

Gestational Trophoblastic Neoplasia

The Unit of Gynecologic Oncology



המרכז הרפואי האוניברסיטאי סורוקה

SOROKA UNIVERSITY MEDICAL CENTER

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The Israeli Society of
Gynecologic Oncology

החברה
הישראלית
לגינקולוגיה
אונקולוגית

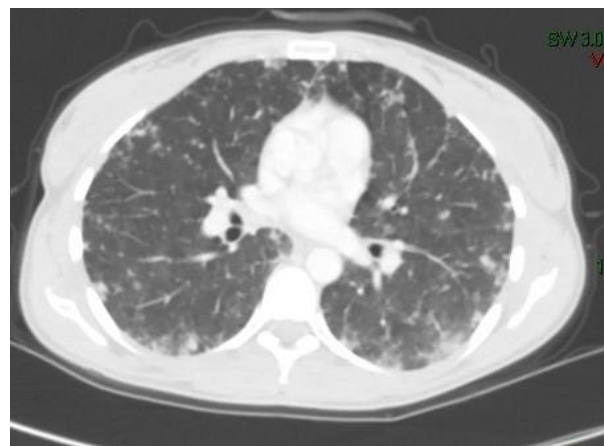


- 43 years old patient
 - mother of two
 - 02/2013 : cesarean section , term , normal healthy newborn
 - Background :
 - Generally healthy
 - Family history of breast cancer
 - Sister diagnosed at the age of 31
 - BRCA1 and 2 mutation status tested just prior to pregnancy
 - 185 del AG, 6174 del T

- About two months following delivery
 - Fatigue, progressive weakness
 - Anemia (Hb = 7.4)
 - Persistent cough -> hemoptysis
 - CXR : multiple lung lesions , bilateral



- 05/2013
 - Admitted to internal medicine/pulmonology ward
 - CT of chest abdomen and pelvis
 - Multiple lung lesions, considered metastatic spread
 - no other abnormal findings
 - Tumor markers within normal limits
 - No HCG level
 - Trans vaginal US : normal findings



- Referral for gynae oncology opinion
 - On examination
 - red , firm, round mass, 3 cm on the clitoris
 - Otherwise normal gynaecologic examination
 - HCG level :> 20000 mIU/ml

The FIGO Cancer Committee Guidelines for the diagnosis of GTN

- 1. Four values or more of hCG plateaued over at least 3 weeks :
- 2. An increase in hCG of 10% or greater for 3 or more values over at least 2 weeks
- 3. The histologic diagnosis of CCA
- 4. Persistence of hCG 6 months after molar evacuation / index pregnancy.

- GTN should be considered and an **hCG test performed in any woman in the reproductive age group who presents with**
 - abnormal uterine bleeding
 - **unexplained metastatic disease**
- GTN following a term or preterm gestation usually presents with uterine bleeding due to invasion of tumor, or bleeding from a metastatic site
 - Patients who develop extensive pulmonary metastases may present with dyspnea, cough, or chest pain.

What would you do next?

- 1. CT guided biopsy of the lung lesions
- 2. Excision of the vulvar mass
- 3. CNS imaging (brain MRI ?)
- 4. Plan for chemotherapy

- Gestational trophoblastic neoplasia (GTN) is a **clinical diagnosis made based upon elevation of serum human chorionic gonadotropin (hCG)**, after a nonmolar pregnancy and other etiologies of an elevated hCG have been excluded
- Imaging findings of uterine enlargement or pathology consistent with GTN, bilateral ovarian theca lutein cysts, or metastatic disease support the diagnosis
- **Unlike other solid tumors, a tissue diagnosis is not required prior to treatment**
 - Risk of profuse bleeding from biopsy sites

