Banner MD Anderson Cancer Center

Making Cancer History®

Breast Cancer

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Breast Cancer

- Most common cancer among women in the US
- 2nd leading cause of death in women
- 1 in 8 women will develop breast cancer over a lifetime
- Incidence increases with age starting at age 40
- Mortality rates have declined

Identifying Women at risk

- Age: starting at age 40
- Gail Model: estimates 5 yr risk/chemoprevention
  - Age
  - Onset of menarche
  - Age of first pregnancy
  - Number of breast bxs
  - Number of first degree relatives
  - Race/ethnicity

Identifying Women at Risk

- Obesity (BMI > 30)
- ETOH (2-5 drinks per day)
- Prior chest wall irradiation (NHL/Hodgkin's)
- HRT
- Breast Density
- Family history (familial vs genetic risk)

Chemoprevention (5 years)

- Use of endocrine therapies (chemoprevention) to mitigate risk of future breast CA
  - Gail model scores > 1.67%
  - Pts with LCIS
  - Pts with ADH, ALH
- Premenopausal women: Tamoxifen
- Postmenopausal women: Anastrozole, Exemestane, Tamoxifen, Raloxifene

Question #1

- Which of the following is NOT a risk factor for developing Breast CA?
- A. First full term pregnancy after age 30
- B. Heavy daily ETOH use
- C. Age > 70 years old
- D. Heavy daily caffeine use
- E. Breast Density

Breast Cancer Detection

- Clinical exam
- Ultrasound
- Mammogram
- MRI

Non invasive vs invasive Breast Disease

- Ductal Carcinoma in Situ (Intraductal Carcinoma)
  - Think of it as cancer cells contained in the ducts, NO INVASION. Most often picked up on mammogram by calcifications.
- Lobular Carcinoma in Situ
  - Think of this as a “marker lesion” which indicates breast tissue at risk for a lifetime **bilaterally** in developing invasive/noninvasive breast dz
  - 20-40% lifetime risk
  - Tx: 5 years chemoprevention and close lifetime surveillance VS bilateral mastectomy
- Ductal Carcinoma (85%), Lobular CA (10-15%)

Two Goals of therapy with Breast Disease

- **Local** control (in situ and invasive)
  - Lumpectomy/RT versus Mastectomy
    - Equivalent survival but increased local relapse with breast conservation
  - Mastectomy + RT
  - Prophylactic contralateral mastectomy
- **Systemic** control (invasive)
  - Risk assessment based on pathologic features
  - Use of chemotherapy, endocrine therapy and engineered antibodies

Sentinel Lymph Node Biopsy

- Sentinel lymph node is the first lymph node to receive lymphatic drainage from the breast
- Lymphatic mapping done by injecting blue dye or radiolabeled tracer into the breast parenchyma near the area of cancer/mass or, alternatively, in a periareolar location
- Lymph node or nodes are removed

Prognostic Pathologic Features of Interest with Invasive Disease

- Tumor size
- Grade (I-III)
- LN involvement
- ER/PR Status
- HER 2 neu status (IHC/FISH)
- Other (Gene expression profiles in select patients)

Gene Expression Profiles

- Oncotype Dx
- Mammoprint

Oncotype Dx

- The Oncotype Dx 21-gene recurrence score is a prognostic predictive assay and allows us to identify patients who are least and most likely to derive benefit from adjuvant chemotherapy
- Indicated for women with ER positive, HER2 negative breast cancer and up to 3 + LNs.
- Primarily validated in pts with tumors 1 cm or greater. Smaller fraction of pts with tumors 5-9 mm were included in data set.

Oncotype Dx

- RT- PCR to generate a recurrence score and % likelihood of recurrence in the next 10 years with endocrine therapy alone +/- chemotherapy
- Categorizes the tumor as low, intermediate or high risk
- Low risk- adjuvant endocrine therapy alone
  - Tamoxifen versus Aromatase inhibitor
- High risk- chemotherapy
  - TC, AC-T, TAC

How to determine Stage? What is appropriate clinical testing?

