Gynecologic Oncology topics for the primary care provider
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Disclosures
- Educational speaker for Clovis Oncology

Objectives: Gynecologic Malignancies
- Have basic familiarity with the types of gynecologic cancers
- Be able to describe symptoms of gynecologic cancers
- Review screening and prevention of gynecologic cancers
- Approach to diagnosis of these cancers

Types of gynecologic malignancies
- Uterine
- Ovarian
- Cervical
- Vulvar
- Uncommon types

Uterine malignancies
- Sarcomas
- Endometrial cancers

Uterine Sarcoma
- Rare (3-7/100,000) in USA and generally aggressive cancer
- Symptoms same as fibroids/leiomyomata
  - Bleeding, mass, pelvic pain, pressure
- No screening/prevention
- Risk factors
  - Pelvic irradiation, a history of childhood retinoblastoma, and hereditary leiomyomatosis and renal cell carcinoma syndrome
  - Tamoxifen (very small)
- Treatment
  - Surgery +/- chemo
Uterine Sarcoma: Diagnosis

- Tissue
- Clinical suspicion: refer to specialist

Examples of leiomyosarcoma (LMS)

- 60 yo woman presented to UTC with complaints of abdominal pain. Mass was palpated and she presented to ER. HGB 7.4, PLT 55k
- Patient underwent surgery and LMS was diagnosed
- She underwent chemotherapy and subsequent resection for residual disease

Examples of LMS

- 41 yo was diagnosed with pelvic masses (3.5 and 2.6 cm) after TLH for fibroid uterus with morcellation at vagina. Pathology was remarkable for benign leiomyoma with bizarre nuclei (not enough to merit LMS diagnosis). She was offered surgery 5/2018 and was lost to follow up. She represented 11/2018 and was noted to have a palpable mass. Surgery was complicated and revealed LMS.

Uterine Sarcoma: Dr. Amy Reed

F.D.A. Dissuages Procedure in Uterine Surgery

- Doctors should stop using a procedure performed on tens of thousands of American women a year in the course of uterine surgery, because it poses a risk of spreading cancerous tissue. The food and Drug Administration said Thursday.

The procedure, power morcellation, involves using a device to cut tissue into pieces that can be pulled out through the tiny incision made during minimally invasive surgery. The devices, known as morcellators, have been widely used in laparoscopic operations to remove fibroid tumors from the uterus, or to remove the entire uterus.

Endometrial cancer

- Endometrium
Endometrial Cancer

Symptoms include:
- Post menopausal bleeding (not a UTI!)
- Irregular bleeding, heavy cycles
- Risk factors (to prevent cancer, mitigate risk factors)
  - Unopposed estrogen, Tamoxifen
  - Anovulatory cycles (PCOS)
  - Obesity
  - HTN, DM, etc.
  - Lynch syndrome
  - The only time screening is considered is with increased risk
  - Consider screening with biopsies

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Endometrial Cancer: Can it be prevented?
- Risk reduction surgery, screening: Lynch
- Kentucky obesity stats as of 2017
  - 34.3% obesity population
  - 35.2% of all women are obese
  - 20.2% of all HS students

Endometrial Cancer: Diagnosis and subtypes
- Diagnosis
  - Thickened endometrial stripe on TVUS (>5mm in postmenopausal women)
  - Endometrial biopsy
  - Dilation and curettage
- Histology
  - High risk: clear cell, PS, carcinosarcoma
  - Typical cell type: endometrioid
  - Grade

Endometrial Cancer: Treatment
- Surgery: hysterectomy, BSO, +/- UND, +/- omentectomy
- Hormonal management if not surgical candidate or thought to be early stage and desire fertility
- Adjuvant treatment if indicated
  - Radiation [brachytherapy, EBRT]
  - Chemotherapy

Endometrial Cancer: Brachytherapy

Ovarian masses in pediatric and adolescent populations: be aware
- Size >8 cm in postpubertal and >5 cm in pre-pubertal patients more likely to be associated with torsion and require surgical consultation
- Ultrasound preferred as initial imaging
- Complexity of mass is a guide for additional testing and intervention
- Referral to gynecologist, adolescent gynecologist, or gynecologic oncologist
Ovarian Cancer: Symptoms
- Insidious onset
- "Silent killer"
- Abdominal bloating, early satiety, change in bowel/bladder function
- Lifetime risk general population ~1.6%
- 10th most common cancer diagnosed in women, 5th most common cause of cancer death
- Screening not indicated (except in high risk populations); not effective
- Most patients (70%) present with advanced disease (Stage III/IV) and most experience recurrence and die of disease

