


Endometrial Cancer

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MSU SCS Board Review Course

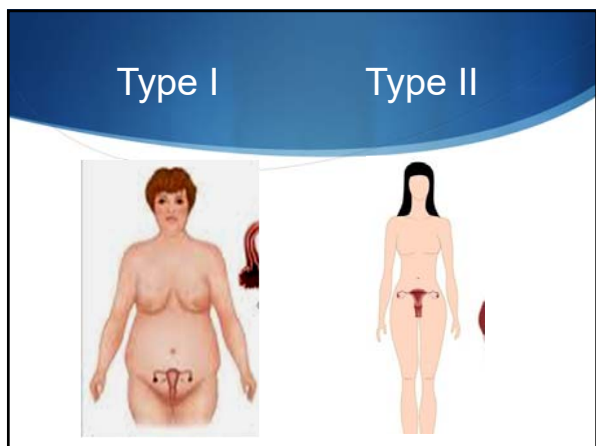


Incidence

- ◆ 53,630 new cases yearly
- ◆ 8,590 deaths yearly
- ◆ 4th most common malignancy in women worldwide
- ◆ Most common GYN malignancy in US
 - ◆ 50% of new GYN cancer diagnosis yearly
- ◆ Most patients present with early stage (curable) disease

Types

- Type I (Most common – 85%)
 - Endometrioid
 - Estrogen-related type
 - Younger patient
 - Typically well differentiated and minimal myometrial invasion (Favorable outcome)
 - Associated with mutations in PTEN and microsatellite instability
- Type II
 - Non-endometrioid
 - Clear cell, Pap serous, Serous
 - Non-estrogen related
 - Older patients
 - Associated with mutations in p53



Screening for asymptomatic patient

- ◆ Postmenopausal patient on exogenous estrogen without progestin
- ◆ Patient from family with lynch syndrome
- ◆ Premenopausal patient with anovulatory cycles (PCOS)

- ◆ EMB or D and C is acceptable

Patient Symptoms

- ◆ Abnormal uterine bleeding
 - ◆ Postmenopausal
 - ◆ Intermenstrual bleeding
 - ◆ Heavy prolonged bleeding
- ◆ Hematometra / pyometra
- ◆ Pelvic pain / pressure, abdominal distention
 - ◆ Advanced disease

Risk Factors

1. Age
 - ◆ ~85% of cases occur in patients >50 y/o (Average 61)
2. Race
 - ◆ Highest in North America, Northern Europe
 - ◆ Lowest in Eastern Europe, Asia, Africa, Latin America
 - ◆ Has to do with obesity rates
3. Nulliparity
 - ◆ Early menarche, late menopause, chronic anovulation

Risk Factors

4. Hereditary (2-5%)
 - Lynch Syndrome (Hereditary Non-polyposis colorectal cancer (HNPCC)
 - Autosomal-dominant cancer with early onset colon, rectal, ovary, small bowel, ureter / renal pelvis, Endometrial Cancer
 - Lifetime risk of EC 40-60%
 - Lifetime risk of ovarian CA 10-12%
5. Endogenous / Exogenous Estrogen
6. Obesity

Obesity and EC

- ◆ Plasma concentrations of androstenedione and estrogens are correlated with body weight in postmenopausal women
- ◆ Aromatization of androstenedione to estrone in adipose cells is believed to be primary mechanism for excess estrogen production
- ◆ Most data says that obesity linked more to type 1 tumors, but some studies show that there is a risk of more high-grade aggressive tumors with obesity

Patients who need EC workup

- ◆ Patient with postmenopausal bleeding
- ◆ Postmenopausal women with pyometra
- ◆ Postmenopausal women with endometrial cells on PAP smear (Esp. if atypical)
 - ◆ PAP with adenocarcinoma in situ, Atypical glandular cells of undetermined significance (AGUS)

Patients who need EC workup

- ◆ Perimenopausal women with intermenstrual bleeding or increasingly heavy periods
- ◆ Premenopausal women with AUB (Esp. if history of anovulation)


EXAM

- ◆ Pelvic
 - ◆ Vulva, Vagina and Cervix
 - ◆ Exclude metastatic spread of other disease site
 - ◆ Uterus
 - ◆ Bulky at times
 - ◆ Recto-vaginal exam
 - ◆ Evaluate ovaries, fallopian tubes, cul-de-sac
 - ◆ May find ovarian tumors or metastatic endometrial cancer to these sites.