- Emphasis on clinical grounds
  - H&P along with routine labs are highly predictive
  - Clinical stages I/II have an extremely low likelihood of positivity on any scans: PET/CT, CT CAP, bone scan, brain scan etc
  - Clinical Stage III pts start to have positivity between 10-20% and requests for CT CAP and bone scan is reasonable. PET/CT would be as good or better but often denied by insurance.

Staging (TNM)

- 0- DCIS
  - >98% 5 year survival
- I - <2 cm, negative LN
- II- ≤ 2 cm 1-3 positive LN or > 2 cm-5 cm if negative LN

Staging

- III- Any tumor size with >4 LN, infraclavicular, ipsilateral internal mammary, supraclavicular LN, tumors >5 cm with >1 LN, chest wall or skin involvement
  - 30-50% 5 year survival

- IV- Distant Mets
  - 18% 5 year survival

Basic Tenets of Adjuvant Radiation Therapy

- Main objective: add to local control of surgery and reduce the risk of local recurrence
- Side effect risks are local: skin, underlying structures (lung, heart with L Breast CA) LNs and lymphatic network (lymphedema)
- External beam irradiation
  - Whole breast plus neighboring LNs
  - Accelerated partial breast
- Brachytherapy (implanted device in biopsy cavity)

Main Systemic Treatment Options:

- Endocrine therapy (Serms, AIs) for all pts with ER or PR +
  - Tamoxifen (block estrogen)
    - **Hot flashes**, mood, vaginal dryness
    - DVT/PE (3/100), CVA (3/100 in > 60 yo), Endometrial CA (3/1000)
    - Estrogen like effects on bone and lipids
  - Aromatase Inhibitors (reduce estrogen)
    - **A/M**, mood, hot flashes, vaginal sx
    - Bone density effects (Ca, Vit D, exercise)

Main Systemic Treatment Options

- Chemotherapy
  - Anthracyclines (Doxorubicin, Epirubicin)
  - Taxanes (Paclitaxel, Docetaxel)
  - Cyclophosphamide
  - Carboplatin
- Her 2 neu Monoclonal Antibodies (1 year total)
  - Trastuzumab (Herceptin)
  - Pertuzumab (Perjeta)

Patient Case #1

- 65 yo woman undergoes a routine screening mammogram which shows calcifications in the left breast that have increased since her last two mammograms. Biopsy comes back consistent with DCIS
- Local: Lumpectomy/RT or Mastectomy (some lump only exceptions)
- Systemic: if ER/PR positive, consider endocrine therapy. Tamoxifen (pre) or AI (post)

Question #2

- The purpose of systemic endocrine therapy in cases of DCIS is to prevent distant metastases. TRUE or FALSE

Patient Case #2

- 61 yo female breast with a mass in her right breast.
- Mammogram/US confirms solid mass. BX confirms Grade III IDC ER 90%, PR 50%, Her 2 neu **negative**. She chooses RMRM. Final path: 3.8 cm primary with 1 microscopic involved LN
- Oncotype Dx score: 51 (high risk) 34% risk of recurrence
- Recommendation: ddAC followed by weekly Taxol, then adj AI x 10 years

Patient #2

- 3 years later…Pt feels lump in R neck at sternocleidomastoid junction. Feels hard, non mobile. CT chest confirms mass as well as suspicious pulmonary nodules and mediastinal LNs.

- Bx requested of R neck mass. **Why**?

  Two reasons:

Patient #2

- Reasons for biopsy:
  - 1 We always want to biopsy first recurrence. Is it her breast CA? Is it a new primary? It's her Breast CA again.
  - 2 Biologic features may have changed. They actually did….
    - ER 92%
    - PR 15%
    - Her 2 neu **POSITIVE**

Patient Case #3

- 54 yo female who presents with a very painful and swollen left breast and palpable lymph nodes
- Mammogram confirms a 6.5 cm breast mass and left axillary LN
- Biopsy is c/w IDC ER/PR negative, her2neu positive
- Staging CT scans are negative for distant disease
- Now what?

