

Frequently Asked Questions (FAQ): A Guide to Breast Implant-Associated Anaplastic Large Cell Lymphoma

Breast implant-associated Anaplastic Large Cell Lymphoma (BIA-ALCL) is a rare cancer that can develop around breast implants (Fig. 1). In January 2011, the US Food and Drug Administration (FDA) released a statement that women with breast implants “may have a very small but increased risk of developing” anaplastic large cell lymphoma.¹ An update in 2016 reported that 258 BIA-ALCL adverse event reports have been received to the FDA, and emphasized that physicians should report all confirmed cases to both the FDA and the PROFILE registry. This has understandably created concern among the plastic surgery community as well as among the patients we treat. However, the FDA confirms that breast implants have a reasonable assurance of safety and efficacy.¹ Additional research is critical to identify patients at risk of developing this disease, characterize the early signs and symptoms, and determine best practices for treatment. Physicians must be aware of this rare disease to ensure that patients are treated appropriately and in a timely manner. The following summary of frequently asked questions (FAQ) and answers about BIA-ALCL serves as a starting point to facilitate a discussion in our plastic surgery community.

About the disease

Q: What is Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL):

This is a rare form of lymphoma, a cancer of the immune system developing from lymphocytes, and is a malignancy of the blood.^{2,3} BIA-ALCL is a distinct type of ALCL involving the capsule or effusion surrounding a breast implant. On average, BIA-ALCL occurs at a mean of eight years following implantation. Some unique technical characteristics include that it is most commonly a purely T-cell lymphoma, does not have an anaplastic lymphoma kinase gene translocation (ALK -), and is CD30 receptor protein positive on immunohistochemistry (Fig.2).⁴

Q: How common is BIA-ALCL?

There are an estimated 10 to 11 million women worldwide with breast implants. While total numbers vary in the literature, 118 distinct cases have been reported, and MD Anderson Cancer Center recognizes 160 cases worldwide of pathologically confirmed BIA-ALCL to date from fifteen countries. Less than ten patients are diagnosed per year with this disease. The only epidemiological study demonstrating an association between breast implants and BIA-ALCL estimated an incidence of 1 in 300,000.⁵ However, determining the true incidence will be dependent upon improved physician awareness and reporting as well as formal disease recognition.

Q: Should BIA-ALCL be included on surgical consent forms?

Following recommendations made by the FDA in 2011, implant manufacturers added language warning of the existence of BIA-ALCL to all breast implant package inserts within the United States and Canada. The American Society of Plastic Surgeons (ASPS) includes the risk of BIA-ALCL in breast implant informed consents. Examples of informed consents are available for download from the website, www.plasticsurgery.org. Therefore, the recommendation is that surgeons should consider including BIA-ALCL in breast implant informed consents. Discussion with breast implant patients can include the existence

of BIA-ALCL, common presenting symptoms such as a mass or delayed seroma/effusion, and to see their physician if these symptoms occur.

Symptoms

Q: How would I know if I had a case of BIA-ALCL?

Patients receiving an implant should be aware of common presenting symptoms such as a spontaneous seroma or effusion after one year from implantation (Fig. 3). Although common causes of a delayed seroma are infection or trauma, suspicious effusions should receive a fine needle aspiration sent for pathologic review. A complete physical examination will help detect the one in eight cases that present with lymphadenopathy. Ideally, the diagnosis should be made prior to surgical exploration to allow for proper oncologic workup.

Risks Factors

Q: Are there any modifiable risk factors that make a patient more susceptible to BIA-ALCL?

At this time, there are no known modifiable risk factors or specific patient populations known to be at a higher risk of developing this disease. There is roughly an even number of aesthetic cosmetic and reconstructive breast implant patients, and both saline and silicone implants are involved with a few reported polyurethane implants. However, the vast majority of known involved devices have been in textured, rather than smooth, implants. Recent studies have demonstrated a possible pathogenic mechanism of chronic T-cell stimulation with local antigenic drive, ultimately leading to the development of lymphoma.^{6,7} Preliminary reports have hypothesized a role for chronic biofilm leading to malignant degeneration⁸, and therefore standard of care precautions such as antibiotic prophylaxis, antibiotic irrigation, sterility, and skin preparation should all be maintained when placing an implant.^{9,10,11} The FDA does not recommend screening or prophylactic implant removal for asymptomatic patients or patients with familial susceptibility.¹

Q: What do I do if I have a suspected case of ALCL?

