During pregnancy, it is possible for the tissue surrounding the embryo to degenerate. Such degeneration typically manifests itself in hydatidiform moles and choriocarcinoma. These tumors are difficult to diagnose and are associated with an increased level of beta hCG. Treatment involves the complete removal of the tumorous growth. The characteristics of the tumors are described in more detail below.

Hydatidiform Moles

Definition of a hydatidiform mole
Hydatidiform moles represent a **hydropic degeneration** of the placental chorionic villi. The vascularization of the degenerated villi is reduced and may even be completely absent. Hydatidiform moles are divided into two different types: **complete** and **partial**. In complete hydatidiform moles, no signs of fetal development are present. In partial moles, some hydropic trophoblastic tissue and fetal tissue may be evident.

### Types of hydatidiform mole

<table>
<thead>
<tr>
<th>Complete mole</th>
<th>Partial mole</th>
</tr>
</thead>
<tbody>
<tr>
<td>46, XX</td>
<td>Triploid</td>
</tr>
<tr>
<td>All villi edematous and completely</td>
<td>Some villi edematous and partially</td>
</tr>
<tr>
<td>surrounded by trophoblastic proliferation</td>
<td>surrounded by trophoblastic proliferation</td>
</tr>
<tr>
<td><strong>No fetal parts</strong></td>
<td><strong>Fetal parts</strong></td>
</tr>
<tr>
<td><strong>Higher risk for choriocarcinoma</strong></td>
<td><strong>Lower risk for choriocarcinoma</strong></td>
</tr>
</tbody>
</table>

### Epidemiology of a hydatidiform mole

In the countries of Southeast Asia, including **China**, the incidence of hydatidiform moles is **twenty times higher** as in the USA or Europe. Generally speaking, women under 20 or over 40 years of age are also at a higher risk.

### Etiology of a hydatidiform mole

The tumorous change occurs due to the fertilization of a **defective egg** from which the mother’s genetic material has been lost. The paternal set of chromosomes reduplicates itself, often in an **XXX** configuration. Triploid chromosome sets are a common occurrence in partial hydatidiform moles.

### Pathogenesis of a hydatidiform mole
In a hydatidiform mole, *hydropic* or fluid-filled *cysts* appear. These are typically the size of a hazelnut and are connected to each other via small peduncles. Because the cysts are not vascularized during the course of proliferation, the *supply of blood and oxygen is deficient*. This situation means that the fetus is no longer viable.

The proliferation of trophoblasts leads to the release of increased amounts of *beta hCG*. This means that a higher-than-usual concentration of the hormone can be measured in the serum.

**Clinical symptoms of a hydatidiform mole**

*Vaginal bleeding* occurs in early pregnancy. This means that a hydatidiform mole is an important differential diagnosis in patients with bleeding during pregnancy. Bleeding due to a hydatidiform mole is often distinguished by the presence of clear vesicles in the bloody discharge.

Lutein cysts form on the ovaries due to the excessive production of beta hCG. Non-specific symptoms such as Hyperemesis gravidarum and nausea may also occur.

**Diagnosing a hydatidiform mole**

Generally, there is a discrepancy between the size of the uterus and the gestational age (the uterus is significantly bigger than it should be). A *sonographic* examination usually reveals an irregular distribution of hypoechoic (= *cystic*) and hyperechoic (= *solid*) areas.

In complete hydatidiform moles, no fetal tissue is present; in partial moles, fetal development with abnormalities may be detected. Abnormalities might include growth retardation or other deformities. A *significantly increased level of beta hCG in the serum* is also an important indication, with the concentration expected to be around twice as high as in a normal pregnancy. Beta hCG is the tumor marker for a hydatidiform mole.

**Differential diagnosis of a hydatidiform mole**

From a diagnostic point of view, a workup for spontaneous *abortion* should also be carried out, since this can also cause bleeding in early pregnancy.

**Treatment for a hydatidiform mole**

Initially, light bleeding is treated conservatively, with prostaglandins or oxytocin administrated to stimulate *spontaneous expulsion* of the mole. Thereafter, curettage
of the uterine wall should be carried out as carefully as possible to avoid perforations. In cases of more severe bleeding, the preceding step is skipped, and **curettage** is carried out immediately. A **hysterectomy** may be performed as the last resort.

Since choriocarcinoma can develop from a hydatidiform mole, regular monitoring of beta hCG levels is essential.

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**Invasive Hydatidiform Mole**

**Definition of an invasive hydatidiform mole**

An invasive hydatidiform mole is a **benign** tumor. Due to its **invasive growth**, it frequently creates a malignant perforation. It is also commonly referred to as a **chorionepithelioma**.

