Recurrence Surveillance in Breast Cancer Survivors

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Gillian Lieberman, MD
Agenda

• Patient
  – Presentation
  – Radiological findings

• Breast cancer
  – Staging
  – Treatment

• Recurrence of breast cancer
  – Companion patient
  – Guidelines for surveillance
  – Sensitivity and specificity of modalities

• Take Home Points
• Summary
Our Patient: Clinical Presentation

• 63 year old female with history of breast cancer (age 47) comes to BIDMC Breast Center 4/2012 to establish care
  – Complained of chronic right chest wall tenderness over the site of her mastectomy scar, worsening over the last 5 months
  – Yearly mammography
    • Last 7/2011 (outside hospital): “BI-RADS 1, negative”
  – Sees her primary care physician regularly
Our Patient: Medical History

• PMH:
  – At age 47, she was diagnosed with right breast cancer stage IIA, ER-PR+, negative lymph nodes
  – Treatment:
    • Modified radical mastectomy
    • 6 cycles of adjuvant chemotherapy (cyclophosphamide, methotrexate and fluorouracil 5FU)
    • Tamoxifen x 5 years

• Family History
  – Ashkenazi Jewish heritage; refused genetic testing
Our Patient: Physical Exam

• Breast physical exam:
  – No visible changes: no erythema, rashes, dimpling, or skin lesions; on the left, no nipple discharge, nipple excoriation, or nipple retraction
  – No palpable nodules nor masses bilaterally
  – No axillary lymphadenopathy
  – Tenderness along the length of the surgical scar with deep palpation mainly between the ribs.

• Plan: Reassurance, scheduled for regular yearly mammography
Our Patient: Primary Care Presentation

• 1 month later:
  – Presents to her primary care physician with a 2 week history of dry cough
  – ROS: denied fever, chills, night sweats or weight loss
Our Patient: Pleural Effusion on Plain Film

Bilateral small pleural effusions and bibasilar opacities

Antero-Posterior (AP) Upright Chest Plain Film

AP Lateral Chest Plain Film
Our Patient: Follow Up

• Despite treatment with azithromycin, levofloxacin and two courses of prednisone, the cough persists for 6 more weeks

• Her primary care physician ordered a chest computed tomography (CT) without contrast
Our Patient: Pleural Effusion on Chest CT

Moderate – large right sided pleural effusion

Right radical modified mastectomy

Axial chest CT without contrast
Our Patient: Differential Diagnosis

**PLEURAL EFFUSION**

<table>
<thead>
<tr>
<th>Transudate</th>
<th>Exudate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular failure</td>
<td>Malignancy</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>Parapneumonic effusions</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>Benign asbestos effusion</td>
</tr>
</tbody>
</table>

Modified from Maskell et al. *Thorax* 2003

Transudate: balance of hydrostatic and oncotic forces favors pleural fluid accumulation
Exudate: local factors leads to leaky capillaries causing shift of fluids into the pleura.
Our Patient: Lung Nodules on Chest CT

Multiple Lung Nodules

Axial chest CT without contrast
Our Patient: Chest Wall Mass on Chest CT

Right Chest
Wall Mass
Rib fracture
Our Patient: Diagnosis and Treatment

• High suspicion for recurrent right breast cancer in the chest wall with metastases to the lungs
• Pleural effusion cytology: + adenocarcinoma
• Core biopsy: invasive carcinoma consistent with breast origin
• Started treatment with chemotherapy for metastatic breast cancer
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Breast Cancer: Epidemiology

- 12% lifetime risk for average American woman
- Causes 15% of cancer related deaths in women
- Gail model for predicting risk

<table>
<thead>
<tr>
<th>Breast Cancer Risk Assessment Tool (Gail Model)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Age</td>
</tr>
<tr>
<td># previous breast biopsies</td>
</tr>
<tr>
<td>Age at first live birth</td>
</tr>
</tbody>
</table>

Fletcher S. Risk Prediction Models for Breast Cancer Screening. *Up-To-Date* 2012
Breast Cancer: Genetic Risk