Berkowitz RS, Goldstein DP, Horowitz NS: UpToDate, Dec 2014

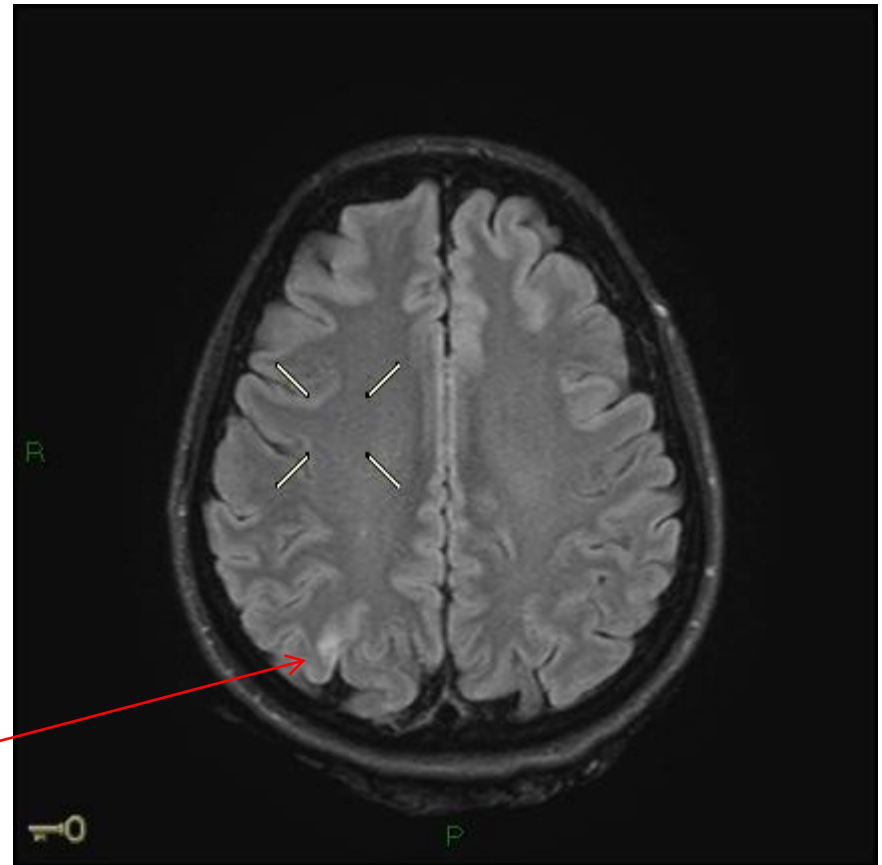
CT guided biopsy of lung lesion

On medical ward, prior to referral

No evidence of malignancy/chronic and focal acute interstitial infiltrate , intra-alveolar hemorrhage

Brain MRI

small right parietal mass, m/p metastatic



Next step?

- 1. Multiple agent chemotherapy
 - High risk GTN
- 2. Single agent chemotherapy
 - Low risk GTN
- 3. Tissue diagnosis
 - Necessary for treatment
- 4. Radiotherapy to the clitoral mass
 - (symptomatic)

High Risk Gestational Trophoblastic Neoplasia

- Metastases outside the lung : stage IV
- Age: 42 = 1
- Pretreatment HCG level > 10000 = 2
- Antecedent pregnancy : term = 2
- Site of metastases : brain = 4

• Therefore : stage IV : 9

FIGO Staging of Gestational Trophoblastic Neoplasia (GTN) (GTN) and modified WHO Prognostic Scoring System as adapted by FIGO

Stage	Disease description	Risk factor	Score			
			0	1	2	4
Stage I	Disease confined to the uterus					
Stage II	GTN extends outside of the uterus, but is limited to the genital structures	Age (years)	<40	≥40	-	-
		Antecedent pregnancy	Mole	Abortion	Term	-
		Interval (months)*	4	4 to 6	7 to 12	>12
Stage III	GTN extends to the lungs, with or without genital tract involvement	Pretreatment serum hCG (mIU/mL)	<10 ³	10 ³ to 10 ⁴	10 ⁴ to 10 ⁵	>10 ⁵
		Largest tumor (including uterus)	<3 cm	3 to 4 cm	≥5 cm	-
Stage IV	All other metastatic sites	Site of metastases	Lung	Spleen, kidney	GI tract	Brain, liver
		Number of metastases	-	1 to 4	5 to 8	>8
		Prior failed chemotherapy	-	-	Single drug	≥2 drugs
The stage should be followed by the sum of the risk factors (eg, III:5)						

FIGO: International Federation of Gynecology and Obstetrics; WHO: World Health Organization; hCG: human chorionic gonadotropin.

