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

Fernando Collado-Mesa

Abstract

Breast implant-associated anaplastic large cell lymphoma is a rare disease first described in 1997. Since then, its incidence has continued to increase. Current estimated lifetime risk in women with textured breast implants range from 1:1000 to 1:30,000. Most cases present with rapid and dramatic breast swelling resulting from peri-implant fluid collection. Palpable mass, pain, and skin lesions also occur. A high index of suspicion in patients who develop a seroma around the breast implant more than one year after implant placement is required. The combination of clinical history, physical exam findings, and appropriate imaging workup can lead to a timely and accurate diagnosis. The disease has excellent prognosis when it is diagnosed earlier, and complete surgery is performed. Radiologists, particularly those involved in breast imaging, can play an essential role in early diagnosis. This chapter presents an overview of the disease, including relevant imaging findings.

Keywords: breast implant-associated anaplastic large cell lymphoma, epidemiology, pathophysiology, diagnosis, treatment, prognosis, mammography, ultrasound, magnetic resonance imaging, fine needle aspiration, needle biopsy, positron emission tomography

1. Introduction

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare disease first described in 1997 when Keech & Creech published the first case report of anaplastic T-cell lymphoma in proximity to a saline-filled breast implant [1]. Following the initial report, additional case reports and case series of this entity have been published [2–4].

A possible association between breast implants and anaplastic large cell lymphoma was announced by the Food and Drug Administration (FDA) in 2011 [5], and in 2016, the World Health Organization (WHO) added BIA-ALCL as a provisionally recognized lymphoma to the family of existing ALCL [6].

In 2019 the FDA issued a safety communication stating, “all individuals who are considering a breast implant of any type be informed of the risk of developing BIA-ALCL”. At the time, most cases of BIA-ALCL were reported to have Allergan’s Biocell textured breast implants, thus, following an FDA recommendation, Allergan

initiated a worldwide voluntary recall of their breast implant products in July 2019 [7].

The incidence of the disease has continued to increase with current estimates of the absolute risk for development of BIA-ALCL ranging from 1 in 3,817 to 1 in 30,000 [8].

BIA-ALCL is characterized by the development of peri-implant fluid collection that occurs >1 year after breast implant placement, and/or by a solid mass arising within the implant's fibrous capsule [9]. Median time since implant placement at diagnosis is estimated at 8–10 years [9].

Overall, the disease has an excellent prognosis, particularly if diagnosed and fully treated at early stage [10]. It is therefore important to increase awareness about this disease amongst health care providers in general and amongst radiologists and provide them with the relevant information for early diagnosis, referral, and treatment.

2. Etiopathogenesis

Although the etiology of BIA-ALCL remains poorly understood, there is evidence demonstrating a preponderance of patients with BIA-ALCL to have been exposed to textured breast implants, developed in the 1980s to reduce implant contractures, which in turn provides clues as to the pathogenesis of this condition [11, 12].

Texturing of the implant shell may lead to a greater inflammatory response of the surrounding fibrous tissue capsule eliciting an increased chronic antigenic stimulation, which in turn could potentially be responsible for the development of ALCL [12]. Other potential causes of chronic inflammation which have been postulated include lipopolysaccharide endotoxin, trauma to the breast pocket, viral infection, and allergens [13].

Currently, there is not enough data to determine whether ALCL may be found more or less frequently in individuals with silicone-filled breast implants compared to individuals with saline-filled breast implants [14].

The presence of germline and somatic mutations, which can increase the susceptibility of the host to BIA-ALCL has been postulated as a contributing factor [12].

Recent molecular studies have identified novel, activating mutations in the Janus kinase (JAK), and signal transducer and activator of transcription factor (*STAT3*) pathway as a major risk factor for the development of BIA-ALCL (the presence of germline and somatic mutations, which can increase the susceptibility of the host to BIA-ALCL). Aberrant *STAT3* signaling has been established as a mechanistic link between chronic inflammation in non-BIA-ALCL cancers, including B- and T-cell lymphomas, and amongst the latter systemic anaplastic large cell lymphomas (the presence of germline and somatic mutations, which can increase the susceptibility of the host to BIA-ALCL) and persistent *STAT3* activation has been definitively linked to improved tumor survival and cell proliferation, increased angiogenesis, and tumor metastasis [13].

3. Epidemiology

Current estimates suggest that each year over 1.8 million people worldwide receive breast implants for cosmetic or reconstructive purposes [15]. In July of 2019 the number of BIA-ALCL reported cases worldwide reached 573, with 320 those cases reported in the US [16]. The estimated lifetime risk of BIA-ALCL in women with textured breast implants range from 1:1,000 to 1:30,000 [17]. A reported

geographic variation of the risk is likely due to variable reporting and less likely to geographic or genetic predisposition [17].

4. Clinical features

Mean age at diagnosis is 53.2 ± 12.3 years [17]. Mean interval from implant placement to diagnosis is 10.7 ± 4.6 years [17]. However, this late-onset diagnoses may reflect delayed diagnosis or misdiagnosis.

