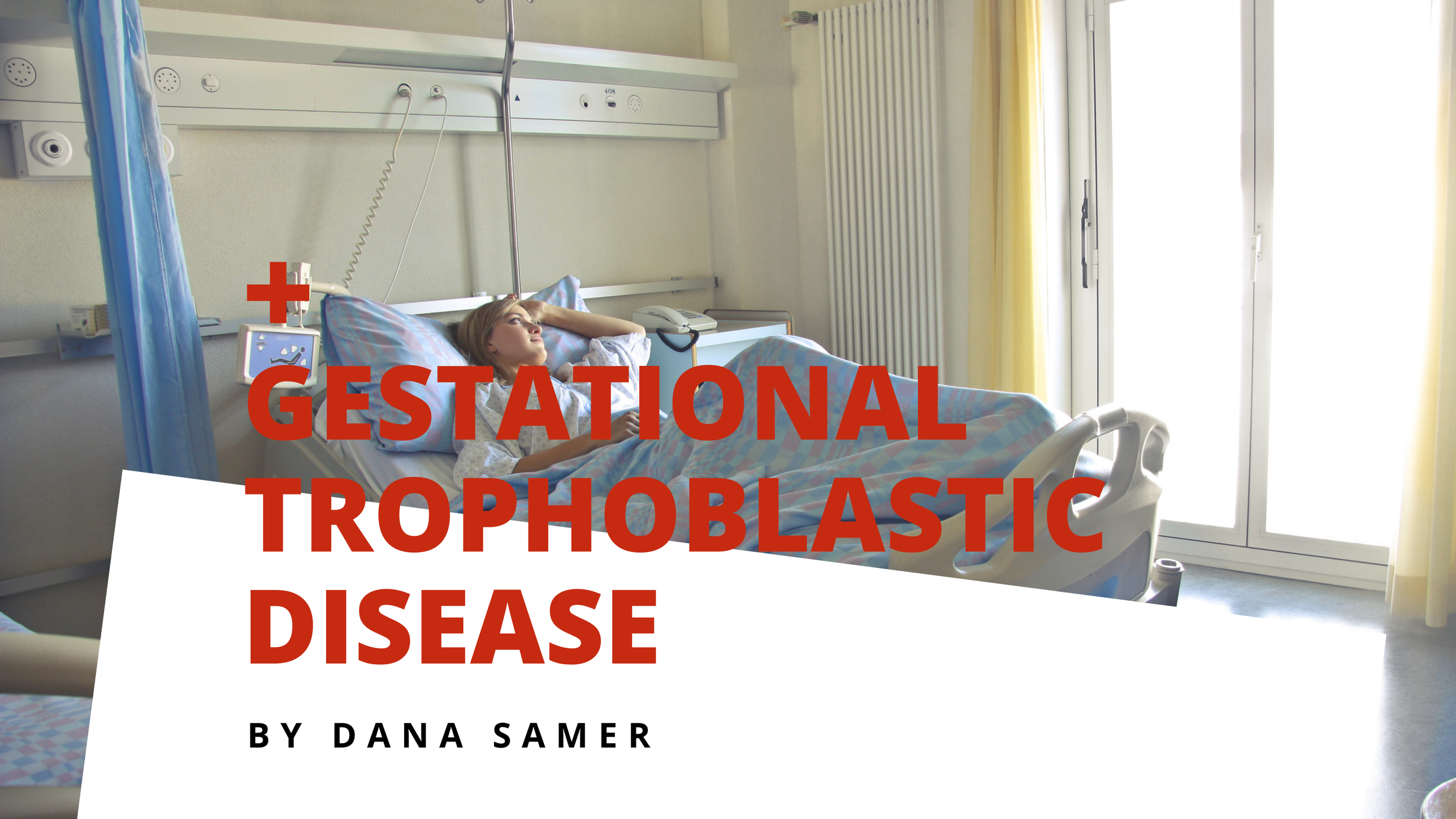


GESTATIONAL TROPHOBLASTIC DISEASE

BY DANA SAMER

- It is a proliferative disorder of trophoblastic cells.
- It defines a heterogeneous group of interrelated lesions arising from the trophoblastic epithelium of the placenta.
- All forms of GTD are characterized by a distinct tumor marker, the beta subunit of human chorionic gonadotropin (hCG).

