Ectopic Molar Pregnancy

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Gestational Trophoblastic Disease (GTD)

- A broad spectrum of benign and malignant tumors derived from the trophoblast of the human placenta.
- These diseases are characterized by a reliable tumor marker, which is the B Subunit of human chorionic gonadotropin (**BhCG**), and have varied tendencies for local invasion and spread.

- **Two distinct types** of molar gestations are recognized: partial and complete hydatidiform moles, both of which have distinct cytogenetic origins, pathologic features, and clinical behavior.
- Most patients with primary molar gestations do not require adjuvant chemotherapy and may be monitored after therapeutic evacuation with serial **hCG** level until either spontaneous regression occurs or the patient develops criteria of malignant sequelae.

EPIDEMIOLOGY AND RISK FACTORS

- The incidence of **GTD** has remained fairly constant at approximately

1 to 2 per 1000 deliveries in North America and Europe,

Although historically higher incidence rates have been reported in parts of Asia .

- Maternal age at the upper and lower extremes carries a higher risk of GTD
- A history of prior unsuccessful pregnancies also raises the risk of GTD For example, previous spontaneous abortion at least doubles the risk of molar pregnancy .
- A personal history of GTD increases the risk of developing a molar gestation in a subsequent pregnancy at least tenfold.

- Vitamin A deficiency and low dietary intake of carotene are associated only with a higher risk of complete moles.
- Prior COC use approximately doubles the risk, and longer duration of use also correlates positively with risk.
- Partial moles have been linked to higher education level , smoking, irregular menstrual cycle .

