Gyn Oncology revision

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1. Cervical neoplasms

Pap smear: screen patients > 21 years old every 3 years.
HPV test: screen patients >30 years old every 5 years.

- **Why > 30?** Because 80-90% of HPV infection in patients 20-30 y.o. clear spontaneously. Only 10-20% persist > progress > change DNA > tumor grow.
- Viral protein E6 suppresses tumor suppressor gene p53, while E7 suppress retinoblastoma gene.
- Infection takes 10-15 years to progress into cancer. Less time in immunocompromised.
- Patients who are +ve or already show dysplasia can still receive HPV vaccine, as it can protect them from other strains of HPV.

Pap smear results can be:

- **Normal**
- **Cancer:** Squamous cell carcinoma (70%) or Adenocarcinoma (20%). Main presenting complaint is poscoital bleeding.
- **Low grade neoplasia** (ASCUS[1] "most common" & LSL[2])
- **High grade neoplasia** (HSL[3] & AGC[4]) .

Preinvasive cervical neoplasms:

Low grade	High grade
Don't jump into LEEP or cone biopsy. **In case of ASCUS (most common), do HPV test:** • **+ve HPV >** proceed to colposcopy. • **-ve HPV >** routine follow up after 3 years. (50 % decrease need for colposcopy) If colposcopy shows a lesion you can take intralesional biopsy. If not, take a random biopsy.	**Cone biopsy (preferred):** • measuring diameter of the lesion. • if margins are -ve > patient is treated. No need for further therapy. **LEEP:** • laser burns the edges and thus doesn't give information regarding the margins.

Staging is clinical (not histopathological):

Stage	Characters	Management
1A1	Microinvasive. Width <7 mm. Depth 0-3 mm.	• **Cone biopsy with -ve margins.** • Or **simple hysterectomy.**
1A2	Microinvasive. Width <7 mm. Depth 3-5 mm.	**Radical hysterectomy + LN dissection.** Or **trachelectomy[5] + LN dissection** with the following: • Women who wish to preserve fertility. • Adenocarcinoma or squamous carcinoma only. • < 2cm lesion. • -ve LN biopsy • After pregnancy > cerclage > deliver by CS
1B1	Invasive > 5mm. < 4 cm.	
1B2	Invasive > 5mm. > 4 cm.	
2A1	Upper ⅔ vagina. < 4 cm.	
2A2	Upper ⅔ vagina. > 4 cm	
2B	+ve **margins** +ve **LN** +ve **Parametria**	>2B "To be or not to be" • **No role of surgery.** • **Chemoradiotherapy:** Low dose chemo for sensitization to radiotherapy. Radiotherapy can be used alone in patients who can't tolerate chemo (cisplatin) toxicity.
3A	Lower ⅓ vagina	
3B	Pelvic sidewall +/- hydronephrosis	
4A	Rectum / bladder	
4B	Distant metastasis	**Palliative therapy:** analgesics, antiemetics, etc…

[1] ASCUS: Atypical squamous cells of undetermined significance.
[2] LSIL: (Low-grade squamous intraepithelial lesion). CIN 1 (and CIN 2 in women > 25 y.o.)
[3] HSIL (high-grade squamous intraepithelial lesion). CIN 2,CIN 3, or CIS (carcinoma in situ)
[4] AGC: (atypical glandular cells)
[5] A **trachelectomy** is a surgical procedure used to treat eligible women with early stage **cervical** cancer who wish to preserve their fertility, by removing only the **cervix**, upper vagina and parametrium.

2. Ovarian cancer

1. **Benign ovarian lesions (not important):**

Most common in pregnancy is dermoid cyst. Other common lesions are serous/ mucinous cystadenoma. Surgical treatment is definitive.

2. Malignant ovarian lesions:

Non specific symptoms: abdominal distension, ascites, intestinal obstruction, paraneoplastic syndrome e.g. weight loss.