TYPES OF GTD

1.Hydatidiform mole (complete or partial)>>benign, noninvasive, localized tumors that develop as a result of an aberrant fertilization event that leads to a proliferative process.Molar pregnancies are considered to be premalignant because they have the potential to develop into a malignancy.

They comprise 90 percent of GTD cases.

2.Persistent/invasive gestational trophoblastic neoplasia (GTN)

3.Choriocarcinoma

4.Placental site trophoblastic tumors

malignant >> because of their potential for local invasion and metastases.

Malignant GTD can develop from a molar pregnancy or can arise after any gestational experience: spontaneous or induced abortion, ectopic pregnancy, or preterm and term pregnancy.

EPIDEMIOLOGY

- The incidence of hydatidiform mole ranges from 23 to 1299 cases per 100,000 pregnancies, while malignant GTD is less common.
- In the United Kingdom, the incidence of complete mole is approximately 1 per 1000 pregnancies, and the incidence of partial mole is 3 per 1000.

RISK FACTORS

1)Prior molar pregnancy– Prior HM predisposes to another molar pregnancy. The risk for repeat molar pregnancy after the first mole is approximately 1 to 1.5 percent (approximately 10 to 15 times the risk for the general population) . The recurrence rate after two molar pregnancies has been reported to range from 11 to 25 percent.

2)Extremes of age—increased in those older than age 35 and slightly increased in those under age 20]. Paternal age does not appear to influence the risk of GTD.

RISK FACTORS

3) ASSISSTED REPRODUCTIVE TECHNOLOGY

4) MATERNAL BLOOD TYPE AB ,A ,B

5) CURRENT SMOKING MORE THAN 15 CIGARETTES PER DAY

6) HISTORY OF INFERTILITY, NULLIPARITY

COMPLETE HYDATIDIFORM MOLE

·A complete mole is a result of fertilization of an empty ovum by two sperms or a single sperm that duplicates, resulting in a 46 XX or 46 XY karyotype.

•all genetic material are from paternal chromosome(no maternal) >>no embryo.

•The presence of a complete mole (which lacks a fetus) often leads to excessive uterine size for the expected "gestational age". Uterine enlargement is due to the tumor itself and/or intrauterine hemorrhage with retained clot.

•The marked elevation in serum hCG associated with a complete mole can lead to complications. These include ovarian enlargement due to theca lutein cysts; hyperemesis gravidarum; early development of preeclampsia (before 20 weeks of gestation); and hyperthyroidism, which is most often subclinical]. These complications occur in approximately 25 percent.

•Theca lutein cysts are a form of ovarian hyperstimulation resulting from high circulating levels of hCG that are associated with GTD. These cysts are multiloculated, often bilateral, and resolve a few weeks or months after treatment of GT.

PARTIAL HYDATIDIFORM MOLE

•A partial mole is the result of fertilization of a haploid ovum by two sperm or duplication of one sperm, resulting in a triploid karyotype (69 XXY, 69 XXX, 69 XYY)>>paternal+maternal genetic material.

•Partial moles are the only type of GTD that are associated with the presence of a fetus, and fetal cardiac activity may be detected. However, there is a high rate of intrauterine death related to triploidy.

•Thus, a partial mole is often misdiagnosed as an incomplete or missed abortion and the correct diagnosis of GTD is made only after histologic review of the surgical specimen.

•These pregnancies are infrequently associated with excessive uterine size, ovarian enlargement, preeclampsia, hyperemesis, or hyperthyroidism because hCG levels are generally lower than those observed with a complete mole.

Distinction between complete and partial molar pregnancy

Feature	Complete mole	Partial mole
Incidence	1/1500 pregnancies	1/750 pregnancies
Karyotype	Diploid: 46,XX (less than 15 percent are 46,XY)	Triploid: 69,XXX, 69,XXY (rarely 69,XYY)
Embryonic/fetal tissue	Typically absent (may be present in few cases)	Present
Villi	Diffusely hydropic	Hydropic villi with marked scalloping mixed with normal appearing chorionic villi and fetal tissue; hydropic changes are focal and less prominent than in complete mole
Trophoblastic proliferation	Hyperplastic	Less trophoblastic hyperplasia than in complete mole; trophoblastic stromal inclusions can be seen
Trophoblastic atypia	Often present	Infrequent
Immuncoytochemistry	hCG*, rare PLAP•	hcG, PLAP, p57
Uterine size	Often large for dates	Often small for dates
Theca lutein cysts	Present in ≤25 percent	Rare
Persistent mole	15 to 20 percent	3 to 5 percent
Choriocarcinoma	3 percent	0.1 percent

