Introduction to Gynecologic Cancer

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Endometrial Cancer

The most common gyn cancer
• 37,400 new cases in 1999
• 6,400 deaths
• Five year survival rates: 95% if Stage I
  – 26% if Stage III/IV
• Up to 25% of patients have Stage III/IV disease at diagnosis and account for 54% of the deaths

Endometrial Cancer

Presentation
• PMB is most common
• Endometrial cells on pap smear
• 30% have multiple sxs, including increasing abdominal girth and abdominal pain
• ROS should include questions about bowel and bladder function, early satiety, pain, and bloating

Endometrial Cancer

Type I versus Type II phenotype
• Younger, obese, comorbidities of HTN and DM-- usually early stage, low grade endometrioid tumors
• Older, thin, no comorbidities, African-American-- usually deep myometrial invasion, high grade, high risk histology, advanced stage

Endometrial Cancer

Risk Factors
• older age
• caucasian
• infertility
• exogenous unopposed estrogen
• obesity

Endometrial Cancer

Histologic Subtypes
• Endometrioid
• Mucinous
• Squamous
• Papillary Serous
• Clear Cell
Endometrial Cancer
Patterns of spread
- most commonly via lymphatics to pelvic and para-aortic nodes
- via direct extension into the cervix
- transperitoneally via fallopian tubes
- hematogenously to lung (rare)

Endometrial Cancer
Physical Examination
- Supraclavicular and inguinal nodal regions
- Ascites and hepatosplenomegaly
- Gross cervical or vaginal involvement
- Parametrial spread
- Rectal involvement

Endometrial Cancer
Preoperative Testing
- Chest x-ray (regardless of age)
- Mammogram
- Electrolytes, CBC
- CA-125
  - correlates with depth of invasion, nodal spread, extra-uterine disease, and survival
- Other tests at the discretion of the surgeon

Endometrial Cancer
Staging
- Staging is surgical
- Stage I: confined to the uterus
- Stage II: spread to the cervix
- Stage III: spread to nodes, pelvic structures, or positive peritoneal cytology
- Stage IV: upper abdominal or distant disease

Endometrial Cancer
Prognostic Factors
- Tumor grade, depth of invasion, cx extension
- cell type
- pelvic/para-aortic nodes
- lymph vascular space invasion
- adnexal spread, positive cytology, extrauterine disease

Endometrial Cancer
Surgery
- Crucial diagnostic and therapeutic modality
- Staging includes washings, exploration, TAH/BSO, pelvic and para-aortic lymphadenectomy when indicated
- High-risk histologies (clear cell and UPSC) mandate inclusion of omentectomy and peritoneal biopsies
Endometrial Cancer

Management
• Surgery: the primary treatment modality and is the standard of care
• Radiation: primary treatment modality in extremely medically compromised patients BUT cure rates are lower
• Radiation in the adjuvant setting can be curative even in advanced stage disease

Summary
• Usually diagnosed early stage due to recognizable symptom
• Surgery is diagnostic and therapeutic
• Radiation is the mainstay of adjuvant treatment
• Chemotherapy and hormonal therapy are important in advanced stage and recurrent disease

Ovarian Cancer

Overview
• Second in incidence but first in mortality
• Vague presenting symptoms
• Majority of women (70%) have advanced stage disease at diagnosis
• Treatment involves both surgery and chemotherapy

Presentation
• Dyspepsia and early satiety
• Increasing abdominal girth and bloating
• Change in bowel or bladder habits, eg, constipation or frequency
• Pain is an infrequent symptom

Epidemiology
• Risk increased: Nulliparity, infertility, FHx, PMHx breast cancer, early menarche, late menopause
• Risk decreased: OCP use, Multiparity
• Familial cases account for 5-10% – Genes implicated: BrCA1, BrCA2, mismatch repair genes
Patterns of spread
- most commonly via transperitoneal shedding of cells -> ascites -> pleural effusion
- via lymphatics to pelvic/para-aortic nodes
- direct extension to involve contiguous pelvic structures
- hematogenously to liver/lung/spleen parenchyma

Physical Examination
- Supraclavicular, axillary, and inguinal nodes
- Decreased breath sounds and dullness to percussion -> pleural effusion
- Omental cake
- Ascites and hepatosplenomegaly
- Pelvic mass

Preoperative Testing
- Chest x-ray (regardless of age)
- Mammogram
- Electrolytes, CBC
- CA-125
  - If elevated at diagnosis, changes reflect activity of disease
- CT scan abdomen/pelvis

Staging
- Staging is surgical
- Stage I: confined to the ovaries
- Stage II: spread to pelvic structures
- Stage III: spread to nodes or upper abdomen
- Stage IV: liver/spleen parenchymal mets or pleural disease

Histologic subtypes
- endometrioid
- mucinous
- papillary serous
- clear cell
- transitional cell
- Brenner