	Epithelial tumors (80%)	Germ-cell tumors	Sex-cord tumors
	> 50 y.o. Aggressive Present late at stage 3 or 4	young pts. Very aggressive	very young pt. May recur after 40 years > follow up for life
Types	**Serous cystadenocarcinoma** "Most common" Tumor marker: CA 125	**Dysgerminoma** Tumor marker: LDH	**Granulosa cell tumor** Tumor marker: inhibin & AMH secretes estrogen
	Mucinous cystadenocarcinoma Tumor marker: CA 199 and CEA	**Yolk sac (endodermal sinus)** Tumor marker: AFP	**Sertoli- Leydig cell tumor**
	Rare types: Clear cell / endometriod cancer	**Immature teratoma** Tumor marker: non specific, AFP	Very aggressive
Dx.	• **CT scan** may show Omental cake[6] or Peritoneal carcinomatosis. If these lesions are present you can take a biopsy. If not, don't take a biopsy from an ovarian lesion as it may spread. • **Cytology, Omental and peritoneal biopsy**		
Rx.	3 cycles of neoadjuvant chemo > interval **debulking (cytoreduction)**[7] > 3 cycles of adjuvant chemo **Or:** primary debulking > 6 cycles of adjuvant chemo	**Unilateral salpingo oophorectomy** Stage 2 and above = **+** chemotherapy [8] (3-4 cycles)	**Unilateral salpingo oophorectomy** Stage 1c and above = **+** chemotherapy **pt>40 = TAH-BSO**
	Debulking: Suboptimal > 2 cm left (useless!). Optimal < 2 cm left. Complete < 1 cm left. Radical = 0cm.		

3. Borderline tumors (non-invasive but can metastasise):

- Good prognosis (80-90%). But may recur as low grade malignant tumor.
- They don't respond to chemo nor radiation, the gold standard is surgical resection.

4. Metastatic ovarian cancer:

- Krukenberg tumors: most common is metastatic from the **stomach**.

5. Familial ovarian tumors:

- **BRCA1&2.** Risk of breast CA in both is 60-80%. Risk of ovarian CA in BRCA1=40%, BRCA2: 20%
- **Lynch syndrome** (cancer of colon 60-80%, ovaries 5-10%, endometrium 40%, bladder, ureter, biliary, brain)

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[6] **omental cake** is **abnormally thickened greater omentum** in radiology due to metastasis.
[7] Debulking (cytoreduction) = TAH-BSO + LN removal + omentectomy + any visible disease.
[8] BEP: bleomycin, etoposide and cisplatin (Platinol) or paclitaxel-carboplatin

3. Endometrial cancer

Risk of progression of hyperplasia (premalignant) to malignancy:

- **Simple hyperplasia** without atypia: 1% with atypia (x10): 10%
- **Complex hyperplasia** without atypia: 3% with atypia (x10): 30%

90% of patients present early (stage 1) due to AUB (abnormal uterine bleeding).
Perform endometrial biopsy for any patient with AUB whose age > 35 or with risk factors e.g obesity even if younger than 35.
Most common cause of AUB is genital atrophy.
Benign changes can be treated by prophylactic hysterectomy or high dose progesterone.
High dose progesterone for treating a patient with low grade endometriod endometrial cancer (80% response to treatment):

- **Conditions:** wish to preserve fertility, low parity, grade 1 endometroid endometrial cancer, no myometrial invasion, LN< 1 cm on MRI (MRI is used instead of surgical biopsy)
- **Follow up** in 3 months, if biopsy is -ve, refer to IVF. if still+ve, double the dose of progesterone and repeat the biopsy in 3 months. If she is still +ve, repeat MRI, if still showing no lymphadenopathy and no myometrial invasion, continue medical treatment for 3 more months. After 3 months (9 months from diagnosis), if still +ve, medical therapy failed and patient has to undergo complete surgical staging.

	Type 1 cancer	Type 2 endometrial cancer
Risk factors	DM, HTN, PCOS, nulliparity, infertility, obesity [9], younger pt.	No specific risk factors! (not related to hyperestrogenism) Postmenopausal patients
Histopathology	Low grade endometriod cancer	• High grade endometriod cancer • Papillary / Clear cell carcinoma
Management	**TAH-BSO** + pelvic LN excision	**TAH-BSO** + pelvic and para-aortic LN excision + omentectomy

Staging is surgical (histopathological after surgical biopsy):

Stage	Characters	Management
1A	Endometrial invasion < 50%	**TAH-BSO** No need for neoadjuvant chemo or vaginal brachytherapy[10].
1B	Endometrial invasion > 50%	TAH-BSO **+ vaginal brachytherapy**
2	Extension to the cervix	**Radical** hysterectomy + BSO + pelvic lymphadenectomy Or Pelvic radiation followed by simple hysterectomy (both options are valid) Staging + **+ chemotherapy (6 cycles)** + radiotherapy
3A	Invasion of ovaries, tubes, or serosa.	
3B	Invasion of parametrium or vagina.	
3C1	Pelvic LN	
3C2	Para-aortic LN	
4A	Bladder / rectum	
4B	Distant metastasis.	**Palliative therapy:** chemotherapy or supportive care

[9] due to increased aromatization to estrogen and decrease protein binding > increase free estrogen
[10] **Brachytherapy** is a form of radiotherapy where a sealed radiation source is placed inside or next to the area requiring treatment.