• Genetic mutations (BRCA)
  – Mutation carriers have up to 60-80% risk of developing breast cancer in their lifetime
  – Higher prevalence of BRCA gene mutations in Ashkenazi Jews
# Breast Cancer: Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>% Diagnosed</th>
<th>% 5 year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>20.8</td>
<td>93</td>
</tr>
<tr>
<td>I</td>
<td>38.2</td>
<td>88</td>
</tr>
<tr>
<td>II</td>
<td>24.8</td>
<td>74-81</td>
</tr>
<tr>
<td>III</td>
<td>8.5</td>
<td>41-67</td>
</tr>
<tr>
<td>IV</td>
<td>3.7</td>
<td>14</td>
</tr>
<tr>
<td>Unknown</td>
<td>3.9</td>
<td></td>
</tr>
</tbody>
</table>

Modified from [http://www.facs.org/cancer/ncdb](http://www.facs.org/cancer/ncdb)
National Cancer Data Base (2001, 2009)
Breast Cancer: Treatment

• Dependent on the stage
• Equivalent survival benefit:
  – Breast conserving surgery with radiation therapy
  – Mastectomy +/- reconstruction
• Axillary lymph node biopsy + staging
• Adjuvant therapy:
  – Tamoxifen
  – Radiation
  – Chemotherapy
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Breast Cancer: Recurrence

- 5-40% risk of locoregional recurrence (average 10%) after invasive breast cancer treatment
- 9-25% of above will have distant metastases
- Majority occur within 5 years of primary treatment

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence</td>
<td>Ipsilateral chest wall (including skin and muscle) or mastectomy scar</td>
</tr>
<tr>
<td>Regional spread</td>
<td>Ipsilateral axillary, supraclavicular, infraclavicular or internal mammary lymph nodes</td>
</tr>
<tr>
<td>Distant spread</td>
<td>metastases to any other location</td>
</tr>
<tr>
<td>Spread to contralateral breast</td>
<td>metastasis versus new primary tumor</td>
</tr>
</tbody>
</table>
Breast Cancer: Prognostic Factors for Recurrence

• Influenced by:
  – Tumor size
  – Tumor grade
  – Number of lymph nodes
  – Presence of lymphovascular space invasion
  – Surgical margin status
  – Involvement of fascia or skin
  – Percentage of nodal involvement

• Chest wall recurrence is a poor prognostic factor

Blanco et al. British Journal of Cancer 1990
Chagpar et al. Annals of Surgical Oncology 2003
Companion Patient: Clinical Presentation

- 46 year old female
- Family history: Breast cancer in Mother (age 41), Sister (31)
- BRCA negative
- Age 43 had bilateral prophylactic nipple sparing mastectomy with breast reconstruction
- Pathology from the mastectomy showed DCIS
- Age 46 found a palpable mass
- Breast Magnetic resonance imaging (MRI) ordered
Companion Patient: Adenocarcinoma on MRI

Axial MRI with Gadolinium enhancement

Saline Implant

Adenocarcinoma
Modalities for Surveillance: Clinical Exam

• Clinical Breast Exam

http://www.siumed.edu/breastcenter/screenings.html
Modalities for Surveillance: Mammography

- Clinical Breast Exam
- Mammography
  - Contralateral breast only in patients with mastectomy
  - Both breasts in breast-conserving therapy
Modalities for Surveillance: Ultrasound

- Clinical Breast Exam
- Mammography
- Ultrasound

Sagittal ultrasound of right breast mass
Modalities for Surveillance: MRI

- Clinical breast exam
- Mammography
- Ultrasound
- MRI

Axial MRI
Modalities for Surveillance: FDG-PET scan

- Clinical breast exam
- Mammography
- Ultrasound
- MRI
- Fluorodeoxyglucose Positron Emission Tomography (FDG-PET scan)
Breast Cancer Screening: Intermediate Risk
ACR Appropriateness Criteria

- Compiled by American College of Radiology (ACR)
- Intermediate risk group: personal history of breast cancer, lobular neoplasm, atypical ductal hyperplasia, dense breasts, 15-20% lifetime risk

<table>
<thead>
<tr>
<th>Radiologic Procedure</th>
<th>Rating</th>
<th>Comments</th>
<th>RRL*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography screening</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI breast without and with contrast</td>
<td>7</td>
<td>See statement regarding contrast in text under “Anticipated Exceptions.”</td>
<td>O</td>
</tr>
<tr>
<td>US breast</td>
<td>5</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>FDG-PEM</td>
<td>2</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>Tc-99m sestamibi BSGI</td>
<td>2</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>MRI breast without contrast</td>
<td>1</td>
<td></td>
<td>O</td>
</tr>
</tbody>
</table>

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

*Relative Radiation Level

Meiniero et al. ACR Appropriateness Criteria 2012
Breast Cancer Screening: High Risk
ACR Appropriateness Criteria