Survival
- Stage I: 90%
- Stage II: 65%
- Stage III: 35%
- Stage IV: 10-15%
- Overall: 50%
Prognostic factors
- Age
- Stage
- Tumor grade
- Amount of residual disease at completion of surgery

Surgery
- Diagnostic: Up to 35% of patients with clinical stage I disease have microscopic advanced stage disease
- Therapeutic: Removing masses > 1cm leads to improved survival statistics
- Therapeutic: Improve symptomatology by removing omental cake and ascites

Surgery
- Staging includes washings, exploration, USO, pelvic and para-aortic lymphadenectomy, omentectomy, peritoneal biopsies
- Debulking or cytoreduction refers to removing all gross tumor > 1 cm

Chemotherapy
- Only Stage Ia/b grade 1/2 patients do not receive chemotherapy
- Current standard of care is 6 cycles of taxol and carboplatinum
- Other active drugs include doxil, topotecan, gemcitabine, taxotere, HMM, VP-16, ifosfamide, and 5-FU

Surgery vs Neoadjuvant chemotherapy
- The problem of Meig’s syndrome
- Paracentesis vs Thoracentesis

Chemotherapy
- Initial response rates are 75-80%
- Unfortunately, the majority of advanced stage patients will develop recurrence
- Retreatment drugs depend upon the disease free interval
- Median survival for Stage III patients is 36 months
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<th>Ovarian Cancer</th>
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<tr>
<td><strong>Summary</strong></td>
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<tr>
<td>• Usually diagnosed late stage due to lack of recognizable symptoms</td>
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<td>• Surgery is diagnostic and therapeutic</td>
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<tr>
<td>• Chemotherapy in addition to surgery is required for the majority of patients</td>
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<td>• Ca-125 can be used to follow disease activity</td>
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<th>Cervical Cancer</th>
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<tr>
<td><strong>Epidemiology</strong></td>
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<td>• 13,700 new cases in the U.S.</td>
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<td>• 4,900 deaths in the U.S.</td>
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<td>• 400,000 cases annually worldwide</td>
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<td>• A big problem in developing nations</td>
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<tr>
<th>Cervical Cancer</th>
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<td><strong>The Sad Facts</strong></td>
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<tr>
<td>• 50% of women with newly diagnosed cervical cancer in the U.S. have never had a Pap smear</td>
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<td>• 10% have not had a smear within 5 years of diagnosis</td>
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<td><strong>Risk Factors</strong></td>
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<tr>
<td>• Lower socioeconomic status</td>
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<td>• First coitus at young age</td>
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<td>• Multiple (&gt; 5) sexual partners</td>
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<td>• Large number of pregnancies</td>
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<tr>
<td>• Smokers</td>
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<td>• Immunosuppression</td>
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<td><strong>Presentation</strong></td>
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<tr>
<td>• post-coital spotting</td>
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<td>• abnormal uterine bleeding</td>
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<td>• abnormal vaginal discharge</td>
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<tr>
<td>• pain</td>
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<td>• bowel/bladder symptoms (hematuria, rectal bleeding)</td>
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<td>• constitutional symptoms (weight loss, fatigue)</td>
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<td><strong>Staging</strong></td>
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<tr>
<td>• Based on clinical criteria, not surgical</td>
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<td>• Stage I: confined to the cervix</td>
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<td>• Stage II: spread into the proximal vagina or parametria</td>
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<td>• Stage III: spread to lower vagina, pelvic sidewall, or ureteral obstruction</td>
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<td>• Stage IV: distant dz or mucosal involvement</td>
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Cervical Cancer

Patterns of spread
- locally via direct extension into the parametria, the vagina, or into the bladder or rectum
- via lymphatics into the pelvic and para-aortic nodes
- hematogenously to liver or lung (rare)

Cervical Cancer

Physical Examination
- Supraclavicular or inguinal adenopathy
- Pelvic examination
  - Tumor may be exophytic, ulcerative, or endophytic (barrel lesion)
  - Involvement of the vagina, supporting ligaments, bowel or bladder mucosa

Cervical Cancer

Diagnostic Evaluation
- Labs: CBC, Cr, LFTs, UA
- CXR
- IVP/BE vs. CT vs. MRI
  - CT scan is 97% specific, 25% sensitive

Cervical Cancer

Histologic Subtypes
- Squamous
- Adeno
- Adenosquamous
- Small Cell
- Melanoma

Cervical Cancer

Epidemiological Prognostic Factors
- younger age
- African American race
- low socioeconomic status
- anemia
- HIV +

Cervical Cancer

Pathologic Prognostic Factors
- tumor size
- endometrial extension
- lymph node involvement
Cervical Cancer

**Survival**
- Stage I: 80-90%
- Stage II: 70-80%
- Stage III: 35-45%
- Stage IV: 15%

**Treatment**
- Stage I and IIa: surgery or chemoradiation
- Stage IIb-IVa: chemoradiation
- Stage IVb: chemoradiation or clinical trials or palliative care