For suspicious cases, patients should receive an ultrasound evaluation to confirm the presence and extent of an effusion, determine if there is presence of a mass, and evaluate regional lymph node basins for lymphadenopathy. Fine needle aspiration is performed of an effusion, which is sent to an experienced hematopathologist for culture, flow cytometry, and cytology. It is critical to include a clinical history and to direct the pathologist to “rule out BIA-ALCL” as well as to perform CD30 surface protein immunohistochemistry.¹² Ultrasound is an acceptable screening tool for the two-thirds of patients presenting with an effusion or the one-third with a mass.¹³ PET/CT and MRI are reserved for confirmed cases and there does not appear to be a role for mammography.

Confirmed Cases

Q: What are the essential studies performed for the preoperative evaluation after confirming a case?

Physicians are strongly encouraged to include a lymphoma oncologist for medical management and future disease surveillance. Preoperative evaluation includes a bone marrow biopsy to distinguish from other

systemic forms of ALCL, which have a more aggressive clinical course and poor prognosis. Patients should also receive a preoperative PET/CT scan to evaluate for baseline extent of disease, masses, and involved lymph nodes. Physicians with confirmed cases have a responsibility to report their cases to the PROFILE Registry, a collaboration between the US FDA and The Plastic Surgery Foundation, which can be found at www.thepsf.org/PROFILE.

Treatment

Q: How should I manage a confirmed case of BIA-ALCL?

Definitive treatment for most patients is removal of the implants and total capsulectomy, which includes complete resection of any mass associated with the capsule (Fig. 4).¹⁴ Physicians should consider possible removal of contralateral breast implants with capsulectomy as several bilateral cases have been detected incidentally. The implant, capsule, and effusion should all be sent to pathology for evaluation. Suspicious lymph nodes should also be excised. At this time, there does not appear to be a role for routine sentinel lymph node biopsy or for full axillary dissection if no clinically positive nodes are present. Surgeons are strongly encouraged to include a *surgical oncologist* for resection of disease as well as resection of involved lymph nodes. Surgery should be performed with strict oncologic technique including use of specimen orientation sutures and placement of surgical clips within the tumor bed. Complete surgical resection may be sufficient treatment for the majority of patients. The role for further adjunctive therapy such as chemotherapy (CHOP regimen: cyclophosphamide, doxorubicin, vincristine, prednisolone), clinical trials of targeted immunotherapy (Brentuximab vedotin), and chest wall radiation therapy for unresectable tumors or positive margins is the subject of ongoing research.

Q: How should BIA-ALCL patients be reconstructed?

Ideal type and timing of reconstruction remains controversial. Replacement of textured implants is not advised in a patient that has already demonstrated a propensity for malignant degeneration. Placement of smooth implants has been performed without reported progression or recurrence of disease however the safety of this strategy is still being investigated. Autologous reconstructions that do not require a breast implant are advisable. Reconstruction is suggested following a sufficient (one year) surveillance period to confirm complete eradication of the disease.

Prognosis

Q: What is the prognosis of patients that are diagnosed with BIA-ALCL?

The disease course is commonly indolent and the majority of patients may be adequately treated with complete capsulectomy and implant removal. *Even if appropriately treated*, however aggressive variants have been reported which include lymph node metastases and death. The presence of a mass has a slightly higher but significant disease recurrence and progression (Fig.5).¹⁵

Q: How are patients followed for surveillance of BIA-ALCL?

Confirmed cases of BIA-ALCL that have been adequately treated are followed with serial PET/CT scans and physical examination every 6 months for approximately 2-4 years. An experienced lymphoma oncologist ideally performs surveillance.