Patients most commonly present with rapid onset of a spontaneous fluid collection (60–90%) or capsular mass (10–40%) [9]. Approximately 30% of patients report pain, and about 25% present with skin lesions, most commonly erythema, subcutaneous nodules, eruption, erosion, or ulcer [9].

Implant capsule contracture is present in approximately 30% of cases [9]. When this occurs, there is a preponderance of grade III and IV contracture, defined as clinically symptomatic and visible contracture of the implant capsule [18].

BIA-ALCL disseminates locally in a small proportion of cases [19]. When local dissemination takes place it most commonly involves the ipsilateral axillary lymph nodes [19]. The prevalence of lymphadenopathy at diagnosis ranges from 2–14% [19].

Distant disease is uncommon. There are case reports of and distant lymph nodes and bone marrow involvement [19]. Systemic symptoms, such as unexplained weight loss, fever, or night sweats, are also uncommon affecting approximately 8% of patients [19].

5. Radiologic features

5.1 Mammography

In general, mammography findings include nonspecific capsular thickening, and circumferential asymmetry around the implant (**Figures 1 and 2**) [19, 20].



Figure 1. 63-year-old female with history of saline breast implants with textured surface placed 19 years ago presented with pain and swelling throughout the right breast and a palpable abnormality in the posterior third of the right breast at 7 o'clock for 1 month. Bilateral digital mammogram shows bilateral retro glandular saline breast implants. The right breast is larger than the left and shows a homogeneous and circumferential area of increased density (arrow) surrounding the implant, including the area of palpable abnormality noted by triangular marker in the posterior third of the right breast lower quadrants (source: Collado-Mesa et al. [20]).

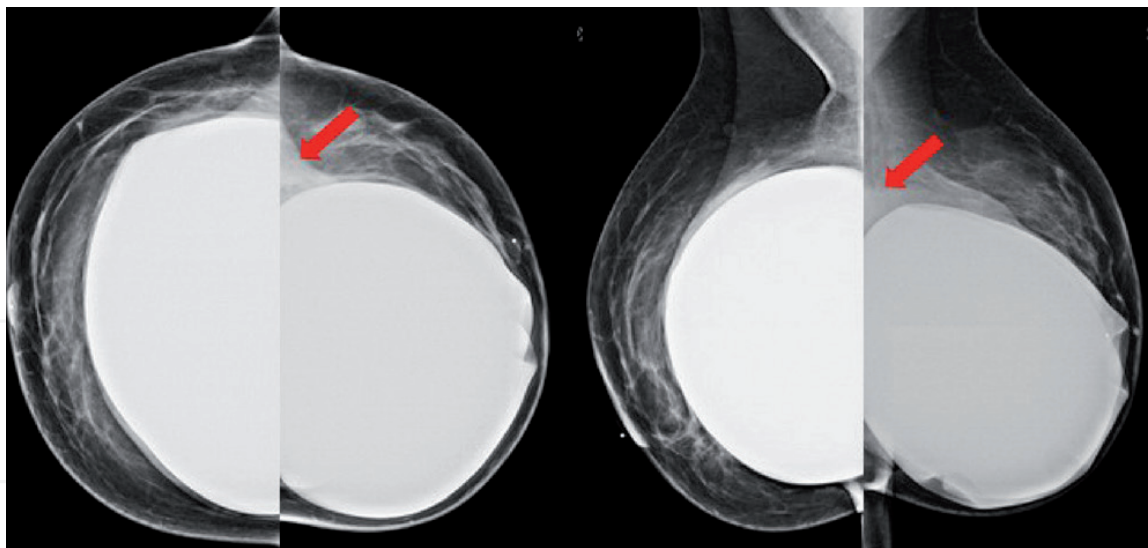


Figure 2. 54-year-old female status post left breast mastectomy for DCIS and right breast prophylactic mastectomy, followed by immediate bilateral breast silicone implant with textured surface reconstruction 11 years ago presented with sudden onset of right breast swelling and enlargement with associated discomfort. She denied fever or general symptoms. Bilateral mammogram shows irregular contours of the right breast silicone implant with associated focal-peri-implant increased density (arrows) (source: Collado-Mesa et al. [20]).

Unlike with primary breast cancer, mammography is not accurate for detection of either peri-implant effusion or mass-forming BIA-ALCL.

Overall, mammography has a lower sensitivity and specificity than both ultrasound and Magnetic Resonance Imaging (MRI) for any abnormality due to BIA-ALCL, at 73% and 50% respectively [21].

5.2 Ultrasound

Ultrasound (US) is the imaging exam of choice. Findings most commonly include a homogeneous peri implant effusion with inflammatory changes in the periprosthetic breast tissue (Figures 3 and 4).

