History

• 49 year-old post-menopausal female presenting with acute onset right breast erythema and skin thickening
• Right breast mammogram showed skin thickening and right axillary adenopathy
• A 1-week course of antibiotics was recommended, after which the erythema improved
• She received an additional 2 weeks of antibiotics after which the erythema was entirely resolved but the induration remained present
History

• In-office ultrasound demonstrated persistent mixed echogenicity at the 9 o’clock position

• She was told to follow-up in 1 month, at which point given the lack of resolution of ultrasound changes, a skin punch biopsy and core needle biopsy were performed
Physical examination approximately 1 month following completion of final course of antibiotics
PMH/PSH: Negative
Reproductive History: Menarche age 10
  G2P2 (First birth: 23 years)
  LMP: 1 year prior
  No hormone exposure
Medications: None
Allergies: Keflex, Sulfa
Social History: Works as a hairdresser. Never smoker. 2-3 drinks/week.
ROS: +Fullness of right breast. No headaches, changes in vision, SOB, cough, nausea, vomiting, diarrhea or bone pain.
Family History: No Ashkenazi Jewish ancestry.

- **Mother** – Lung cancer (Age 71).
- **Maternal Aunt** – Breast cancer (Age 70s).
- **Father** – Melanoma (Age 60).
- **Paternal Aunt** – Breast cancer (Age 44).
- **Paternal First Cousin** – Breast cancer (Age 30).
- **Second Paternal First Cousin** – Breast cancer (38).
- **Third Paternal First Cousin** – Breast cancer (Age 33).
- **Fourth Paternal First Cousin** – Lung cancer (Age 53).
Imaging: Mammography

Skin thickening

Enlarged axillary lymph nodes
Differential Diagnosis

- Inflammatory breast cancer
- Infectious Mastitis
- Breast abscess
- Ductal ectasia
- Locally advanced breast cancer
- Lymphoma of the breast
- Leukemia of the breast
Pathology

- Core Needle Biopsy: Invasive ductal carcinoma, poorly differentiated (modified Bloom-Richardson grade III/III), measuring at least 0.6 cm. No lymphovascular invasion is identified.
  - Estrogen receptor: Positive (>95%, strong)
  - Progesterone receptor: Positive (5%, moderate to strong)
  - HER2/NEU: Negative (1+)

- Skin, Punch Biopsy: High-grade carcinoma present within dermal lymphatics
Definition of IBC

• International Expert Panel Diagnostic Features:
  1. Rapid onset of breast erythema, edema and/or peau d’orange and/or warm breast
  2. Duration of history of no more than 6 months
  3. Erythema occupying at least one-third of the breast
  4. Pathologic confirmation of invasive carcinoma

• Dermal lymphatic invasion is neither required nor sufficient by itself for a diagnosis of IBC

Clinical Presentation

• Ipsilateral axillary disease is common (50-90%). 1-3

• 30% Stage IV at initial presentation.

• Contralateral axillary nodal disease in 38/177 (22%) patients in MDACC study; only site of M1 disease in 47% of them. 4
  – For those treated with chemotherapy, surgery (bilateral mastectomy and ALND), and RT, 4/13 durable NED

Characteristics of IBC

• 1-5% of all breast cancers in the United States
• Younger age at diagnosis and increased likelihood of being estrogen receptor negative compared to locally-advanced advanced breast cancer
• Less favorable outcome compared to locally-advanced or early-stage breast cancer
  – LRR: 10-27% versus 7-10%
  – OS5: 40-60% versus 40-86%
• Hypothesis that IBC is not a unique biologic entity but rather is a subset of the non-IBC tumors

Initial Evaluation

• Multi-disciplinary evaluation
• Biopsy for confirmation of diagnosis and receptor studies
• Bilateral diagnostic mammograms (ultrasound if necessary for biopsy)
• CT C/A/P and bone scan or PET-CT
Recommended Treatment

