Aesth Plast Surg (2020) 44:1–12
https://doi.org/10.1007/s00266-019-01521-3

ORIGINAL ARTICLE BREAST SURGERY

Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) and the Textured Breast Implant Crisis

Anne K Groth[1,2,3,4] · **Ruth Graf**[1,5,6]

Received: 12 August 2019 / Accepted: 5 October 2019 / Published online: 17 October 2019

Abstract Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is an uncommon T-cell, CD-30+/ALK lymphoma. Late (9 years) periprosthetic fluid (seroma) is the most common presentation (90% of the cases). A combination of textured breast implant, bacterial contamination, and genetic predisposition seems to be necessary for BIA-ALCL to occur. There are 35 million patients with implants in the world, and at the present moment, 573 cases of BIA-ALCL have been reported. The risk of developing BIA-ALCL in Australia varies from 1:2832 to 1:86,029, with texture grades 3 and 4 seeming to pose a higher risk than grades 2 and 1. NCCN has established guidelines for diagnosis and treatment, and early diagnosis is the key to cure. At an early stage and for the vast majority of patients, the treatment consists of capsulectomy and implant removal. However, at stages II to IV, a systemic treatment is warranted, including chemotherapy, radiotherapy (residual disease), and brentuximab vedotin. The majority of patients can be cured, and complete capsular removal is the most important factor. So far, 33 patients have died from BIA-ALCL worldwide, with deaths related to delay in diagnosis and treatment. Textured implants have been in the midst of the current implant crisis, and Biocell was recalled worldwide after the latest FDA update on the disease. At the present moment, no medical society or regulatory agency has recommended implant removal. It is about time that we start robust breast implant registries to determine risks. Besides, based on scientific criteria, we must consider all the benefits and risks associated with the available breast devices.
Level of Evidence III This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Breast implants · Silicone elastomers · Lymphoma, large cell, anaplastic: breast

✉ Anne K Groth
annegroth@gmail.com

1 Brazilian Society of Plastic Surgery, Curitiba, Brazil

2 Plastic Surgery and Microsurgery Department, Erasto Gaertner Hospital, Curitiba, PR, Brazil

3 Positivo University Medical School, Curitiba, Brazil

4 Curitiba, Brazil

5 Federal University of Parana, Curitiba, Brazil

6 Pieta Medical Center, Rua Solimões 1175, Curitiba, PR, Brazil

Definition

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is an uncommon T-cell lymphoma, CD30-positive, ALK-negative, that typically presents itself as a spontaneous periprosthetic fluid collection or a capsular mass on the implant [1]. Non-Hodgkin lymphomas in the breast are rare (< 1% of breast neoplasms), and only 10% of them are T-cell lymphomas [2].

BIA-ALCL was first described in 1997 [3]; however, it was only after the communication by the US Food and Drug Administration (FDA) in 2011 that physicians have increased their attention to this disease.

The World Health Organization (WHO) recognized BIA-ALCL as a provisional entity in 2016, with morphological and immunophenotypic features indistinguishable from the ALK-negative anaplastic large cell lymphoma

(ALCL) but arising primarily in association with breast implants [4].

Etiology

At present, the development of BIA-ALCL seems to be associated with a textured breast implant, plus bacterial contamination (biofilm), and individual genetic predisposition [5].

Textured silicone breast implants have been developed in response to the search for more natural-looking implants with less silicone leakage has led to the development of textured silicone breast implants. They promote the stability of the breast pocket by increasing adherence to the breast tissue while decreasing capsular contracture [6].

Long-term safety of textured implants has been demonstrated in several recent studies [7]. Randquist [8] analyzed over 6000 textured implants and detected low rates of capsular contracture and reoperations. Adams et al. [9] investigated a series of 42,000 Biocell textured implants and found an overall contracture rate of 2.2%, a result similar to that also found by McGuire et al. [10], for Biocell implants (2.3–4.1%). However, complications not observed in smooth implants, like late seroma, double capsule, and lately BIA-ALCL, have been reported [9]. The presence of capsular contracture for smooth and textured implants is subjected to some controversy; while Zingaretti et al. [10] found similar capsular contracture rates in the submuscular pocket between smooth and textured implants, and Namnoum et al. [11] observed lower capsular contracture rates in textured implants.