Exam

- ◆ Abdominal
 - ◆ Ascites
 - ◆ Omental masses
 - ◆ Otherwise normal

Diagnosis



- ◆ Endocervical curettage and EMB
 - ◆ EMB pipelle has detection rate of 91-99%
- ◆ Negative biopsy in a symptomatic patient warrants further workup with Dilatation & Curettage
 - ◆ Hysteroscopy at time of D&C to rule out polyps or other tumors in endometrial cavity
 - ◆ No prospective studies have been performed and it is uncertain what effect positive cytology washing caused by hysteroscopy has on overall prognosis (pelvic washings removed from FIGO staging)

Ultrasound

- ◆ Less invasive tool to examine AUB
- ◆ Endometrial Thickness < 4 mm can be considered negative for EC
 - ◆ But if continues to bleed then need to sample endometrial cavity
- ◆ Endometrial thickness > 4 mm
 - ◆ Endometrial Biopsy
 - ◆ D&C Hysteroscopy
 - ◆ Saline infusion Sonohysteroscopy

Pre-Op Evaluation for staging surgery

- ◆ CBC
- ◆ Creatinine and Electrolytes
- ◆ Liver Function Tests
- ◆ UA
- ◆ CT scan with contrast
 - ◆ Chest / Abdomen / Pelvis
 - ◆ To rule out metastatic disease

CT or MRI Needed

- ◆ MRI with Gadolinium
 - ◆ Useful to determine depth of myometrial invasion
 - ◆ Little usefulness in examining metastatic disease
- ◆ CT scan with contrast
 - ◆ Useful to determine metastatic disease
 - ◆ Especially if you have: Abnormal liver function tests, Hepatomegaly, Upper abdominal mass, extrauterine disease on exam, Ascites, High-risk histology

Treatment

- ◆ Surgery
 - ◆ For anyone who can tolerate surgery
- ◆ Radiation therapy
 - ◆ Patients with significant medical comorbidities who cannot tolerate surgery
 - ◆ Severe cardio-pulmonary disease, Advanced Age, Decreased Performance status
 - ◆ Used to control vaginal bleeding
- ◆ Chemotherapy
 - ◆ If advanced disease and not a surgical candidate as above

Surgery

- ◆ Hysterectomy with bilateral salpingoophorectomy, pelvic lymphadenectomy ± para-aortic lymphadenectomy is procedure of choice
- ◆ Omentectomy only if high-risk histology or advanced disease
- ◆ LAVH, Total laparoscopic hysterectomy, Abdominal hysterectomy, Robotic Hysterectomy

FIGO Staging

- ◆ IA - < 50% myometrial invasion
- ◆ IB - ≥ 50% myometrial invasion
- ◆ II – Invades cervical stroma
- ◆ IIIA – Serosa of uterus or Adnexa
- ◆ IIIB – Vaginal / Parametrial involvement
- ◆ IIIC1 – Positive Pelvic LN's
- ◆ IIIC2 – Positive Para-aortic LN's
- ◆ IVA – Bladder / Bowel Mucosa
- ◆ IVB – Distant Mets (Intra-abdominal / Inguinal LN's)

Stage I

Stage IA Endometrial Cancer

<50 % Myometrial Invasion

Stage IB Endometrial Cancer

≥50% Myometrial Invasion

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Stage IIIC

Stage IIIC Endometrial Cancer

Aorta
Cancer in lymph nodes
Myometrium
Endometrium
Uterus
Cancer in lymph nodes

IIIC1 – Pelvic LN
IIIC2 - Para-aortic LN

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Stage IVA

Stage IVA Endometrial Cancer

Small intestine
Large intestine (part of the bowel)
Cancer
Cervix
Bladder
Uterus
Endometrium

