



Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

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Accepted: 18 April 2024 / Published online: 25 June 2024

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Abstract

Purpose of Review This review aims to provide a comprehensive overview of the current understanding of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), including its incidence, risk factors, clinical presentation, and diagnostic criteria. The aim is to enhance awareness among healthcare professionals and patients about BIA-ALCL, its management strategies, and the importance of surveillance in individuals with breast implants.

Recent Findings Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare form of T cell lymphoma characterized by the presence of the CD30 biomarker. Although BIA-ALCL is more prevalent than other primary breast lymphomas, its incidence rate is extremely low. Textured implants have been associated with nearly all instances of BIA-ALCL. A significant proportion of BIA-ALCL patients exhibit an excellent prognosis after the extraction of the implants and capsules. Unfavorable outcomes are seen in instances of tumor bulk and implant capsule invasion.

Summary This review provides an in-depth understanding of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), focusing on its incidence, risk factors, clinical presentation, diagnostic criteria, and imaging evaluation. BIA-ALCL management techniques, treatment modalities, effectiveness, and outcomes are examined to improve patient care and awareness.

Keywords Breast implant · Textured implants · Lymphoma · Anaplastic large cell lymphoma · BIA-ALCL

Introduction

Breast surgery may result in psychosexual morbidity. Breast reconstruction has played a crucial role in the restoration of feminine identity and self-esteem among women who have undergone breast surgery [1•]. One common approach to breast reconstruction is the use of implants, which are used

on a global scale in both breast augmentation and reconstruction procedures [1•, 2]. Breast-implant based reconstruction may be performed in several stages, including an initial tissue expander placement followed by an exchange for a permanent implant [3]. Tissue expanders and breast implants can be smooth or textured. Textured surfaces maximize tissue ingrowth to improve the stability of the breast pocket and improve aesthetic outcomes [4]. Textured tissue expanders prevent port rotation and maintain the fluid injection direction. Implant contraction and migration have been mitigated with the use of textured implants [5••].

Textured implants have been linked to breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), a treatable non-Hodgkin type T cell lymphoma positive for CD30 biomarker [1•, 6]. BIA-ALCL was first described in the 1997 by John Keech Jr. and Brevator Creech [7••]. Reported cases are split equally between cosmetic and reconstructive surgery patients, which may suggest that prior malignancy is not an independent risk factor [1•]. Textured implants were first introduced in the late 1980s, and no cases of BIA-ALCL were documented prior to the textured implant era [2]. Although ALCL of the breast has been reported in both women with and without breast implants, a study by de Jong et al. established that implants increased the risk by a factor of 18 [2].

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In 2016, the World Health Organization (WHO) provisionally recognized BIA-ALCL as a distinct lymphoma and established National Comprehensive Cancer Network (NCCN) guidelines to delineate the detection, treatment, and care for patients with BIA-ALCL [8]. Allergan Corporation's Biocell textured implants were the subject of a class I device recall by the U.S. Food and Drug Administration (FDA) in July 2019. Additionally, Allergan issued a voluntary global recall of its textured surface breast tissue implants and expanders [1•, 8].

Most cases of BIA-ALCL have an acute onset, and if diagnosed and treated promptly, follow an indolent clinical course [1•]. Treatment may include exploration with capsulectomy, chemotherapy, and radiation [2]. Because the median onset of BIA-ALCL is more than a decade after initial breast tissue implantation, there may be a delay in diagnosis for these patients [6]. The FDA recommends periodic magnetic resonance imaging (MRI) to monitor for ruptures following silicone implants but does not address saline implants [3]. Due to insufficient follow-up of the implanted devices, a lack of knowledge about the condition, or insufficient training or expertise among medical professionals in examining breast implants, there may be a delay and/or error in the diagnosis of BIA-ALCL [3]. Thus, it is crucial for healthcare professionals to understand the complexity and long-term implications of the disease in this patient population.

Epidemiology

Anaplastic Large Cell Lymphoma (ALCL) is a rare form of non-Hodgkin lymphoma. Additionally, breast lymphomas comprise approximately 1 to 2 percent of all extranodal lymphomas and approximately 0.04 to 0.5 percent of all breast malignancies [9]. The reported incidence of BIA-ALCL varies in literature, from 1 in 355 patients to 1 in 30,000 patients [10]. This variability is likely linked to lack of global reporting, incomplete breast implant sales data, relative rarity of the disease, or long initial implant to onset exposure times [1•, 10].