Further Reading

Q: Where can I learn more about this rare cancer and what can I do to help?

Many resources exist for oncologists and surgeons treating a BIA-ALCL patient, and a number of credible online resources are available such as the FDA recommendations which are posted on the www.fda.gov website. Physician and patient resources can be found on the MD Anderson Cancer Center website <http://www.mdanderson.org/> to introduce BIA-ALCL patients to a supportive community where they may receive insights and potential leads on developing therapies. Most importantly, physicians with confirmed cases of BIA-ALCL have a responsibility to report and share their cases with our national societies as information gathered from every single case brings us closer to a cure. The Plastic Surgery Foundation, the American Society of Plastic Surgeons and the FDA have created the PROFILE Registry (Patient Registry and Outcomes For breast Implants and anaplastic large cell Lymphoma etiology and Epidemiology) to increase the scientific data on BIA-ALCL, to support research characterizing BIA-ALCL, and to elucidate the role of breast implants in the etiology of the disease. Treating physicians are encouraged to report confirmed cases to the PROFILE Registry at www.thepsf.org/PROFILE.

Disclaimer

This document was developed to assist physicians in clinical decision making and was developed through a review of the scientific literature and consideration of relevant clinical experience, and describes a range of generally acceptable approaches to diagnosis, management, or prevention of specific diseases or conditions. This document attempts to define principles of practice that should generally meet the needs of most patients in most circumstances.

However, this document should not be construed as a rule, nor should it be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the appropriate results. It is anticipated that it will be necessary to approach some patients' needs in different ways. The ultimate judgment regarding the care of a particular patient must be made by the physician in light of all the circumstances presented by the patient, the available diagnostic and treatment options, and available resources.

This document is not intended to define or serve as the standard of medical care. Standards of medical care are determined on the basis of all the facts or circumstances involved in an individual case and are subject to change as scientific knowledge and technology advance and as practice patterns evolve. This document reflects the state of current knowledge at the time of publication. Given the inevitable changes in the state of scientific information and technology, this document will be reviewed, updated and revised periodically.

Resources

The Plastic Surgery Foundation, PROFILE Registry: www.thepsf.org/PROFILE

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United States Food and Drug Administration, Preliminary Findings and Analyses: <http://www.fda.gov/>

US National Cancer Institute, Treatment for health professionals: <http://www.cancer.gov/>

Example Figures

Figure 1: Breast Implant-Associated Anaplastic Large Cell Lymphoma with characteristic reniform shaped nuclei, abundant vacuoles, and anaplastic morphology.

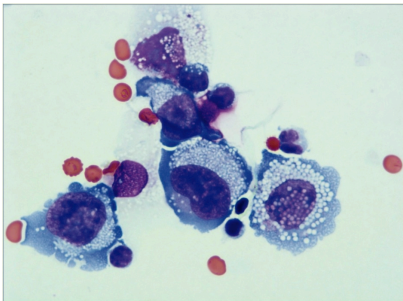


Figure 2: Example of immunohistochemistry (IHC) staining for CD30 cell membrane protein (TNF receptor family). CD30 staining is characteristic of ALCL.

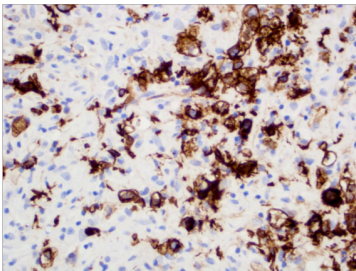


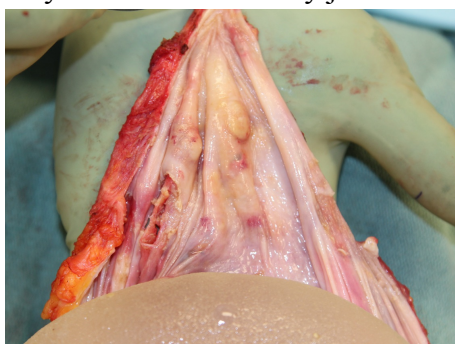
Figure 3: Patient presenting with a large effusion of the right breast seven years after receiving a breast implant for breast cancer reconstruction. Fine needle aspiration confirmed the diagnosis of BIA-ALCL.



