GTN (gestational trophoblastic neoplasia) PART 2

PART 2

Malignant GTN

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The malignant GTN can be classified into:

- the non-metastatic: invasive mole
- and the metastatic: choriocarcinoma and the PSTT

Malignant disease can be suspected when

- 1- Plateauing or rising B-hCG value over a period of 3 consecutive weeks.
- 2- A rise of B-hCG over a period of 2 weeks.
- 3- Persistence of a detectable B-hCG after 6 months of evacuation

The frankly malignant disease is further subdivided into

1. **Good prognosis** group (low risk group)
2. And the **poor prognosis** group (high risk group).

Choriocarcinoma:

The incidence:

- between 1:10 000 to 1:70 000 deliveries in the west.
- And between 1:250 to 1:6000 deliveries in Asia

Choriocarcinoma

The *antecedent pregnancy* is

1- H. mole in 50%,

2- normal pregnancy in 25%

3- abortion or ectopic pregnancy in 25%.

Clinical Presentation

1- Vaginal bleeding is the most common symptom.

2- Lower abdominal pain because of invasion of the surrounding structures.

3- Abdominal AND/OR vaginal mass.

4- Amenorrhea may precede bleeding caused by the high B-hCG produced by the tumor mass.

Clinical Presentation

5- Pulmonary metastasis may cause **dyspnoea and haemoptysis** it may be misdiagnosed as pulmonary T.B and it can be diagnosed by CXR.

6- **Neurological abnormality** may indicate brain invasion.

7- *High index of suspicion is required to diagnose it especially if it follows normal pregnancy or abortion.*

8- it **invade the myometrium and metastasizes to the lungs, brain, liver, and other organs.**

On examination:

- Most of the patients have **enlarged uterus** as well as ovarian enlargement by **theca lutein cysts**.
- Sites of metastasis should be looked for especially in the vagina cervix and the adnexia

Investigations:

1- B-hCG level in the serum or the urine.
   it is very high > 100 000 IU / L
2- U/S for the pelvis, liver, kidneys…
3- CXR.
4- CT for the brain, liver, and pelvic organs metastasis.
5- MRI for the brain metastasis.
6- Lumber puncture: CSF to measure the B-hCG level in the CSF it should be greater than 1:40 (the ratio of the level in the CSF to that in the serum)
7- CBP, LFT, RFT, and the coagulation study.

Confirmation of the diagnosis is made by Histopathology of curettage products but curettage carry high risk of uterine perforation and dissemination of the disease, so it can be diagnosed basically depending on the clinical suspicion and high B-hCG levels

Staging of the disease

FIGO anatomic staging:

- **Stage I: disease is confined to the uterus.**
- **Stage II: disease extends outside the uterus but limited to the genital tract.**
- **Stage III: disease extends to the lungs with or without genital tract invasion.**
- **Stage IV: all other metastasis**

Classification of the disease according to the prognostic factors:

1- Good prognosis metastatic disease:

2- Poor prognosis metastatic disease:

1- Good prognosis metastatic disease (criteria)

a- short duration (<4 months) between the antecedent pregnancy and chemotherapy.

b- Serum B- hCG <40 000 mIU /ml

c- No metastasis to the brain and the liver.

d- No prior chemotherapy.

2- Poor prognosis metastatic disease (criteria)

a- long duration from the antecedent pregnancy (>4 months) to chemotherapy.

b- Serum B- hCG >40 000 mIU /ml.

c- Metastasis to the brain.

d- Unsuccessful prior chemotherapy.

e- If the disease is following term pregnancy.

Another scoring system is the FIGO scoring:

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Table 15.2 FIGO scoring system

Scores	0	1	2	4
Age	<40	≥40	-	-
Antecedent pregnancy	Mole	Abortion	Term	-
Months from index pregnancy	<4	4–6	7–13	≥13
Pre-treatment hCG	<1000	1000–10,000	1000–100,000	>100,000
Largest tumour size	<3 cm	3–5 cm	≥5 cm	-
Site of mets	Lung	Spleen, kidney	Gastro-intestinal	Brain, liver
Number of mets	-	1–4	5–8	>8
Previous chemotherapy	-	-	Single agent	Two or more drugs

the **WHO scoring system** which is based on an individual risk factors has two categories:

- low risk
- and high risk categories based on total score:
- If score 0-6 (low risk)
- If score of 7 and more (high risk)

Treatment

***For the non metastatic GTD*:**

1- Single agent chemotherapy: either **methotrexate (MTX)** or **actinomycin –D** (dactinomycin).

2- Combined chemotherapy with hysterectomy in female who not wish to preserve reproductive function and her disease is confined to the uterus.

Table 15.3a Methotrexate/folinic acid treatment schedule

Day 1	Methotrexate 50 mg im at noon
Day 2	Folinic acid 30 mg po at 6 p.m.
Day 3	Methotrexate 50 mg im at noon
Day 4	Folinic acid 30 mg po at 6 p.m.
Day 5	Methotrexate 50 mg im at noon
Day 6	Folinic acid 30 mg po at 6 p.m.
Day 7	Methotrexate 50 mg im at noon
Day 8	Folinic acid 30 mg po at 6 p.m.

