GESTATIONAL TROPHOBLASTIC DISEASE

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INTRODUCTION

- GESTATIONAL TROPHOBLASTIC DISEASES (GTD) INCLUDE:
  - 1. **HYDATIDIFORM MOLES** (both complete and partial)
  - 2. INVASIVE MOLES
  - 3. **CHORIOCARCINOMA**.

- They typically arise from the abnormal **FERTILIZATION** of the **OVUM**.

- **HYDATIDIFORM MOLES** are benign.

- **INVASIVE MOLES** AND **CHORIOCARCINOMA** are malignant lesions with a tendency to **METASTASIZE** to other organs, especially the **LUNGS**.
Blastocyst

The stage at which embryonic and extra-embryonic tissues are segregated (about 5 days post fertilization).

Consists of:

1. The **Inner Cell Mass (ICM)** which will give rise to the embryo

2. The **trophoblast** which will give rise to the placenta
HYDATIDIFORM MOLE

- CLASSIFIED AS COMPLETE OR PARTIAL MOLES
- BENIGN TROPHOBLASTIC DISEASE
- PROLIFERATES WITHIN THE UTERUS WITHOUT MYOMETRIAL INFILTRATION OR HEMATOGENIC DISSEMINATION
- MAY DEVELOP MALIGNANT TRAITS AND BECOME AN INVASIVE MOLE
  - NO HISTOLOGIC SIGNS OF MALIGNANCY IN THE PRIMARY TUMOR
  - TROPHOBLASTS INFILTRATE THE MYOMETRIUM AND GAIN ACCESS TO THE VASCULAR SYSTEM.
  - HEMATOGENIC DISSEMINATION LEADS TO METASTATIC GROWTH IN DIFFERENT ORGANS (BRAIN, LUNGS, LIVER).
CASE

• 27 YEARS OLD FEMALE GRAVIDA 2 PARA1 PRESENTS TO YOUR CLINIC AFTER A POSITIVE PREGNANCY TEST. HER LAST PERIOD WAS 9 WEEKS AGO SHE HAD AN APPOINTMENT TO BE SEEN LATER THIS WEEK. BUT DECIDED TO COME IN THIS MORNING BECAUSE SHE IS PASSING GRAPE LIKE CLOTS . HER PREVIOUS PREGNANCY WAS COMPLETELY NORMAL AND RESULTED IN SPONTANEOUS VAGINAL DELIVERY BOY AT 39WEEKS AND 4 DAYS. THIS PREGNANCY HAS BEEN COMPLICATED BY SEVERE VOMITING WHICH CAUSED HER TO GO TO THE ER TWICE WHERE SHE WAS GIVEN FLUIDS AND DISCHARGED ON DOXYLAMINE/B6.

• VITAL SIGNS ARE NORMAL. PELVIC EXAM IS REMARKABLE FOR TWO RED TRANSLUCENT GELATINOUS LIKE MASSES (APPROXIMATELY 1 CM IN DIAMETER FREELY SETTING ON THE FLOOR OF VAGINAL VAULT.)
• FIRST THING YOU HAVE TO DO ON HER IS TO MAKE SURE THAT SHE IS ACTUALLY PREGNANT SOME OF THESE AT HOME PREGNANCY TEST CAN GIVE FALSE POSITIVE AND IT’S NOT UNCOMMON FOR A WOMEN TO MISS HER PERIOD OR AT LEAST HAVE HER PERIOD AND NOT REALIZED IT SO YOU WANT TO MAKE SURE THAT SHE IS CLINICALLY PREGNANT.

• LAST PERIOD WAS 9 WEEKS AGO INDICATED THAT SHE PROBABLY IS INDEED PREGNANT BECAUSE SHE SHOULD HAVE TWO PERIODS RIGHT NOW. SHE ALSO HAVING SIGNIFICANT NAUSEA THAT ALSO POINTS TO PREGNANCY.