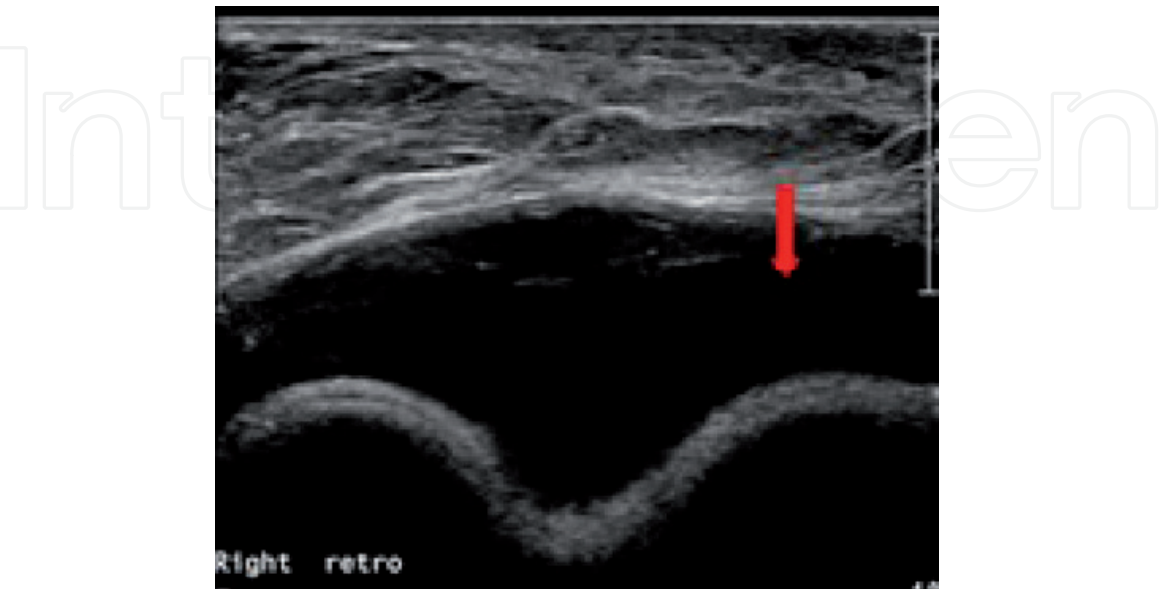


Figure 3. 63-year-old female with history of saline breast implants with textured surface placed 19 years ago presented with pain and swelling throughout the right breast and a palpable abnormality in the posterior third of the right breast at 7 o'clock for 1 month. Grey scale ultrasound shows right breast peri-implant fluid collection (arrow) (source: Collado-Mesa et al. [20]).

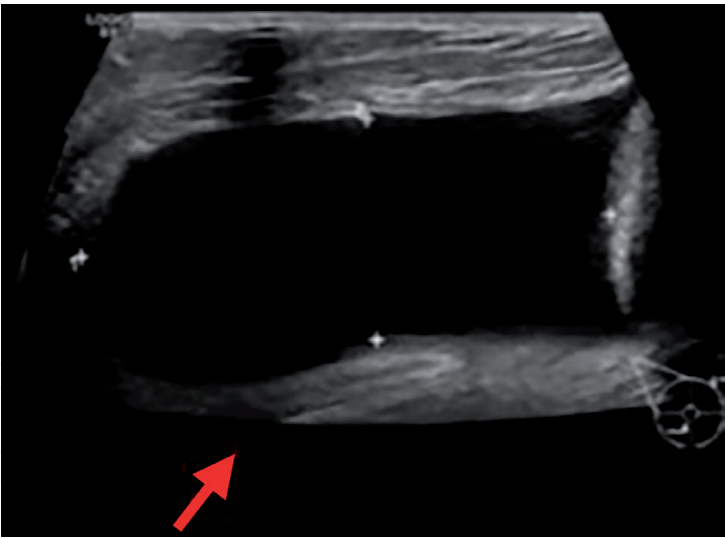


Figure 4.
Effusion-only BIA-ALCL in a 55-year-old woman after mastectomy for breast cancer. The initial breast implant was exchanged after 9 years; 7 years later, she experienced sudden new marked implant-associated swelling. Transverse US image shows a large seroma with septa surrounding the intact implant (arrow). US-guided fine-needle aspiration yielded cloudy yellow fluid, cytologic analysis of which demonstrated ALK-negative BIA-ALCL (source: Sharma B et al. [19]).

When a solid mass is present, it frequently appears as an oval, hypoechoic, circumscribed mass, without hypervascularity (**Figure 5**) [19, 20]. Less frequently, it appears as a complex cystic and solid mass [19, 20].

Some cases may present with abnormal ipsilateral axillary lymph nodes, including the presence of nodal cortical thickening or diffusely hypoechoic without evident fatty hilus.

Amongst the commonly used breast imaging modalities, the highest sensitivity for detection of peri-implant fluid collection is reported for ultrasound (84%) [21]. Ultrasound is also reported to have the highest specificity for detection of solid mass (100%) [21].



Figure 5.
63-year-old female with history of saline breast implants with textured surface placed 19 years ago presented with pain and swelling throughout the right breast and a palpable abnormality in the posterior third of the right breast at 7 o'clock for 1 month. Grey scale ultrasound shows a 4 × 1.4 × 2.4 cm mixed echogenicity, oval, partially indistinct mass (arrow) abutting the fibrous capsule in the right breast at 7 o'clock, 5 cm from the nipple, corresponding to palpable abnormality (source: Collado-Mesa et al. [20]).

5.3 Magnetic resonance imaging

Breast Magnetic Resonance Imaging (MRI) is the imaging test of choice after US, and it particularly add value when US results are indeterminate.