Considering that the morphology of the outer shell in textured implants is not uniform for all providers, Jones et al. [12] proposed a new classification for the likelihood of bacterial growth on implant surfaces based on the surface area and roughness, with micro- and macrotextures. This classification goes from 1 to 4 (minimal, low, intermediate, and high), and the risk of BIA-ALCL is significantly higher for surfaces in classes 3 and 4 [13]. Each manufacturer has a particular method to create texture, which seems to have a direct correlation to lower or higher incidence of BIA-ALCL [7].

Deva et al. hypothesized that bacterial contamination introduced at the time of breast implant surgery might, over time, develop a biofilm that triggers an inflammatory and immune system response characterized by a predominantly T-cell lymphocytic infiltrate [14–16]. In genetically predisposed patients, such a response could lead to the development of BIA-ALCL [15]. This hypothesis led to several further studies, some of which suggested that implants with a higher surface area could allow a more significant bacterial load, which would promote increased lymphocyte stimulation and transformation [15, 17], while others indicated that textured and rough surfaces could be irritating and abrasive, further stimulating inflammatory responses [7].

Studies comparing bacteria in breast implant capsules from capsular contracture and BIA-ALCL revealed that Gram-positive bacteria are predominant in cases of capsular contracture, whereas the majority of bacteria present in BIA-ALCL are Gram-negative [15]. Bacterial biofilm, therefore, could lead to two pathologic pathways: The biofilm of Gram-positive bacteria (e.g., *Staphylococcus*) would promote capsular contracture due to inflammation and fibrosis; on the other hand, the biofilm of Gram-negative bacteria (e.g., *Ralstonia pickettii*, *Pseudomonas*) could lead to lymphocyte stimulation/transformation and eventual lymphoma [15].

There are various examples in the literature of infectious diseases leading to cancer, such as Helicobater pylori and gastric MALT lymphoma [18], and lymphomas associated with infections by Epstein Barr virus (EBV), human herpes virus 8 (HHV 8), and leukemia/lymphoma virus 1 (HTLV-1) [19]. EBV is involved in extranodal NK/T-cell lymphoma [19], and Aladily [2] describes a case that mimics BIA-ALCL symptoms, but further research is mandatory to confirm this hypothesis. Obtaining the medical history of previous infections in patients with BIA-ALCL should help and clarify any role of infections in BIA-ALCL development.

Betadine (50% or higher concentration) (povidone–iodine [PI] 10% solution, 1% available iodine [Purdue Frederick Company, Stamford, CT]) is one of the few antiseptic agents that is effective against *R. pickettii* [20]. Therefore, the use of Betadine was reviewed by the US FDA in 2017, at the request of a breast implant manufacturer, to introduce changes in the Directions for Use (DFU) that removed warnings regarding the use of Betadine [21].

Blombery et al. [22] sequenced the genome of 11 confirmed cases of BIA-ALCL and detected variants leading to JAK/STAT activation in 10 of 11 patients, indicating that genetic predisposition may be likewise a critical factor. Geographic variation in incidence might also be explained by genetic predisposition.

Incidence

Although there are no accurate numbers of breast implant surgeries performed, it is estimated that there are approximately 35 million patients with breast implants worldwide [23]. The first case of BIA-ALCL was reported in 1997 [3], and the American Society of Plastic Surgery (ASPS) and FDA have recognized a total of 573 cases worldwide until August 5, 2019 [24]. Australia's Therapeutic Goods