* Interval (in months) between end of antecedent pregnancy and start of chemotherapy.

Original figure modified for this publication. Berkowitz RS, Goldstein DP. Current management of gestational trophoblastic diseases. *Gynecol Oncol* 2009; 112:654.

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What chemotherapy regimen?

- 1. EMA –EP
 - Etoposide, ActD, MTX, Cisplatin
- 2. MAC
 - MTX, ActD, Chlorambucil
- 3. EMA-CO
 - Etoposide, MTX, ActD, Cyclophosphamide, Vincristine
- 4. CHAMOCA
 - MTX, ActD, Cyclophosphamide, Doxorubicine, Melphalan, Hydroxyurea, Vincristine

Combination chemotherapy for primary treatment of high risk gestational trophoblastic tumour (Review)

Deng L, Zhang J, Wu T, Lawrie TA, 2012



- EMA/CO is currently the most widely used first-line combination chemotherapy for high-risk GTN
 - retrospective studies have reported primary remission rates for EMA/CO of up to 91%
 - this regimen has not been rigorously compared to other combinations such as MAC or FAV in RCTs.
- Other regimens may be associated with less acute toxicity than EMA/CO;
 - however, proper evaluation of these combinations in high-quality RCTs that include long-term surveillance for secondary cancers is required

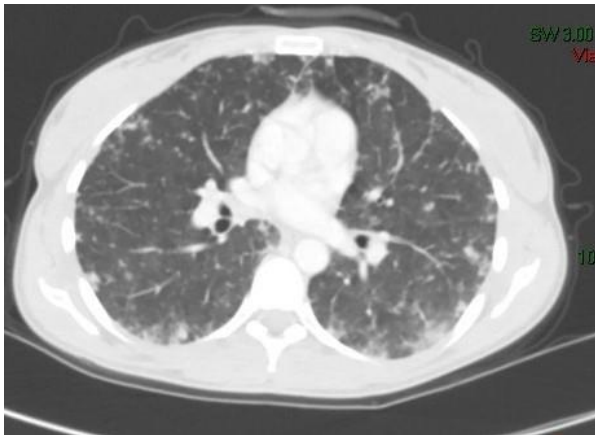
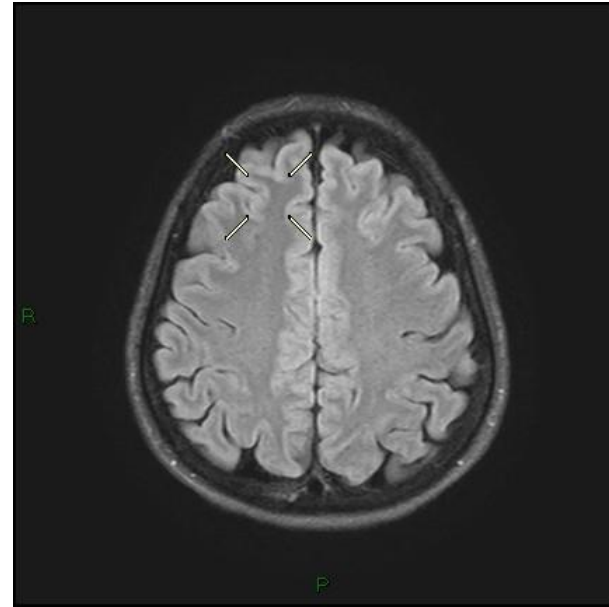
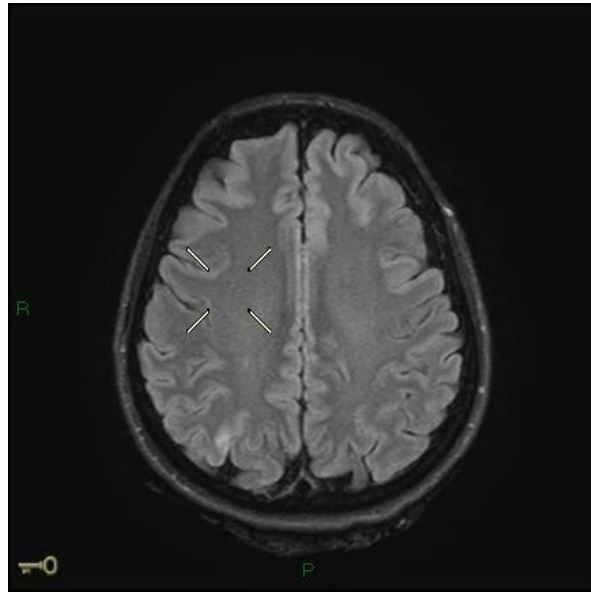
EMA – CO