MRI findings include peri-implant tissue edema and effusion, as well as peri-implant mass lesions, including small-volume mass components not detected with US. Enhancement with intravenous gadolinium contrast material may also help with characterization of some findings (**Figures 6–10**) [19, 20].

MRI also serves to evaluate for the presence of implant rupture when there is a silicone implant [19].

MRI is the imaging modality with the second highest sensitivity for peri-implant fluid collection at 82% and with the second highest specificity for mass at 93% [21].

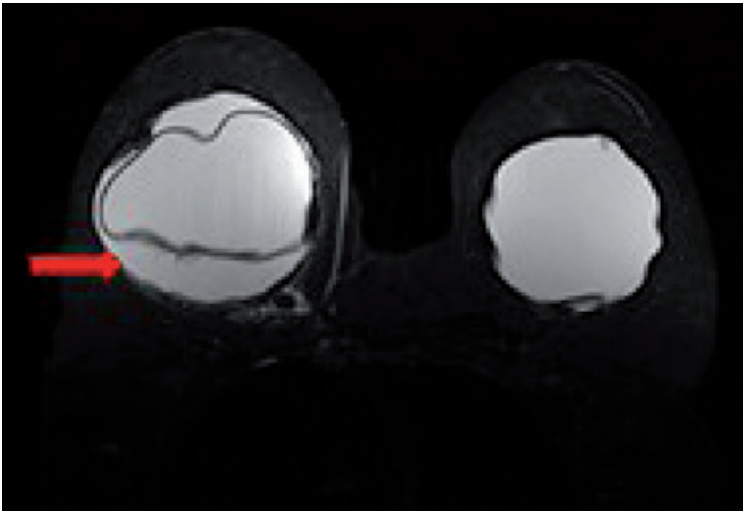


Figure 6. 63-year-old female with history of saline breast implants with textured surface placed 19 years ago presented with pain and swelling throughout the right breast and a palpable abnormality in the posterior third of the right breast at 7 o'clock for 1 month. Breast MRI axial T2-weighted fat-saturated sequence shows right breast peri-implant fluid collection (arrow) (source: Collado-Mesa et al. [20]).



Figure 7. 63-year-old female with history of saline breast implants with textured surface placed 19 years ago presented with pain and swelling throughout the right breast and a palpable abnormality in the posterior third of the right breast at 7 o'clock for 1 month. Breast MRI axial T1-weighted fat saturated postcontrast subtraction shows a 4 × 1.7 × 2 cm oval heterogeneously enhancing mass (arrow) arising from the fibrous capsule in the right lower outer quadrant (source: Collado-Mesa et al. [20]).

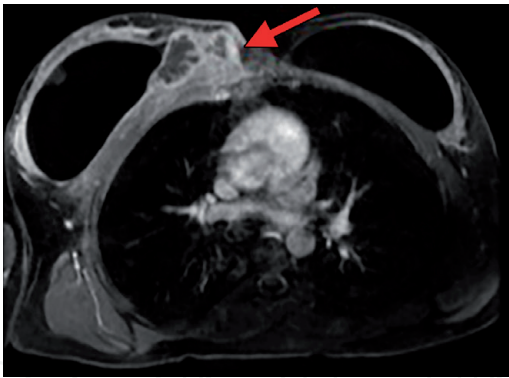


Figure 8.
Mass forming BIA-ALCL in a 29-year-old woman with a right upper inner breast mass 3 years after bilateral breast augmentation with TRF-520 implants (Allergan). Axial gadolinium enhanced fat-saturated breath-hold volume MR image shows a large implant-associated lobulated mass with a central necrotic area and intense rim enhancement (arrow) infiltrating the pectoralis major muscle and threatening the intercostal muscles. Biopsy demonstrated BIA-ALCL (source: Sharma B et al. [19]).

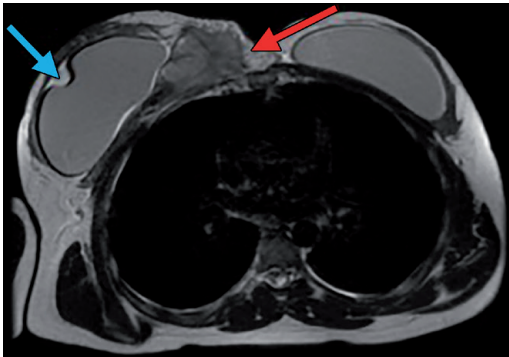


Figure 9.
BIA-ALCL with chest wall invasion in a 29-year-old woman who underwent bilateral breast augmentation with TRF-520 implants (Allergan) and developed a right upper inner breast lump 3 years after surgery. Axial fast spin-echo T2-weighted image with breath holding 4 months later shows irregular surface of the implant (blue arrow) and rapid enlargement (estimated at 7 cm axially) of the lobulated mass (red arrow), which is characterized by a central necrotic area. Biopsy demonstrated large atypical CD30-positive cells infiltrating the fibrous tissue. The final diagnosis was BIA-ALCL (source: Sharma B et al. [19]).