CLINICAL MANIFESTATIONS

- Vaginal bleeding
- Enlarged uterus >>more with complete mole
- Pelvic pressure or pain
- Theca lutein cysts
- Anemia
- Hyperemesis gravidarum
- Hyperthyroidism >>hcg same alpha subunite with TSH.
- Preeclampsia before 20 weeks of gestation
- Vaginal passage of hydropic vesicles

·Women with HM typically present to their obstetric clinician with missed menstrual periods, a positive pregnancy test, and signs and symptoms consistent with early pregnancy or early pregnancy complications (bleeding, pelvic discomfort, hyperemesis gravidarum)]. Molar pregnancy may be suspected based upon unusually high human chorionic gonadotropin (hCG) levels or only after pathology evaluation of a failed pregnancy.\

•In many cases, particularly in partial mole, a patient is presumed to have a spontaneous abortion, and a molar pregnancy is detected only after pathology evaluation of a uterine curettage sample.

If the products of conception are not examined histologically, the diagnosis of HM may be missed. In these patients, hCG monitoring to detect persistent disease is generally omitted and early diagnosis of gestational trophoblastic neoplasia (GTN) is delayed. Alternatively, women with early disease may be diagnosed before they develop symptoms, based upon an unusually high serum hCG or ultrasound findings.

Previously complete mole typically presented with late effects as hyperthyroidism and PET.

Globally, complete mole is now diagnosed more frequently in the first rather than the second trimester. Thus, there are fewer late onset symptoms.

EVALUATION

Human chorionic gonadotropin

•The serum hCG concentration is always elevated in women with GTD and is usually higher than that observed with intrauterine or ectopic pregnancies of the same gestational age.

•About 40 percent of complete moles are associated with hCG levels >100,000 mIU/mL (normal nonpregnant <5 mIU/mL and peak normal pregnancy level typically <100,000 mIU/mL).

