CASE 1
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Clinical History
• 46 year-old female with a suspicious left breast mass on screening mammogram with ultrasound
• Past Medical History: Hysterectomy, left salpingo-oophorectomy
• Family History: Mother breast cancer (55), sister triple negative breast cancer (42), maternal grandmother ovarian cancer (50)
• Image guided needle biopsy performed
• Interpreted as grade 1 triple negative breast carcinoma
• Referred to our institution for treatment
Core biopsy

Differential Diagnosis

- Sclerosing adenosis
- Invasive mammary carcinoma, low grade
  - Tubular carcinoma
  - Microglandular adenosis

<table>
<thead>
<tr>
<th>Sclerosing Adenosis</th>
<th>Wire</th>
<th>Tubular Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gland Shape</td>
<td>Compressed/Variable</td>
<td>Round</td>
</tr>
<tr>
<td>Architectural Pattern</td>
<td>Lobular</td>
<td>Infiltrative</td>
</tr>
<tr>
<td>Myoepithelial Cells</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Basement Membrane</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Apical Snouts</td>
<td>Variable</td>
<td>Absent</td>
</tr>
<tr>
<td>Cytologic Atypia</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Eosinophilic Secretions</td>
<td>Not prominent</td>
<td>Present</td>
</tr>
<tr>
<td>S-100</td>
<td>Variable/Weak</td>
<td>Present/Strong</td>
</tr>
<tr>
<td>ER</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>EGFR</td>
<td>Negative</td>
<td>Positive</td>
</tr>
</tbody>
</table>

ER
p-63
SMMHC
Calponin
p-63
S-100
p-63
Core biopsy

Final Diagnosis – Core Biopsy

• Microscopic focus of invasive mammary carcinoma, NST, low combined histologic grade and high grade DCIS associated with microglandular adenosis (MGA) with features of atypical microglandular adenosis (AMGA).

Microglandular Adenosis (MGA)

• Uncommon proliferative lesion of the breast (first described 1968, well characterized 1983)
• Female breast, wide age range (most 45-55 yo)
• Palpable masses or mammographically detected
• Pure (ordinary) form and atypical forms (AMGA)
• Carcinoma, in-situ or invasive, described to arise in MGA/AMGA in significant number of cases (about 27%)

• Disordered proliferation of round glandular structures
• Single layer of epithelial cells
• Lack of myoepithelial cell layer
• Eosinophilic secretions
• Surrounding basement membrane
• Non-reactive fibrous stroma or embedded in adipose tissue
• ER, PR, HER2 negative; S-100 positive

Atypical Microglandular Adenosis (AMGA)

• Retains elements of MGA but…
• Complex architecture
  • Large irregular glands, interconnected acini, microcribriform nests
  • Simple to stratified epithelium to solid nests
  • Partial to complete loss of intraluminal secretions
• Cytologic atypia
  • Prominent nucleoli, variable pleomorphism
  • Mitosis and apoptosis present

Carcinoma arising in MGA/AMGA

• Carcinoma in-situ (CIS) to invasive carcinomas retaining the acinar growth pattern
  • CIS – solid expansion, cytologic atypia, basement membrane (BM)
  • Invasive – coalescent nests, high nuclear grade, absent BM
• Ordinary type DCIS, LCIS
• Invasive carcinomas with basoloid features, secretory or squamous differentiation, matrix-producing carcinomas, adenoid cystic carcinomas
• ER, PR, HER2, CK5/6, 34bE12 negative; EGFR positive (triple negative, basal-like immunophenotype)
Clinical History

- Additional testing
  - MRI
  - Genetic counseling with BRCA testing (germline BRCA1 deleterious mutation; exon 14-20 del 26kb)
- Total mastectomy with surgical axillary staging
BREAST SPECIALTY CONFERENCE - CASE 1

Mastectomy

SMA

p-63

Biomarkers

ER

HER2
Proliferative activity parallels progression


Immunohistochemistry

- Myoepithelial cell markers: Negative
- E-cadherin: Positive
- ER/PR/HER2: Negative
- p53: Positive in areas of AMGA to CIS
- Ki-67: Higher in areas AMGA to CIS

Final Diagnosis – Mastectomy Specimen

- Multiple microscopic foci of invasive carcinoma, NST, intermediate combined histologic grade in a background of MGA, atypical MGA and high grade DCIS, solid and comedo type.
- Two axillary sentinel lymph nodes negative for carcinoma by morphology and immunohistochemistry.
- pT1a pN0(i-)(sn)

MGA/AMGA Progression to Carcinoma

- Shin SJ, et al, 17 cases, cCGH
- Guerini-Rocco E, et al, 10 cases MPS
- MGAs genetically heterogeneous; variable copy number alterations and chromosomes affected, recurrent gains (1q, 8q) and losses (5q, 14q); TP53 most frequently mutated (not in MGA)
- Concordant alterations in matched samples
- Subset MGA may represent a non-obligate precursor of a subgroup of triple negative breast cancer

New Concept on MGA

- Geyer FC, et al, re-analysis, targeted MPS, 10 MGA/AMGA (8 associated with cancer), and 6 acinic cell carcinomas (6 non-acinic carcinoma component)
- Both entities are likely related and harbor similar genomic profiles and recurrent TP53 mutations
- Low grade morphology but recapitulate triple negative breast cancer at the molecular level
- Likely represent low grade forms of triple negative disease with potential to progress to high grade triple negative breast cancer

Take Home Messages

- MGA can simulate carcinoma both clinically and pathologically
- Low grade glandular proliferations of the breast in core biopsies require correlation with myoepithelial stains and biomarkers
- MGA likely represents a non-obligate precursor of breast cancer requiring excision and assessment of margins
- Thorough sampling of specimens with MGA is crucial due to high number of cases associated with carcinoma
- Staging based on invasive component regardless of the lesion size (radiologic or macroscopic)
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