Administration (TGA) has confirmed a total of 76 cases to date [25]. The average woman's risk of developing breast cancer in her lifetime is 1:8 [26]. Doren et al. [29] reported a BIA-ALCL incidence of 1:30,000 in women with a textured breast implant. Implant-specific risk was estimated in Australia using sales data between 1999 and 2015 for Allergan, Mentor, and Silimed (polyurethane) in 2017 [17]: The risk estimated was higher in the Biocell textured implants (1:3817), followed by polyurethane (1:7788), and Siltex (1:60,631). Magnusson [27] updated the numbers in February 2019 for the risk of polyurethane (1:2832), Biocell (1:3345), and Siltex (1:86,029), showing that Biocell poses a 16.5-fold higher risk compared to Siltex, and polyurethane poses a 23.4-fold higher risk compared to Siltex. Ruffenach et al. [28] recently reported 36 cases of BIA-ALCL in France, with patients from the ANSM and the French Lymphopath Network, and found that 72% of the explanted implants were of the Biocell brand, while no records involved smooth implants.

This lack of precise risk estimates is due to the unstructured data collection, potential duplicate records, unclear clinical and pathological data, lack of information on the number of implants inserted as a denominator, and, most importantly, undiagnosed cases [19, 29].

Clinical Presentation

The most common clinical presentation of BIA-ALCL is late seroma, which is present in 60–90% of confirmed cases [28]. It usually occurs several years (7–10) after breast implant insertion and is described as an abrupt increase in breast volume due to periprosthetic fluid accumulation [29].

It should be highlighted that not all late seromas are associated with BIA-ALCL; however, approximately 9% of late seromas (i.e., present after 1 year of implant surgery) are associated with BIA-ALCL [30]. Accordingly, any seroma after 1 year of surgery that cannot be explained by trauma or infection should be further investigated and considered as suspicious of BIA-ALCL.

Other presentations of BIA-ALCL include a mass development, which occurs in 10–40% of all cases, besides cutaneous manifestations [31, 32], capsular contracture, and lymphadenopathy.

A total of 414 medical device reports (MDR) were present in the database of the FDA Manufacturer and User Facility Device Experience (MAUDE) until September 30, 2017 [33]. Of these MDRs, 272 contain information associated with the implant surface, with 242 implants identified as textured and 30 as smooth. No cases of BIA-ALCL were found in patients with documented smooth devices. Brody et al. [26] reviewed 79 published and 94 previously unreported cases and found that 100% of the patients had a textured implant or previously used one.

Diagnosis

The National Comprehensive Cancer Network (NCCN) established guidelines for the diagnosis and treatment of this disease in 2016 and updated in 2019 [1, 34].

Because the most common form of clinical presentation is a seroma (Fig. 1), it is crucial to collect the fluid through fine-needle aspiration (FNA) and submit it to cytologic evaluation and flow cytometry.

The initial exam in the disease workup is an ultrasound (Fig. 2), and mammograms are not useful. In a minority of cases that do not present any fluid, ultrasound-guided, or open biopsy may be necessary to collect samples of capsular mass, abnormal skin, or enlarged and suspicious lymph nodes.

As much fluid as possible should be collected through FNA and submitted to cytopathology and flow cytometry (Figs. 3, 4, 5) as soon as possible after collection to avoid misreads and false negatives. Because flow cytometry is not available in small/medium health centers in Latin America, the diagnosis is usually based only on cytopathologic findings and immunochemistry [35].

Cytopathologic diagnosis of BIA-ALCL is based on the presence of large cell, atypical, pleomorphic, and anaplastic morphology with eosinophilic cytoplasm. Immunohistochemistry will show large sheets of tumor

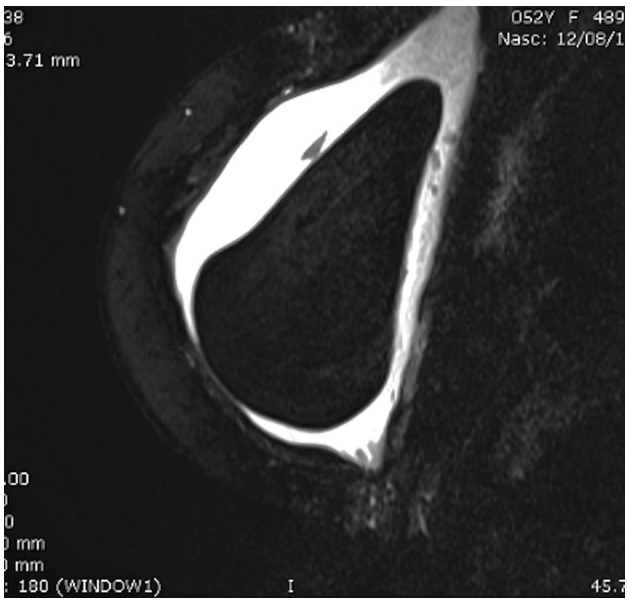

Fig. 1 Seroma in the breast of a BIA-ALCL confirmed patient (from the authors)