4. Gestational Trophoblastic Disease

GTD:

Complete mole	Incomplete mole
Fertilization of **EMPTY ovum** with 2 sperms or 1 sperm that will divide later on	Fertilization of **normal ovum** with 2 sperms or 1 sperm that will divide later on
No fetal components	**fetal components present**
5-15% risk of malignancy	<1% risk of malignancy
Most common genetic 46 XX - followed by 46 XY	**Most common genetic 69 XXY - followed by 69 XXX**

Presentation: Large uterus, vaginal bleeding, hyperemesis gravidarum, thyrotoxicosis.
Diagnosis:

- **Quantitative bHCG:** extremely high bHCG levels (can reach up to million)
- **US:** snowstorm appearance (COMPLETE MOLE), hydropic villi, theca lutein ovarian cysts (no need to treat them, they regress after resolution of GTD)
- Patient should be followed weekly with bhcg until 3 consecutive -ve results then monthly for 6 months.
- **Recurrence:** 1% after 1 molar, 23% after 2 molar pregnancies

GTN:

- Bhcg is not dropping as expected, plateauing or rebounding, or
- if still +ve after 6 months from the time of evacuation, or
- if histopathology after the evacuation of molar pregnancy came +ve for choriocarcinoma.

1. **Invasive mole**
2. **Choriocarcinoma**
   Both responds to chemo 95% with an excellent prognosis.
3. **Placental site trophoblastic tumours (PSTTs):**

- After miscarriage or normal pregnancy (not after molar).
- bHCG is high (usually in few thousands), but not as high as molar (100 thousands up to a million)
- Human placental lactogen (HPL) is elevated .
- US: highly vascular lesion.
- Biopsy (D&C), sometimes -ve (difficult diagnosis)
- Locally invasive, doesn't metastasize. Resistant to chemo and radiotherapy.
  - **Rx. :** hysterectomy or wedge resection to preserve fertility if low or no parity.

Bhcg, CXR, CT BRAIN, ABDOMEN, USS PELVIS ARE USED TO DEFINE THE SCORE AND THE STAGE.

WHO PROGNOSTIC SCORING

SCORES	0	1	2	4
AGE IN YRS	<40	>40	-	-
ANTECEDENT PREGNANCY	H.MOLE	ABORTION	TERM	-
INTERVAL SINCE LAST PREGNANCY	<4 MONTHS	4-6	7-12	>12
BHCG	<1000	10^3-10^4	10^4-10^5	>10^5
LARGE SIZE TUMOR	3-4	5	-	-
SITE OF METATSTASIS		SPLEEN,KIDNEY	GI	LIVER, BRAIN
NUMBER OF METASTASIS		1-4	5-8	>8
PREVIOUS FAILED CHEMO			SINGLE DRUG	TWO OR MORE DRUG

Adapted from FIGO
Low risk score <6 ,High risk score >7

FIGO Anatomic Staging Of GTN

Stage I	**Disease confined to the uterus**
Stage II	**GTN extends outside of the uterus but is limited to the genital structures (adnexa, vagina, broad ligament)**
Stage III	**GTN extends to the lungs, with or without known genital tract involvement**
Stage IV	**All other metastatic sites (brain, liver)**

Management:

GTD	GTN	
Complete & incomplete	**Low score (<7)**	**High score (7-12)**
Suction evacuation (+gentle curettage to avoid perforation)	**Single agent chemo:** MTX or Actinomycin D	**Multiple agents chemo:** EMACO[11]
Follow up every week until 3 -ve bhCG, then every month for 6 months.	Follow up for 1 year (Patient should be followed weekly with bhcg until 3 consecutive -ve results then monthly for 12 months).	Follow up for 2 years (Patient should be followed weekly with bhcg until 3 consecutive -ve results then monthly for 24 months).
Hormonal Contraception for 6 months. IUD is allowed when bhcg is zero.	Hormonal Contraception for 1 year. IUD is allowed when bhcg is zero.	Hormonal Contraception for 2 years. IUD is allowed when bhcg is zero.

بالتوفيق يارب <3
- لولوه الصغيّر

[11] EMACO (etoposide, methotrexate, actinomycin D, cyclophosphamide, Oncovin/vincristine)