Modified WHO Classification of GTD

Hydatidiform mole

1.Complete

2.Partial

3.Invasive mole

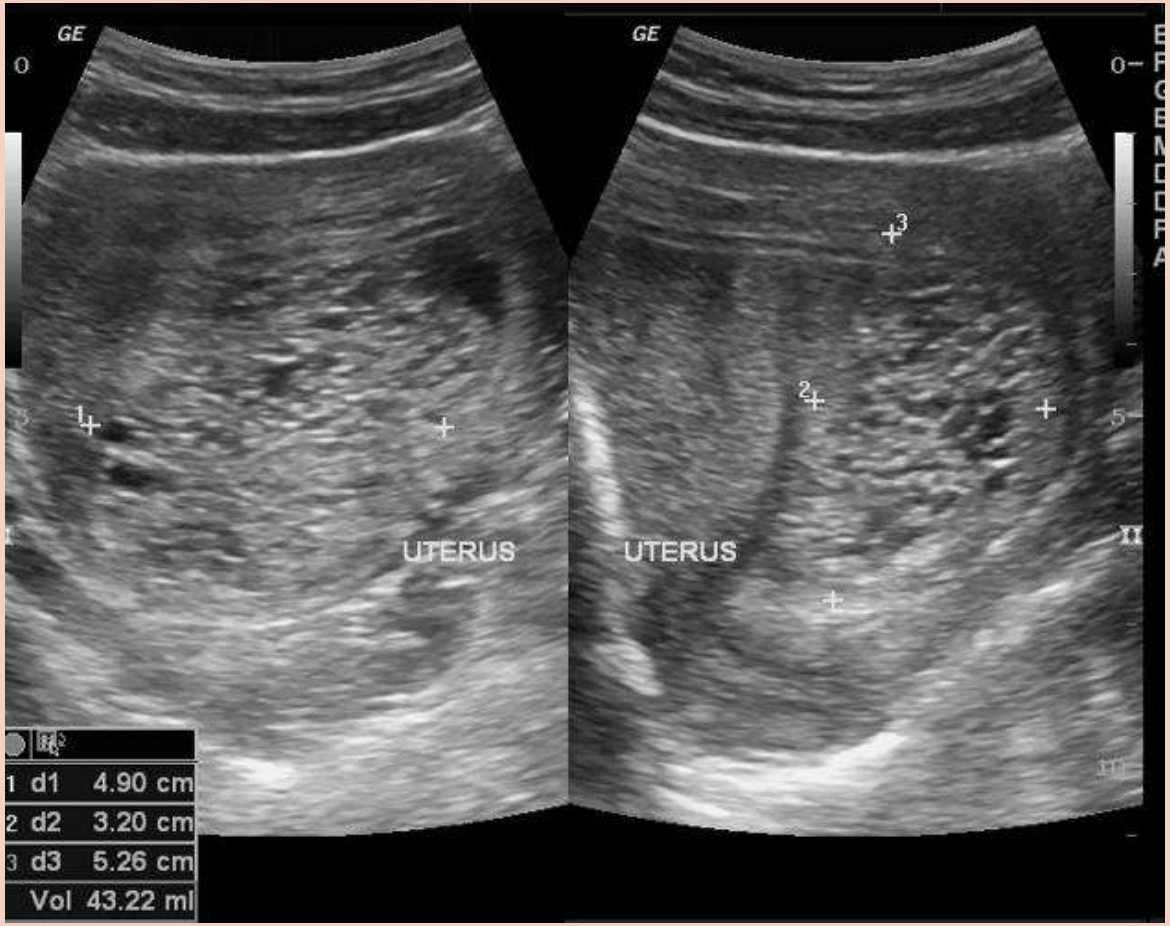
Trophoblastic tumors

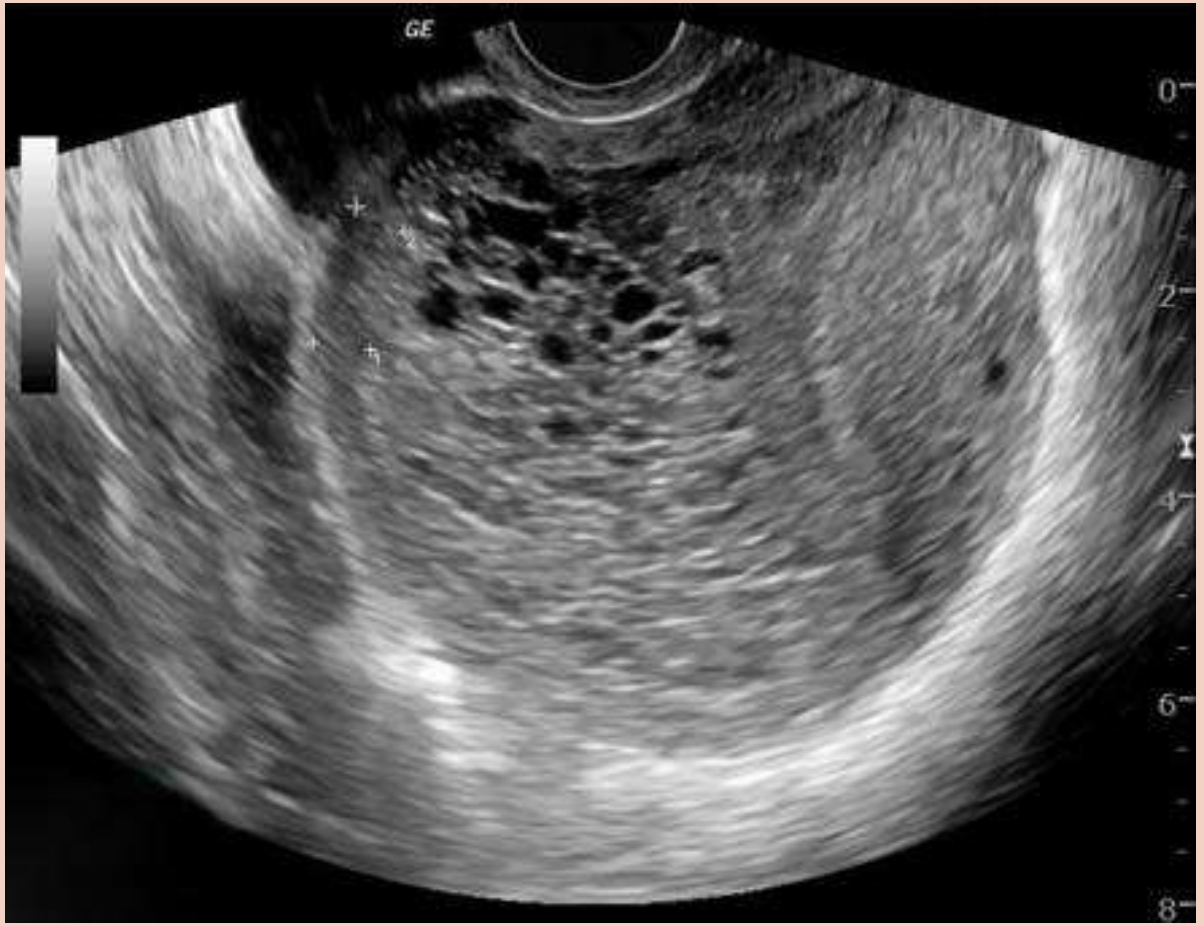
1.Choriocarcinoma

2.Placental site trophoblastic tumor

3.Epithelioid trophoblastic tumor

Ultrasonographic Picture Of hydatid Mole





Ectopic Molar Pregnancy

- Ectopic molar pregnancy is an uncommon event in clinical practice.
- The true incidence of **GTD** developing outside the uterine cavity approximates 1.5 per 1 million births & with any ectopic pregnancy, initial management usually involves surgical removal of the conceptus and histopathologic evaluation.

GESTATIONAL TROPHOBLASTIC NEOPLASIA

- This term characterized by aggressive invasion of the endometrium and myometrium by trophoblast cells.
- Most cases follow a hydatidiform mole.
- Rarely, GTN develops after a live birth, miscarriage, or termination.

GESTATIONAL TROPHOBLASTIC NEOPLASIA :Histologic Classification

1.Invasive Mole

- This common manifestation of **GTN** is characterized by whole chorionic villi that accompany excessive trophoblastic overgrowth and invasion .
- These tissues penetrate deep into the myometrium, sometimes to involve the peritoneum, adjacent parametrium, or vaginal vault.
- Such moles are locally invasive but generally lack the pronounced tendency to develop widespread metastases typical of choriocarcinoma.
- Invasive moles originate almost exclusively from a complete or a partial hydatidiform mole .

2.Gestational Choriocarcinoma

- This extremely malignant tumor contains sheets of anaplastic trophoblast and prominent hemorrhage. necrosis, and vascular invasion.
- However, formed villous structures are characteristically absent.
- Gestational choriocarcinoma initially invades the endometrium and myometrium but tends to develop early blood-borne systemic metastases .

Spread of GTN

Apart from the local spread, vascular erosion takes place early and hence distant metastases occur rapidly.

The common sites of metastases are lungs (80%), anterior vaginal wall (30%), brain (10%), liver (10%) and others.

