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.[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.[b]**

Diagnosis

- **Tumor cells are CD30+, ALK-, large anaplastic morphology on cytology, and demonstrate a single T-cell clone.[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.[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.[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.[f]**
  - **May consider immediate (early stage) or delayed (advanced stage) breast reconstruction with autologous tissue or smooth surface breast implants.[g]**
  - **Local disease relapse may be amenable to re-excision surgery alone without requiring systemic therapies.**

See Clinical Presentation (BIAA-1)

[a] Mehta-Shah N, Clemens MW, Horwitz SM. How I treat breast implant-associated anaplastic large cell lymphoma. Blood 2018;132:1889-1898.
[b] Collins MS, Miranda RN, Medeiros LJ, et al. Characteristics and treatment of advanced breast implant-associated anaplastic large cell lymphoma. Plast Reconstr Surg 2019;143(3S):41S-50S.
[c] Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016,127:2375-2390.
[d] Quesada AE, Medeiros LJ, Clemens MW, et al. Breast implant-associated anaplastic large cell lymphoma: A review. Mod Pathol 2019;32:166-188.
[e] Lyapichev KA, Pina-Oviedo S, Medieros LJ, et al. A proposal for pathologic processing of breast implant capsules in patients with suspected breast implant anaplastic large cell lymphoma. Mod Pathol 2019 [Epub ahead of print]
[f] Clemens MW, Medeiros LJ, Butler CE, et al. Complete surgical excision is essential for the management of patients with breast implant-associated anaplastic large cell lymphoma. J Clin Oncol 2016;34:160-168.
[g] Lamaris GA, Butler CE, Deva AK, et al. Breast reconstruction following breast implant-associated anaplastic large cell lymphoma. Plast Reconstr Surg 2019;143(3S):51S-58S.

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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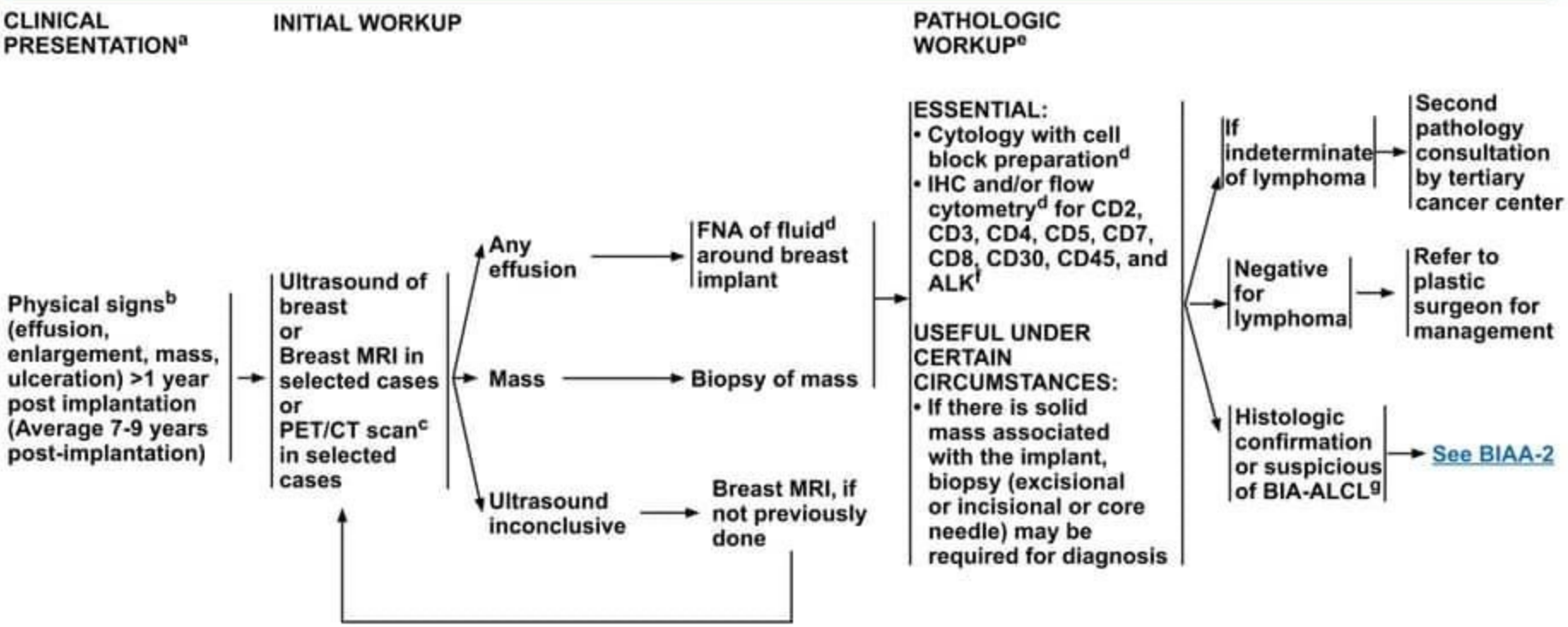