Most case series report BIA-ALCL onset at a median exposure time of 7.5 to 11 years, although shorter onset times (0.4–2 years) have been reported [10]. Nelson et al. reported an estimated incidence of 1.79 per 1000 patients and 1.15 per 1000 implants for development of BIA-ALCL [10]. The cumulative incidence was 6.66 per 1000 implants beyond 14 to 16 years [10].

Pathogenesis

Anaplastic large cell lymphoma (ALCL) is a type of non-Hodgkin lymphoma characterized by the presence of large anaplastic lymphoid cells that express the cell-surface

protein CD30 [2, 6]. The WHO further classifies ALCL into two major variants, one of which expresses anaplastic lymphoma kinase (ALK) protein and the other that does not, which is more aggressive in nature [2]. Having a positive ALK protein occurs in 60–80% of systemic ALCL (sALCL) cases, whereas the remaining sALCL cases are characterized by specific gene rearrangements, including *Dusp22* and *TP63* [1•]. BIA-ALCL, a pure T-cell lymphoma, is a subset of systemic ALCL that is Triple Negative (ALK-, *Dusp22*-, *TP63*-) and CD30 positive [1•, 2, 3, 6].

BIA-ALCL arises in the capsule or the fluid surrounding the breast implant [2]. The proposed pathogenesis for the development of BIA-ALCL complex involves the textured implant surface invoking an immune response, chronic inflammation, and bacterial biofilm growth [3]. With textured implants, tissue growth into the implant pores may prolong chronic inflammation [3]. Chronic inflammation leads to extensive immune cell clonal expansion and lymphomagenesis in a genetically susceptible individual [1•]. Additionally, the time for development of BIA-ALCL is consistent with the time needed for a chronic bacterial biofilm to produce an immune activation, chronic inflammation, and subsequent malignant cell transformation [3]. BIA-ALCL cells have been pathologically classified as CD30+, which traditionally marks activated B and T cells, and epithelial membrane antigen positive [1•, 3].

Other proposed mechanisms for BIA-ALCL development include allergen driven carcinogenesis: from contaminants derived from the implant surface or from the operating suite [1•]. Genetics may also be a risk factor for disease development, with oncogenic mutations in *TP53*, *DNMT3A*, and the *JAK-STAT3* pathway noted in patients with BIA-ALCL [1•, 3]. Additional proposed oncogenic drivers include chronic trauma to the breast pocket or viral infections [1•].

Presentation and Spectrum of Disease

The mean age at onset of BIA-ALCL is 51 years, with breast reconstruction patients being older compared with cosmetic surgery patients (57 vs 46 years of age) [3]. Most patients are initially seen with a seroma, and the most common clinical presentation is a late peri-implant fluid collection [3, 8]. Patients may present with a mass, both a mass and seroma, with capsular contracture, axillary lymphadenopathy, skin lesions, or B type symptoms (fever, night sweats, and weight loss) [3]. Right and left breasts are affected equally and patients with silicone implants are affected more than those with saline implants (61% vs. 39%) [3]. If left untreated, cells within the seroma fluid may coalesce and present as a solid mass [1•]. There are two distinct histological subtypes of BIA-ALCL, in-situ

and infiltrative disease: in-situ disease remains confined within the breast implant capsule, whereas the infiltrative subtype extends into or beyond the fibrous capsule [1•].

Diagnostic Workup and Treatment

Generally, BIA-ALCL has a favorable prognosis when diagnosed and treated promptly [1•]. Accurate imaging assessment of BIA-ALCL is challenging with multiple imaging modalities used in clinical practice [11–14]. Patients suspected to have BIA-ALCL are usually first evaluated with breast ultrasound. The most common ultrasound finding is a peri-implant fluid collection, which sometimes may be associated with an irregular contour of the implant capsule, or a well-circumscribed, hypoechoic, typically low vascularity mass. Complex cystic masses with or without per-implant fluid are a less common finding on breast ultrasound. For a definitive diagnosis, ultrasound-guided aspiration of peri-implant fluid with flow cytometry or a needle biopsy of the mass are performed [11, 12, 15].