ULTRASOUND FINDINGS

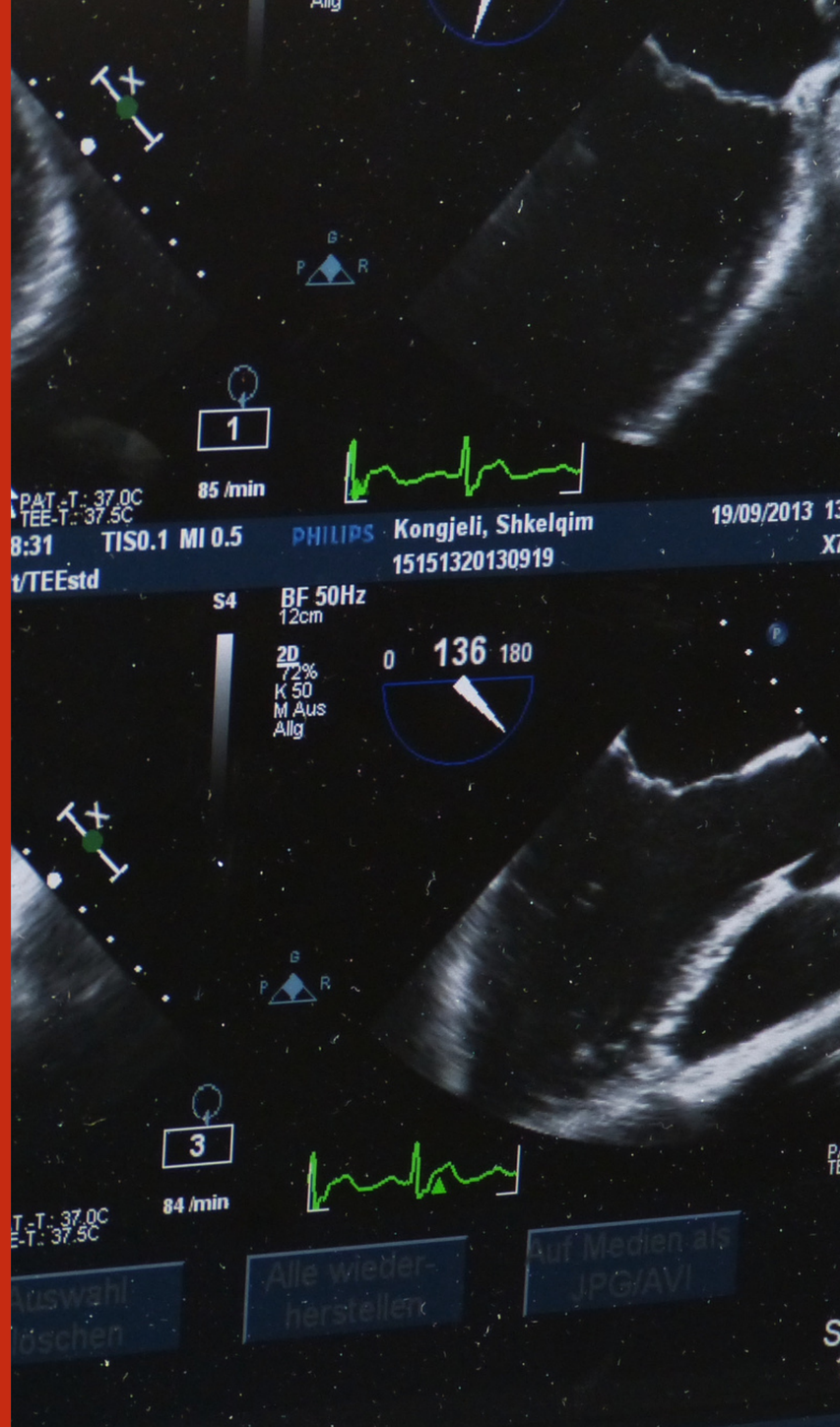
Complete mole

•The absence of an embryo or fetus

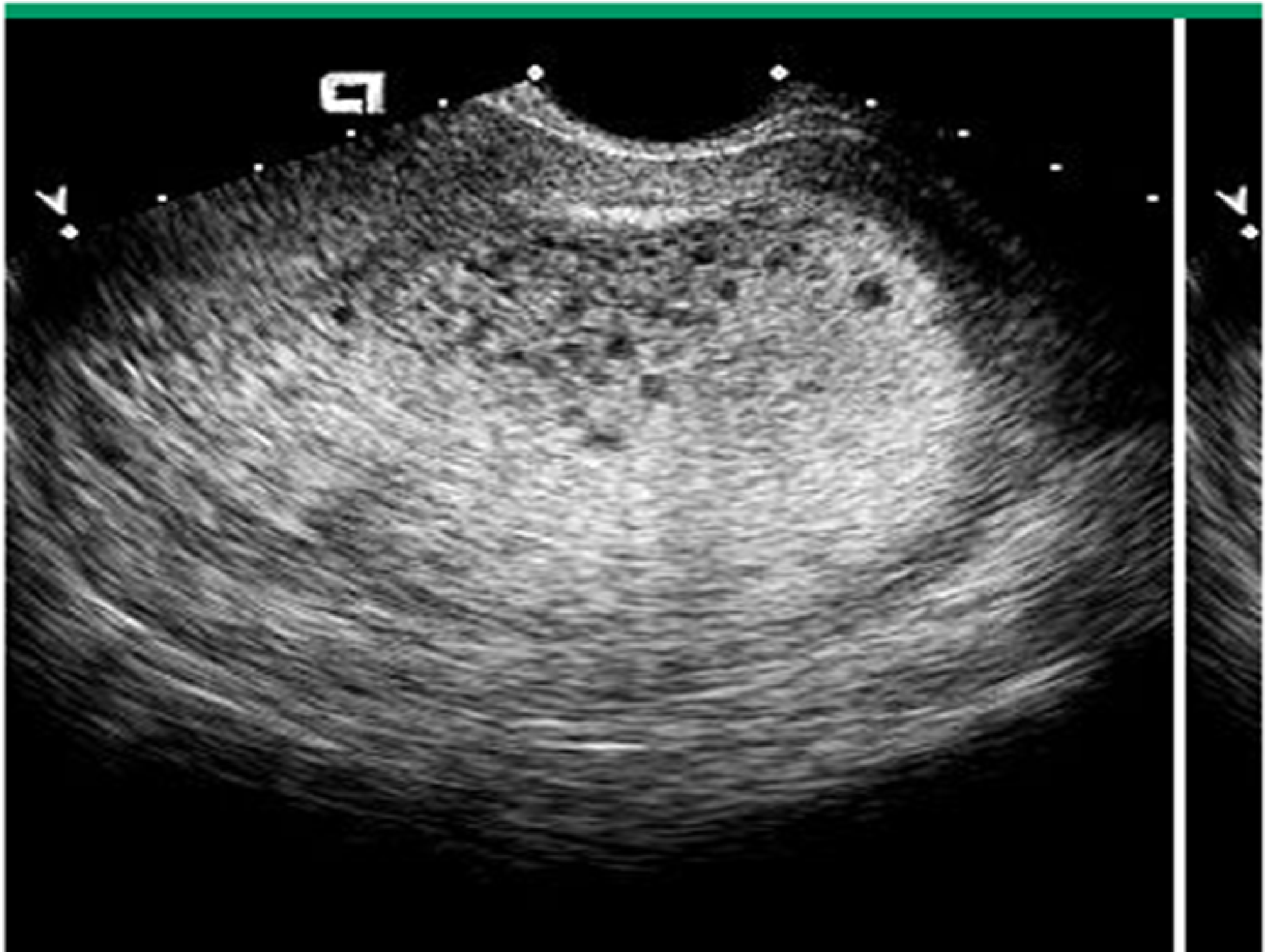
2.No amniotic fluid

3.Central heterogeneous mass with numerous discrete anechoic spaces, which correspond to diffuse hydatidiform swelling of the hydropic chorionic