WE CAN'T DIAGNOSE THIS AS MOLAR PREGNANCY UNTIL WE GET HCG LEVEL AND DO AN ULTRASOUND.
DEFINITION

• MOLAR PREGNANCY IS AN ABNORMAL FORM OF PREGNANCY IN WHICH A NON-VIABLE FERTILIZED EGG IMPLANTS IN THE UTERUS AND WILL FAIL TO COME TO TERM.
ETIOLOGY

• RISK FACTORS
• PRIOR MOLAR PREGNANCY
• HISTORY OF MISCARRIAGE
• PATIENTS $\leq 15$ AND $\geq 35$ YEARS
ETIOLOGY

• COMPLETE MOLE
  • DOES NOT CONTAIN ANY FETAL OR EMBRYONIC PARTS
  • CAUSED BY FERTILIZATION OF AN EMPTY EGG THAT DOES NOT CARRY ANY CHROMOSOMES → THE (PHYSIOLOGICAL) HAPLOID CHROMOSOME SET CONTRIBUTED BY THE SPERM IS SUBSEQUENTLY DUPLICATED.
  • IN RARE CASES, THE FORMATION OF A COMPLETE MOLE MAY ALSO RESULT FROM SIMULTANEOUS FERTILIZATION OF AN EMPTY EGG BY TWO SPERMS.

• FETAL KARYOTYPES
  • 46XX: MORE COMMON (~ 90% OF CASES)
  • 46XY: LESS COMMON (~ 10% OF CASES)
  • A 46YY KARYOTYPE HAS NEVER BEEN OBSERVED BECAUSE IT IS NONVAILABLE.
Dissociation

Empty Egg

23X

46,XX

23X

Empty Egg

46,XX

23X

Empty Egg

46,XY

23X

23Y
• **COMPLETE MOLE** IS THE RESULT OF **PATERNAL DISOMY**!

• **PATERNAL DISOMY**: A GENOTYPIC ANOMALY IN WHICH AN INDIVIDUAL RECEIVES TWO COPIES OF ONE CHROMOSOME FROM A SINGLE PARENT AND NO COPIES FROM THE OTHER
HYDROPIC DEGENERATION OF CHORIONIC VILLI with concomitant PROLIFERATION OF CYTOTROPHOBLASTS and SYNCYTIOTROPHOBLASTS.

HYDROPIC DEGENERATION: THE ACCUMULATION OF WATER IN CELLS IN RESPONSE TO INJURY. IMPAIRED NA+/K+-ATPASE PUMP FUNCTION (E.G., DUE TO HYPOXIA) DECREASES ATP PRODUCTION, WHICH LEADS TO NA+ ACCUMULATION IN THE CELL.

CHORIONIC VILLI: VILLI ARISING FROM THE CHORION THAT INVADE THE ENDOMETRIUM TO FORM THE PLACENTA AND ESTABLISH THE PLACENTAL-MATERNAL INTERFACE. THEY ARE FORMED BY CYTOTROPHOBLASTS AND SYNCYTIOTROPHOBLAST
CLINICAL FEATURES