See References on BIAA-A

[a] Rare cases with parenchymal breast or nodal involvement may have an aggressive course more in line with systemic ALK-positive ALCL (See TCEL-3). Optimal treatment of these cases is not well defined and management should be individualized.
[b] A majority of cases have been seen in textured implants (Miranda RN, et al. J Clin Oncol 2014;32:114-120).
[c] Patients with T-cell lymphomas often have extranodal disease, which may be inadequately imaged by CT. PET scan may be preferred in these instances.
[d] Larger volume of fluid yields a more accurate diagnosis. If possible, obtain >50 mL for cytology and cell block; >10 mL for flow cytometry immunophenotype.
[e] See Principles of Molecular Analysis in T-Cell Lymphomas (LYMP-A).
[f] Breast implant-associated ALCL (BIA-ALCL) is usually ALK-negative but has a good prognosis.
[g] The FDA recommends reporting all BIA-ALCL cases to the PROFILE Registry: www.thepsf.org/PROFILE.

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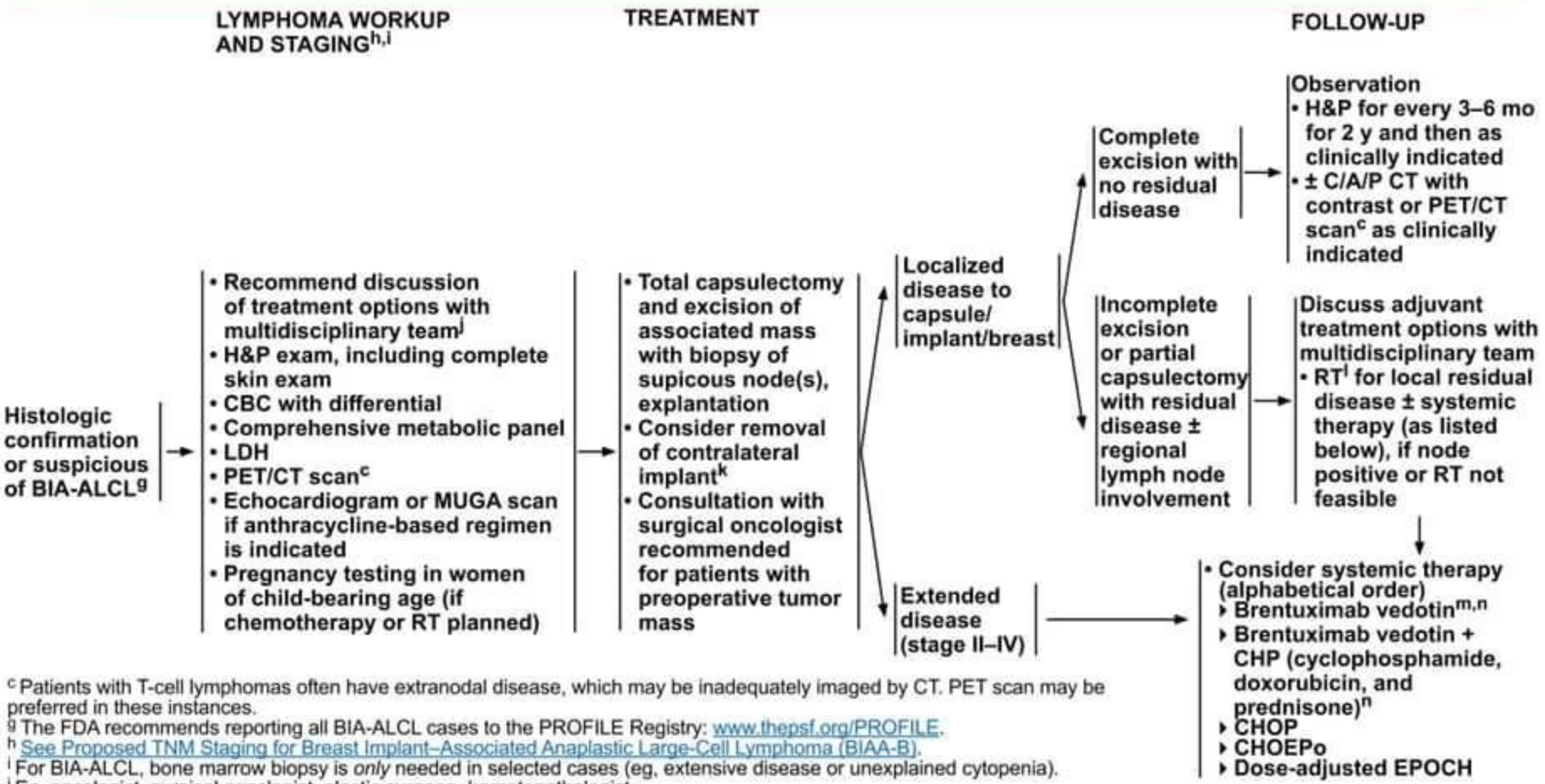