villi. This has classically been described as a "snowstorm pattern" on older ultrasounds

4.Theca lutein cysts



Sonogram of a complete hydatidiform mole



•Partial mole

1.A fetus is present, may be viable, and is often growth restricted

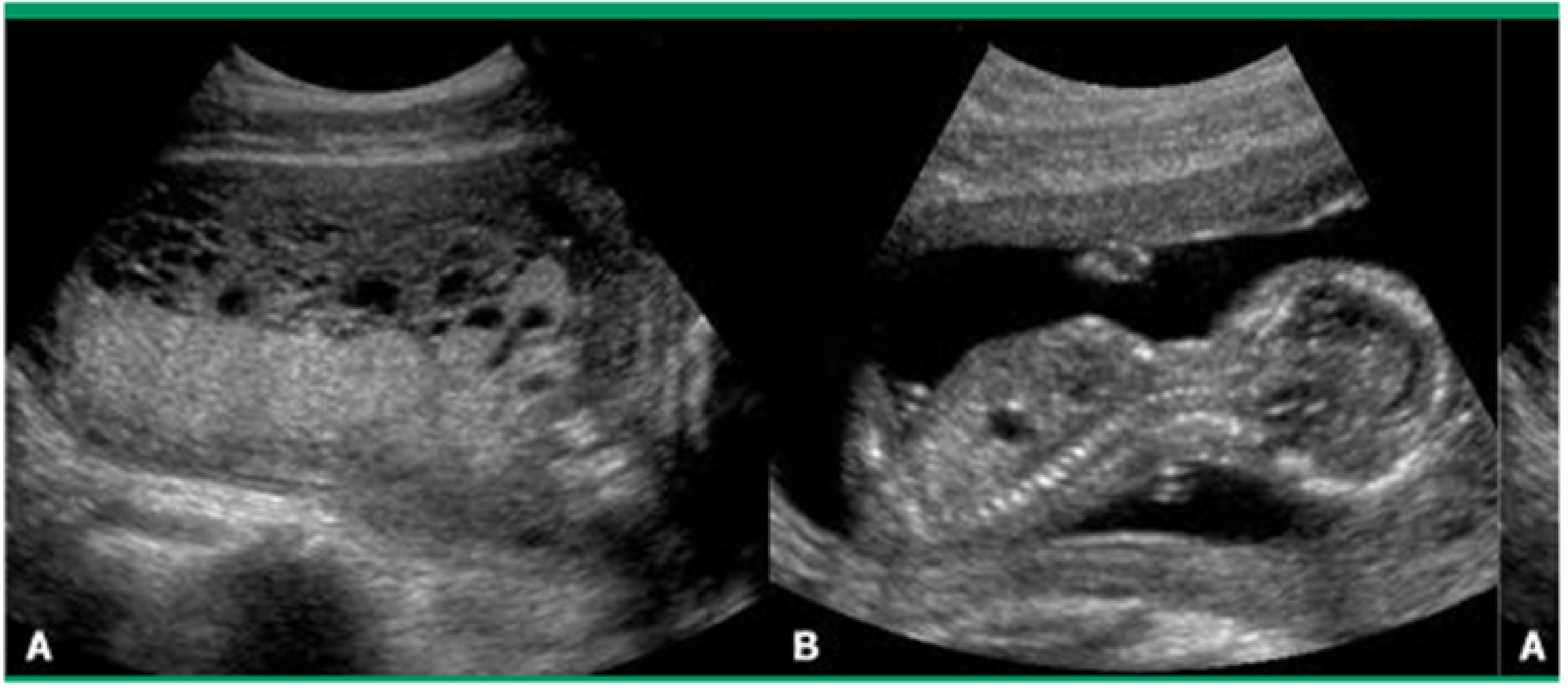
2.Amniotic fluid is present, but may be reduced

