What is Pleomorphic Lobular Carcinoma

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Objectives

• Distinguish Pleomorphic from classic invasive lobular
  – Histologic features
  – Cytologic features
  – Molecular pattern
  – Immunohistochemical pattern

• Does it make a difference?
History

• Invasive pleomorphic lobular carcinoma was described by Page in 1987 as a distinct variant of classic invasive lobular carcinoma.
  – Maintaining the loosely cohesive growth pattern, but unique cytologic features
  – Other names used to describe pleomorphic lobular have been: myoid and histiocytoid
  – Presumed apocrine differentiation (GCDFP-15 reactive)
  – Today classic lobular is about 5-15% of invasive breast cancers while the pleomorphic variant is less than 1%
Histologic Features

• Tumor cells grow in single files or loosely cohesive clusters through the stroma.
  – Linear strands
  – Targetoid appearance around ducts
  – Trabecular
  – Frequent intracytoplasmic lumen
  – Both are E-Cadherin negative by IHC
  – PLC is often grade II-III; while classic lobular is grade I-II.
  – Can be seen with classic LCIS (80%) or PLCIS (35%), mixed (15%)
Histology

Linear and strands and single tumor cells
Histology

Targetoid pattern of tumor infiltration
Cytologic Features

• Cytologic features distinguish pleomorphic from classic invasive lobular carcinoma
  – Enlarged nuclei (4x a lymphocyte)
  – Greater nuclear irregularity
  – Hyperchromsia
  – Prominent nucleoli
  – Increased eosinophilic cytoplasm
  – Increased mitotic activity
Cytology

Abundant eosinophilic cytoplasm
Cytoplasmic lumens
Cytology

Hyperchromatic nuclei

Enlarged, irregular, hyperchromatic nuclei with prominent nucleoli
Immunohistochemistry

- Pleomorphic lobular is more likely to be Estrogen and Progesterone Receptor negative more often than classic lobular.
- Pleomorphic lobular has a Ki-67 rate of greater than 10%
- Loss of E-Cadherin in greater than 90% of classical and 80% of pleomorphic lobular carcinomas
- Both are generally Her-2 negative
- Pleomorphic lobular is often reactive to P53 while classical is not
Invasive Lobular Carcinoma

A. H&E;  B. Estrogen Receptor reactive; C. Her-2 negative; D. Ki-67 negative
Invasive Pleomorphic Lobular Carcinoma

A. H&E; B. Estrogen Receptor negative; C. Her-2 negative; D. Ki-67 reactive
Molecular

• Both classic and pleomorphic demonstrate loss of E-Cadherin expression through loss of CDH1 gene (loss of 16q)
• Classic and pleomorphic exhibit gains of 1q in the majority of cases
• Classic and pleomorphic have los of beta Catenin
• PLC is similar to high-grade IDC, with chromosomal gains on 8p, 8q, 13q and losses on 1p, 8p, 12p, 14q, 18q, 19p, and 19q
Molecular
## Patient and Tumor Characteristics (PLC vs. ILC)

<table>
<thead>
<tr>
<th></th>
<th>PLC (n=52)</th>
<th>ILC (n=298)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>59 (36-86)</td>
<td>61 (34-89)</td>
<td>0.300</td>
</tr>
<tr>
<td>Median tumor size, mm (range)</td>
<td>20(2-75)</td>
<td>15(1-90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multicentric/multifocal (%)</td>
<td>29 (58.0%)</td>
<td>147 (49.3%)</td>
<td>0.453</td>
</tr>
<tr>
<td>Lymphovascular invasion (LVI)</td>
<td>10(19.2%)</td>
<td>3(1.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median No. of positive nodes (range)</td>
<td>1(0-19)</td>
<td>0(0-37)</td>
<td>0.027</td>
</tr>
<tr>
<td>Number with positive nodes</td>
<td>30 (57.7%)</td>
<td>135 (45.3%)</td>
<td>0.132</td>
</tr>
<tr>
<td><strong>ER-positive</strong></td>
<td>50/52 (96.1%)</td>
<td>273/290 (94.1%)</td>
<td>0.749</td>
</tr>
<tr>
<td>Mastectomy rate (%)</td>
<td>33(63.5%)</td>
<td>115 (38.6%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

LVI, lymphovascular invasion; PLC, pleomorphic lobular carcinoma; ILC, invasive lobular carcinoma
What does this Really Mean
Roswell Park Cancer Institute Study

