OVERVIEW OF BREAST IMPLANT-ASSOCIATED ANAPLASTIC LARGE CELL LYMPHOMA (BIA-ALCL)

Definition
- BIA-ALCL is an uncommon and emerging peripheral T-cell lymphoma (PTCL) most frequently arising around a textured surface breast implant or in a patient with a history of a textured surface device.\textsuperscript{a}
- BIA-ALCL commonly presents with delayed periprosthetic effusion and breast asymmetry occurring greater than one year (average 7–9 years) after implantation. Rarely, BIA-ALCL can present with a mass, regional lymphadenopathy, overlying skin rash, and/or capsular contracture.
- The majority of patients with BIA-ALCL exhibit an indolent clinical course with slow progression of disease and an excellent prognosis.
- Regional lymph node metastasis and more rarely distant organ and bone marrow metastasis may be seen in advanced stages.\textsuperscript{b}

Diagnosis
- Tumor cells are CD30+, ALK-, large anaplastic morphology on cytology, and demonstrate a single T-cell clone.\textsuperscript{c}
- The histopathologic findings of BIA-ALCL need to be correlated with a clinical presentation and history of a breast implant to achieve a definitive diagnosis.\textsuperscript{d}
- Diagnosis from effusions requires a sufficient volume of fluid (minimum 50 mL) to achieve diagnosis. Prior serial aspirations may decrease or dilute tumor burden and make diagnosis more challenging; therefore, pathology review of the first aspiration is advisable.
- Multiple systematic scar capsule biopsies may be necessary to determine early invasive disease and mass formation, which have implications for prognosis.\textsuperscript{e}
- Secondary review by a tertiary referral center is recommended for equivocal pathology.

GENERAL PRINCIPLES OF BIA-ALCL
- A multidisciplinary team approach involving lymphoma oncology, surgical oncology, hematopathology, and plastic surgery is often optimal for the management of patients with BIA-ALCL, particularly those with advanced disease.
- Given the rarity of the disease, the U.S. FDA recommends reporting of cases to national disease registries for tracking of cases. (www.thepsf.org/PROFILE)
- Goals of therapy should be individualized but often include:
  - Generally, complete surgical resection alone of the implant, capsule, and associated mass is used in earlier stage disease confined to the periprosthetic scar capsule.\textsuperscript{f}
  - May consider immediate (early stage) or delayed (advanced stage) breast reconstruction with autologous tissue or smooth surface breast implants.\textsuperscript{g}
  - Local disease relapse may be amenable to re-excision surgery alone without requiring systemic therapies. See Clinical Presentation (BIAA-1)


Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
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Breast Implant-Associated ALCL

CLINICAL PRESENTATION
- Physical signs (effusion, enlargement, mass, ulceration) >1 year post implantation (Average 7-9 years post-implantation)

INITIAL WORKUP
- Ultrasound of breast or Breast MRI in selected cases or PET/CT scan in selected cases
- Any effusion
- FNA of fluid around breast implant
  - Mass
  - Biopsy of mass
  - Ultrasound inconclusive
  - Breast MRI, if not previously done

PATHOLOGIC WORKUP
- ESSENTIAL:
  - Cytology with cell block preparation
  - IHC and/or flow cytometry for CD2, CD3, CD4, CD5, CD7, CD8, CD30, CD45, and ALK
- USEFUL UNDER CERTAIN CIRCUMSTANCES:
  - If there is a solid mass associated with the implant, biopsy (excisional or incisional or core needle) may be required for diagnosis
- Histologic confirmation or suspicious of BIA-ALCL
  - See BIAA-2

If indeterminate of lymphoma
- Second pathology consultation by tertiary cancer center
- Negative for lymphoma
- Refer to plastic surgeon for management

See References on BIAA-A

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### Breast Implant-Associated ALCL

#### LYMPHOMA WORKUP AND STAGING

- Recommend discussion of treatment options with multidisciplinary team
- H&P exam, including complete skin exam
- CBC with differential
- Comprehensive metabolic panel
- LDH
- PET/CT scan
- Echocardiogram or MUGA scan if anthracycline-based regimen is indicated
- Pregnancy testing in women of child-bearing age (if chemotherapy or RT planned)

#### TREATMENT

- Total capsulectomy and excision of associated mass with biopsy of suspicious node(s), explanation
- Consider removal of contralateral implant
- Consultation with surgical oncologist recommended for patients with preoperative tumor mass

#### FOLLOW-UP

- Observation
  - H&P for every 3–6 mo for 2 y and then as clinically indicated
  - ± C/A/P CT with contrast or PET/CT scan as clinically indicated
- Complete excision with no residual disease
- Localized disease to capsule/implant/breast
- Incomplete excision or partial capsulectomy with residual disease ± regional lymph node involvement

### Extended disease (stage II–IV)

- Consider systemic therapy (alphabetical order)
  - Brentuximab vedotin
  - Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone)
  - CHOP
  - CHOP
  - Dose-adjusted EPOCH

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Proposed TNM Staging for Breast Implant–Associated Anaplastic Large-Cell Lymphoma

<table>
<thead>
<tr>
<th>TNM</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T: tumor extent</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Confined to effusion or a layer on luminal side of capsule</td>
</tr>
<tr>
<td>T2</td>
<td>Early capsule infiltration</td>
</tr>
<tr>
<td>T3</td>
<td>Cell aggregates or sheets infiltrating the capsule</td>
</tr>
<tr>
<td>T4</td>
<td>Lymphoma infiltrates beyond the capsule</td>
</tr>
</tbody>
</table>

| N: lymph node                          |
| N0 | No lymph node involvement               |
| N1 | One regional lymph node (+)             |
| N2 | Multiple regional lymph nodes (+)       |

| M: metastasis                         |
| M0 | No distant spread                      |
| M1 | Spread to other organs/distant sites    |

<table>
<thead>
<tr>
<th>Stage Designation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>T1 N0 M0</td>
</tr>
<tr>
<td>IB</td>
<td>T2 N0 M0</td>
</tr>
<tr>
<td>IC</td>
<td>T3 N0 M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T4 N0 M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T1–3 N1 M0</td>
</tr>
<tr>
<td>III</td>
<td>T4 N1–2 M0</td>
</tr>
<tr>
<td>IV</td>
<td>T any N any M1</td>
</tr>
</tbody>
</table>


2 Bilateral breast implantation for ALCL is not considered in this staging system. Complete excision of bilateral disease may be recommended if it is determined that 2 independent primaries are present (one on each side). Pathologic staging should be assessed in both sides. Identification of clonal abnormalities in bilateral cases is desirable and may help in determining if the disease represents metastasis.

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