- IN COMPLETE MOLE THERE IS VERY HIGH HCG (HCG MIMICS TSH LH AND FSH)
- MOST WOMEN WILL PRESENT WHEN THEY NOTES GRAPE LIKE CLUSTERS PER VAGINA
- OTHER SYMPTOMS NAUSEA AND VOMITING DUE TO HIGH HCG
- IRRITABILITY DIZZINESS AND PHOTOPHOBIA (THAT PREECLAMPTIC SIGNS). WE ARENT SURE HOW PREECLAMPSIA HAPPENS BUT WE KNOW IS SOMETHING RELATED TO PATHOLOGY OF PLACENTA AND MOLAR PREGNANCY IS ALSO PATHOLOGY OF PLACENTA. SO ITS PROBABLY FOR THAT REASON WE GET PREECLAMPTIC SIGNS.
- SO IF WE HAVE SWELLING HTN AND PROTEINURIA IT IS PATHOLOGY FOR MOLAR PREGNANCY.
- PREECLAMPSIA TENDS TO HAPPEN 2ND AND 3RD TRIMESTER NOT IN 1ST TRIMESTER. SO IF THE SIGNS OCCUR IN 1ST TRIMESTER THINK ABOUT MOLAR PREGNANCY.
- NERVOSNESS TREMORS DUE TO HYPERTHYROIDISIM.
• VAGINAL BLEEDING DURING THE FIRST TRIMESTER
• UTERUS SIZE GREATER THAN NORMAL FOR GESTATIONAL AGE
• PASSAGE OF VESICLES THAT MAY RESEMBLE A BUNCH OF GRAPES THROUGH THE VAGINA
• ENDOCRINE SYMPTOMS
  • PREECLAMPSIA (BEFORE THE 20TH WEEK OF GESTATION)
  • HYPEREMESIS GRAVIDARUM (A CONDITION OF SEVERE, PERSISTENT NAUSEA AND VOMITING DURING PREGNANCY THAT IS ASSOCIATED WITH > 5% LOSS OF PRE-PREGNANCY WEIGHT AND SEVERE DEHYDRATION. MORE COMMON AMONG YOUNG, PRIMIGRAVID WOMEN AND WOMEN WITH MULTIFETAL GESTATION OR MOLAR PREGNANCY.)
  • OVARIAN THECA LUTEIN CYSTS: BILATERAL, LARGE, CYSTIC, ADNEXAL MASSES THAT ARE TENDER TO THE TOUCH (A TYPE OF FUNCTIONAL OVARIAN CYST THAT IS THOUGHT TO ORIGINATE FROM EXCESSIVE AMOUNTS OF CIRCULATING GONADOTROPINS SUCH AS B-HCG. TYPICALLY MULTIPLE AND SEEN BILATERALLY, WITH A HIGH ASSOCIATION WITH GESTATIONAL TROPHOBLASTIC DISEASE AND MULTIPLE GESTATIONS. USG SHOWS BILATERAL ENLARGED, MULTilocULAR, CYSTIC MASSES OF THE OVARES. USUALLY RESOLVE SPONTANEOUSLY ONCE THE SOURCE OF BETA-HCG IS REMOVED)
  • HYPERTHYROIDISM (VERY HIGH AMOUNTS OF B-HCG MAY LEAD TO HYPERTHYROIDISM BECAUSE B-HCG STRUCTURALLY RESEMBLES TSH, ITS THYROTROPIC ACTIVITY)
DIAGNOSTICS

• LABORATORY TESTS: **B-HCG** LEVEL MEASUREMENT (INITIAL TEST OF CHOICE), WHICH SHOULD REVEAL **B-HCG** THAT IS MARKEDLY ELEVATED (HIGHER THAN EXPECTED FOR THE GESTATIONAL AGE)

• **TRANSVAGINAL ULTRASOUND**
  - **COMPLETE HYDATIDIFORM MOLE**
    - **THECA LUTEIN CYSTS**
    - ECHOGENIC MASS INTERSPERSED WITH MANY HYPOECHOGENIC CYSTIC SPACES THAT REPRESENT HYDROPIC VILLI (REFERRED TO AS “SWISS CHEESE,” “BUNCH OF GRAPES,” OR “SNOWSTORM”)
    - NO AMNIOTIC FLUID
    - LACK OF FETAL **HEART** TONES

• NOTE: SOME MOLES MAY NOT PRODUCE **HCG** AT ALL!
HCG LEVELS IN EARLY PREGNANCY

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<th>Weeks Of Pregnancy</th>
<th>HCG level miu/ml</th>
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<tbody>
<tr>
<td>1</td>
<td>5-50 (Average=14)</td>
</tr>
<tr>
<td>2</td>
<td>5-50 (Average=21)</td>
</tr>
<tr>
<td>3</td>
<td>5-50 (Average=42)</td>
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<tr>
<td>4</td>
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<td>5</td>
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<td>9-10</td>
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TREATMENT

• UTERINE EVACUATION BY DILATION AND SUCTION CURETTAGE: COMPLETE MOLES HAVE A 20% RISK OF BECOMING INVASIVE AND A 2% RISK OF DEVELOPING INTO CHORIOCARCINOMA. THEREFORE, COMPLETE EVACUATION OF THE UTERINE CAVITY IS THE MAINSTAY OF TREATMENT.

• MONITOR B-HCG LEVELS UNTIL IN REFERENCE RANGE (USUALLY 8–12 WEEKS)

• CHEMOTHERAPY (USUALLY METHOTREXATE) IF UNRESOLVED, AS INDICATED BY ANY OF THE FOLLOWING:
  • B-HCG VALUES DO NOT DECREASE.
  • HISTOLOGICAL FEATURES OF MALIGNANT GTD ARE PRESENT.
  • IF METASTASES ARE PRESENT ON CHEST X-RAY.
PROGNOSIS

• MOST PATIENTS ACHIEVE NORMAL REPRODUCTIVE FUNCTION AFTER RECOVERY.