Female Reproductive System
Kristine Krafts, M.D.
Female Reproductive System Outline

- Cervix
- Uterus
- Ovaries
- Breast
Cervical Carcinoma

• Once the most common cancer in women – now not even in top 10.
• Decrease due to Pap test!
• At the same time, precursor lesions are increasing (early detection)
Cervical Intraepithelial Neoplasia (CIN)

- DUMB name (should be *dysplasia*, not *neoplasia*)
- All carcinomas are preceded by CIN!
- Three grades of dysplasia: I (mild), II (moderate), III (severe)
- The higher the grade, the more likely the lesion will progress to carcinoma
Cervical Carcinoma Risk Factors

- Sex stuff (early age at first intercourse, multiple sexual partners, persistent infection with “high-risk” HPV)
- Smoking
- Immunodeficiency
Cervical Carcinoma and HPV

• HPV is detectable in almost all CIN and cancer.

• “High-risk” types:
  • 16, 18, 45, 31
  • Found in carcinomas
  • Integrate into genome, inactivate p53, RB

• “Low-risk” types:
  • 6, 11
  • Found in condylomas (benign lesions)
  • Do not integrate into genome
CIN grades
normal  CIN I  CIN II  CIN III

CIN cytology (Pap smear)
normal

CIN I

“Low-grade dysplasia”

CIN II

CIN III

“High-grade dysplasia”

CIN cytology (Pap smear)
Invasive Cervical Carcinoma

- Peak age: 45
- Most cases are squamous (from CIN)
- Usually diagnosed early; spreads slowly
- Mortality is related to stage
  - Stage 0 (preinvasive): 100% 5 year survival
  - Stage 4: 10% 5 year survival
Cervical carcinoma
Endometriosis

- Location of endometrial glands outside uterus
- Endometrium undergoes cyclic bleeding
- Causes scarring, pain, sometimes infertility
Endometriosis in ovary ("chocolate cyst")
Endometrial Hyperplasia

- Proliferation of endometrium
- Risk factors involve estrogen excess (obesity, nulliparity, estrogen replacement therapy)
- The more severe the hyperplasia, the greater the chance that it will evolve into carcinoma
Leiomyoma ("Fibroid")

- Benign tumor of smooth muscle
- Common!
- Stimulated by estrogen
- Menorrhagia, metrorrhagia, or asymptomatic
Leiomyosarcoma

- Malignant tumor of smooth muscle
- Necrotic, with atypical cells and lots of mitoses
- Often metastasizes, especially to lungs
- 5 year survival = 40%
Leiomyoma

Leiomyosarcoma
Leiomyoma

Leiomyosarcoma
Endometrial Carcinoma

- Peak age: 60
- Frequently arises in endometrial hyperplasia
- Risk factors involve estrogen excess (obesity, nulliparity, estrogen replacement therapy)
- Symptoms: leukorrhea, irregular bleeding
- Metastasizes late
Surface epithelial tumors
- Cystadenoma
- Cystadenocarcinoma

Germ cell tumors
- Teratoma
- Dysgerminoma
- Yolk sac tumor
- Choriocarcinoma

Sex cord-stromal tumors
- Granulosa-theca cell tumor
- Sertoli-Leydig cell tumor
Origin of Ovarian Tumors

Most common

Surface epithelial tumors
- Cystadenoma
- Cystadenocarcinoma

Germ cell tumors
- Teratoma
- Dysgerminoma
- Yolk sac tumor
- Choriocarcinoma

Sex cord-stromal tumors
- Granulosa-theca cell tumor
- Sertoli-Leydig cell tumor
Cystadenoma

- Benign tumor derived from surface epithelium
- Repeated ovulation, scarring, infolding of epithelium leads to cysts, which can undergo neoplastic transformation (mehhhh...)
- Typically large, occasionally bilateral
Patient with ovarian cystadenoma
Ovarian cystadenoma
Ovarian cystadenoma
Teratoma

- Benign tumor with differentiation along all three germ cell layers (ectoderm, endoderm, mesoderm)
- Usually cystic, with skin inside (“dermoid cyst”)
- Sebaceous material, matted hair, teeth, bone...
- Malignant variant has immature tissues
Teratoma
Ovarian Cancer