Breast MRI is a second-line modality for BIA-ALCL diagnosis if breast ultrasound results are indeterminate. Breast MRI should be performed with intravenous administration of gadolinium contrast. Peri-implant fluid with or without capsular enhancement is the most common MRI finding, followed by presentation as enhancing soft tissue mass. Advantages of breast MRI include the evaluation of the extent of disease and the ability to rule out involvement of the chest wall [13, 15–17].

Whole body imaging techniques such as CT and PET-CT have been also used to evaluate patients with suspected BIA-ALCL. On CT imaging, peri-implant fluid usually presents as non-enhancing fluid with or without capsular abnormality. BIA-ALCL presenting as a mass usually is seen on CT as a diffusely enhancing mass partially surrounding the breast implant with or without associated fluid. CT imaging offers the additional advantages of locoregional staging and the evaluation of the distant extent of the disease [11, 15].

PET-CT is a whole-body functional imaging that is modality of choice for initial evaluation, staging and treatment response assessment of patients with different types of lymphoma. PET-CT shows increased FDG uptake in BIA-ALCL with pericapsular involvement and mass presentation. However, there are a few pitfalls for PET-CT evaluation of the BIA-ALCL patients. PET-CT cannot differentiate malignant from a benign peri-implant effusion, which is the most common presentation of the BIA-ALCL, resulting in low sensitivity. Benign inflammatory pericapsular changes may have FDG uptake leading to false-positive results. Additionally, increased FDG uptake can be seen due to reactive changes in the regional lymph nodes, also resulting in false-positive assessment. The main advantage of the PET-CT is its high sensitivity for detection and staging of distant disease [11, 14, 15].

Individual cases should involve a multidisciplinary team to determine the best management and treatment options. Management options include oncologic en bloc resection of the capsule and associated masses with implant removal, exchange for smooth implant devices, or conversion to autologous tissue reconstruction [8, 10]. En bloc resection includes complete/total capsulectomy with clear margins [1•]. Excisional biopsy of suspicious lymph nodes is recommended, although routine sentinel lymph node biopsy is of limited value [2]. Most BIA-ALCL cases may be managed surgically, with chemotherapy and radiation used for adjuvant therapy in metastatic or recurrent disease [2].

Conclusion

BIA-ALCL is a type of T-cell lymphoma that originates in the capsule or fluid surrounding the breast implant. With prompt diagnosis and appropriate management, BIA-ALCL has a favorable prognosis. It is important for healthcare professionals to understand the complexity and long-term implications of the disease for this patient population.

Author contributions All authors contributed to the conception and design of this review. All authors gave final approval of the version of the review to be published, and all authors agree to be accountable for all aspects of the work.

Data availability The data supporting the information presented in this paper are, as confirmed by the authors, contained within the paper.

Declarations

Competing interests The authors declare no competing interests.

Conflict of interest Ms. Vuong, Mr. Rauch, Ms. Vishwanath, and Ms. Jean declare that they have no conflict of interest. Dr. Moseley is a medical imaging consultant for Merit Medical, Hologic, GE, and Siemens Medical.

Human and Animal Rights This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. ●DeCoster RC, Lynch EB, Bonaroti AR, et al. Breast implant-associated anaplastic large cell lymphoma: An evidence-based systematic review. *Annals of surgery*. 2021;273(3):449–458. This article provides an evidence-based systematic review evaluated primary research studies focusing on the diagnosis and