Ovarian cancer: Genetic considerations
- BRCA, RAD51D, Lynch, others
- Genetic % risk models
- TVGS: CA 125 q 6 months in lieu of better screening options
- Risk reduction surgery in high risk populations
- The only prevention?
- Genetic counselor's role
- Ethical considerations of testing

Ovarian Cancer: Risk Factors
- Infertility
- Nulliparity, endometriosis
- Obesity
- Inconclusive data
- Genetics

Ovarian cancer: Prevention
- Surgery
  - Hysterectomy and tubal ligation (each ~34% risk reduction)
  - Salpingectomy (50% risk reduction)
- OCP use
  - ~20% per every 5 years of use

Ovarian Cancer: Types
- Epithelial: carcinosarcoma, clear cell, mucinous, serous, clear cell, low grade serous/endometrioid, borderline/LMP
- Includes ovarian, fallopian, and primary peritoneal
- "Typical" ovarian cancer
- Germ cell
- Examples: immature teratoma, dysgerminoma
- Sex Cord Stromal
  - Sertoli-Leydig cell

Ovarian masses: adult population approach to diagnosis
- CA 125 tumor marker
- Non-specific
- Indicator of peritoneal inflammation
- Other tumor markers: depend on age of patient, clinical findings
  - Such as testosterone, HCG, AFP, LDH, inhibin
- Imaging: TVUS, CT scan
Ovarian Cancer

Ovarian Cancer: Treatment approach

- Tissue confirmation of diagnosis
- Surgery followed by chemotherapy vs. neoadjuvant chemo/surgery/adjuvant chemo +/- PARP inhibitor (PARPi)
- Surgical goal is reduction of disease
- Subsequent treatment can include repeat surgery, chemotherapy, targeted treatments (bevacizumab, PARPi)

Moore K, et al. Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer

Cervical Cancer: Scope of the problem

- According to the CDC, every year about 14 million Americans become infected with HPV; about 12,000 women are diagnosed with and about 4,000 women die from cervical cancer caused by certain HPV viruses.
- Preventable disease

Cervical Cancer: symptoms

- Postcoital bleeding
- AUB
- Discharge
- Pain

Cervical Cancer: screening/diagnosis

- Pap smear
- Cytology
- HPV testing
  - Consideration of primary screening in women 25 years and older*
  - reflex follow-up testing of unclear Pap test results in women 21 years and older
  - co-testing with a Pap test in women 30 years and older.
- Colposcopy with directed biopsy
- Cervical conization (LEEP, CKC), CO2 laser for CIN, cryoablation CIN
- Consider HIV screening

*not FDA approved recommendation

Huh WK, et al. Use of primary high-risk human papilloma testing for cervical cancer screening: Interim clinical guidance. Gynecologic oncology YGYNO-975741; No. of pages: 5; 4C:
Cervical cancer: screening/diagnosis

- Simple hysterectomy
- Radical hysterectomy
- Current data suggests minimally invasive radical hysterectomy is inferior to abdominal radical hysterectomy from a curative standpoint
- Radiation + Cisplatin
- Rarely: radical trachelectomy, aggressive cone


Cervical cancer: prevention

- Vaccination
- "The U.S. Food and Drug Administration today approved a supplemental application for Gardasil 9 (Human Papillomavirus (HPV) 9-valent Vaccine, Recombinant) expanding the approved use of the vaccine to include women and men aged 27 through 45 years."
- Gardasil 9 is a vaccine indicated in females 9 through 45 years old
- For prevention of cervical, vulvar, vaginal, and anal cancers caused by human papillomavirus (HPV) Types 16, 18, 31, 33, 45, 52, and 58; precancerous or dysplastic lesions caused by HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58; and genital warts caused by HPV Types 6 and 11

FDA news release October 5, 2018: FDA approves expanded use of Gardasil 9 to include individuals 27 through 45 years old

Cervical Cancer

- 31yo diagnosed with cervical cancer.
  Underwent radiation + chemo. Post treatment PET/CT.

Vulvar Cancers

- HPV related
- Tobacco abuse contributing factor to dysplasia, multifocal disease, and recurrence
Vulvar Cancer, VIN: Symptoms
- Lesion: white or red, raised, pigmented (SCC, melanoma)
- Pruritus
- Irritation
- Bleeding, discharge
- Asymptomatic
- Associated with lichen sclerosi

Vulvar Cancer, VIN: Screening
- Evaluate at annual
- Visualize vulva if symptomatic
- Low threshold to biopsy = diagnosis
- Don’t assume yeast infection

Vulvar Cancer: Treatment
- Surgery
- Radiation/chemotherapy

Rare Gynecologic Cancers
- Bartholin’s gland
  - Increased with age >45
- Vaginal
  - Primary (away from cervix)
  - History of hysterectomy for cervical dysplasia
  - Bleeding
  - Mass
  - Can be detected on exam, pap smear