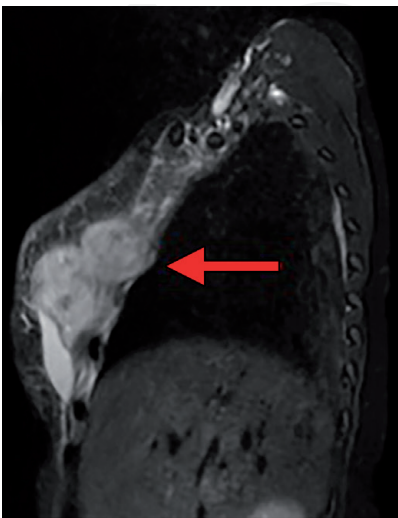


Figure 10.
BIA-ALCL with chest wall invasion in a 29-year-old woman who underwent bilateral breast augmentation with TRF-520 implants (Allergan) and developed a right upper inner breast lump 3 years after surgery. Sagittal short τ inversion-recovery (STIR) image obtained 4 months later shows the mass (arrow) infiltrating the pectoralis major muscle and threatening the intercostal muscles. Biopsy demonstrated large atypical CD30-positive cells infiltrating the fibrous tissue. The final diagnosis was BIA-ALCL (source: Sharma B et al. [19]).

6. Diagnosis and histologic features

A high index of suspicion of BIA-ALCL is required to allow a timely diagnosis.

Breast ultrasound should be obtained in patients with suspicious signs and symptoms such as breast swelling, palpable mass, pain, and skin lesions which have developed more than one year after implant placement (average 8–10 years).

If a peri-implant effusion is noted, then fine needle aspiration of at least 50 ml should be performed [22]. In cases where a peri-implant mass is present, either core needle biopsy or surgical excisional biopsy should be performed [22].

In cases with inconclusive findings on ultrasound, a breast MRI should be obtained [22].

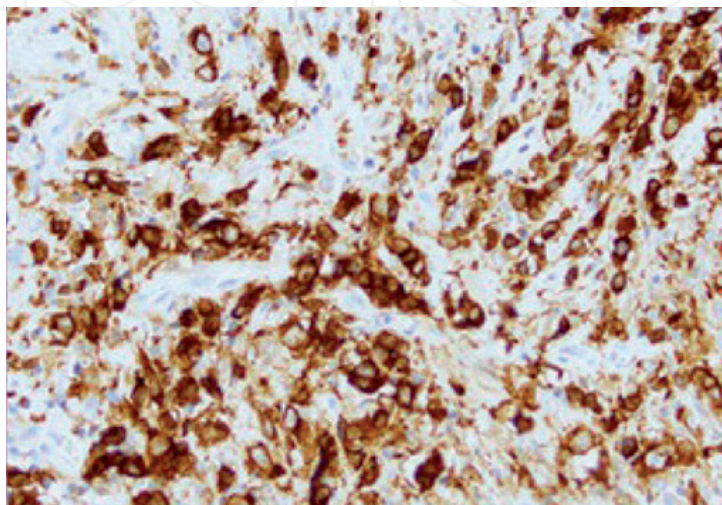


Figure 11. Photomicrograph of ultrasound-guided core needle biopsy samples of solid mass showed in **Figure 5** shows most of the cells to be strongly and uniformly positive for CD30 (CD30 immunohistochemistry, $\times 60$) (Source: Collado-Mesa et al. [20]).

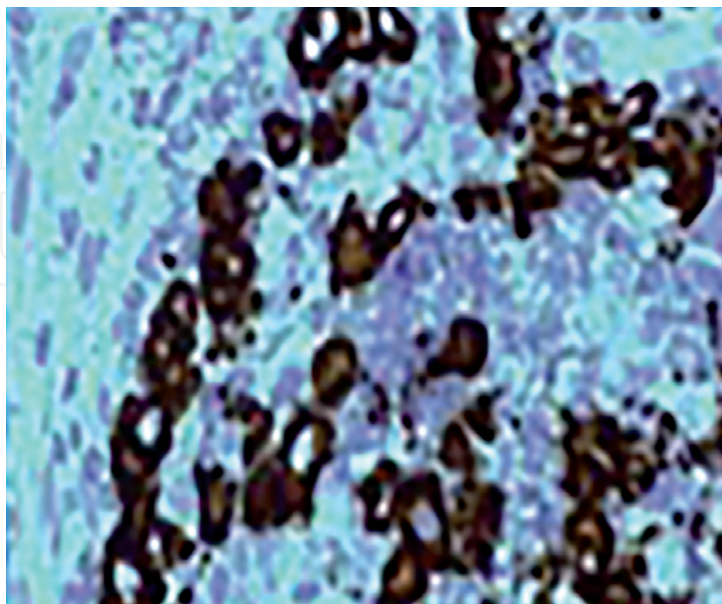


Figure 12. Effusion-only BIA-ALCL in a 55-year-old woman after mastectomy, axillary node dissection, implant reconstruction, chemoradiotherapy, and immunotherapy. After 9 years, the implant was exchanged; 7 years later, sudden new marked swelling of the right breast developed. At US, a large seroma surrounded the intact right breast implant; diagnostic aspirate yielded cloudy yellow fluid, which was ALK-negative at cytologic analysis. Immunohistochemistry slides show that the infiltrate is positive for CD30 (source: Sharma B et al. [19]).

