RADY Case Presentation

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July 2018

Ed. John Lilly, MD
67-year-old female with right breast mass
Ms. AS is a 67-year-old female presenting to the UNCH Breast Multidisciplinary Clinic to seek a second opinion on treatment for her newly diagnosed right breast cancer.

* Past medical history of well-controlled hypertension and type 2 diabetes mellitus.
* Family history unremarkable for breast, colon or ovarian cancer. She had a daughter that had non-Hodgkin's lymphoma.
* Palpated a mass in her right breast during self exam and brought this to the attention of her primary care provider.
Imaging studies obtained

* Bilateral diagnostic mammogram
* Targeted ultrasound of right breast and right axilla
* Breast MR without and with intravenous contrast with postprocessing images
Note asymmetry right breast upper outer quadrant, mass right posterior depth, and LN.
Compression magnification mammograms confirm findings.
Ultrasound demonstrates multicentric irregular masses, at 2:00 and 9:00.
Ultrasound also confirms abnormal right axillary LN (blue), as compared to normal (white).
Breast MR shows large medial breast mass and enlarged LN.
Pathology results

- At time of surgery, pathology results were as follows:
  - Multicentric Invasive ductal carcinoma with micropapillary and lobular features, lesion 1 = 2.6 cm and lesion 2 = 4.5 cm
  - Nottingham combined histologic grade: 2 (of 3)
  - Ductal carcinoma in situ grade 3 with comedonecrosis
  - Estrogen receptor: Positive
  - Progesterone receptor: Positive
  - HER2/neu by immunohistochemistry: Negative
  - 5/30 LN involved by tumor
Clusters of neoplastic cells floating in empty, clear spaces surrounded by delicate strands of stroma (hematoxylin-eosin, original magnification x50).
Clinical course

* When the tumor was first diagnosed, she declined treatment.
* After 2nd opinion at UNC, she underwent modified radical mastectomy.
* She was found to have lymphovascular invasion and perineural invasion with involvement of 5/30 lymph nodes. The size of the largest metastasis was 1.3 cm with extracapsular extension present.
* She was started on postsurgical chemotherapy with AC (Adriamycin + Cyclophosphamide) followed by Taxol with very good response.
* She also received postsurgical radiation.
* She is now on Anastrazole (Arimidex) and tolerating it well without signs of return of her cancer.
Histologically, IMPC is a rare variant of invasive breast carcinoma characterized by pseudopapillary and tubuloalveolar arrangement of tumor cell clusters in sponge-like, clear empty spaces, mimicking extensive lymphatic invasion.

This subtype of breast cancer accounts for 3 - 6% of all primary breast cancers, resulting in relatively few major studies and small sample sizes in even the largest IMPC-focused case control studies.

UNC study cohort (see accompanying slide) has contributed to understanding
Discussion: IMPC

* Patients with invasive micropapillary breast carcinomas commonly present as stage II or stage III tumors, rapid spread to axillary lymph nodes, and are more likely to have axillary nodal involvement compared to IDC. Distant metastases are very rare, however.

* IMPC are well-differentiated tumors
* IMPC Immunohistochemistry: Most are ER positive, PR positive, and Her2-neu negative (>95%), and have a better prognosis than other stage II and stage III breast cancers

* Genetics
  * Majority are classified as luminal-type
  * This yields a more favorable stage in the new AJCC Clinical Prognostic Staging
70 patients with confirmed histologic diagnosis of IMPC, with complete records in 60:

* 61 tumors in 60 patients
* Patient age mean of 55 years
* Immunohistochemistry: 82.0% ER positive, 67.2% PR pos, and 21.3% HER2 pos
* IMPC histopathologic grade: 2.9% grade 1, 50.0% grade 2, and 45.6% grade 3
* Molecular subtyping: 50.8% Luminal A and 29.5% Luminal B
* Tumor mass size mean was 2.8 cm (range 0.5 cm to 9 cm)
* The surgical treatments included 56.7% mastectomy, 46.7% breast-conserving surgery, and 10.0% receiving both in tandem therapy
* Despite the high grade of primary tumor and high percentage of axillary lymph node involvement, 41 of 42 known cases (98%) have 5-year-survival documented.
Discussion: IMPC at UNC *(article submitted)*

Our observations and conclusions:

* High percentages of grade 2 and 3 tumors with mixed molecular subtyping and unusually high lymph node involvement.
* Despite metastatic involvement of locoregional lymph nodes, these patients uniformly do well. These outcomes can be explained by important changes in the newly published 8th edition American Joint Committee on Cancer (AJCC) Cancer Staging Manual.
* Understanding that IMPC has high lymph node involvement should guide imagers to target axillary LN with more vigilant interrogation.
* These patients may be uniquely suited to TAD (targeted axillary dissection) protocol.
Discussion: IMPC at UNC (article submitted)

Traditional Sequence
Traditional management pathway for invasive micropapillary carcinoma of the breast.

Desired Sequence
Management of IMPC with greater understanding of behavior of this particular subtype of breast cancer.
Sequence Incorporating Targeted Axillary Dissection (TAD)
Ideal management of invasive micropapillary carcinoma of the breast with the use of targeted axillary dissection.
References