Patient Case #3

- Neoadjuvant chemotherapy- Her2neu targeted therapy
- Surgery (Mastectomy)
- Radiation

Patient Case #4

- 54 yo female with history of breast cancer diagnosed 7 years ago
- Lumpectomy, SLN followed by radiation and 5 years of Tamoxifen
- Back pain for past 3 months
- Exam is unremarkable
- Treated supportively with NSAIDS, physical therapy

Patient Case #4

- X-ray and CT scan of her spine- widespread bone mets
- PET scan- Bone lesions but no other sites of disease
- Biopsy is done and shows IDC ER/PR positive and Her2neu negative

Patient Case #4

- Anastrozole plus a cyclin dependent kinase 4/6 inhibitor (e.g. Ibrance) until progression
- Denosumab or Bisphosphonate monthly to reduce risk of fractures and hypercalcemia
- Chemotherapy if any evidence of visceral crisis or progressed on multiple lines of endocrine therapy

Questions

- A 50 yo woman underwent breast conservation surgery and radiation for Stage I triple negative breast cancer. She declined adjuvant chemotherapy. Two years later she is found to have a 1.5 cm ipsilateral relapse that on biopsy is again triple negative. Bone scan and CT scans are all negative

Questions

- Which of the following treatment plans would provide the greatest reduction in risk of future relapse?
- A) Mastectomy
- B) Mastectomy with adjuvant chemotherapy
- C) Mastectomy with radiation and adjuvant chemotherapy

Questions

- B) Mastectomy with adjuvant chemotherapy

Questions

- A woman presents with a primary breast cancer, with a 3cm axillary lymph node which is triple negative (ER/PR/Her 2 neu)

Questions

- Which of the following best determines whether or not she should receive preoperative chemotherapy or proceed with initial surgery?
  - A) Neoadjuvant chemotherapy has been proven to improve survival in this situation
  - B) Initial surgery has been associated with improved survival in this situation
  - C) Neoadjuvant chemotherapy is associated with a reduction in the need for mastectomy and possibly axillary lymph node dissection

Questions

- C) Neoadjuvant chemotherapy is associated with a reduction in the need for mastectomy and possibly axillary lymph node dissection

Questions

- A 65 yo woman has a resected Her2neu positive breast cancer. She has been told that adjuvant trastuzumab/pertuzumab are beneficial

Questions

- Which of the following is the appropriate length of time for her to receive adjuvant Her2neu directed therapy?
  - A) 6 months
  - B) 1 year
  - C) 2 years
  - D) Adjuvant Her2neu directed therapy is only necessary during the time that she is receiving adjuvant chemotherapy

Questions

- Which of the following patients would you refer for genetic counseling?
  a) Men with breast cancer
  b) Women diagnosed at or under the age of 50, or with Ashkenazi heritage, and/or a strong family history of breast or ovarian cancer.
  c) Women with triple negative breast cancer up to age 60
  d) All the above

Male Breast Cancer

- <1% of all breast cancer cases
- BRCA positive, Li-Fraumeni, Cowden’s syndrome, Lynch, syndrome, Klinefelter's syndrome, hepatic dysfunction, marijuana use
- ER/PR positive breast cancer
- Primarily treated with mastectomy +/- RT locally
- Tamoxifen +/- chemotherapy

Breast CA Survivorship

- Regular followup and emphasis on H&P
- Followup Breast imaging (Mammo +/- US) if native tissue remains
- Regular Labs including tumor markers and scans of all types done on asymptomatic patients have not been shown to alter outcomes.
- ASCO guidelines and breast cancer research protocols list all other testing as only when “clinically indicated”.