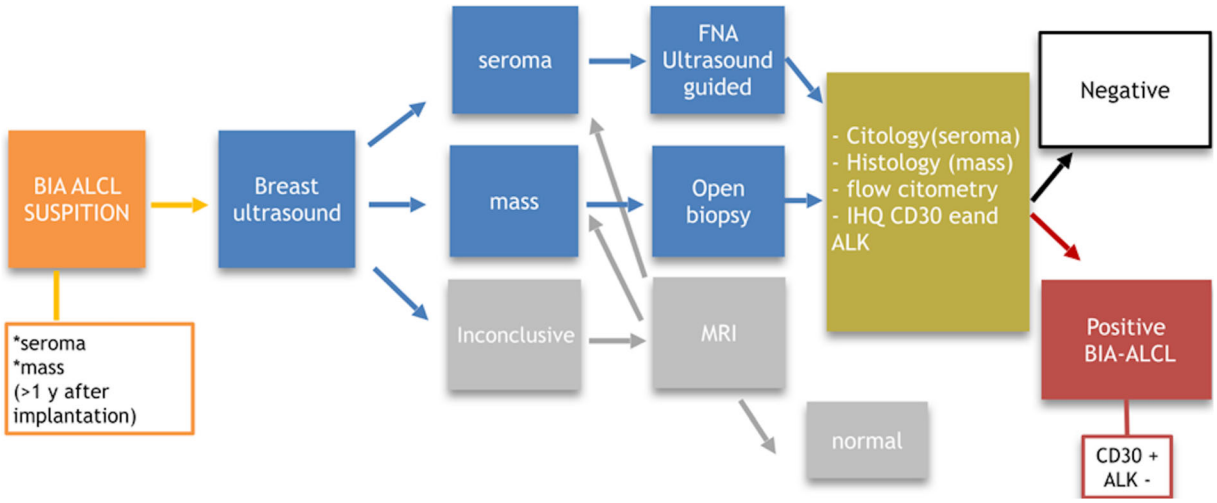

Fig. 2 BIA-ALCL diagnostic workup

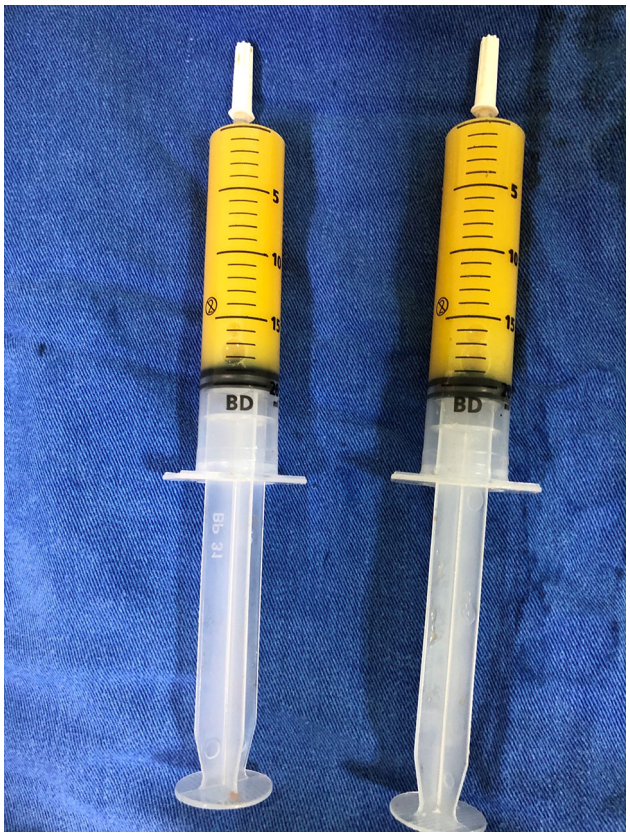

Fig. 3 Seroma in ultrasound FNA aspirate

cells expressing CD30, and a single T-cell clone is evident on flow cytometry.