3.Focal anechoic spaces and/or increased echogenicity of chorionic villi (swiss cheese pattern)

4.Increased transverse diameter of the gestational sac

5.Theca lutein cysts are usually absent

Partial molar pregnancy



DIAGNOSIS

Complete and partial mole

•When complete or partial mole is suspected based upon sonographic findings and hCG determination, the diagnosis must be confirmed by histologic examination of tissue. The accuracy of histologic diagnosis is further enhanced by flow cytometry to determine the karyotype.

•Tissue is obtained by evacuation of the uterine contents by suction curettage.

•Twin pregnancy may be complicated by GTD: either a mole (partial or complete) and a viable fetus or two moles. The diagnosis of mole is suggested by ultrasound examination and confirmed by cytogenetic studies and histopathologic examination.

PRETREATMENT EVALUATION

•Blood tests are obtained to assess renal and hepatic function , thyroid function, peripheral blood counts, and baseline serum hCG levels.

•Radiographic evaluation includes pelvic ultrasound, both to look for evidence of retained trophoblastic tissue, and to evaluate the pelvis for local spread.

•Chest imaging is also required, as the lungs are the most common site of metastatic disease

•In the absence of pulmonary and vaginal involvement, brain and liver metastases are rare.

•Asymptomatic patients with normal chest and pelvic imaging do not require further imaging of brain or liver.

•CT scan or magnetic resonance imaging (MRI) of the brain is recommended in women with persistent disease who have vaginal or lung metastases and in all patients with choriocarcinoma. Cerebral involvement can also be assessed by measuring beta-hCG levels in the cerebrospinal fluid (CSF)

MANAGEMENT OF HYDATIDIFORM MOLE

- Initial management of suspected complete or partial mole is evacuation of the uterine contents by suction curettage.
- Evacuation is indicated for pathologic confirmation of the diagnosis, relief of symptoms, and to prevent complications related to molar pregnancy.
- This procedure is a definitive therapy for most patients.

MANAGEMENT OF HYDATIDIFORM MOLE

•Suction curettage is the preferred approach because it is less likely to result in uterine perforation or intrauterine adhesions than sharp curettage, and evacuates the uterus more completely than medical methods.

•Patients who have no desire for future fertility may opt for hysterectomy, which eliminates the risk of local invasion, but does not prevent metastasis. The adnexae may be retained; if prominent theca lutein cysts are present, these may be drained at the time of surgery.

PROCEDURE

•Under adequate anesthesia, oxytocin is administered and the cervix is dilated to allow passage of the suction cannula.

•During dilation of the cervix, brisk uterine bleeding is often encountered, which generally slows significantly once suction evacuation has commenced. Heavy bleeding is nearly always self-limited, and inappropriate transfusion should be avoided.

•A suction catheter of 12 mm is usually sufficient to evacuate a complete molar pregnancy since there is no fetus. A larger catheter may be needed to evacuate a partial mole with a coexistent fetus greater than 12 weeks of gestation.