8 cycles

- [Etoposide](#) – 100 mg/m² IV over 30 minutes on days 1 and 2
- [MTX](#) – 100 mg/m² IV bolus followed by 200 mg/m² IV over 12 hours on day 1
- [ActD](#) – 0.5 mg IV bolus on days 1 and 2
- [Leucovorin](#) calcium – 15 mg orally every 12 hours for four doses, starting 24 hours after start of MTX
- [Cyclophosphamide](#) – 600 mg/m² IV on day 8
- [Vincristine](#) – 1.0 mg/m² IV on day 8

Brain Metastases

- Multidisciplinary approach
 - Surgery
 - Radiotherapy
 - Chemotherapy
 - High dose Methotrexate 1000 mg / sqm
- With appropriate management, the outlook for patients with brain metastases from high-risk gestational trophoblastic tumors is good
 - the majority of patients can achieve sustained remission and probably a cure with **chemotherapy as the dominant form of treatment**
 - When the tumor is sufficiently chemosensitive, the blood-brain barrier does not prevent disease elimination
 - Newlands ES, Holden L, Seckl MJ et al, J Reprod Med, 2002



05/2013

08/2013

- 08/2013
 - CT of chest, abdomen and pelvis and MRI of brain : no abnormal findings, radiologic complete response
- 08/2014
 - Free of disease
 - Had risk reducing BSO
- 01/2016
 - Contemplates IVF pregnancy – egg donation

תאריך	מדבקה	תוצאה	טווח ויחידות
20/11/2013 13:07	15927929	<7	mIU/mL
21/08/2013 11:24	15924096	<7	mIU/mL
14/08/2013 13:53	15922516	<7	mIU/mL
07/08/2013 11:22	15922151	<7	mIU/mL
31/07/2013 10:30	15917792	<7	mIU/mL
25/07/2013 11:30	15917525	<7	mIU/mL
17/07/2013 09:50	15917124	<7	mIU/mL
10/07/2013 09:55	15879764	7.0	mIU/mL
03/07/2013 11:23	15879381	9.8	mIU/mL
26/06/2013 10:38	15878999	20.3	mIU/mL
19/06/2013 12:11	15878629	47.6	mIU/mL
12/06/2013 11:06	15878254	135.2	mIU/mL
05/06/2013 14:32	15876925	348.6	mIU/mL
29/05/2013 11:33	15876447	1913.5	mIU/mL
21/05/2013 14:37	15869997	12113.7	mIU/mL
16/05/2013 10:55	15869713	19614.9	mIU/mL
12/05/2013 08:43	15869449	20676.8	mIU/mL
06/05/2013 11:33	15869175	18759.2	mIU/mL
05/05/2013 11:45	15869100	20367.5	mIU/mL

Thank you



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