BIA-ALCL does not express the anaplastic lymphoma kinase translocation (i.e., it is ALK-negative), which is critical to differentiate from systemic ALK-positive ALCL [30].

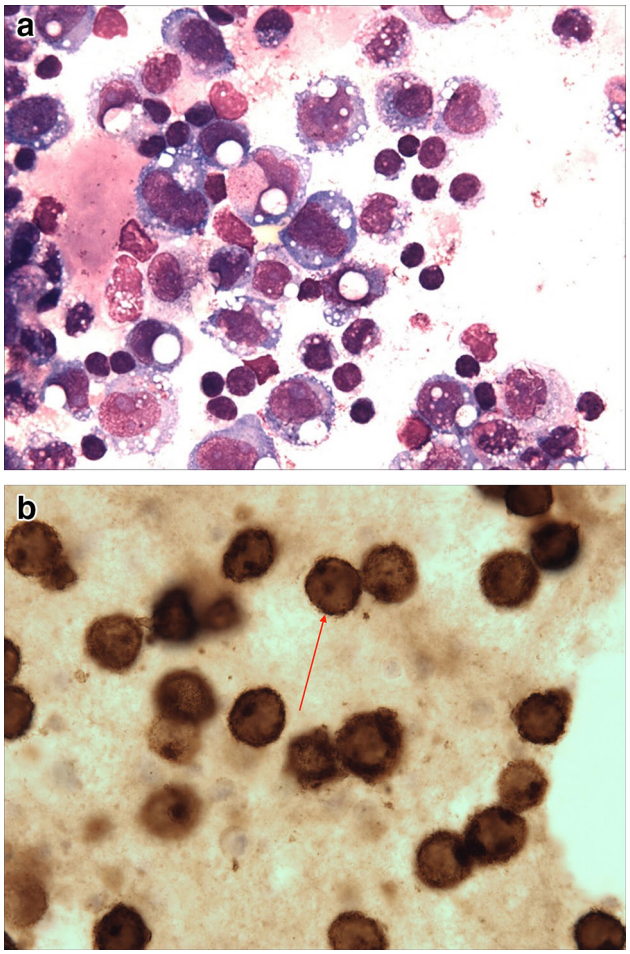

Fig. 4 Histological aspect of large and pleomorphic cells (red arrow). Immunohistochemistry test showing expression of the CD30 protein (red arrow) on large cells (from the authors)