- PLC was in general larger at time of diagnosis and more likely to develop metastases than ILC and IDC.
- Rate of recurrence was higher for PLC (11.5%) vs ILC (3.7%)
- PLC had a recurrence free survival similar to IDC
Roswell Park Cancer Institute Study

• Conclusions:
  – PLC is a unique distinctive breast cancer
  – Morphology, negative E-cadherin, and lacking basal keratins similar to ILC
  – Aggressive clinical behavior, occasional HER2+ and triple negative, high rate of p53 reactivity resembling IDC
Follow-up, Recurrence and Disease Status Data (PLC vs. ILC)

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<th>ILC (n=298)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean follow-up, years (range)</td>
<td>3.8 (0-9.3)</td>
<td>4.4 (0.1-9.3)</td>
<td>0.076</td>
</tr>
<tr>
<td>Distant recurrence (%)</td>
<td>6(11.5%)</td>
<td>11(3.7%)</td>
<td>0.027</td>
</tr>
<tr>
<td>Any recurrence (%)</td>
<td>6 (11.5%)</td>
<td>15 (5.0%)</td>
<td>0.120</td>
</tr>
<tr>
<td>Time to 1st recurrence, years (range)</td>
<td>2.2 (0.2-4.2)</td>
<td>2.7 (1.5-4.0)</td>
<td>0.519</td>
</tr>
<tr>
<td>NED (%)</td>
<td>44 (84.6%)</td>
<td>273 (91.6%)</td>
<td>0.110</td>
</tr>
</tbody>
</table>

PLC, pleomorphic lobular carcinoma; ILC, invasive lobular carcinoma

## Patient and tumor characteristics (PLC vs. ILC)

<table>
<thead>
<tr>
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<th>PLC (n=7)</th>
<th>ILC (n=58)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>35-69</td>
<td>30-88</td>
<td>.20</td>
</tr>
<tr>
<td>Grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0/7</td>
<td>11/58</td>
<td>.59</td>
</tr>
<tr>
<td>II</td>
<td>5/7</td>
<td>47/58</td>
<td>.62</td>
</tr>
<tr>
<td>III</td>
<td>2/7</td>
<td>0/58</td>
<td>.01</td>
</tr>
<tr>
<td>LVI present</td>
<td>2/7</td>
<td>7/58</td>
<td>.25</td>
</tr>
<tr>
<td>Lymph node</td>
<td>Unknown</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>4/7</td>
<td>37/58</td>
<td>.70</td>
</tr>
<tr>
<td>N1a</td>
<td>1/7</td>
<td>12/58</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>N2a</td>
<td>0/7</td>
<td>2/58</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>N3a</td>
<td>2/7</td>
<td>3/58</td>
<td>.09</td>
</tr>
</tbody>
</table>

LVI indicates lymphovascular invasion

### Patient and tumor characteristics (PLC vs. ILC)

<table>
<thead>
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<th>Characteristic</th>
<th>PLC (n=7)</th>
<th>ILC (n=58)</th>
<th>P</th>
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<tbody>
<tr>
<td>ER $&gt; 1%$</td>
<td>4/7</td>
<td>All positive</td>
<td>.001</td>
</tr>
<tr>
<td>Her-2</td>
<td>All negative</td>
<td>All negative</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Ki-67 $&gt; 10%$</td>
<td>5/7</td>
<td>7/58</td>
<td>.002</td>
</tr>
<tr>
<td>Follow-up (median, 29mo)</td>
<td>None</td>
<td>1/7</td>
<td>.30</td>
</tr>
<tr>
<td>NED</td>
<td>5/7</td>
<td>51/58</td>
<td>.25</td>
</tr>
<tr>
<td>Metastases</td>
<td>1/7</td>
<td>4/58</td>
<td>.45</td>
</tr>
<tr>
<td>Deceased</td>
<td>0/7</td>
<td>1/58</td>
<td>&gt;.99</td>
</tr>
</tbody>
</table>

NED, no evidence of disease

Summary

- PLC is a unique variant of ILC
- It lacks E-cadherin generally, similarly to ILC
- Histologically it is similar to ILC
- It has more aggressive features similar to high grade IDC
- It has mixed molecular finding between ILB and IDC
Summary

• Distinguishing Pleomorphic Lobular carcinoma as a distinct variant of Classic Lobular carcinoma...

DOES MAKE A DIFFERENCE!
References


