**Gestational trophoblastic neoplasia**

* Classification of GTN :
  + Benign :
    - Hydatidiform mole :
      * Complete mole
      * Partial mole
  + Malignant :
    - Invasive mole
    - Choriocarcinoma
    - Placental-site trophoblastic tumor
* Risk factors :
  1. Previous molar pregnancy
  2. Extremities of age
* Benign mole can metastasize as well as fibroid too .
* **Hydatidiform mole :**
* Genetics :
  + Complete mole: the majority , and have a 46XX or 46XY karyotype, both X chromosomes are paternally derived, result from normal haploid sperm fertilizing an empty ovum.
  + Partial mole: the karyotype is usually a triploid, normal ovum fertilized by 2 sperms , often 69XXY, the remaining lesions are 69XXX or 69XYY .
* Clinical presentation :
* Complete mole :
  1. **Vaginal bleeding**: the most common presenting symptom, occurs in 97%of cases
  2. Excessive uterine size: large for date is one of the classic signs, occurs in 50% of cases
  3. Toxemia: PET is observed in 27%, usually develops early in the pregnancy
  4. **Hyperemesis Gravidarum**: Occurs in 25% of cases (due to very high Bhcg)
  5. **Hyperthyroidism**: clinically evident hyperthyroidism is observed in 7% (aplha subunit of hcg looks like TSH and induce thyroid gland to secrete hormones)
  6. Trophoblastic Embolization: respiratory distress develops in approximately 2%
  7. Theca lutein ovarian cysts: prominent cysts >6cm develop in 50% of cases (hcg looks like LH and FSH so when its high it’ll stimulate ovaries )
  8. Lower abdominal pain, expulsion of vesicles
* Partial mole :
  1. Patients with Partial HM usually do not have the clinical features of complete HM
  2. In general, these patients present with signs and symptoms of incomplete or missed abortion
  3. The diagnosis may be made only after **histologic** review of the curetting
* Diagnosis :
  + Ultrasonography is a reliable and sensitive technique of **Complete** HM, “**Snow storm**” pattern (snow storm pattern can also be seen in missed miscarriage on fibroid )
  + Serum **B-HCG**  higher than normal pregnancy values
  + Chest film
  + Blood tests: FBC, BGRH, Coagulation profile, LFT, KFT
  + Comparison between complete and partial mole :

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| --- | --- | --- |
| **FEATURE** | **PARTIAL HM** | **COMPLETE HM** |
| **Karyotype** | Most commonly 69,XXX Or 69,XXY | Most commonly 46,XX or 46,XY |
| **Fetus** | Often present | Absent |
| **Amnion, fetal RBC’s** | Usually present | Absent |
| **Villous edema** | Variable, focal | Diffuse |
| **Trophoblastic proliferation** | Focal, slight to moderate | Diffuse, slight to severe |
| **Diagnosis** | Missed miscarriage | Molar gestation |
| **Uterine size** | Small for date | 50% larger for date |
| **Theca lutein cysts** | Rare | 15-25% |
| **Post molar malignant sequelae** | <5% | 9-20% |