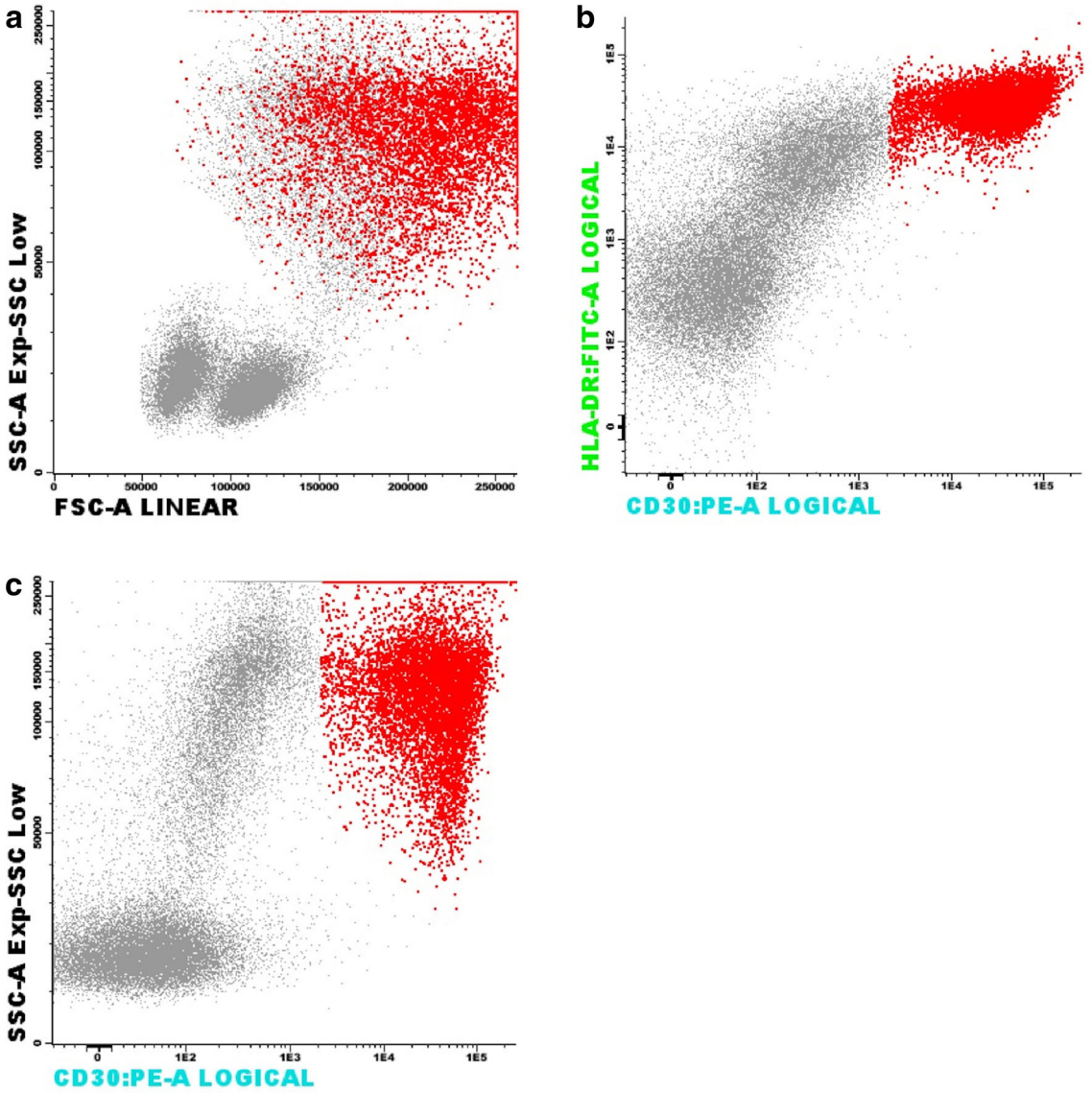

Fig. 5 Flow cytometry in a confirmed BIA-ALCL case. The red area shows atypical large CD 30 + expressing cells (from the authors)

It should be noted that such immunohistochemistry panels are not performed in routine fluid evaluations, so it is necessary to provide a clinical history and indicate the suspicion of BIA-ALCL for CD30 and ALK testing [36].

Staging

NCCN [29] has developed a staging system for BIA-ALCL associated with a solid tumor (Fig. 6). In the early stages of the disease, malignant cells are found solely in the periprosthetic fluid (stage IA) or the internal aspect of the capsule (stage IB) or a mass confined to the capsule (stage IC). If the tumor extends beyond the capsule, it is considered a T4 (stage II). If there are any lymph nodes or distant organs affected, this suggests disease progression (stages IIB, III, and IV).

A patient should not be submitted to surgery if the BIA-ALCL diagnosis is unconfirmed, and patients with confirmed BIA-ALCL should be referred to a clinical oncologist for proper evaluation and staging before surgery. PET scans are useful for scanning extracapsular disease and distant metastasis [29].

Treatment

One of the most critical aspects of treatment is for the plastic surgeon to be aware that the case consists of confirmed BIA-ALCL. It is not good practice to perform surgery before a complete BIA-ALCL diagnostic workup.

