CHALLENGES IN THE DIAGNOSIS
AND
MANAGEMENT OF HYDATIDIFORM MOLE

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Case Summary

• Mrs X, 26yrs, P1,L1, admitted in a state of shock with evidence of intraperitoneal bleed.

• USG showed evidence of hemoperitoneum and multiple highly vascular uterine masses.

• Diagnosis - Invasive mole with perforation

• H/o medical abortion at 8wks of amenorrhea with USG diagnosis of Anembryonic pregnancy, 6 months back

• There was no tissue available for histopathological study & hCG was not done.
USG Doppler-Invasive Mole

- Highly vascular multiple masses in the myometrium
- Serum $\beta$-hCG >300,000 IU/L
Laparotomy

- Subtotal hysterectomy
- Blood transfusion
**Metastatic Work up**

- **X-Ray chest – CT, Multiple secondaries**
- **CT abdomen – no liver Mts**
- **MRI brain – no brain Mts**
- **High-Risk GTN**
- **EMA-CO, 5 courses for remission**
First Trimester H.mole

- Early pregnancy evaluation by USG
- Classical appearance of H.mole will be absent.
- Diagnosed as Anembryonic pregnancy, Blighted ovum, Failing pregnancy, missed abortion
- Termination by medical abortion
- No histopathology
- Early evacuation of H.mole – do not reduce incidence of GTN
- GTN diagnosed late - Higher Morbidity
Diagnosing 1\textsuperscript{st} Trimester H.mole

- Suspicious cases, hCG level also with USG
- Repeat USG & hCG after one week
- All products must be examined by experienced pathologist for diagnosing molar change
- USG, hCG and Histopathology will help in Diagnosis
- Follow-up
Diagnosing 1st Trimester H.mole

Normal regression

• After Delivery - hCG neg by 2wks
• After abortion - 4wks
• GTD - later
• hCG to be tested after 4 weeks of abortion evacuation
p57kip2

- p57kip2 (p57) is the protein product of the paternally imprinted but maternally expressed gene CDKN1C located on chromosome 11p15.5.5
- CHM lack maternal genome and hence p57
- Immunohistochemical analysis for p57 has been shown to be a valuable tool in the diagnosis of a CHM
- However, immunohistochemical analysis for p57 cannot distinguish a PHM from an HA.

p57

- p57 staining in a partial mole shows strong nuclear staining in the villous cytotrophoblast and stromal cells
p57kip2 immunohistochemistry

- p57 staining in a complete mole shows lack of staining in the villous cytotrophoblast
- Incidence of GTN following CHM is 15-20%
- GTN incidence after PHM 0.5-5%
Twin with complete mole and coexisting fetus

- Referred as partial mole
- 3-D ultrasound shows normal placenta with fetus and molar tissue separate
- Amniocentesis - normal karyotype
Baby with mole

- Delivered normally at term
- Follow up – normal regression
- Conceived and delivered again after two years
Placental mesenchymal dysplasia mimicking partial mole – Beckwith-Wiedemann syndrome

- Referred as partial mole at 16 weeks.
- Baby was normal on USG
- Molar appearance – partial mole
- Amniocentesis - Normal karyotype
- Pregnancy continued
- Baby developed growth restriction
- C. section
- Placenta - mesenchymal dysplasia.
Two sisters were referred to us for follow up after evacuation of the hydatidiform moles. The eldest sister had 10 unsuccessful pregnancies. 4 were confirmed as complete mole including the last one in 2003. She developed GTN and treated with MTX/FA. The youngest sister had 4 early pregnancy loss of which two are confirmed as complete moles. The 2nd and 3rd sisters are having normal children. No h/o consanguinity. The aim was to confirm whether these are familial recurrent moles-mutation of NLRP7.
Biparental Familial Recurrent Moles

Is an autosomal recessive condition
A recessive maternal locus responsible for this condition
was mapped to 19q13.3-13.4
Most cases are due to mutations in the NLRP7 gene
Women experience recurrent pregnancy loss – CHMs
Genetically diploid but biparental in origin
Normal pregnancies are extremely rare
Similar risk of developing GTN
First reported from Mumbai, India- Ambani et al, 1980
Fluorescent microsatellite genotyping was performed on FFPE tissue from the most recent molar tissue of the elder affected sister.