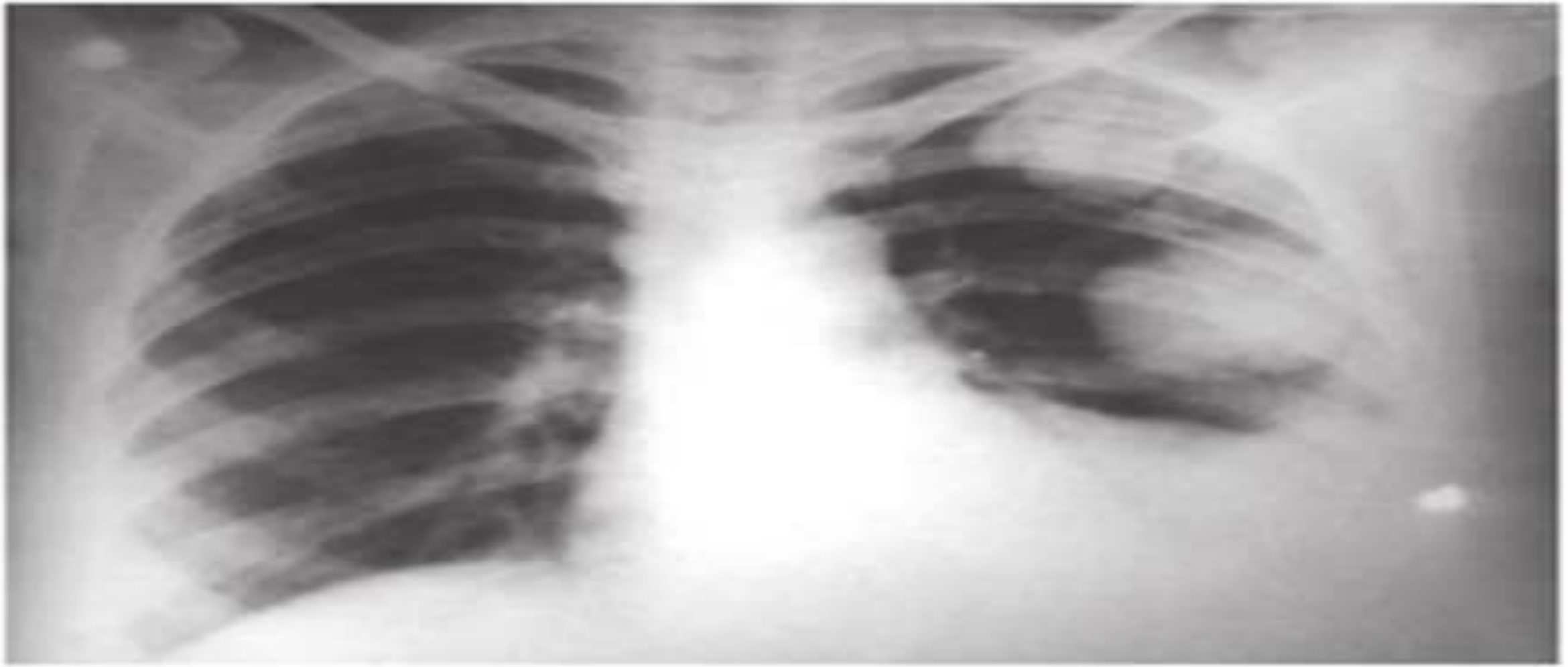


Fig. 23.17: Cannon ball shadow in the left apical and mid region of the lung with pleural effusion in choriocarcinoma [*By courtesy* — Eden Hospital, MCH, Kolkata]

Is Histological Diagnosis Necessary For Treatment ?

- Patients may be treated for malignant **GTN** on the basis of clinical, radiographic, and **hCG** level determinations without a definitive histologic diagnosis.
- For this reason, the generic term of gestational trophoblastic neoplasia is useful, especially when treating patients with metastatic disease that is not readily accessible for pathologic evaluation.
- Except for **PSTT**, the initial histologic features of any lesion identified as GTN are less important than the clinical data and hCG level.

Treatment Of Molar Pregnancy

Surgical: -Suction evacuation of the uterus as early as the diagnosis is made.

-Surgical evacuation should be done in theater room then follow up by BhCG and sonar.

Chemotherapy:

Do all cases of molar pregnancy need chemotherapy?.....**NO**.

When we should give chemotherapy?

PROPHYLACTIC CHEMOTHERAPY

-80% of patients undergo spontaneous remission.

-Chemotherapy is used with advantages in the following circumstances:

(i) If the hCG level fails to become normal by (10-12 weeks) or re-elevation at 4-8 weeks

(ii) Rising β hCG level after reaching normal levels

(iii) Post evacuation hemorrhage

(iv) follow up facilities are not adequate

(v) Evidences of metastases irrespective of the level of hCG

(vi) high risk patient

Treatment Of GTN

- Low risk group receive single agent chemotherapy (usually methotrexate).
- High risk group combination chemotherapy (usually EMA-CO)
- Hysterectomy
- Following hysterectomy or chemotherapy, regular follow-up is essential.

If there is any clinical or radiographic evidence of extrauterine metastases, the patient is classified as **having metastatic GTN**.

These patients are further divided into **good-prognosis** and **poor-prognosis** categories on the basis of factors that predict the failure of primary single-agent chemotherapy with methotrexate or dactinomycin.

Follow up

Follow up is mandatory for all patients at least for 2 years.

Serum hCG is measured weekly until it is negative for three consecutive weeks.

Thereafter it is measured monthly for 6 months and 6 monthly thereafter for life.

Future childbirth: There is no adverse effect on the subsequent pregnancy provided the conception occurs after 1 year of completion of chemotherapy

Pregnancy should be confirmed by USG early and hCG level is to be measured 6 weeks after delivery to exclude persistent GTN.

Incidence of placenta accreta is increased.

Modality Of Chemotherapy

In practical events we refer the patients to medical oncologist.

Curative Chemotherapy

MANAGEMENT OF GTN	
A. Stage I Low risk GTN	- Single agent chemotherapy.
High risk or Resistant	- Combination therapy - Family completed→ hysterectomy.
B. Stage II and III Low risk GTN	- Single agent chemotherapy. - Hysterectomy (family completed) to reduce tumor mass.
High risk or Resistant	- Combination therapy - Hysterectomy — to reduce (trophoblastic) tumor mass.
C. Stage IV	- Combination chemotherapy. - Surgery (hepatic resection, craniotomy). - Radiation (cerebral metastasis).

-Non metastatic disease (confined to the uterus)

-Metastatic disease:

A. *Low risk (good prognosis)*

– Disease is present < 4 months duration
– Initial serum hCG level < 40,000 mIU/ml
– Metastasis limited to lung and vagina
– No prior chemotherapy
– No preceding term delivery

B. *High risk (poor prognosis)*

– Long duration of disease (> 4 months)
– Initial serum hCG > 40,000 mIU/ml
– Brain or liver metastasis
– Failure of prior chemotherapy
– Following term pregnancy
– WHO score > 8

Prognostic factors and treatment groups

Table 42.3 International Federation of Gynecology and Obstetrics (FIGO) prognostic scoring system employed for assessing the intensity of the initial chemotherapy treatment.

Scores*	**0**	**1**	**2**	**4**
Age (years)	<40	≥40	–	–
Antecedent pregnancy	Mole	Abortion	Term	–
Months from index pregnancy	<4	4–6	7–13	≥13
Pretreatment hCG (IU/L)	<1000	1000–10 000	1000–100 000	>100 000
Largest tumour size	<3 cm	3–5 cm	≥5 cm	–
Site of metastases	Lung	Spleen, kidney	Gastrointestinal	Brain, liver
Number of metastases	–	1–4	5–8	>8
Previous chemotherapy	–	–	Single agent	Two or more drugs

* Scoring is done using data obtained within 24 hours prior to starting chemotherapy.

EMA/CO chemotherapy.