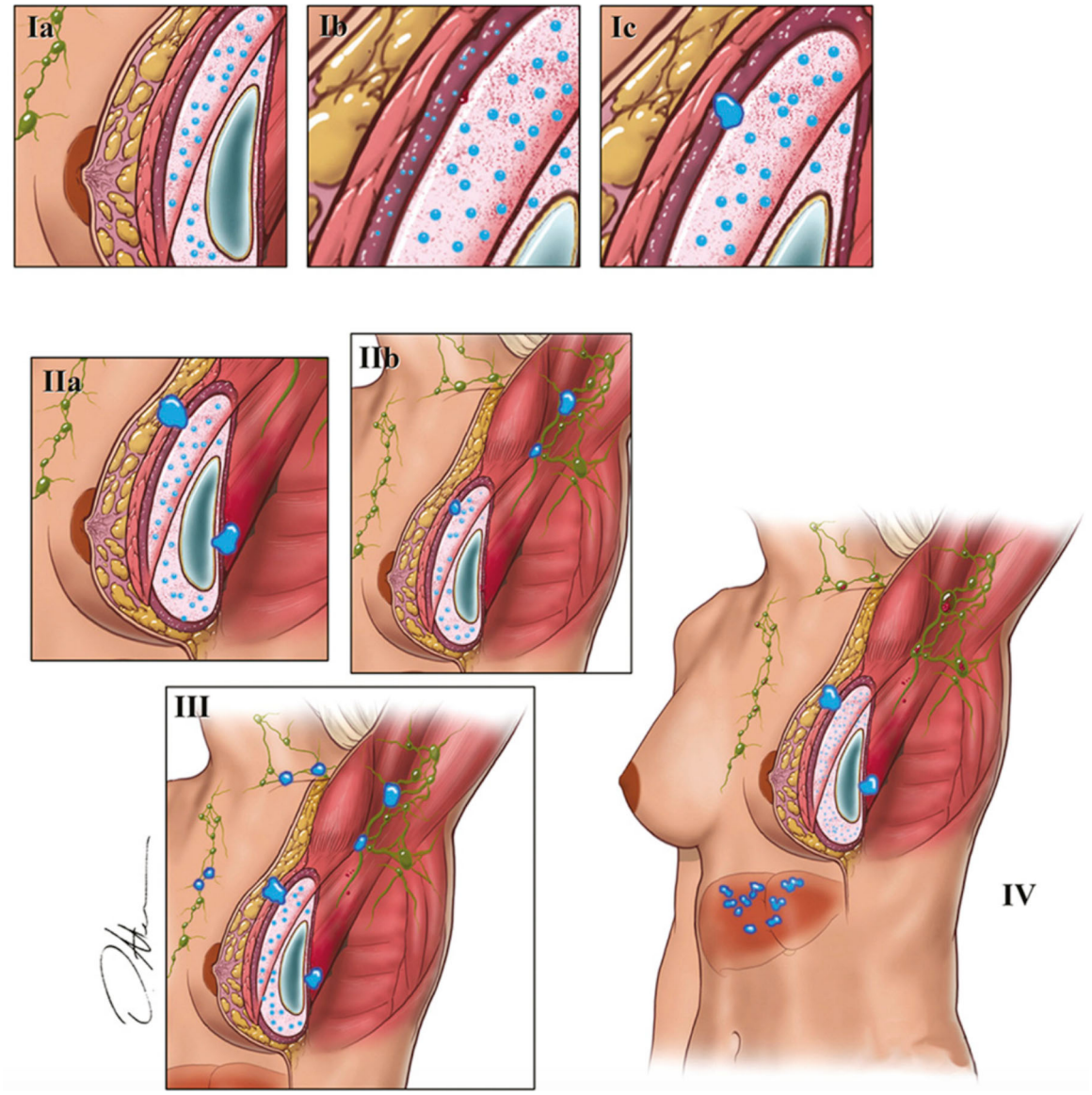

Fig. 6 BIA-ALCL STAGING. From Clemens et al. [44]. Reprinted with permission. © (2016) American Society of Clinical Oncology. All rights reserved

Surgical treatment consists of the removal of the implant, total capsulectomy (Figs. 7, 8, 9), and, for advanced stages (II, III or IV), lymphadenectomy, in which case the patient should be referred to a surgical oncologist. Sentinel-node biopsy appears to not be applicable in the treatment of BIA-ALCL [36].