- Peak age: 50
- About 22,000 new cases / 14,000 deaths in 2016
- 5th commonest, 5th deadliest cancer in women
- Danger: no definitive signs until advanced
- Most are cystadenocarcinomas
Papillary cystadenocarcinoma
Papillary cystadenocarcinoma
Ovarian Cancer

Symptoms

- Feeling of fullness or bloating
- Pelvic pain
- Back pain
- Abnormal menses

Risk factors

- Estrogen excess (e.g., nulliparity)
- Family history (BRCA gene mutation)
- *NOT* using oral contraceptives!
Ovarian Cancer

- Treatment: surgery, radiation, chemotherapy
- Prognosis depends on stage
  - Cancer inside ovary: 5y survival 70%
  - Cancer outside ovary: 5y survival 13%
Most breast lumps are benign
Fibrocystic Change

- Super common (not even a disease anymore)
- Exaggeration of normal breast cycles
- Very rarely associated with increased cancer risk
Fibrocytic change
Normal breast
Fibrocystic change
Fibroadenoma

- Peak age: 20s
- Most common benign breast tumor
- Stimulated by estrogen
- Solitary, discrete, moveable mass
- Fibrous tissue with compressed ducts and lobules
Fibroadenoma
Fibroadenoma
Breast Carcinoma

- 233,000 new cases / 40,000 deaths in 2014
- Most common, 2nd deadliest cancer in women
- Lifetime risk: 1 in 8
- 75% of patients are >50
- Rate was increasing but now stable
Breast Carcinoma Risk Factors

- Age
- Family history
- Increased estrogen exposure
- Alcohol consumption
- High-fat diet
What about family history?

- 5-10% of all cases are hereditary
- Most have BRCA-1 or BRCA-2 mutations
- Genetic testing difficult (lots of mutations)
- About half of carriers get cancer by age 70
Breast Carcinoma Clinical Findings

If discovered by palpation
- Solitary, painless, moveable mass
- 2-3 cm in diameter
- Axillary nodes positive in 50% of patients

If discovered by mammography
- 1 cm in size
- Axillary nodes positive in only 15% of patients

As disease progresses
- Fixation to chest wall
- Adherence to overlying skin
- Peau d’orange
Mammogram of Left Breast, Original Screening

Mammogram of Left Breast, Two Years Later

Abnormal Mass
Advanced breast carcinoma: fixation to skin
Peau d’orange
Breast Carcinoma Histologic Types

Non-invasive
- Ductal carcinoma in situ (DCIS)
- Lobular carcinoma in situ (LCIS)

Invasive
- Ductal
- Lobular
- Inflammatory
- Others
Lobular carcinoma in situ
Low-grade invasive ductal carcinoma
High-grade invasive ductal carcinoma
Inflammatory breast carcinoma
Breast Carcinoma Prognostic Factors

- Size of tumor
- Lymph node involvement
- Distant metastases
- Grade of tumor
- Histologic type of tumor
Sentinel node biopsy
## TNM* staging system for breast cancer

<table>
<thead>
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<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>5-year survival</th>
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<tr>
<td>Stage 0</td>
<td>DCIS</td>
<td>0</td>
<td>M0</td>
<td>92%</td>
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<tr>
<td>Stage I</td>
<td>&lt;2 cm</td>
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<td>M0</td>
<td>87%</td>
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<tr>
<td>Stage II</td>
<td>&lt;5 cm</td>
<td>&lt;3</td>
<td>M0</td>
<td>75%</td>
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<tr>
<td></td>
<td>&gt;5 cm</td>
<td>0</td>
<td>M0</td>
<td></td>
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<td>Stage III</td>
<td>&lt;5 cm</td>
<td>4+</td>
<td>M0</td>
<td>46%</td>
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<tr>
<td></td>
<td>&gt;5 cm</td>
<td>1+</td>
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<tr>
<td></td>
<td>Any T</td>
<td>10+</td>
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<td></td>
<td>Any T</td>
<td>Any N</td>
<td>skin or chest wall</td>
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<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td>13%</td>
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* Tumor (size), nodes (# positive), metastases