Week 1	
Day 1	Actinomycin D 0.5 mg i.v. Etoposide 100 mg/m^2 i.v. Methotrexate 300 mg/m^2 i.v.
Day 2	Actinomycin D 0.5 mg i.v. Etoposide 100 mg/m^2 i.v. Folinic acid 15 mg p.o. 12-hourly × 4 doses Starting 24 hours after commencing methotrexate
Week 2	
Day 8	Vincristine 1.4 mg/m^2 (maximum 2 mg) Cyclophosphamide 600 mg/m^2

TABLE 23.20 MAC PROTOCOL IN LOW-RISK CASES

Methotrexate	1–1.5 mg/kg	IM/IV	Days 1, 3, 5 and 7
Folinic acid	0.1–0.15 mg/kg	IM	Days 2, 4, 6 and 8
Actinomycin D	12 µg/kg	IV	Days 1–5
Cyclopho-sphamide	3 mg/kg	IV	Days 1–5

The courses are to be repeated at interval of 2 weeks

TABLE 23.21 EMA-CO PROTOCOL IN POOR PROGNOSIS METASTATIC DISEASE

	Drug	*Dose*
Day 1	Etoposide	100 mg/m² in 200 mL saline infused over 30 minutes
Day 1	Actinomycin D	0.5 mg IV bolus
	Methotrexate	100 mg/m² bolus followed by 200 mg/m² IV infusion over 12 hours
Day 2	Etoposide	100 mg/m² in 200 mL saline infused over 30 minutes
	Actinomycin D	0.5 mg IV bolus
	Folinic acid	15 mg IM every 12 hours for 4 doses beginning 24 hours after starting methotrexate
Day 8	Cyclophosphamide	600 mg/m² IV in saline over 30 minutes
	Vincristine (oncovin)	1 mg/m² IV bolus

The course will restart after 7–14 days, if possible. Generally 2 additional courses are given after the hCG levels become normal.

The Story Of Our Patient

➢ Long story lasing from15/6/2020 up to now.

A 25 -year-old lady P3 +1 from Boraa, housewife , presented to the emergency department with lower abdominal pain ,spotting per vagina since 3 weeks, amenorrhea since two and half months with N&V.

The pain progressive, dull aching in nature. She has history of abortion and D&C 3 months ago. Systemically free and no significant family history.

- **Clinical examination** revealed soft abdomen with severe tenderness in the right iliac fossa. Per vaginal examination revealed bulky uterus and cervical tenderness was positive. There was no evidence of palpable mass lesion. Systemically free .
- **Ultrasonography** of the pelvis showed right adnexal mass 7x5cm heterogeneous irregular outline adjacent to right ovary and uterus was corresponding to 9 weeks,
- urine, blood teste for pregnancy positive .
- **Routine hematological and biochemical** test were within normal limits.

Diagnosis and Decision

- **Ectopic pregnancy was suspected and laparotomy was decided.**
- Explorative laparotomy was performed. Intraoperatively, there was bulky uterus both tubes are normal, no free fluid in Douglas pouch and no any localized mass was seen, so no specimen can be taken for histopathological evaluation.
- But only needle aspiration was taken from undemarkated, retroperitoneal vascularized flat lesion close to the fallopian tube and sent for cytology. The result was clotted blood with congested blood vessels (On 7/7/2020).

Postoperative Follow UP

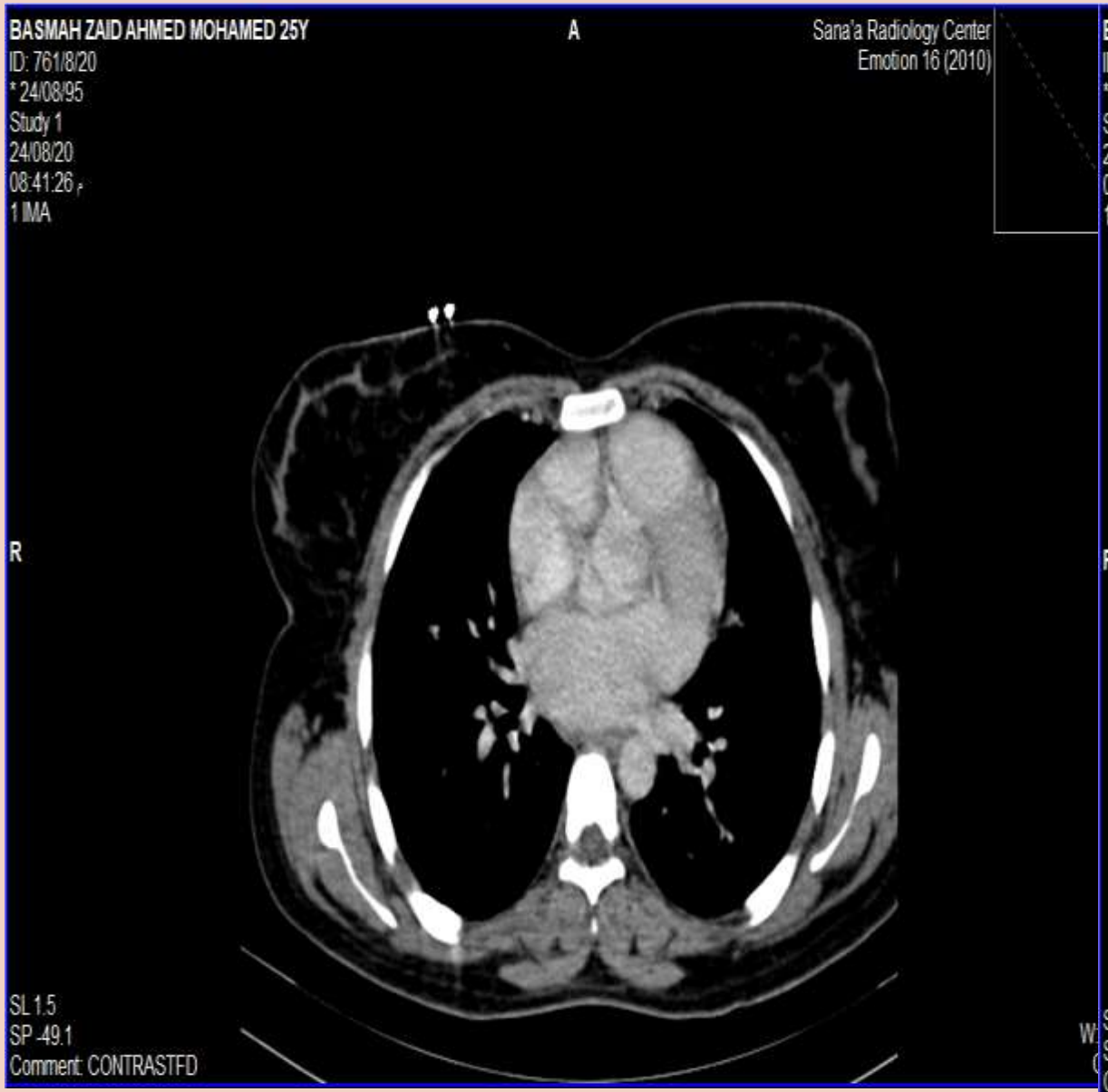
1st day post operation, **BHCG** was 73300 IU (**on 16/6/2020**) and the patient still in pain. , so she was referred to medical oncologist.