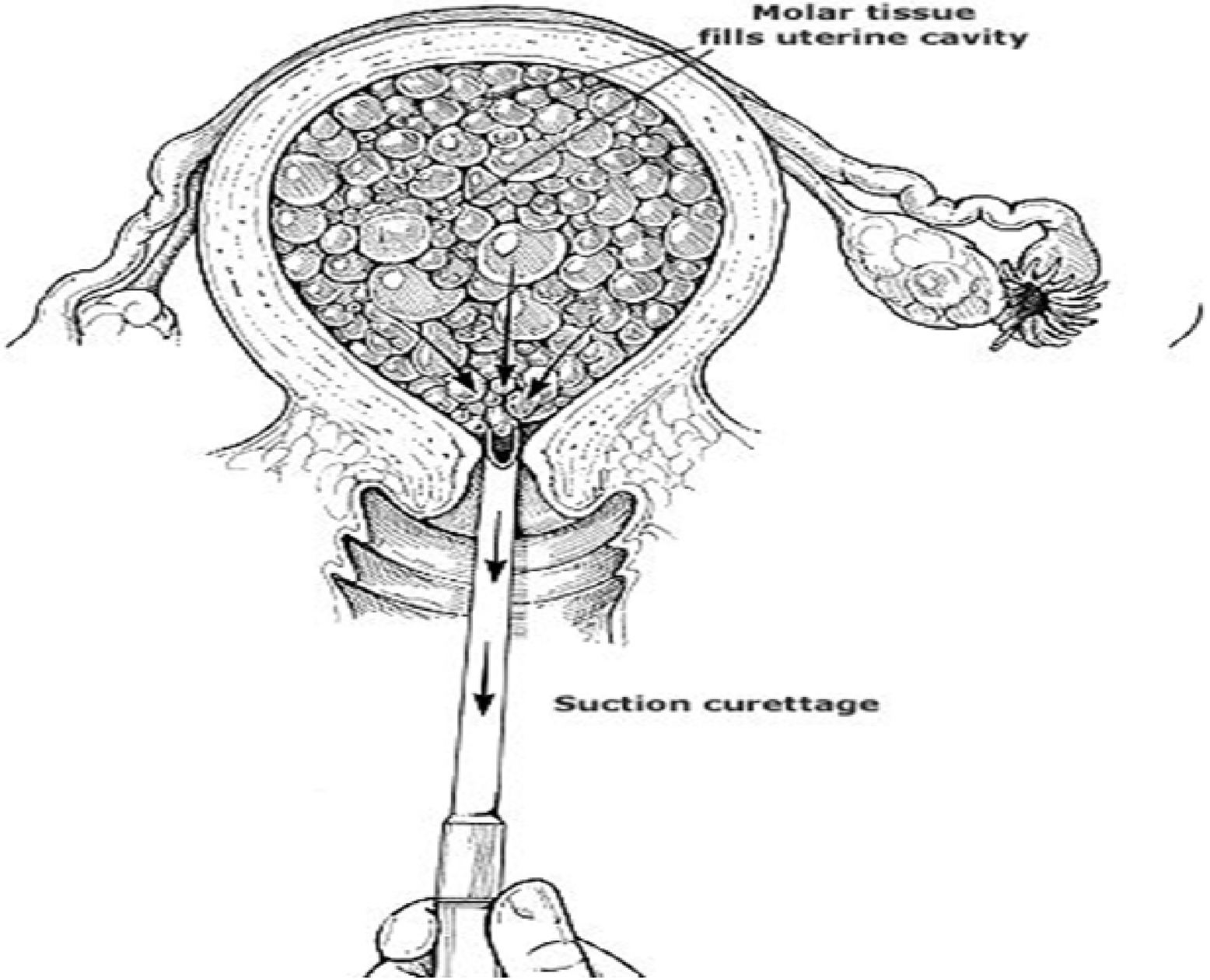
•The suction curette is not advanced to the fundus; instead, it is placed just inside the internal os.

•Vacuum pressures of 50 to 60 cm Hg are then applied and the hydropic placental tissue is drawn into the curette.

PROCEDURE

- As additional tissue is evacuated, the uterus will contract and the suction curette may then be advanced to the fundus.
- Suction curettage can be performed under ultrasound guidance if needed to facilitate the procedure and confirm complete evacuation of uterine contents.
- Intravenous oxytocin is administered, and for uteri over 14-weeks size, we suggest fundal massage to stimulate myometrial contraction