- High Risk Group: BRCA gene mutation, first degree relative with BRCA mutation, history of chest irradiation between ages 10-30, greater than 20% lifetime risk of breast cancer

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<tr>
<td>Mammography screening</td>
<td>9</td>
<td>Beginning at age 25-30 or 10 years before age of first-degree relative with breast cancer or 8 years after radiation therapy, but not before age of 25. Mammography and MRI are complementary examinations, both should be performed.</td>
</tr>
<tr>
<td>MRI breast without and with contrast</td>
<td>9</td>
<td>Mammography and MRI are complementary examinations, both should be performed. See statement regarding contrast in text under “Anticipated Exceptions.”</td>
</tr>
<tr>
<td>US breast</td>
<td>6</td>
<td>If patient cannot have MRI.</td>
</tr>
<tr>
<td>FDG-PEM</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Tc-99m sestamibi BSGI</td>
<td>2</td>
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Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

Meiniero et al. ACR Appropriateness Criteria 2012
Recurrence Surveillance: ASCO Recommendations

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>NOT RECOMMENDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Exam</td>
<td>Routine blood tests</td>
</tr>
<tr>
<td>Patient education</td>
<td>Imaging studies (CXR, bone scan, liver ultrasound, CT)</td>
</tr>
<tr>
<td>Referral for genetic counseling</td>
<td>Tumor markers (CA 15-3, CA27.29, CEA)</td>
</tr>
<tr>
<td>Breast self-exam</td>
<td>FDG-PET</td>
</tr>
<tr>
<td>Mammography*</td>
<td>Breast MRI</td>
</tr>
<tr>
<td>Coordination of care</td>
<td></td>
</tr>
<tr>
<td>Pelvic exam</td>
<td></td>
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</table>

Modified from Khatcheressian et al. *Journal of Clinical Oncology* 2006

*Mammography Recommendations: starting 1 year after initial mammogram that lead to diagnosis (no earlier than 6 months after definitive radiation therapy). Then surveillance mammo every 6-12 months.
- If mastectomy, mammography of contralateral breast
# Recurrence Surveillance: Modality Accuracy

- Review of modality accuracy for detection of ipsilateral breast cancer recurrence

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<thead>
<tr>
<th>Breast Imaging Modality</th>
<th>Sensitivity range (%)</th>
<th>Specificity range (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography (for breast conserving treatment)</td>
<td>64-67</td>
<td>85-97</td>
</tr>
<tr>
<td>MRI</td>
<td>86-100</td>
<td>93</td>
</tr>
<tr>
<td>Clinical exam</td>
<td>50-89</td>
<td>76</td>
</tr>
<tr>
<td>Ultrasound (for symptomatic presentation)</td>
<td>43-87</td>
<td>31-73</td>
</tr>
<tr>
<td>PET-CT</td>
<td>96</td>
<td>89</td>
</tr>
<tr>
<td>CT</td>
<td>40-92</td>
<td>41-100</td>
</tr>
</tbody>
</table>

Robertson et al. *Health Technology Assessment* 2011  
Pennant et al. *Health Technology Assessment*  2010  
Pan et al. *Journal of Cancer Research and Clinical Oncology* 2010
Recurrence Surveillance: MRI

• Very sensitive imaging modality for identifying breast cancer recurrence

• Surveillance must be both clinically effective AND cost effective
  – Debate about reduction of mortality with MRI
  – MRI is 10 x more expensive than mammography

• More data required to determine if MRI is improving outcomes for women with recurrent breast cancer
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Take Home Points

• Risk of recurrence persists past 5 year disease-free-survival after primary breast cancer treatment

• Screening recommendations depend on risk stratification
  – Intermediate risk: Mammogram with clinical exam
  – High risk: Mammogram + MRI with clinical exam

• MRI has a very high sensitivity but is currently only recommended in high-risk women
Summary

• Patient with a 16 year disease-free-interval who had recurrent ipsilateral breast cancer
• Breast cancer epidemiology, screening, staging and treatment
• Rates and risk of recurrence
• Surveillance recommendations for breast cancer survivors
References


15. Pennant M, Takwoingi Y, Pennant L. A systematic review of positron emission tomography (PET) and positron emission tomography/computed tomography (PET/CT) for the diagnosis of breast cancer recurrence. *Health Technology Assessment* 2010;14(50):1-103.


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