During the treatment cycle or once per week we have to check the RFT, LFT, CBC and platelet count

Treatment should be stopped when:

When the patient's condition deteriorates:

- WBC<3000
- PLAT <100 000,
- elevated liver enzymes
- or severe side effects: severe stomatitis, GIT ulceration or febrile course.

Switching to alternative chemotherapy when:

When the patient is not responding to this agent like in rising or plateauing titer or when new metastasis appear while the patient on treatment and if the hormone is detectable after 5 courses of chemotherapy which indicate treatment failure.

This will indicate switching to new agent

*Contraception should be continued for 1 year following remission.

* Chemotherapy is continued for 1 cycle following negative hCG titer.

* The advantage of single agent chemotherapy is less toxic but treatment failure is about 6-10%

follow up program:

- B-hCG weekly until 3 consecutive negative titer, then monthly for a year, then 2 monthly for another year, then 6 monthly for life,
- the follow up need Pelvic examination and CXR together with the hCG titer

Poor prognosis (high risk) metastatic disease group:

- those respond poorly (<40% response rate) to single agent chemotherapy.
- Prior unsuccessful chemotherapy is one of the worst prognostic factors because of considerable toxicity and depleting bone marrow reserves.

Combined chemotherapy for high risk group

- *CURRENTLY*: **EMA-CO**: (etoposide, MTX, actinomycin-D, cycloph., and vincristine).
- This protocol gives the best response rate (80%), the treatment cycle should be repeated every 2 weeks and the same investigations are done (RFT, LFT, CBC …)

Other combinations are:

- **MAC (MTX, actinomycin-D, chlorambucil or cyclophosphamide)**
- **Modified BAGSHAWE protocol {CHAMOCA: cycloph., hydroxyurea, MTX, vincristine(oncobin), cycloph., actinomycin-D}.**

IF RESISTANCE to the previously mentioned combinations OCCURS

- **Adjuvant surgery: hysterectomy, thoracotomy or craniotomy for chemotherapy resistant malignant masses.**
- **Other combinations including platinum based drugs are to be used which give better results of response but with higher side effects.**

Example of treatment course

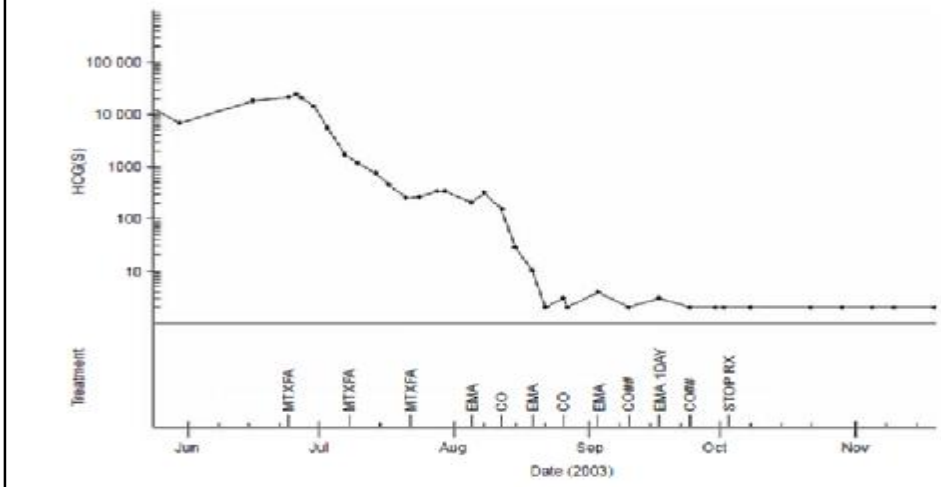

Fig. 15.2 An individual example of the pattern of hCG levels during the course of management.

PSTT

- Derived from intermediate trophoblast
- Local invasion occurs into the myometrium and lymphatics and less commonly into the vasculature,
- it occur with any type of pregnancy or months to years later.
- It is treated by hysterectomy because of resistance to chemotherapy
- if there is metastasis it is an indication for chemotherapy.

Prognosis of GTD:

1. For H.Mole the prognosis is excellent,
2. and for the non metastatic disease the prognosis is very good.
3. For the good prognostic group the cure rate is 75-85%,
4. and for the poor prognosis group if there is liver metastases the survival from (0-60%).
5. The survival is <20% if previous failed chemotherapy or when metastases to the CNS occur in the 1st few months following termination of chemotherapy

Secondary tumor induction:

patients with multiple agent chemotherapy especially (Etoposide) have increased risk to develop myeloid leukemia and colonic cancer.

Subsequent pregnancy

- There are no extra complication during pregnancy but require good follow up by U/S and B-hCG levels because of the 2% risk of recurrence after 1 mole and 20% after 2 moles and 50% after 3 moles.
- After delivery placenta should be sent for histopathological study, and B-hCG level must be measured 6 weeks postpartum.