• Pre-operative chemotherapy including anthracycline and taxane; HER2-directed therapy if HER2-positive

• If adequate response, then total mastectomy and Level I/II axillary dissection, then radiation therapy, including comprehensive regional nodal radiotherapy

• If inadequate response, consider additional chemotherapy and/or pre-op radiation therapy
Case Management

- PET-CT performed: Showed skin thickening of the right breast, multiple FDG-avid right axillary lymph nodes. No evidence of distant disease.
- Diagnosis: T4dN1M0 (Stage IIIB) ER+/PR+/HER2- Inflammatory Breast Cancer
- Genetic counseling and testing revealed a BRCA2 mutation
Imaging: PET-CT

No evidence of FDG-avid distant metastatic disease.
Case Management

• The patient completed four cycles of dose-dense Adriamycin, Cytoxan followed by four cycles of dose-dense Taxol
• She went on to modified radical mastectomy with pathology as follows:
  – Residual invasive ductal carcinoma, spanning a 1.4 x 1.0 cm zone of fibrosis
  – Lymphatic invasion focally present
  – Deep margin free of invasive carcinoma
  – Metastatic ductal carcinoma in 7 of 20 lymph nodes, largest foci 11.0 mm, without extranodal extension
  – Miller-Payne response grade 3; residual cancer burden = 3.434 (RCB class III)
Radiation Therapy

• Adjuvant radiotherapy was recommended
  – CT Sim: Supine, breast board
    • Wires placed at midline, mastectomy scar
  – Radiation delivered to the chest wall, supraclavicular and axillary lymph nodes
    • 50 Gy in 25 fractions to chest wall, supraclavicular and axillary lymph nodes
      – 1.0 cm bolus every other day during CW+regional lymph nodes, including to inferior anterior supraclavicular field
    • 10 Gy chest wall boost (Total Dose: 60 Gy)
      – 1.0 cm daily bolus during CW boost
  – Full Axilla (including levels I-III) targeted 2/2 bulk of axillary disease and incomplete response to systemic therapy
  – Adequate margin on medial disease pre-chemotherapy required some extension across midline
Radiation Therapy: Supraclavicular and Full Axilla

Teaching Point: Lateral border of the AP and PA fields set to include adequate margin on levels I-III lymph nodes when treating full axilla.

Levels I-III and supraclavicular lymph nodes contoured based on RTOG Atlas.
Radiation Therapy: CW Tangents
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Radiation Therapy: CW Tangents
# Radiation Therapy: DVH

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Radiation Therapy Approaches

- Dose acceleration, bolus, and/or total dose escalation have been utilized in an attempt to improve local control
- Selected Approaches:
  - MD Anderson: If age <45, positive margins, or poor chemo response → 66 Gy BID (1.5 Gy/fx). Otherwise 60-66 Gy (2Gy/fx) PRN Bolus.
  - Cleveland Clinic and University of Florida retrospectively showed better control with doses (CW + boost) higher than 60 Gy (1.8-2Gy/fx)
  - MSKCC: 50.4 Gy (1.8 Gy/fx) and daily bolus (0.5-1.0 cm)
  - DFCI: 50 Gy to chest wall with every other day bolus + 10 Gy to scar with daily bolus
Radiation Therapy Approaches

• International Expert Panel:
  • No “standard” dose
  • However, consider dose escalation to 66 Gy in:
    • Women age <45
    • Close or positive surgical margins
    • 4 or more positive LN following pre-op chemo
    • Poor response to pre-op systemic treatment

Teaching Points

• Data on dose-escalation are variable and unlikely to be definitively proven by a randomized trial given rarity of the disease
• Risk of distant disease in this population is very high so escalation of local therapy needs to be considered in this context
• At our institution, coverage of the full axilla and internal mammary nodes determined on a case-by-case basis based on extent of disease and individual anatomy
References

• Tsai, Am J Clin Oncol. 2013. [EPub].