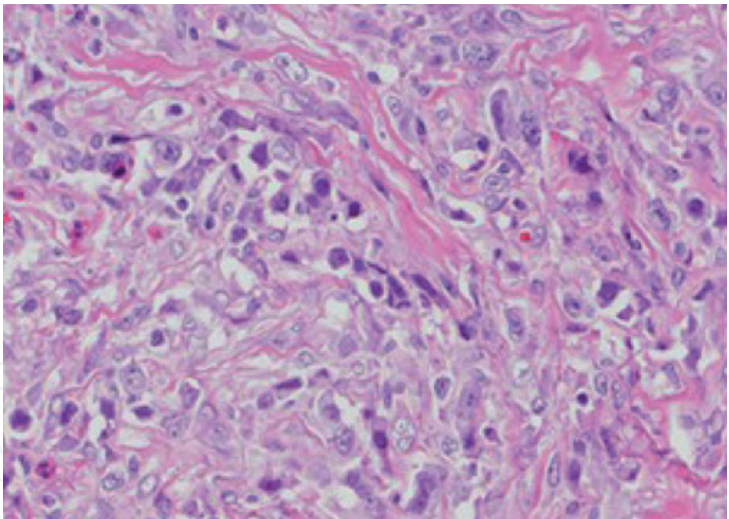


Figure 13.
Photomicrograph of ultrasound-guided core needle biopsy samples of solid mass showed in Figure 5 shows large and pleomorphic neoplastic cells with irregular nuclei, large prominent nucleoli, conspicuous mitotic activity, and moderate cytoplasm (hematoxylin and eosin [H&E], ×60) (source: Collado-Mesa et al. [20]).

Samples should be sent for cytology, flow cytometry, immunohistochemistry for CD30 (**Figures 11 and 12**) and additional differentiation markers (CD2 – CD5, CD7, CD8, CD45, and ALK [19, 20, 22]).

The presence of large neoplastic cells that have pleomorphic nuclei, abundant eosinophilic cytoplasm, and irregular cell membranes is required for diagnosis (**Figure 13**). Uniform CD30 expression, evidence of a single T-cell clone, and an absence of ALK expression are also observed [22]. Epithelial membrane antigen (EMA) is also often expressed by neoplastic cells [23]. “Hallmark cells” with eccentric kidney or horseshoe-shaped nuclei are not uncommonly seen [23].

If results are indeterminate, a referral to a cancer center is recommended. If results are negative, then it should be treated as a benign seroma. Patients with positive results require a disease workup [22].

7. Staging

The traditional staging for all lymphoma is the Ann Arbor classification. However, BIA-ALCL is not a classical non-Hodgkin lymphoma and it usually progress locally and/or regionally like a solid tumor; thus, it is better suited to the TNM system for staging solid tumors.

TNM	Criteria
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 involved
N2	Multiple regional lymph nodes involved

TNM	Criteria
M: Metastasis	
M0	No distant spread
M1	Spread to other organs/distant sites
Stage	TNM
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

Modified from source: (Clemens et al. [22]).

Table 1.
TNM stage classification of BIA-ALCL.

The 2019 update of the National Comprehensive Cancer Network guidelines now include a TNM disease staging system based on clinical and pathological evaluation first proposed in 2016 by MD Anderson Cancer Center and which may be more applicable for predicting a prognosis and for evaluating treatment regimens in patients with BIA-ALCL [22].

In this TNM classification for BIA-ALCL the disease is considered extended (not localized) if there is tumor invasion beyond the fibrous capsule, spread to one or more regional lymph nodes, or spread to any organs/distant sites (Table 1).

8. Treatment

8.1 Surgical treatment

A surgical oncology consultation is not compulsory but may be beneficial for plastic surgeons unaccustomed to optimal surgical resection of a malignancy.

The goals of surgery are to remove the implant with the surrounding fibrous capsule and any associated capsule mass. Complete surgical excision prolongs both overall survival and event-free survival compared with all other therapeutic interventions [10].

All attempts should be made to gain complete surgical resection because retained or unresectable disease likely indicates the need for adjuvant treatments.

An estimated 2–4% of patients develop bilateral disease, and therefore surgeons may consider removal of the contralateral implant and capsule [10].

Currently, there is no clear role for radical mastectomy or sentinel lymph node biopsy. Full axillary dissection has been used rarely for gross involvement of multiple lymph nodes.

8.2 Adjuvant treatments

No data from prospective trials is available to guide management of patients with disseminated BIAS-ALCL. Current treatment is based on experiences from treating primary cutaneous and systemic ALCL.

Radiation therapy with 24–36 Gray (Gy) to the local or involved site is suggested for patients with local residual disease, positive margins, or unresectable disease with chest wall invasion [22].

Systemic therapy for patients with stage IIB-IV disease can be as combination anthracycline based chemotherapy or as a combination with brentuximab vedotin [22].

9. Surveillance and prognosis

In patients with complete response to treatment, surveillance should include history and physical exam and either a CT chest, abdomen, and pelvis with contrast or a whole-body PET-CT every 6 months for two years and then as clinically indicated (**Figures 14** and **15**) [22].

