Case history

• The patient is a 37 year old female with stage IIA invasive ductal carcinoma of the left breast diagnosed in July 2013.
• After lumpectomy and adjuvant chemotherapy, she underwent bilateral mastectomy and breast reconstruction surgery in February 2014.
• In April 2020, she presented with right breast swelling, and a fine needle aspiration was performed to rule out recurrent disease.

Disclosure

• No conflict of interest to disclose

Whole slide digital image - #10

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Cytomorphology (PAP stain)

Histomorphology (H&E cell block)
Immunohistochemistry (cell block)

Immunohistochemistry (cell block)

Immunohistochemistry (summary)

- Positive
  - CD30 (strong)
  - MUM1 (strong)
  - CD5 (large subset)
  - EMA (large subset)
  - CD43 (small subset)
  - TIA1 (focal)
  - Perforin (focal)
  - Granzyme B (focal)

- Negative
  - CD2
  - CD3
  - CD4
  - CD7
  - CD8
  - CD20
  - PAX5
  - ALK1
  - CD68
  - Pankeratin
  - HMB45

Diagnosis

- CD30-positive hematolymphoid malignancy consistent with breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)

Milestones on BIA-ALCL

### Incidence of BIA-ALCL

<table>
<thead>
<tr>
<th>Study</th>
<th>Years</th>
<th>n</th>
<th>Incidence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Boer et al. 2010</td>
<td>2000-2010</td>
<td>52</td>
<td>6.9-12.8</td>
</tr>
<tr>
<td>Wang 2006</td>
<td>2000-2012</td>
<td>2</td>
<td>46.4 (9.4-160)</td>
</tr>
<tr>
<td>Largent 2012</td>
<td>1996-2007</td>
<td>3</td>
<td>14.8 (5.8-40.7)</td>
</tr>
<tr>
<td>Doren 2017</td>
<td>1995-1999</td>
<td>130</td>
<td>2.0 (1.7-2.9)</td>
</tr>
<tr>
<td>Preadt 2013</td>
<td>2003-2018</td>
<td>0</td>
<td>0.0 (0.0)</td>
</tr>
<tr>
<td><strong>Summary</strong></td>
<td></td>
<td>176</td>
<td>3.2 (1.7-5.7)</td>
</tr>
</tbody>
</table>

Retrospective case-control studies from the Netherlands (de Boer), USA (Largent, Wang and Doren), Australia/New Zealand (Loch-Wilkinson) and Germany (Preadt)

### Implant and risk of BIA-ALCL

**Implant and risk of BIA-ALCL**

Prospective study from MSK:
- 3546 patients received textured breast implantation
- 10 developed BIA-ALCL
- Medium follow-up 8.1 years
- Overall risk 1/355 women or 0.311 cases per 1000 person-years (95% CI: 0.118-0.503)

[Condeiro PG et al, J Plastic Reconstr Aesthetic Surg (2020)]

**Implant and risk of BIA-ALCL**


### Microbiome and BIA-ALCL

[Hu H et al, Plast Reconstr Surg (2015)]

### Genetics of BIA-ALCL

[Hish N et al, Blood (2018)]
Clinicopathological features

- Mean age at diagnosis – about 50 years
- Interval from implantation to diagnosis varies from 2.2-44 years with a mean of 9 years.
- More frequently associated with textured than smooth shell surface implant
- Physical findings
  - Swelling, asymmetry or pain, usually unilateral
  - Peri-implant effusion or seroma most common (80%)
  - Mass lesion(s) around the implant (10-20%)
  - Loco-regional or systemic lymphadenopathy (rare)
- Genetic and epigenetic driver genes mutations
- Excellent prognosis with appropriate management

Pathology workup

- Diagnosis
  - Fine needle aspiration of fluid/effusion
    - Cytomorphology
      - Smear – Reparative and bright-Giemsa
      - H&E sections
      - Immunohistochemistry
    - Flow cytometry
    - T-cell receptor gene PCR
  - Incisional/needle core biopsy of mass
    - Histomorphology
    - H&E sections
    - Immunohistochemistry
    - Flow cytometry
    - T-cell receptor gene PCR
- Staging
  - En-block resection/total capsulectomy with explantation
  - Excision of extracapsular mass
  - Excision of lymph nodes
Diagnosis - cyto/histomorphology

Jaffe ES et al, J Clin Oncol (2020)
Tumer SD et al, Am J Pathol (2020)

Diagnosis - immunohistochemistry

Adapted from Quesada AE et al, Mod Pathol (2019)

Diagnosis - flow cytometry

Jaffe ES et al, J Clin Oncol (2020)

Diagnosis - T-cell receptor gene PCR

Lee A et al, JCEP (2010); Quesada AE et al, Mod Pathol (2019)

Differential diagnosis

- Hematolymphoid malignancies
  - Systemic ALCL - ALK-positive and ALK-negative
  - Primary cutaneous ALCL
  - Extranodal NK/T cell lymphoma
  - Plasmablastic lymphoma
  - (Extracavitary) Primary effusion lymphoma
  - Diffuse large B-cell lymphoma

- Non-hematolymphoid malignancies
  - Metastatic carcinoma
  - Metastatic melanoma
  - Sarcoma

Pathology workup

- Diagnosis
  - Fine needle aspiration of fluid/effusion
    - Cytomorphology
    - Smear – Preparation and Wright-Giemsa stains
    - H&E sections
    - Immunohistochemistry
  - Flow cytometry
  - T-cell receptor gene PCR
- Incisional/needle core biopsy of mass
  - Histomorphology
  - H&E sections
  - Immunohistochemistry
  - Flow cytometry
  - T-cell receptor gene PCR

- Staging
  - En-bloc resection/total capsulectomy with explantation
  - Excision of extracapsular mass
  - Excision of lymph nodes
Staging of BIA-ALCL

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Infiltration of implant or subcutaneous tissue</td>
</tr>
<tr>
<td>T2</td>
<td>Infiltration of breast tissue</td>
</tr>
<tr>
<td>T3</td>
<td>Infiltration of skin</td>
</tr>
<tr>
<td>T4</td>
<td>Infiltration of muscle</td>
</tr>
</tbody>
</table>

Staging of BIA-ALCL

Patient follow-up

- Bilateral capsulectomy with implant removal (no residual lymphoma, stage 1A) and re-construction in May 2020.
- PET from skull to abdomen shows s/p bilateral mastectomy with breast implants in place and low level homogenous activity around the implants.
- No evidence of disease recurrence at her last clinic visit on July 17, 2020.
Other seroma-associated ALCL

- Tibial implant-associated ALCL
- Dental implant-associated ALCL/MCU
- Chest port-associated ALCL
- Bariatric implant-associated ALCL
- Gluteal implant-associated ALCL


Selective references

- De Boer et al. JAMA Oncol 2018;4(3): 335-41
- Lyapichev KA et al. Mod Pathol 2020; 33: 367-79
- Prantl L et al. J Clin Med 2020; 9, 1247
- Quesada AE et al. Mod Pathol 2019; 32: 166-88
- Walker JN et al. Scientific Reports 2019; 9: 10391