On17/6 /2020 U/S finding was: extra uterine heterogeneous, irregular outline ,hyper vascular mass about **9 x7cm** with normal uterus.

On 24/ 6/2020 BHCG was 50000 IU,**U/S** finding was **12x7cm** highly vascular cystic degeneration in close contact with the base of **UB**

Postoperative Follow UP

- **On 29/6/2020** She was given single agent chemotherapy (Methotrexate).
- **On 24/8/2020**, After 5 doses of Methotrexate with folonic acid, the pain subsided but still persistent increase in **BHCG** >45000 mIU/ml .
- **I referred** the patient to Sana,a for **Dr. Salwa Alghomairi** who in turn refer her for oncologist **Dr.Soaad Alareky**, **Dr. Ahmed Shamalan** he did for her BHCG, U/S and CT. **CT** showed picture of invasive mole with potential malignant degeneration evidenced by a mass **22× 9 ×10 cm** extending to lateral and posterior of uterus, with several nodules noted in the base of pulmonary field the largest measured **19× 12mm** and **BHCG** was **53000 MIU /ML on 12/9/2020 .**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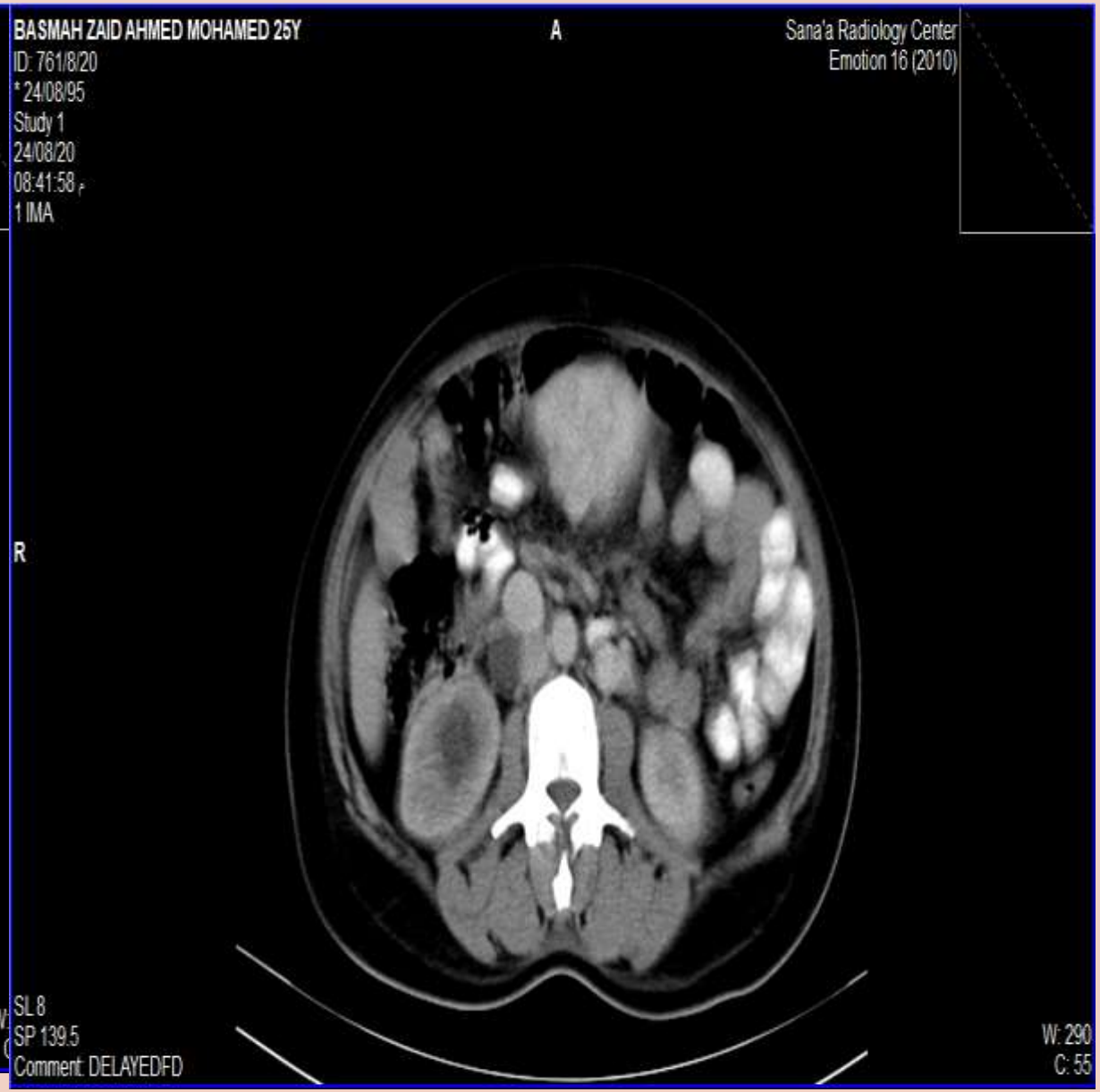
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In Sanaa oncology center the patient was seen and given combined chemotherapy (**EMA/CO protocol**)and referred her to complete her treatment in Hodeida oncology center.