BIA-ALCL has shown to have an excellent prognosis when the disease is diagnosed earlier (localized disease), and when complete surgery, consisting of explantation, capsulectomy, and removal of any associated capsule mass, is performed [9, 10].

Compared to stage I disease, stage II and stage III disease have a rate of disease events and recurrence which are 2.6-fold higher and 2.7-fold higher respectively [10].

Patients with T1–T3 disease have 0% rate of disease events following complete surgical excision as compared to T4 disease have a 14.3% in patients with T4 disease [10]. Local recurrence is most common if incomplete resection or partial capsulectomy took place [10].

A study of causes of death in patients diagnosed with BIA-ALCL showed that all the patients who died had incomplete surgical excision or did not receive targeted therapy [24]. The study also reported delay in diagnosis or treatment for an average of 1–2 years [24]. Direct extension into the chest wall leading to respiratory failure was a common cause of death [24]. Other less commonly reported causes of death included stem cell transplant complication and development of a second unrelated lymphoma [24].

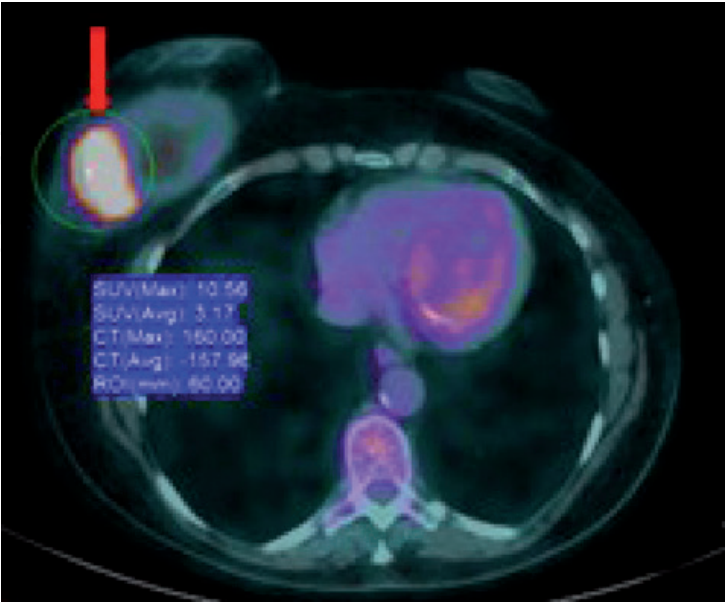


Figure 14.
63-year-old female with history of saline breast implants with textured surface placed 19 years ago presented with pain and swelling throughout the right breast and a palpable abnormality in the posterior third of the right breast at 7 o'clock for 1 month. Screen capture of a whole body 18F-FDG PET/CT shows FDG activity of SUV 10.56, corresponding to a soft tissue mass (arrow) in the lower outer quadrant of the right breast adjacent to the implant measuring 3.2 × 4.8 cm × 2.5 cm (source: Collado-Mesa et al. [20]).



Figure 15. 63-year-old female with history of saline breast implants with textured surface placed 19 years ago presented with pain and swelling throughout the right breast and a palpable abnormality in the posterior third of the right breast at 7 o'clock for 1 month. Screen capture of a whole body 18F-FDG PET/CT obtained 6 months after bilateral breast explantation and total capsulectomy shows no abnormality (source: Collado-Mesa et al. [20]).

10. Conclusion

In the absence of infection or trauma, the development of a new peri-implant effusion more than one year after breast implant placement should prompt consideration for the diagnosis of BIA-ALCL. As the clinical symptoms are often nonspecific, radiologists, particularly those involved in breast imaging, play an important role in its diagnosis. While mammography may demonstrate subtle abnormalities, ultrasound and MRI have higher sensitivity and specificity. Diagnosis requires sampling of peri-implant fluid or mass and/or lymph node. Suspicion of BIA-ALCL should be communicated to the pathologist, and immunohistochemistry for CD30 ordered. Once diagnosed, oncology referral and multi-specialty team care including plastic surgery and radiation therapy is recommended. Prompt diagnosis and complete treatment appear to lead to excellent prognosis.

Conflict of interest

The authors declare no conflict of interest.

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Author details

Fernando Collado-Mesa
University of Miami Miller School of Medicine, Miami, Florida,
United States of America