Sequencing of the coding exons of NLRP7 was performed on DNA from all four sisters and their parents.
The molar tissue from the elder sister was found to be diploid and biparental consistent with a diagnosis of familial recurrent hydatidiform moles.

Both affected sisters were found to be homozygous for a base substitution (c.1738G>T) in exon 4 of *NLRP7*, resulting in a novel amino acid change from glutamic acid to a stop codon, p.E580*.

Both unaffected sisters and the parents of the four sisters were found to be heterozygous carriers of the mutation.
Novel Mutation Found in Affected Individuals

NLRP7 protein

Mutation

p.E580*

PYD domain  NACHT domain  Leucine Rich Region
Pedigree Showing Inheritance of the Mutation in the Family

\[ \downarrow = \text{mutated base at position c.1738 - in a normal individual this should be G/G} \]

- \text{Mother} (Heterozygous G/T)
- \text{Father} (Heterozygous G/T)
- \text{Mrs Z} (Homozygous T/T)
- \text{Mrs S} (Heterozygous G/T)
- \text{Mrs U} (Heterozygous G/T)
- \text{Mrs M} (Homozygous T/T)
Complete Mole

- Classic snow-storm appearance
- Generalized swelling of the chorionic villi
- No gestational sac or embryo
Theca Lutein Ovarian Cysts

- 20-25% of complete mole
- Usually bilateral, multicystic, 6-12cm
- Ovarian hyperstimulation by high hCG
Partial Hydatidiform mole

- excessively enlarged placenta.
- cystic spaces within the placenta,
- gestational sac with embryo/fetus
- Focal cistern formation
**Suction Evacuation**

- **Suction evacuation under anesthesia irrespective of the size using 12-14 mm canula.**
- **Gentle curettage**
- **Oxytocin i/v during evacuation**
Molar Tissue

- Gross appearance of complete mole
- Histopathological exam in all cases
Hysterectomy with Mole-in-situ

- Elderly multiparous women
- Does not prevent Metastatic disease.
- Need hCG follow up
Chemoprophylaxis

• **Prophylactic Chemotherapy at the time of evacuation remains controversial.**

• **Risk of persistent disease in high risk patients can be reduced though not eliminated.**

• **Those who develop persistent disease after prophylactic chemotherapy will have a more resistant disease**
Follow up after molar evacuation

- **Serum hCG** every week till Negative, three more
- **Serum hCG** every month for 6 months.
- hCG –neg. by 8 wks, only 6 more months follow up
- hCG 6 & 10 weeks after subsequent pregnancy
- Contraception during follow-up
- Low-doe OCP
Diagnosis of GTN

- Rise in hCG – 3 values over two weeks
- Plateauing of hCG - 4 values over three weeks
- Persistence of hCG after 6 months
- hCG > 20,000 IU/L after 4 wks
- Tissue diagnosis of choriocarcinoma.
- hCG assay should pick up all forms of hCG- free β-hCG, hCG–H, nicked hCG, hCG missing terminal carboxyl segment.
USG with Doppler

- When GTN is diagnosed with hCG titer, Doppler study may show evidence of invasive mole
Sub urethral Nodule

- Do not try to excise as it will lead to heavy bleeding
- Pack the Vagina keeping a urethral catheter
- Give chemotherapy
Management of GTN

- **Depends on Stage & Risk Score**
  - **Stage I, II, & III Risk score ≤ 6**
  - **Single agent Chemotherapy**
  - **Stage I, II, III with risk score ≥ 7 & Stage IV**
  - **Combination Chemotherapy**
GTN - The Calicut Experience

- No.H.Mole -- 1746
- Incidence of GTN -- 361 (21%)

- Single agent
  - Mx/FA -- 319 (88.37%)
  - Mx/FA & hysterectomy -- 14 (3.9%)
- Multiple agents
  - Mx/FA followed by Act-D -- 10
  - Mx/FA – MAC -- 7
  - Mx/FA- EMA-CO -- 6

Sekharan PK, Sreedevi NS, Rasheedabeesam O, Radhadevi VP, Jayandhiraghavan T, Beena Guhan: Management of Postmolar Gestational Trophoblastic Diseases with Methotrexate and Folinic acid: 15 years of experience,

All products of conception should be taken for histopathologic evaluation.
hCG estimation to be done before & 4 weeks after abortion.
Early abortion before the appearance of molar change will not exclude the possibility of GTN.
Thank You