**Epidemiology of invasive hydatidiform moles**

This condition is significantly more common in Asia than in the Western world. In Asian countries, chorionepithelioma occurs in around one of every 20,000 births. Older
pregnant women and first-time mothers are at highest risk.

Etiology of invasive hydatidiform moles

In one half of all cases, an invasive hydatidiform mole occurs following a previous non-invasive hydatidiform mole. The tumorous change can also occur following an abortion or an ectopic pregnancy. Rarely, it occurs spontaneously during the pregnancy.

The development of an invasive hydatidiform mole occurs due to a movement of trophoblast cells into the endometrium. A metastasis occurs as soon as the trophoblast cells reach the bloodstream. Typical sites of metastasis include the lungs, bones, liver, brain and vagina. However, these generally respond well to treatment.

Clinical symptoms of an invasive hydatidiform mole

Typically, the patient will have an enlarged, soft uterus that does not shrink of its own accord. This may be accompanied by recurrent vaginal bleeding that continues despite evacuation of a hydatidiform mole or termination of pregnancy. Significantly increased beta hCG levels continue to be present in the blood. Organ-specific symptoms typically occur once metastasis has taken place.

Diagnosing an invasive hydatidiform mole

As a first step, the beta hCG value should be determined. The results of a sonographic examination will be similar to those obtained in the case of a non-invasive hydatidiform mole. In addition, irregular tumorous regions will be visible in the myometrium.

In a histological perspective, invasive hydatidiform moles are distinguished from complete hydatidiform moles by increasing trophoblast proliferation and invasion of the myometrium. The diagnosis can be confirmed using curettage; however, this is not always possible. Depending on the site of metastasis, a further diagnostic aid, such as a chest x-ray, may be needed.

Treating an invasive hydatidiform mole

Chemotherapy is the method of choice. Despite the occurrence of metastasis, this type of tumor has a good prognosis. Once a year of follow-up care has passed, it no longer represents a contraindication for pregnancy.

Choriocarcinoma

Definition of choriocarcinoma
Choriocarcinoma is a **malignant trophoblast tumor** that consists of degenerated chorionic villi. At a histological level, the villi can no longer be detected; only **anaplastic cells** are present.

**Epidemiology of choriocarcinoma**

Choriocarcinoma is one of the **rarest carcinomas** occurring in the female genital tract. It accounts for around 1% of all female tumors.

**Etiology of choriocarcinoma**

Choriocarcinoma frequently develops from a **hydatidiform mole** or following a spontaneous abortion; occasionally, it also occurs after a normal pregnancy. If occurring after a normal pregnancy, the tumorous growth need not always appear immediately. The period of latency may last months or even years.

Risk factors include the age of the woman, first pregnancies and previous abortions.

**Clinical symptoms of choriocarcinoma**

From a clinical perspective, it is not possible to distinguish choriocarcinoma from an invasive hydatidiform mole. As with an invasive hydatidiform mole, the uterus is soft and **enlarged** and is slow to shrink. Vaginal bleeding is typical. If metastasis has occurred in the vagina, blue or hemorrhagic metastases may be seen during the clinical examination. Systemic symptoms, including fatigue, tiredness and weight loss, are frequently reported.

A choriocarcinoma should always be suspected when there is a **latency period of 4-6 months** between the end of the pregnancy and the appearance of the tumor, when a significantly **raised concentration of beta hCG** is measured in the blood and when **hematogenous metastasis** is detected in the liver, bones and CNS.

**Diagnosing choriocarcinoma**

The diagnostic procedure is similar to that for an invasive hydatidiform mole. It is important that **curettage** is carried out and that the **beta hCG concentration in the blood is determined**. A **chest x-ray**, an **MRI** and a **sonography** of the abdomen could also form a part of the diagnostic process.
Treatment of choriocarcinoma

Treatment of choriocarcinoma is chemotherapy-based, often using methotrexate. 5-6 cycles of cytostatic therapy is typically deployed as treatment. This depends on the levels of beta hCG. The concentration of the hormone should be monitored at regular levels, since it serves as a tumor marker.

Review Questions

The answers are below the references.

1. Which of the following sites of localization is not typical for the hematogenic metastasis of a choriocarcinoma?
   - A. Lungs
   - B. Liver
   - C. Brain
   - D. Adrenal glands
   - E. Spinal cord

2. What is the therapy of choice for treating a hydatidiform mole?
   - A. Chemotherapy with methotrexate
   - B. Combination chemotherapy
   - C. Curettage
   - D. Hysterectomy
   - E. Beta hCG

3. Which of these is less of a risk factor for choriocarcinoma than the rest?
   - A. First pregnancy
   - B. Getting pregnant at an older age
   - C. Intrauterine device
   - D. Threatened abortion
   - E. Incipient abortion

References


Correct answers: 1D, 2C, 3C

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