Gestational Trophoblastic Neoplasia

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MSU SCS Board Review Coarse

Gestational Trophoblastic Disease

- Partial or complete mole based on pathology, morphology and karyotype

Pathology

- Complete mole
  - Absent embryonic / fetal tissue
  - Chorionic villi show hydatidiform swelling and diffuse trophoblastic hyperplasia
  - 46XX karyotype, entirely paternal origin
  - Ovum in which nucleus is absent or inactive and fertilized by haploid sperm
  - 10% show 46XY karyotype
  - Empty egg fertilized by 2 sperm

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Pathology

- Partial mole
  - Chorionic villi of various size with focal hydatidiform swelling and cavitation
  - Marked villous scalloping
  - Focal trophoblastic hyperplasia
  - Prominent stromal trophoblastic inclusions
  - Embryonic or fetal tissue
- Chromosomes
  - Triploid karyotype (69 chromosome)
  - Extra haploid set from the father

Clinical Features

- Complete mole
  - Vaginal bleeding is presenting symptom
  - Excessive uterine size
  - Preeclampsia
  - Hyperemesis gravidarum
  - Hyperthyroidism
  - Trophoblastic emboli
  - Theca lutein cysts
- Partial mole
  - No symptoms as above
  - Present with signs and symptoms of a missed abortion

Progression

- Complete mole
  - 15% of patients have local uterine invasion after evacuation
  - 4% have metastasis
- Partial mole
  - 2-4% will have persistent post molar tumor
Diagnosis / treatment

- Diagnosis
- US usually

Treatment
- If done childbearing then consider hysterectomy
- Suction curettage for others

Follow - up

- BhCG weekly until negative for 3 consecutive weeks
- Then monthly for at least 3 months
- Contraception during the follow-up period

Gestational Trophoblastic Neoplasia

- Can form non-metastatic and metastatic disease after removal of a complete or partial molar pregnancy
- It's the cancerous form of GTD
How to determine GTN

- FIGO guidelines:
  - A plateau in BhCG over at least 3 weeks
  - 10% or more increase in BhCG for 3 or more values over at least 2 weeks
  - Persistent BhCG level 6 months after evacuation
  - Histology showing choriocarcinoma
  - Presence of metastatic disease

GTN workup

- H and P
- BhCG level
- Liver, thyroid, renal function test
- WBC and PLT count
- Stool guaiac test
- Chest X-ray
- Pelvic US
  - Rule out pregnancy and detect pelvic disease, retained tissue or invasion

Metastatic workup

- Chest CT if chest x-ray positive
- Ultrasound or CT of abdomen / pelvis
- MRI or CT of head
Staging

- Stage I – Disease confined to the uterine corpus
- Stage II – Disease extends outside the uterus, but limited to genital structures (broad ligament, vagina, adnexa)
- Stage III – Disease extends to the lungs, with or without genital tract involvement
- Stage IV – All other met sites (brain, liver, kidneys, GI tract)

Prognostic Scoring System

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>&lt;40</td>
<td>≥40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior Preg</td>
<td>Mole</td>
<td>Abortion</td>
<td>Term</td>
<td></td>
</tr>
<tr>
<td>Months from prior preg</td>
<td>&lt;4</td>
<td>4 - &lt;7</td>
<td>≥7 - &lt;13</td>
<td>≥13</td>
</tr>
<tr>
<td>PreTrt hCG</td>
<td>&lt;10^3</td>
<td>10^3 - &lt;10^4</td>
<td>10^4 - &lt;10^5</td>
<td>≥10^5</td>
</tr>
<tr>
<td>Largest tumor size</td>
<td>3 - &lt;5 cm</td>
<td>≥5 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site of met</td>
<td>Lung</td>
<td>Kidney/splen</td>
<td>GI / Liver</td>
<td>Brain</td>
</tr>
<tr>
<td># Met</td>
<td>------</td>
<td>1-4</td>
<td>5-8</td>
<td>≥8</td>
</tr>
<tr>
<td>Prior failed chemo</td>
<td>------</td>
<td>Single drug</td>
<td>2 or more drugs</td>
<td></td>
</tr>
</tbody>
</table>