Bladder or Bowel Mucosa Involvement

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Stage IVB

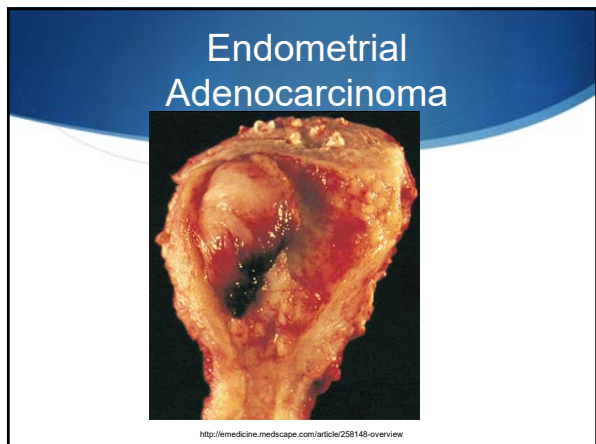
Stage IVB Endometrial Cancer

Endometrial cancer has spread to parts of the body beyond the pelvis.

Cancer
Blood
Lymph nodes
To other parts of the body
Cancer in endometrium
Abdomen
Pelvis
Lymph nodes

Distant Mets (Intra-abdominal / Inguinal LN)

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Post surgical Treatment?

- ◆ Stage IA and IB (low risk of recurrence)
 - ◆ Can monitor postop with pelvic exams q3-4 months
- ◆ Stage IB and stage II (intermediate risk)
 - ◆ Brachytherapy and possible pelvic RT
- ◆ Stage III / IV (high risk)
 - ◆ Chemotherapy + RT or only chemotherapy

Patterns of EC spread

- ◆ Direct Extension
 - ◆ Most common
 - ◆ Penetration of myometrium and progresses to serosa
- ◆ Fundal tumors
 - ◆ Will involve the adnexa before the cervix
- ◆ Low uterine segment tumors
 - ◆ Involve the cervix before the adnexa

Pattern of Spread Continued

- ◆ Transtubal dissemination
 - ◆ Retrograde flow along fallopian tubes
- ◆ Lymphatic dissemination
 - ◆ To pelvic (External iliac / Obturator LN's) and para-aortic LN's
- ◆ Hematogenous Spread
 - ◆ Lung mets most common
 - ◆ Other sites – Liver, Brain, Bone

Histology

- ◆ Endometrioid Adenocarcinoma
 - ◆ Most common 75-80% of cases
- ◆ Mucinous Carcinoma
 - ◆ 1-9% of cases
- ◆ Serous Carcinoma
 - ◆ ~10% of cases, older woman and advanced disease
- ◆ Clear cell Carcinoma
 - ◆ 4% of EC
- ◆ Squamous Carcinoma
 - ◆ <1% of EC
 - ◆ Diagnosed after primary cervical cancer is ruled out

Prognostic Factors

- Histologic type
 - Endometrioid type better prognosis
 - Clear cell / Pap Serous / Serous – worse prognosis
- Histologic grade
 - Grade 1 better
 - Grade 2 and 3 worse
- Myometrial invasion
 - Less invasion the better
- Vascular space invasion
 - No tumor found in vascular spaces is best
- Tumor size
 - Smaller tumor better

Radiation therapy

- ◆ Brachytherapy
 - ◆ Radiation to the vaginal cuff and 1/2 to 2/3 of vagina
- ◆ External Beam Pelvic RT
 - ◆ To treat pelvic lymph node areas up to obturator and external iliac chains
 - ◆ Treat to 45-50 Gy

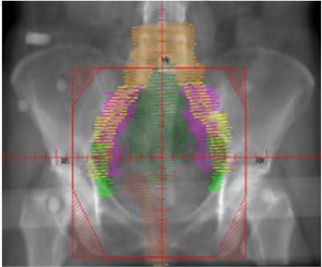
Internal radiation devices or brachytherapy

Labels in diagrams: Tandem, Ovoid, Uterus, Cervix, Vagina, cylinder, radioactive wire, bladder, tube, vagina, rectum.