[c] Patients with T-cell lymphomas often have extranodal disease, which may be inadequately imaged by CT. PET scan may be preferred in these instances.
[g] The FDA recommends reporting all BIA-ALCL cases to the PROFILE Registry: www.thepsf.org/PROFILE.
[h] See Proposed TNM Staging for Breast Implant–Associated Anaplastic Large-Cell Lymphoma (BIAA-B).
[i] For BIA-ALCL, bone marrow biopsy is *only* needed in selected cases (eg, extensive disease or unexplained cytopenia).
[j] Eg, oncologist, surgical oncologist, plastic surgeon, hematopathologist.
[k] In approximately 4.6% of cases, lymphoma was found in the contralateral breast (Clemens MW, Medeiros LJ, Butler CE, et al. J Clin Oncol 2016;34:160-168).
[l] See Principles of Radiation Therapy (LYMP-D).
[m] Brentuximab vedotin may be appropriate for low burden disease in selected patients.
[n] See Supportive Care (LYMP-B).
[o] Oral etoposide dose of 200 mg/m^2 (PO dosing of etoposide is 2x the IV dose) may be substituted on days 2 and 3 for IV etoposide. Consider splitting the daily doses of oral etoposide over 200 mg.

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Proposed TNM Staging for Breast Implant–Associated Anaplastic Large-Cell Lymphoma[1,2]

TNM	Description
T: tumor extent	
T1	Confined to effusion or a layer on luminal side of capsule
T2	Early capsule infiltration
T3	Cell aggregates or sheets infiltrating the capsule
T4	Lymphoma infiltrates beyond the capsule
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

Stage Designation	Description
IA	T1 N0 M0
IB	T2 N0 M0
IC	T3 N0 M0
IIA	T4 N0 M0
IIB	T1–3 N1 M0
III	T4 N1–2 M0
IV	T any N any M1

[1] Clemens MW, Medeiros LJ, Butler CE, et al. Complete surgical excision is essential for the management of patients with breast implant-associated anaplastic large-cell lymphoma. J Clin Oncol 2016;34:160-168.

[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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