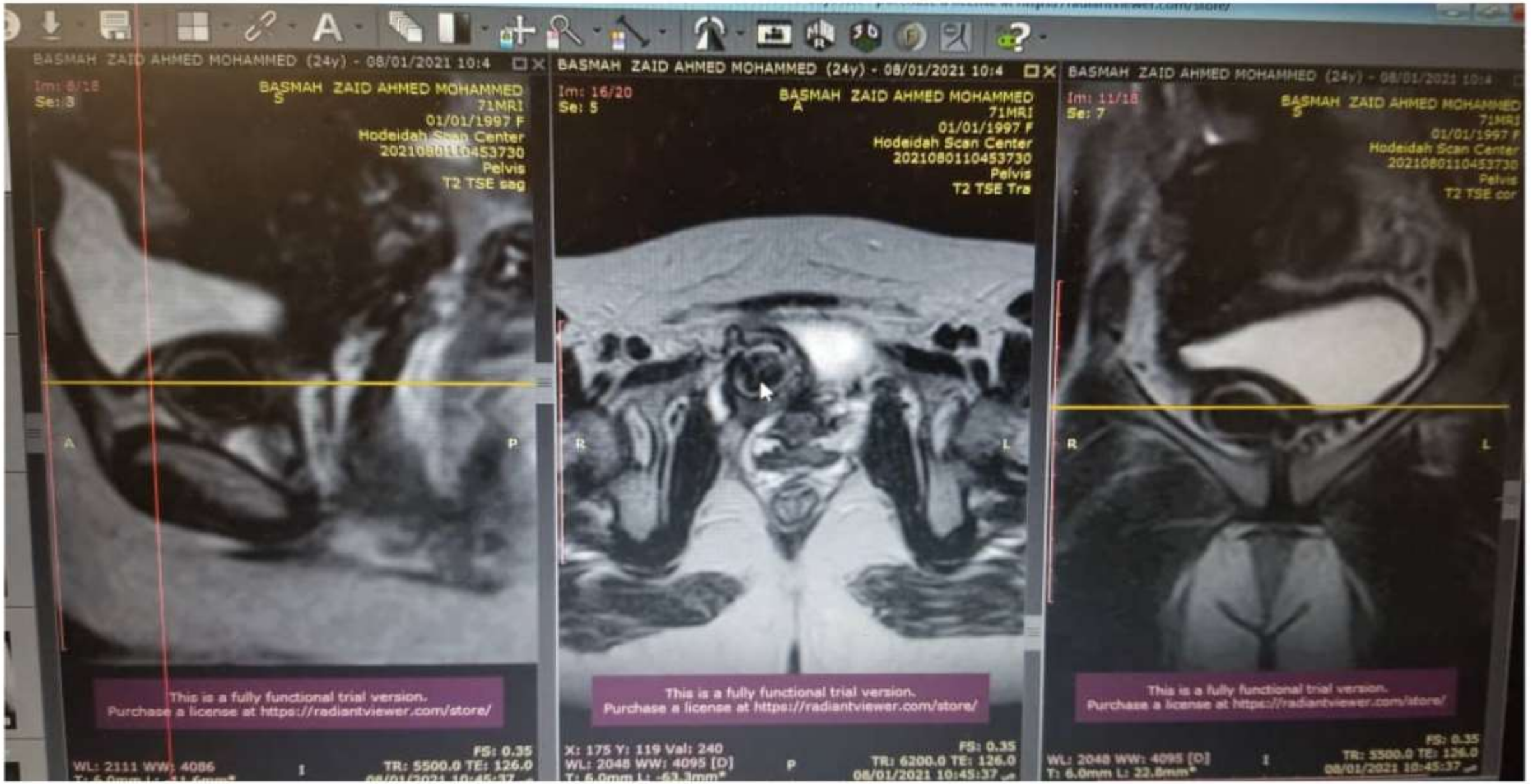
In Hodeida oncology center she was given **EMA/CO** and **EMA/EP** alternatively.

On 29/9/2020 BHCG was **4038 mIU/ml.**

On 15/2/2021 BHCG was **0.100 mIU/ml**but the size of the mass by U/S and CT was not reduced markedly.

On 27/6/2021 She had taken her last dose of chemotherapy .