Suction curettage of molar pregnancy



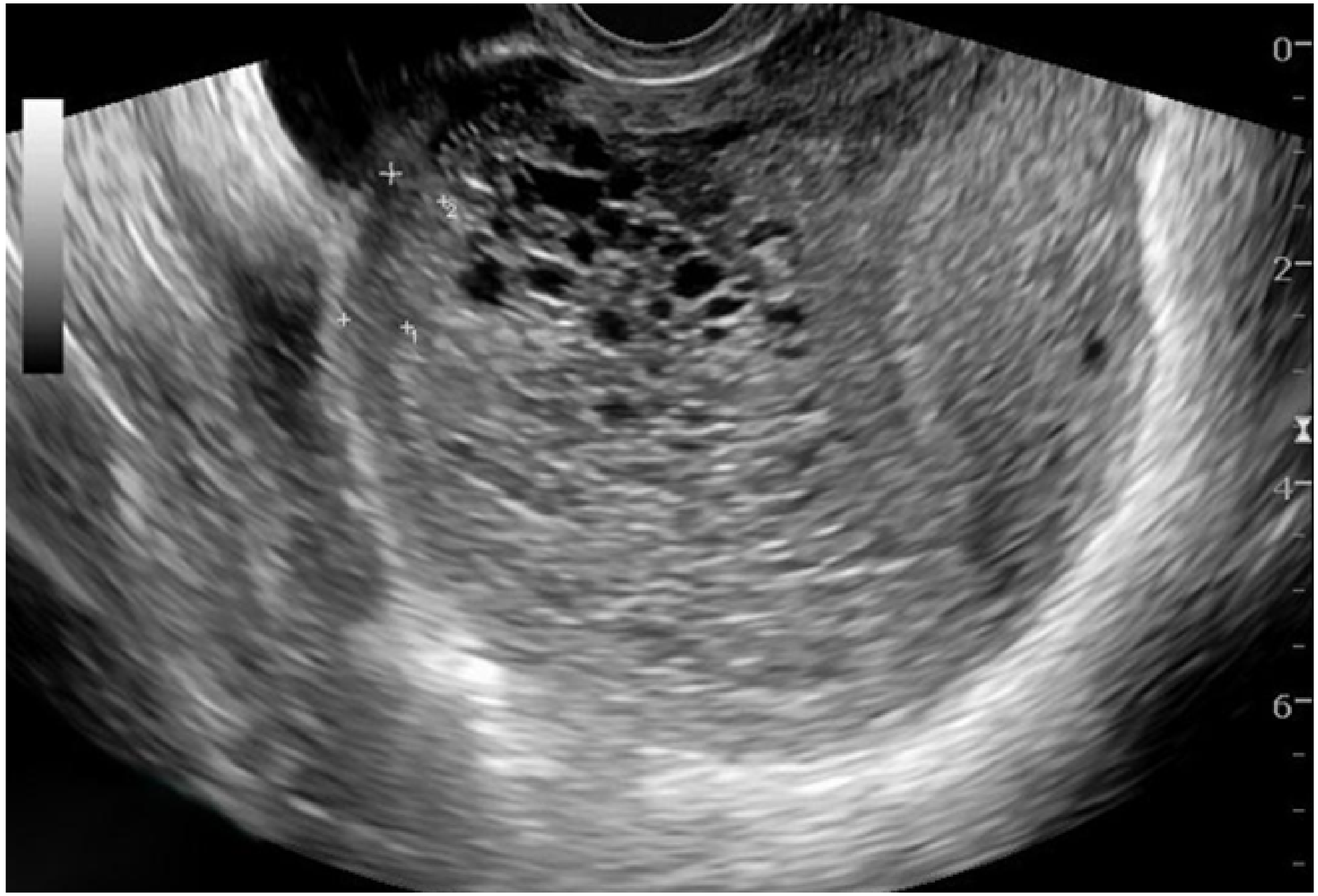
CASE

A 35-year-old woman presents with vaginal bleeding at 8 weeks 3 days' gestation. She has never been pregnant before. Bright red 'spotting' commenced 7 days ago, which she thought was normal in early pregnancy. However since then the bleeding is now almost as heavy as a period. There are no clots. She has no abdominal pain. Systemically she has felt nausea for 3 weeks and has vomited occasionally. She has regular periods bleeding for 5 days every 28 days, and has never had any known sexually transmitted infections.

•On Examination:

The heart rate is 68/min and blood pressure is 108/70 mmHg. The abdomen is soft and non-tender. Speculum reveals a normal closed cervix with a small amount of fresh blood coming from the cervical canal. Bimanually the uterus feels bulky and soft, approximately 10 weeks in size. There is no cervical excitation or adnexal tenderness.

• Beta HCG was 460,514 mIU/mL.



The ultrasound scan shows a mixed echogenicity appearance in the uterus, There is no recognizable gestational sac or fetus.