* + Treatment :
    - desire to preserve fertility :
      * suction curettage “ best method regardless uterine size “ , steps :
        1. oxytocin infusion (in the OR before the procedure)
        2. dilatation and suction curettage
        3. gentle sharp curettage
        4. send specimens from suction and sharp curettage separately for pathology .
    - No desire to preserve fertility :
      * hysterectomy may be performed with mole *in situ*.
      * The ovaries may be preserved even though theca lutein cysts are present
    - Prophylactic chemo :
      * Not indicated in patients with molar pregnancy because 90% have spontaneous remissions
  + Follow up :
    - B-HCG radioimmunoassay is the most reliable method for follow up of patients with GTN .
    - Following molar evacuation or hysterectomy , patients should be followed by weekly determination of B-HCG levels until these are **normal for 3 consecutive weeks** and the by monthly determination until the levels are normal for **6 consecutive months .**
  + Contraception :
    - Should be used during the entire interval of follow-up.
    - Avoid IUCD until the patient achieves a normal B-hCG level (due to high risk for perforation , and also it causes irregular bleeding at first few months so we can’t tell if the bleeding is due to IUCD or due to persistent mole )
    - Hormonal Contraception + barrier (double method ) is the best choice .
* **Invasive mole :**
  + Non-metastatic :
    - Develops in 15% of patients after evacuation of a complete mole .
    - May perforate through the myometrium, causing intraperitoneal bleeding, or erode into uterine vessels, causing hemorrhage .
    - Persistent GTN After molar evacuation may exhibit features of either HM or choriocarcinoma .
    - persistent GTN After nonmolar pregnancy always has the features of choriocarcinoma (worse)
  + Metastatic :
    - Occurs in 4% of patients after evacuation of a complete mole .
    - Metastasis is usually associated with choriocarcinoma .
    - Most common site of mets is Lungs (80%) .
  + FIGO staging system :
    - Stage I: patients with persistently elevated hGC levels and tumor confined to the uterine corpus **(always low risk >> one chemo agent only)**
    - Stage II: Patients with metastasis to the vagina or pelvis
    - Stage III: patients with **lung metastasis** with or without uterine, vaginal or pelvic involvement
    - Stage IV: Patients with advanced disease and involvement of the brain, liver, kidneys, or GIT **(always high risk >> needs more than 1 chemo agent )**
  + FIGO scoring system : (to determine whether high or low risk , used for stage 2 and 3)
    - Dr said don’t memorize numbers just the parameters :
    1. Age (years)
    2. Antecedent pregnancy
    3. Interval from index Pregnancy (months)
    4. Pretreatment hCG level (mIU/ml )
    5. Largest tumor size
    6. Metastatic site
    7. Number of mets
    8. Previous failed chemo
    - 6 or less is low risk , 7 or more is high risk .
  + Diagnostic evaluation :
    1. A complete history and examination
    2. Measurement of the serum hCG value
    3. Hepatic, thyroid and renal function tests
    4. Complete blood count
  + Metastatic work-up :
    1. A chest X-Ray
    2. CT scan of the abdomen and pelvis
    3. CT or MRI scan of the head
    4. Measurement of **CSF hCG** level if any metastatic disease is present and the head CT is negative
    5. Selective angiography of abdominal and pelvic organs if indicated
  + Diagnosis of post HM trophoblastic neoplasia (invasive mole) : one or more of the following
    1. Plateau of hCG lasts for **four measurement** over a period of 3 weeks or longer, i.e for days 1, 7,14 and 21
    2. A rise in hCG level for **three** weekly consecutive measurements or longer, over a period of at least two weeks or more, i.e on day 1,7and 14
    3. Histological diagnosis of **choriocarcinoma**
    4. When hCG level remains elevated for 6 months or more
  + Chemo therapy :
    - Stage 1 and low risk stage 2 and 3 >> one chemo agent only . (follow up Weekly until normal for 3 wk, then monthly until normal for 12 months)
    - Stage 4 and high risk stage 2 and 3 >> more than 1 chemo agent . (follow up Weekly until normal for 3 wk, then monthly until normal for 24 months)
    - Never get pregnant during follow up .
    - Duration of therapy : give until hcg is normal , and when it becomes normal give at least additional 2 doses to prevent relapse .
    - Invasive mole treated with chemo doesn’t affect fertility .
    - Chemo agents :
      * Methotrexate : it is antifolate , so givefolinic acid to avoid the side effects , associated with less bone marrow, GIT, and liver toxicity
      * Actinomycin D : used in case there is no response to Methotrexate.
  + With each subsequent pregnancy :
    1. Pelvic **USS in 1st trimester** to confirm normal gestation (bcz high risk of recurrence 7-8%),
    2. **histological** review of the placenta,
    3. **HCG** measurement 6 weeks after completion of the pregnancy to exclude occult GTN
* **Choriocarcinoma :**
  1. Highly malignant tumor , haematogenous spread
  2. 3-7% of HM will develop Choriocarcinoma .
  3. Most common organ affected by mets, **lung** .
  4. Some cases manifested by intraperitoneal bleeding seconday to rupture liver or ruptured theca lutein cyst
  5. Patients with pulmonary mets may present with haemoptysis or resp failure
  6. CNS mets presents with neurologic signs resulting from spontaneous bleeding (intracranial bleeding)
  7. 50% of Choriocarcinoma cases occur after HM .
* **Placental Site Trophoblastic Tumor PSTT :**
  1. very rare
  2. can occur after a normal pregnancy, abortion, term delivery, ectopic pregnancy or molar pregnancy
  3. Characterized by **low B-hCG levels**, highf HPL on histologic section and in the serum .
  4. **Diagnosis** is confirmed by dilatation and curettage and hysterectomy
  5. Most cases are confined to the uterus but mets has been reported
  6. **Surgery is the primary treatment of choice**
  7. **Good prognosis** is anticipated in cases localized to the uterus, in case of distant mets or delayed treatment the outcome is poor .

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Look for snow storm pattern on google