Prognostic scoring system

- This is used to determine those at increased risk (stage I - III) who should receive single agent or multi agent chemotherapy
- Stage I – III will be low (single agent) or high risk (multi agent chemo)
- Stage IV is high risk (multi agent chemo)
- If prognostic score is ≥7 then the patient is high risk and needs multi agent chemotherapy
Stage I - III

- Hysterectomy can be done if fertility complete
- Placental site and epithelioid trophoblastic tumor is chemoresistant and hysterectomy is preferred
- Single agent chemotherapy if low risk
- Multi – agent chemotherapy if high risk
- Follow hCG weekly until normal x 3
- Monthly hCG until normal x 12 months
- Contraception during this follow-up

Stage IV

- All use multi-agent chemotherapy
- Brain lesion – can use RT
  - 3000 cGy to the head
- Liver
  - Can resect lesion if acute bleeding
  - Hepatic embolize may be needed to induce remission
- Follow up
  - hCG weekly for 3 negative
  - hCG monthly for 24 months
  - Contraception during follow up

Lung met

- 80% of metastatic GTN
- Present with chest pain, cough, dyspnea, hemoptysis
- Radiology shows
  - Alveolar or snowstorm pattern
  - Discrete, rounded densities
  - Pleural effusion
  - Embolic pattern caused by pulmonary artery occlusion
Other mets

- Vaginal
  - 30% of met patients
  - Highly vascular, violet lesions
  - Lots of bleeding if biopsied
- Liver
  - 10% of met patients
  - Epigastric or RUQ pain
  - Lesions are hemorrhagic and friable
- Brain
  - 10% of met patients
  - Slurred speech, seizure, visual disturbance, headache

Single agent chemo

- Methotrexate
- Actinomycin D

Methotrexate

- Methotrexate 0.4 mg/kg IV or IM for 5 days
- With response treat at same dose
- Fall of βhCG by 1 log
- Without response increase dose to 0.6 mg/kg or switch to actinomycin D
- MTX 40mg/m² IM weekly
- MTX 1mg/kg day 1, 3, 5, 7
- Folinic acid 0.1 mg/kg day 2, 4, 6, 8
Actinomycin D

- 5 day course
- Act D 12 µg/kg IV daily for 5 days
- With response treat at same dose
- Without response add 2 µg/kg to the initial dose or switch to MTX
- Pulse Act D
- Act D 1.25 mg/m² every 2 weeks

Treating with single agent

- βhCG measured weekly after each course of chemotherapy
- Treat patient until βhCG is negative
- Then 1-3 consolidation courses are given

Multi-agent Chemo

- EMA-CO
- EMA-EP
EMA-CO

- Etoposide, MTX, Act-D, Cyclophosphamide, vincristine
- Day 1
  - Etoposide 100 mg/m²
  - Act-D 0.5 mg
  - MTX 100 mg/m² followed by 200 mg/m²
- Day 2
  - Etoposide 100 mg/m²
  - Act D - 0.5 mg
  - Folinic Acid 15 mg IV every 12 hours for 4 doses
- Day 8
  - Vincristine 1 mg/m²
  - Cyclophosphamide 600 mg/m²

EMA-EP

- Etoposide, MTX, Act-D
- Etoposide, cisplatin

Use this protocol if patients become resistant to EMA-CO

Multi-agent treatment

- Chemotherapy continued until BtCG normal x 3
- Then give 2-4 consolidation courses of chemotherapy
Pregnancy following GTD / GTN

- Patients are at an increased risk of a mole after a prior mole
- In new pregnancy
  - US during first trimester (10 weeks) to confirm normal gestation
  - BhCG measurement at 6 weeks PP to exclude GTN