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External Beam Radiation therapy



Chemotherapy

- ◆ Typical first line chemotherapy is carboplatin / paclitaxel
- ◆ In stage III disease chemotherapy is often given in a “sandwich” type fashion
 - ◆ 3 cycles of chemotherapy then pelvic radiation therapy then 3 more cycles of chemotherapy

5- year Survival

- ◆ Stage I
 - ◆ 90-92%
- ◆ Stage II
 - ◆ 80-88%
- ◆ Stage III
 - ◆ 66-74%
- ◆ Stage IV
 - ◆ 30-35%

Special Circumstances

- ◆ Endometrial cancer diagnosed after hysterectomy
 - ◆ CT scan of chest, abdomen, pelvis or PET scan to rule out mets
- ◆ If no mets and early Grade tumor 1 or 2 with <50% myometrial invasion then can observe as low risk
- ◆ If mets then surgery to perform staging and remove mets
- ◆ If ovaries remain then surgery to remove ovaries and can do lymphadenectomy at same time depending on risk factors

Special Circumstances Young Women

- ◆ Fertility sparing indicators
 - ◆ Grade 1 (well-differentiated) endometrioid adenocarcinoma
 - ◆ No or minimal myometrial invasion
- ◆ MRI of the pelvis to examine for myometrial invasion
- ◆ Treatment
 - ◆ Megestrol acetate 160 mg – 320 mg /day
 - ◆ MPA 200 – 500 mg /day
- ◆ Repeat Dilatation and curettage in 3 months
- ◆ If disease regresses then start on OCP or continue a progesterone therapy

Follow-up Exams

- ◆ Pelvic exams
 - ◆ q 3-4 months for first 2 years
 - ◆ q 6 months for next 2 years
 - ◆ Then yearly
- ◆ Biopsy any abnormal lesion seen or palpated on exam

Recurrence

- ◆ Low risk Stage I disease most common recurrence will be at the vaginal cuff
- ◆ High risk stage I without lymphadenectomy
 - ◆ Pelvic sidewall and distant site recurrence
- ◆ Node positive disease (Stage III)
 - ◆ Distant site failures
- ◆ Stage IV
 - ◆ Peritoneal cavity recurrences

Recurrence

- ◆ Vaginal cuff recurrence treat with radiation therapy
- ◆ Distant mets in the abdomen, lung, etc
 - ◆ Treat with chemotherapy
 - ◆ Commonly Carboplatin / paclitaxel

Pearls of Endometrial Cancer

- ◆ Most commonly due to unopposed estrogen
 - ◆ Estrogen-replacement therapy, obesity, anovulatory cycle, estrogen-secreting tumors
- ◆ Common symptom is postmenopausal bleeding or intermenstrual bleeding, heavy prolonged perimenopausal bleeding
- ◆ Diagnosed by EMB or D and C
- ◆ Surgically staged disease
- ◆ Spread
 - ◆ Direct, transtubal, lymphatic, hematogenous
- ◆ Common path is Endometrioid adenocarcinoma
- ◆ HIGH risk Path – clear cell, Pap-serous, Serous

Other Pearls of EC

- ◆ Young women with grade 1 tumor and no myometrial invasion then can try progesterone therapy to get disease to regress
- ◆ Recurrent disease
 - ◆ Locally to the vaginal cuff then treat with pelvic and cuff RT
 - ◆ Distant disease then systemic chemotherapy
- ◆ High risk path (clear cell, pap serous, serous)
 - ◆ Most often will be treated with systemic chemotherapy after surgery no matter the disease stage