Figure 4: Example of a total capsulectomy with removal of an implant, associated effusion and capsule as one specimen with negative margins. Orientation sutures are used to assist with pathologic evaluation.



Figure 5: Example of capsular lining in a patient with nodular disease of BIA-ALCL. Note some patients may have a mass or may just have disease isolated to the peri-prosthetic effusion.

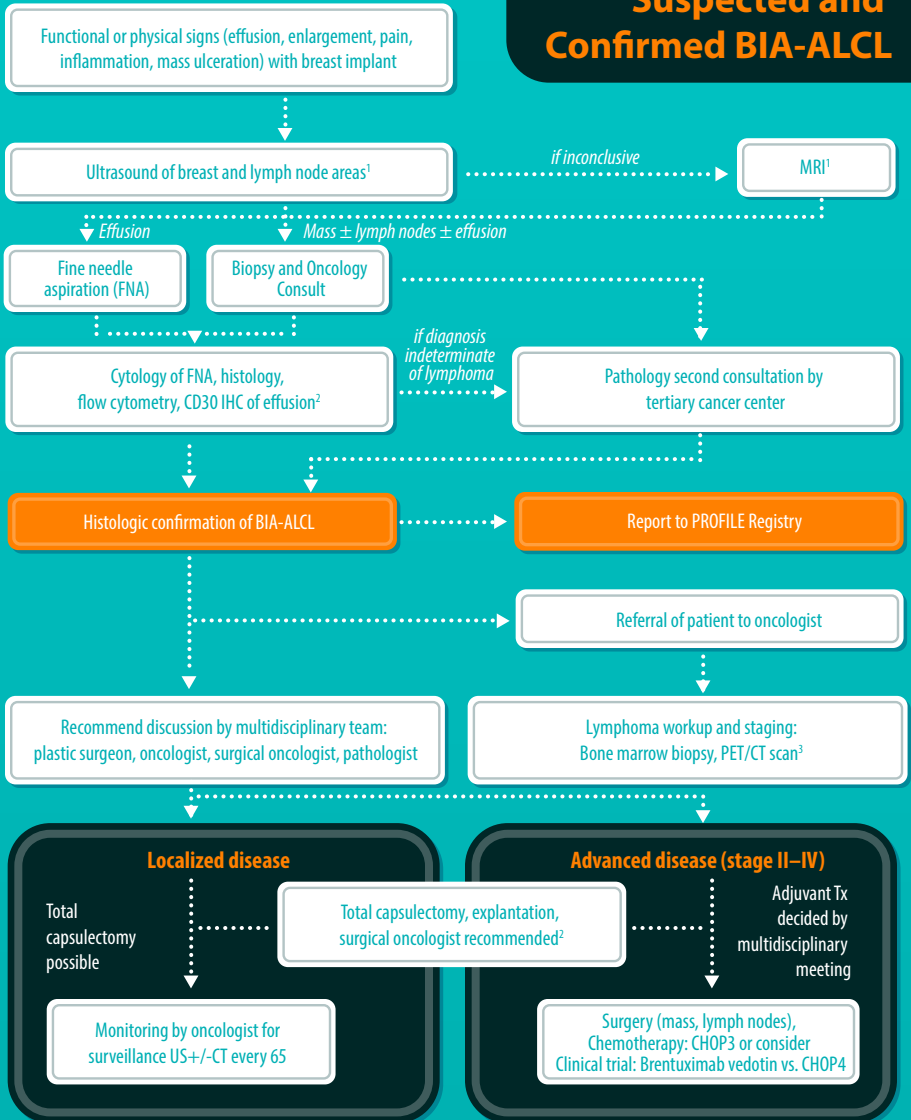


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Management of Suspected and Confirmed BIA-ALCL



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