On 1/8/2021 MRI was done and there was significant reduction of mass to **7.8 × 5× 4 cm** and the lung nodule is **8 x 7 mm**, So she was referred for surgical oncologist **Dr.Anter Alafari** who did TAH and BSO **on 14/8/2021**.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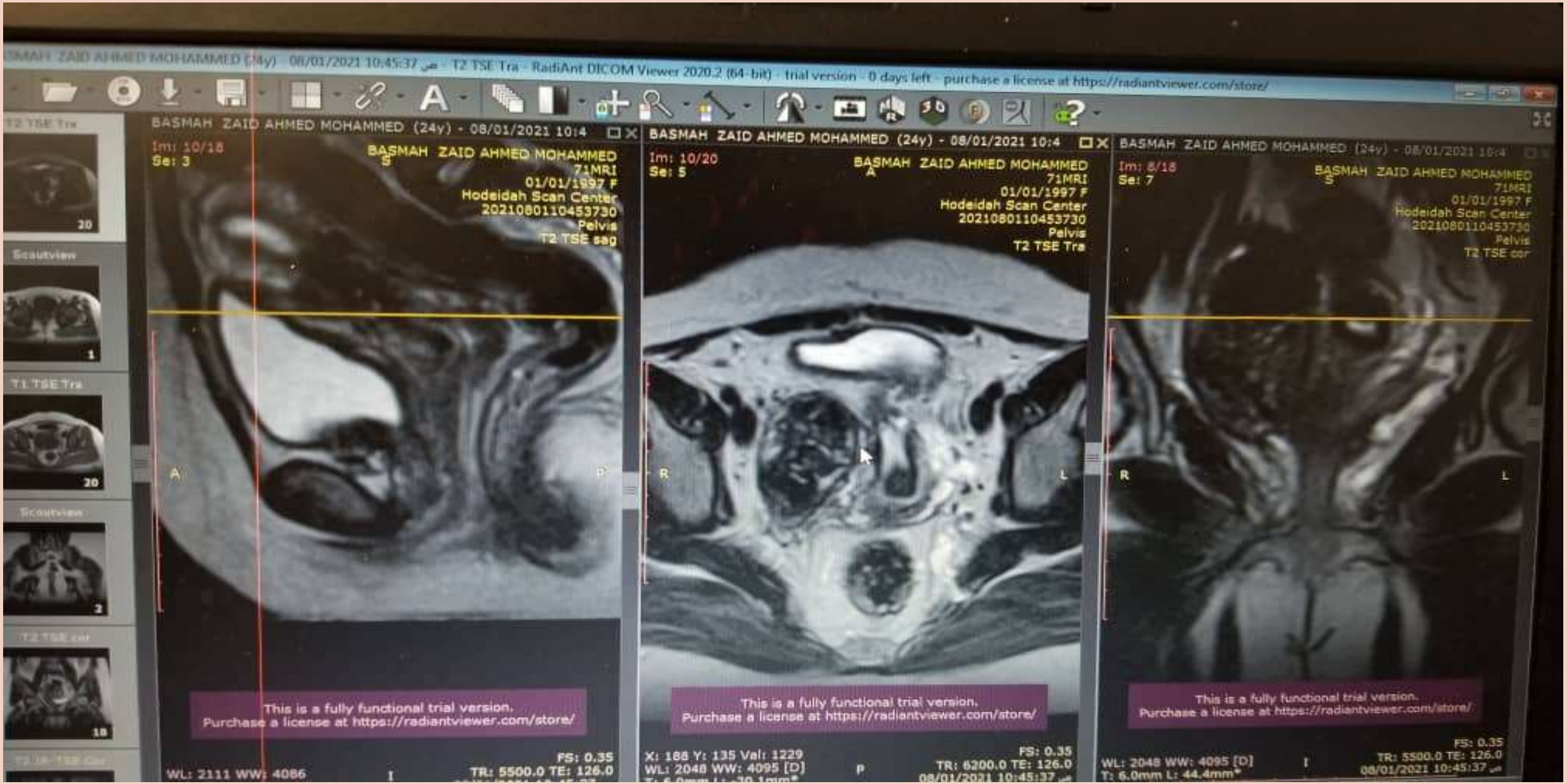
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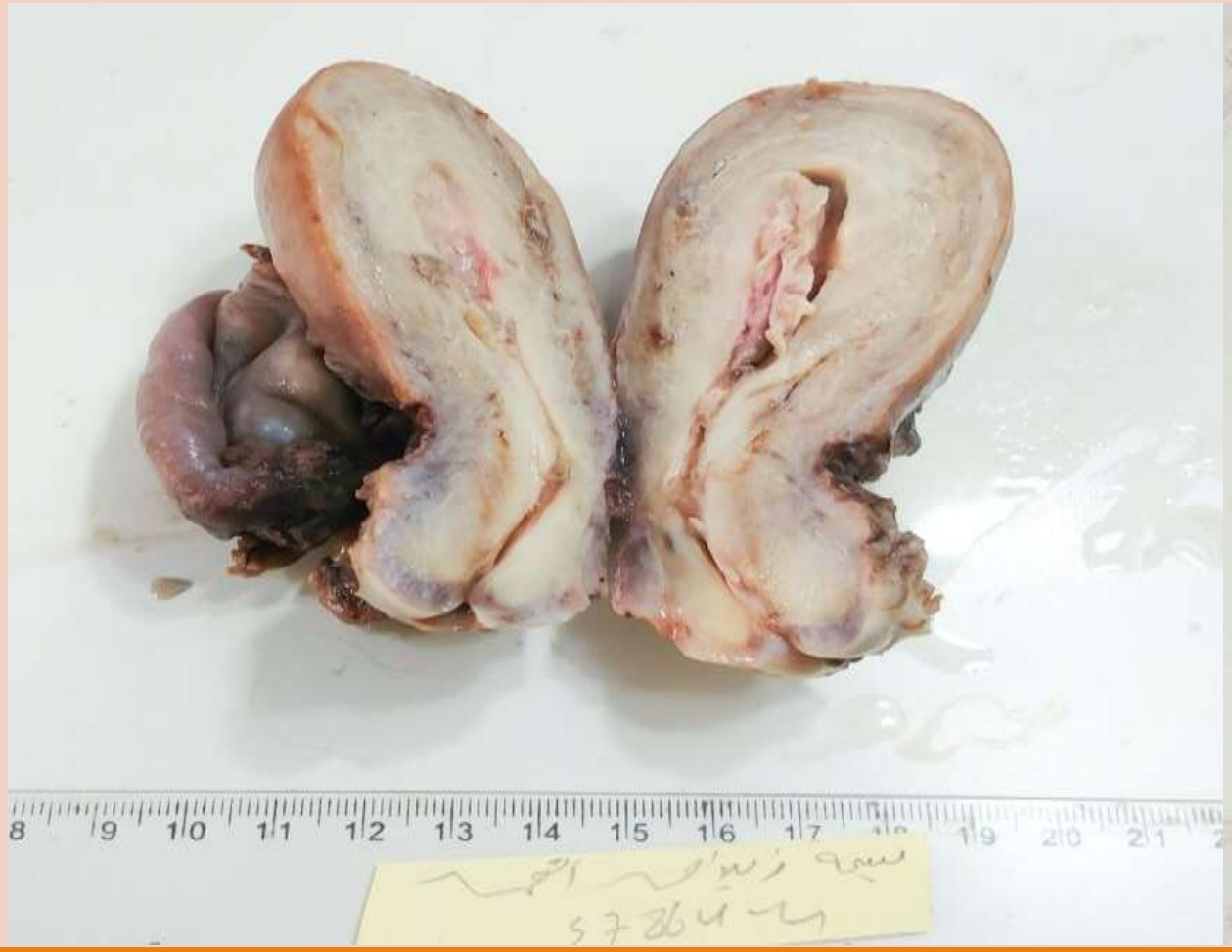