- treatment of BIA-ALCL that were published in PubMed, Google Scholar, and other scientific databases through March 2020.
2. O'Neill AC, Zhong T, Hofer SOP. Implications of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) for breast cancer reconstruction: An update for surgical oncologists. *Ann Surg Oncol*. 2017;24(11):3174–9.
 3. Leberfinger AN, Behar BJ, Williams NC, Rakszawski KL, Potochny JD, Mackay DR, Ravnicek DJ. Breast implant-associated anaplastic large cell lymphoma: a systematic review. *JAMA Surg*. 2017Dec 1;152(12):1161–8.
 4. Lineaweaver WC. Breast Implant-Associated Anaplastic Large Cell Lymphoma and Textured Breast Implants. *Ann Plast Surg*. 2019;82(6):595–6.
 5. ●●Vorstenbosch J, McCarthy CM, Shamsunder MG, Polanco TO, Dabic S, Wiser I, Matros E, Dayan J, Disa JJ, Pusic AL, Cavalli MR. Smooth versus textured implant breast reconstruction: patient-reported outcomes and complications. *Plastic and reconstructive surgery*. 2021 Nov 1;148(5):959–67. **This article addresses patient's postoperative satisfaction with breasts or health-related quality of life following immediate postmastectomy implant-based breast construction.**
 6. Bewtra C & Gharde P. Current Understanding of Breast Implant-Associated Anaplastic Large Cell Lymphoma. *Cureus*. 2022; 14(10) published online.
 7. ●●Keech Jr JA. Anaplastic T-cell lymphoma in proximity to a saline-filled breast implant. *Plastic and reconstructive surgery*. 1997 Aug 1;100(2):554–5. **This article was the first to describe the association between breast implants and anaplastic T-cell lymphoma.**
 8. Tevis SE, Hunt KK, Miranda RN, Lange C, Pinnix CC, Iyer S, Butler CE, Clemens MW. Breast implant-associated anaplastic large cell lymphoma: A prospective series of 52 patients. *Ann Surg*. 2022Jan 1;275(1):e245–249.
 9. Gidengil CA, Predmore Z, Mattke S, Busum K van, Kim B. Breast Implant-Associated Anaplastic Large Cell Lymphoma: A Systematic Review. *Plastic and reconstructive surgery (1963)*. 2015;135(3):713–720.
 10. Nelson JA, Dabic S, Mehrara BJ, Cordeiro PG, Disa JJ, Pusic AL, Matros E, Dayan JH, Allen RJ Jr, Corididi M, Polanco TO. Breast implant-associated anaplastic large cell lymphoma incidence: determining an accurate risk. *Ann Surg*. 2020Sep 1;272(3):403–9.
 11. Sharma B, Jurgensen-Rauch A, Pace E, Attygalle AD, Sharma R, Bommier C, Wotherspoon AC, Sharma S, Iyengar S, El-Sharkawi D. Breast implant-associated anaplastic large cell lymphoma: review and multiparametric imaging paradigms. *Radiographics*. 2020May;40(3):609–28.
 12. Collado-Mesa F, Yepes MM, Net JM, Jorda M. Breast Implant-Associated Anaplastic Large Cell lymphoma: Brief overview of current data and imaging findings. *Breast Dis*. 2021Jan 1;40(1):17–23.
 13. Rotili A, Ferrari F, Nicosia L, Pesapane F, Tabanelli V, Fiori S, Vanazzi A, Meneghetti L, Abbate F, Latronico A, Cassano E. MRI features of breast implant-associated anaplastic large cell lymphoma. *Br J Radiol*. 2021Sep 1;94(1125):20210093.
 14. Siminiak N, Czepczyński R. PET-CT for the staging of breast implant-associated anaplastic large cell lymphoma. *Nuclear Medicine Review*. 2019;22(2):90–1.
 15. Mehdi AS, Bitar G, Sharma RK, Iyengar S, El-Sharkawi D, Tasoulis MK, Attygalle AD, Cunningham D, Sharma B, RMH BIA-ALCL Working Group. Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL): a good practice guide, pictorial review, and new perspectives. *Clinical Radiology*. 2022 Feb 1;77(2):79–87.
 16. Noreña-Rengifo BD, Sanín-Ramírez MP, Adrada BE, Luengas AB, Martínez de Vega V, Guirguis MS, Saldarriaga-Urbe C. MRI for evaluation of complications of breast augmentation. *Radiographics*. 2022 Jul;42(4):929–46.
 17. Fernandez M. Ciudad Fernandez MJ, de la Puente Yague M, Brenes Sanchez J, Benito Arjonilla E, Moreno Dominguez L, et al. Breast implant associated Anaplastic large cell lymphoma (BIA-ALCL): imaging findings. *Breast J*. 2019;25(4):728–30.

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