
GESTATIONAL TROPHOBLASTIC NEOPLASIA (TUMOURS OF THE PLACENTA OR AFTERBIRTH)

Gestational trophoblastic neoplasia (GTN) represents a unique spectrum of diseases that are related to benign or malignant transformation of the placenta (or afterbirth). The disease include benign hydatidiform mole; invasive mole, which can metastasize; and the frankly malignant variety, choriocarcinoma. The majority of patients (80% to 90%) with GTN follow a benign course, with their disease remitting spontaneously. Most patients with metastatic disease can be effectively cured with chemotherapy. This diverse group of diseases has a sensitive tumour marker, hCG (Human Chorionic Gonadotropin), which is secreted by all of these tumours and allows accurate diagnosis and follow-up.

EPIDEMIOLOGY AND ETIOLOGY

The incidence of molar pregnancy is about 1 in every 1500 to 2000 pregnancies in Australia. There is a much higher incidence among Asian women. If a woman has had a molar pregnancy, the risk of a second one is 1% to 3%.

Although the cause of GTN is unknown, it is known to occur more frequently in women younger than 20 years and in those older than 40 years. It appears that GTN may result from defective fertilization, a process that is more common in both younger and older individuals.

COMPLETE MOLE

The majority of hydatidiform moles are “complete” moles and have a 46 XX karyotype ie 46 chromosomes including two female chromosomes. Specialized studies indicate that both of the X chromosomes are derived from the father. Complete molar pregnancy is only rarely associated with a foetus and this may represent a form of twinning.

PARTIAL MOLE

In the “incomplete” or partial mole, the karyotype is usually a triploid, often 69 XXY (80%). These lesions, unlike complete moles, often present with a coexistent foetus. The foetus usually has a triploid karyotype and has congenital abnormalities.

CLASSIFICATION

The term *gestational trophoblastic neoplasia* is of clinical value because often the diagnosis is made and therapy instituted without definitive knowledge of the precise histologic pattern. GTN may be benign or malignant and nonmetastatic or metastatic

Classification of gestational trophoblastic neoplasia

BENIGN

Hydatidiform mole

- Complete mole
- Incomplete (“partial”) mole

MALIGNANT

Invasive mole (“chorioadenoma destruens”)
Choriocarcinoma

The benign form of GTN is called hydatidiform mole. Although this entity is usually confined to the uterine cavity, trophoblastic tissue can occasionally spread to the lungs. The malignant forms of GTN are invasive mole and choriocarcinoma.

HYDATIDIFORM MOLE

SYMPTOMS

Most patients with hydatidiform mole present with irregular or heavy vaginal bleeding during the 1st or early 2nd trimester of pregnancy. In addition, the patient may expel molar “vesicles” from the vagina and occasionally may have excessive nausea. Some patients experience preeclampsia. Patients may occasionally exhibit symptoms relating to hyperthyroidism, such as nervousness and tremors.

Diagnosis of hydatidiform mole

CLINICAL DATA

- Bleeding in the first half of pregnancy
- Abdominal pain
- Toxaemia before 24wks gestation
- Excessive vomiting
- Expulsion of vesicles

DIAGNOSTIC STUDIES

- Ultrasonography – no foetus
- Chest film
- Serum hCG higher than normal pregnancy values

SIGNS

About half of patients with molar pregnancy present with a uterus that is bigger than expected based on their last menstrual period. Ovarian enlargement by theca-lutein cysts occurs in about one-third of women with molar pregnancies.

TREATMENT

Evacuation

The standard therapy for hydatidiform mole is suction evacuation followed by sharp curettage of the uterine cavity, regardless of the duration of pregnancy. Following the evacuation of a hydatidiform mole, the patient must be monitored with weekly serum assays of hCG. The hCG level should progressively decline and return to normal in 8 – 10 weeks.

PARTIAL MOLE

The incomplete or partial mole is usually associated with a developing foetus. Partial moles are usually diagnosed later than are complete moles and generally present as a miscarriage.

Partial moles rarely metastasize, and only rarely is there a need for chemotherapy.

INVASIVE MOLE

Invasive mole is usually a locally invasive tumour, progressively growing into the muscle of the uterus. About 10% of all hydatidiform moles become invasive moles. Rarely, invasive mole is associated with metastases, particularly to the vagina or lungs, although brain metastases have been documented.

CHORIOCARCINOMA

About one half of patients with choriocarcinoma have had a preceding molar pregnancy. In the remaining patients, the disease is preceded by a spontaneous or induced miscarriage, ectopic pregnancy, or normal pregnancy. Trophoblastic disease following a normal pregnancy is always choriocarcinoma. The tumour has a tendency to spread via the blood stream, particularly to the lungs, vagina, brain, liver, kidneys, and bowel.

SYMPTOMS

Vaginal bleeding is a common symptom of uterine choriocarcinoma or vaginal metastasis. Coughing up blood or shortness of breath may occur as a result of lung metastasis. In the presence of central nervous system metastases, there may be headaches, dizzy spells, "blacking out," or a fit. Rectal bleeding or "dark stools" could represent disease that has spread to the bowel.

DIAGNOSIS

Choriocarcinoma is a great imitator of other diseases, so unless it follows a molar pregnancy, it may not be suspected. In females of reproductive age, a serum hCG level to screen for choriocarcinoma should be performed when any unusual symptoms or signs develop.

TREATMENT OF GESTATIONAL TROPHOBLASTIC NEOPLASIA

If the hCG levels do not fall steadily after the mole has been evacuated, chemotherapy is required.

The chemotherapy most often employed is either methotrexate or actinomycin D. In appropriately selected patients, hysterectomy may be the primary therapy for hydatidiform mole.

For patients with disease having a poor prognosis eg those with liver or brain metastases, combination chemotherapy is always used. Regimens that have been successfully employed include the modified "Bagshawe" regimen (EMA-CO), which is a six-drug chemotherapy regimen. The drugs used include etoposide (VP-16), actinomycin D, vincristine, cyclophosphamide, methotrexate, and folinic acid.

FOLLOW-UP STUDIES

Following three normal hCG levels, patients with a good prognosis should be followed with monthly levels for 1 year. Patients with a poor prognosis should have monthly levels for 2 years or more.

PROGNOSIS

About 95% of patients with GTN having a good prognosis are cured of their disease. Patients with poor prognostic features can be expected to be cured in 50% to 70% of cases. The majority of the patients who die have brain or liver metastases.