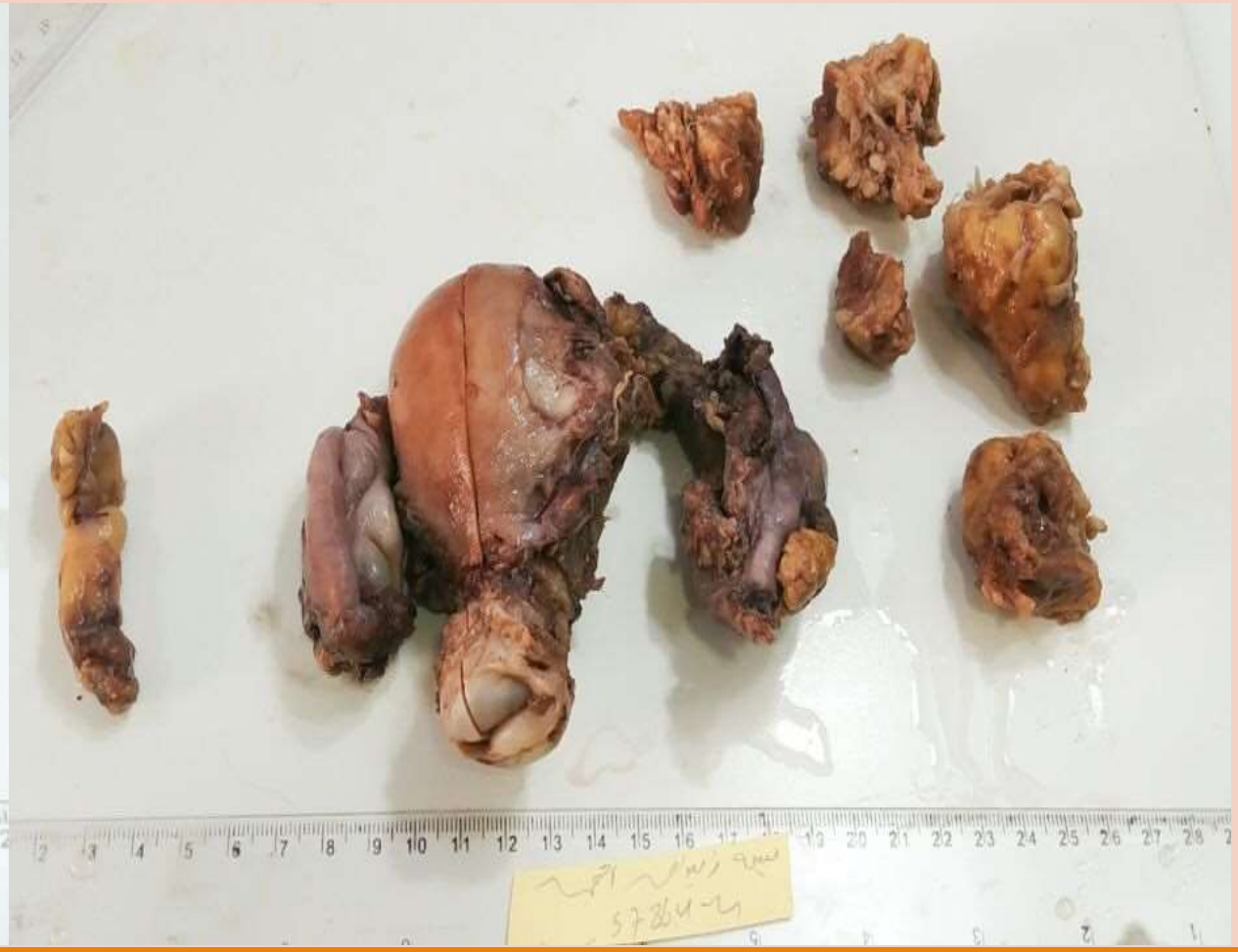

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PATHOLOGY REPORT

CLINICAL INFORMATION	Known case of choriocarcinoma - mostly? Post ectopic pregnancy received12 cycles chemotherapy.
NATURE OF SPECIMEN	T.A.H. + B.S.O. with fragmentation tissue mostly at parauterine area.

GROSS

Specimen received consists of uterus with adnexa. The uterus measures 10x4x4 cm [#A,B,C,D]. The endometriu is 0.8 cm thick. The myometrium is 2 cm thick. The right and left ovaries measure 3x2x1 cm and 4x2x1.5 c respectively. Cut sections of the right ovary are grayish [#R]. Cut sections of the left ovary show a cyst filled w mucus measuring 2x2x1.5 cm [#L1,L2]. The right and left fallopian tubes are 5.5 cm and 8 cm long, respective Multiple fragments measuring 10x8x3 cm in aggregate are also received; grayish brownish cut sections are se [#S1-S4]. An appendix [6 cm long] is also recieved; grayish cut sections are seen [#S5].

PHOTOGRAPHS

MICROSCOPIC

Sections examined from the uterus revealed endometrial lining showing multiple rounded and elongat endometrial glands lined by columnar secreting epithelial cells with elongated nuclei showing focal stratificatic with no atypia. The intervening stroma is formed of spindle cells. The cervix showed mild chro inflammation. The right ovary and tubes are unremarkable. The left ovary reveals corpus luteum. Separate piec showing totally necrotic tissue. No viable tumor tissue seen.

Sections from appendix showing obliteration of lumen by fibrous tissue and nerve tissue, accompanied by tota atrophic mucosa and submucosa with scattered lymphocytic cell infiltrate in muscle layers.

FINAL DIAGNOSIS

Uterus, tubes and ovaries with fragmentation tissue, T.A.H. with B.S.O. & fragmentation tissue at para-uteri area: Simple Endometrial Hyperplasia With Superadded Secretory Changes, Mild Cervicitis. Left Ovarian Corp Luteum. Fibrous Obliterated Appendix. **Totally Necrotic Separate Tissue, No Viable Tumor Tissue Seen.**

Thanks for referer

Postoperative(TAH&BSO) Follow UP

on 11/9/2021 :

BHCG 5.28 mIU/ml

CT for chest is normal

CT for pelvic there is about 23x 18 mm ovide vascular lesion in anterior inferior of pelvic .

On 16/10/2021 :

BHCG 12.4 mIU/ml

Conclusion

Although ectopic molar pregnancy is an uncommon event in clinical practice, it should be suspected in any case of extrauterine conception with continuous increasing of **BhCG** and chemotherapy should be given in spite of absence of histopathological diagnosis of invasive mole or choriocarcinoma .

Conclusion

Follow up should be done by **BhCG**, **US** and imaging for any metastasis by **CT** or **MRI**.

Team of Management And F.Up

Wide team of consultants who shared in management and f.up of this interest case.

Gynecologists: - Dr. Hanan Balobaid, Hodeida. -Dr. Salwa Alghomairy, Sanaa.

Medical Oncologists: -Dr. Abdullah Omeer, Hodeida. -Dr. Ahmed Shamalan, Sanaa.

- Dr.Soaad Alareky, Sanaa.

Surgical Oncologist: -Dr. Anter Alaffary, Sanaa.

Diagnostic Radiologists:-Dr. Fahad Suhail,Hodeida. -Dr.Wadah Almhabashy, Hodeida.

Histopathologist: -Dr. Wael Alabsy, Sanaa.

Allot Of Thanks For All

THANK YOU