**Surgery**
- Cone Biopsy: preservation of fertility
- Simple hyst: transect cervix at vagina (no margins around cervix)
- Modified radical hyst: remove medial half of cardinal and uterosacral ligaments
- Radical hyst: cardinal ligaments taken at pelvic sidewall

**Summary**
- Staging is clinical
- Pap smear screening is effective
- All patients treated with radiation should receive chemosensitization
- Patients not treatable with curative intent should be considered for clinical trials

Vulvar Cancer

**Epidemiology and Pathogenesis**
- Rare, only 4% of gyn malignancies
- Risk factors: genital warts, smoking, abnormal pap smear, chronic immunosuppression, and chronic vulvar inflammation/irritation
- Trend towards younger age in diagnosis

**Clinical Manifestations and Differential Dx**
- Visible lesion
- Most common symptom: pruritus (90%)
- Delay in diagnosis is common
  - Average of 6-12 months
- DDx includes: HPV, VIN, squamous hyperplasia, Paget’s, infection
Vulvar Cancer

Diagnostic Evaluation
- Biopsy +/- Colposcopy
- Co-morbidities
- Physical examination
  - Extension to adjacent structures, nodes
- CXR (regardless of age)

Patterns of Spread
- Local extension to urethra, anus, pubic symphysis
- Hematogenous spread to lungs, liver
- Lymphatic spread to inguinal then pelvic nodes

Staging
- Clinical versus surgical
- TNM staging correlates with FIGO
- Stage I and II: local disease, based on size
- Stage III and IV: Metastatic disease- ipsilateral versus contralateral nodes
- Stromal invasion > 1mm crucial

Histology/Pathology
- Squamous, inc. Verrucous
- Adenoid squamous
- Basal cell
- Transitional cell
- Adenocarcinoma (Bartholin’s glands)
- Paget’s
- Melanoma

Prognosis
- Factors: tumor size, depth of invasion, nodal spread, distant metastasis
- Most important: lymph node mets-- number, unilateral vs. bilateral, volume, and level
- Risk of local recurrence depends upon adequacy of resection margins

Survival for SCCA
- Stage I: 90%
- Stage II: 85%
- Stage III: 60%
- Stage IV: 15%
- NB: Groin recurrence is uniformly fatal
**Vulvar Cancer**

**Treatment**
- Surgery: considerable evolution since the 70s
  - Radical excision via single incision (Bassett or butterfly incision)
  - Triple incision technique
  - Radical local resection with unilateral nodes
- Multi-modality therapy
- Radiation

**Vulvar Cancer**

**Treatment**
- Adjuvant XRT for positive nodes or close margins:
  - improves local control and survival
  - field: groins and lower pelvis if > 1 node +
  - XRT is superior to surgery for + pelvic nodes
  - increased morbidity with XRT plus superficial and deep inguinofemoral lymphadenectomy

**Vulvar Cancer**

**New Directions**
- Sentinel node mapping- GOG study ongoing
- Chemo-XRT

**Vaginal Cancer**

**Epidemiology and Pathogenesis**
- Rare, 1-2 % of gyn malignancies
- 80-90% of vaginal malignancies are mets
  - cervix, endometrium, vulva
- Risk factors for SCCA: low socioeconomic status, Hx genital warts, vaginal irritation, Hx abnl Pap, early hyst
- Risk factors for clear cell: DES exposure

**Vaginal Cancer**

**Clinical Manifestations and Differential Dx**
- 52% involve the upper third
- 58% involve the posterior wall
- If involves cervix or vulva at presentation, that site takes precedence
- Presenting sx: 50-75% with vaginal bleeding
- Other sx: dysuria, pelvic pain

**Vaginal Cancer**

**Pathology**
- Squamous: 80-90%
- Melanoma: 2.8-5%
- Smooth muscle tumors
- Rhabdomyosarcoma: most common type in infants and children
- Other sarcomas
Vaginal Cancer

Prognosis
- Most significant factor: stage
- Nonepithelial tumors have a poor prognosis

Vaginal Cancer

Survival
- Stage I: 80-90%
- Stage II: 25-55%
- Stage III: 40%
- Stage IV: 15%
- Reports of improved survival with surgery plus XRT in stage I and IIb

Vaginal Cancer

Treatment
- Preferred therapy: XRT
  - excellent tumor control and good functional results
- Surgery in selected cases

Gynecologic Cancers

Summary
- In the US, endometrial is most common and ovarian most likely to be fatal
- Worldwide, cervical cancer is the largest problem
- Staging and treatment of most gyn malignancies is surgical

Gynecologic Cancers

Summary
- Combined modality therapy is more common than not
- A gynecologic oncologist is a specialist trained in the surgery, chemotherapy, radiation therapy, and terminal care of women with gynecologic cancers
  - Remember to refer these patients!