*Address all correspondence to: fcollado@med.miami.edu

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References

- [1] Keech JA Jr, Creech BJ. Anaplastic T-cell lymphoma in proximity to a saline-filled breast implant. *Plastic and Reconstructive Surgery*. 1997;**100**:554-555
- [2] Gaudet G, Friedberg JW, Weng A, Pinkus GS, Freedman AS. Breast lymphoma associated with breast implants: Two case reports and a review of the literature. *Leukemia & Lymphoma*. 2002;**43**(1):115-119
- [3] Wong AK, Lopategui J, Clancy S, Kulber D, Bose S. Anaplastic large cell lymphoma associated with a breast implant capsule: A case report and review of the literature. *The American Journal of Surgical Pathology*. 2008; **32**(8):1265-1268
- [4] Miranda RN, Lin L, Talwalkar SS, Manning JT, Medeiros LJ. Anaplastic large cell lymphoma involving the breast: A clinicopathologic study of 6 cases and review of the literature. *Archives of Pathology & Laboratory Medicine*. 2009;**133**(9):1383-1390
- [5] Reports of Anaplastic Large Cell Lymphoma (ALCL) in Women with Breast Implants: FDA Safety Communication. 2011. Available from <https://wayback.archive-it.org/7993/20170111070030/http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm240000.htm> [Accessed: 2021-08-02]
- [6] Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood*. 2016;**127**(20):2375-2390
- [7] US Food and Drug Administration. The FDA requests allergan voluntarily recall natrelle biocell textured breast implants and tissue expanders from the market to protect patients: FDA safety communication. Available from <https://wayback.archive-it.org/7993/20191214045822/https://www.fda.gov/node/390731> [Accessed: 2021-08-02]
- [8] US Food and Drug Administration. FDA In Brief: FDA updates public information about known risk of lymphoma from breast implants. Available from <https://www.fda.gov/news-events/fda-brief/fda-brief-fda-updates-public-information-about-known-risk-lymphoma-breast-implants> [Accessed: 2021-08-02]
- [9] Clemens MW, Brody GS, Mahabir RC, Miranda RN. How to diagnose and treat breast implant-associated anaplastic large cell lymphoma. *Plastic and Reconstructive Surgery*. 2018;**141**(4):586e-599e
- [10] 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. *Journal of Clinical Oncology*. 2016;**34**(2):160-168
- [11] Kadin ME, Deva A, Xu H, Morgan J, Khare P, MacLeod RA, et al. Biomarkers provide clues to early events in the pathogenesis of breast implant-associated anaplastic large cell lymphoma. *Aesthetic Surgery Journal*. 2016;**36**(7):773-781
- [12] Rastogi P, Riordan E, Moon D, Deva AK. Theories of etiopathogenesis of breast implant-associated anaplastic large cell lymphoma. *Plastic and Reconstructive Surgery*. 2019;**143**(3S):23S-29S
- [13] DeCoster RC, Clemens MW, Di Napoli A, Lynch EB, Bonaroti AR, Rinker BD, et al. Cellular and molecular mechanisms of breast implant-associated anaplastic large cell lymphoma. *Plastic and Reconstructive Surgery*. 2021;**147**(1):30e-41e

- [14] US Food and Drug Administration. Questions and answers about breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). Available from <https://www.fda.gov/medical-devices/breast-implants/questions-and-answers-about-breast-implant-associated-anaplastic-large-cell-lymphoma-bia-alcl> [Accessed: 2021-08-02]
- [15] International Society of Aesthetic and Plastic Surgery: International Survey on Aesthetic/Cosmetic Procedures performed in 2018. Available from <https://www.isaps.org/wp-content/uploads/2019/12/ISAPS-Global-Survey-Results-2018-new.pdf> [Accessed: 2021-08-02]
- [16] US Food and Drug Administration. Medical device reports of breast implant-associated anaplastic large cell lymphoma. Available from <https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-breast-implant-associated-anaplastic-large-cell-lymphoma> [Accessed: 2020-02-18]
- [17] Doren EL, Miranda RN, Selber JC, et al. U.S. epidemiology of breast implant-associated anaplastic large cell lymphoma. *Plastic and Reconstructive Surgery*. 2017;**139**(5):1042-1050
- [18] Spear SL, Baker JL Jr. Classification of capsular contracture after prosthetic breast reconstruction. *Plastic and Reconstructive Surgery*. 1995;**96**(5):1119-1123
- [19] Sharma B, Jurgensen-Rauch A, Pace E, Attygalle AD, Sharma R, Bommier C, et al. Breast implant-associated anaplastic large cell lymphoma: Review and multiparametric imaging paradigms. *Radiographics*. 2020;**40**(3):609-628
- [20] 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 Disease*. 2021;**40**(1):17-23
- [21] Adrada BE, Miranda RN, Rauch GM, Arribas E, Kanagal-Shamanna R, Clemens MW, et al. Breast implant-associated anaplastic large cell lymphoma: Sensitivity, specificity, and findings of imaging studies in 44 patients. *Breast Cancer Research and Treatment*. 2014;**147**(1):1-14
- [22] Clemens MW, Jacobsen ED, Horwitz SM. NCCN consensus guidelines on the diagnosis and treatment of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). *Aesthetic Surgery Journal*. 2019, 2019;**39**(Suppl_1):S3-S13
- [23] Pastorello RG, D'Almeida Costa F, Osório CABT, Makdissi FBA, Bezerra SM, de Brot M, et al. Breast implant-associated anaplastic large cell lymphoma in a Li-FRAUMENI patient: A case report. *Diagnostic Pathology*. 2018;**13**(1):10
- [24] Abi-Rafeh J, Safran T, Al-Halabi B, Dionisopolous T. Death by implants: Critical analysis of the FDA-MAUDE database on breast implant-related mortality. *Plastic and Reconstructive Surgery*. *Global Open*. 2019;**7**(12):e2554