After capsulectomy and implant removal, breast reconstruction should be performed with autologous tissue [37] or smooth implants. NCCN advises removing both implants due to some cases of incidental findings in the contralateral breast [18, 34].

The majority of patients do not require further treatment besides implant removal and total capsulectomy (stage I). It should be noted that incomplete removal of the capsule is staged as an advanced disease according to NCCN guidelines, meaning a higher recurrence rate and a decrease in the overall survival [34]; thus, the oncological resection of both implants and capsule (total capsulectomy) is required.

Further treatment may be necessary for advanced stages (II to IV), but there is no standardized therapy so far due to the small number of cases worldwide. NCCN guidelines were updated in 2019 [34] with the recommendation of adjuvant therapy with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) [1]. However, frontline therapy with brentuximab vedotin, an antibody–drug conjugated to a chimeric CD30, has been reported to produce good results, and it is now considered the "preferred" first-

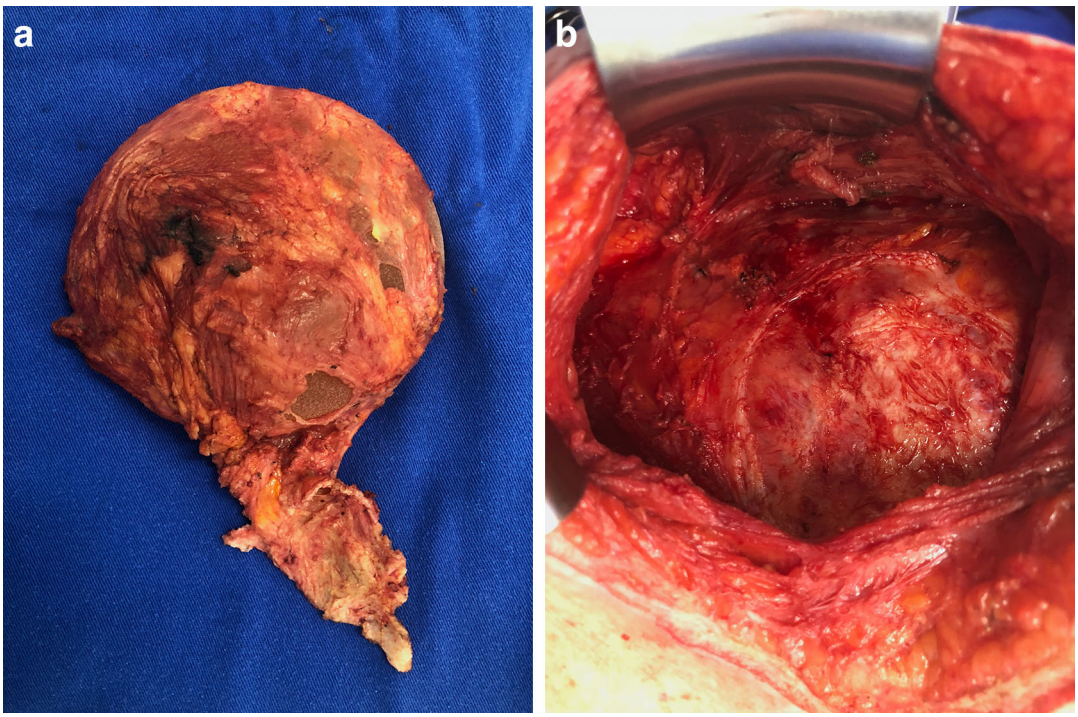

Fig. 7 Surgical treatment of BIA-ALCL. Submuscular Allergan 410 form-stable implant for breast reconstruction. Right: costal arches and intercostal muscles after posterior capsulectomy (from the authors)

line therapy [38, 39]. Residual or unresectable disease may eventually require radiotherapy [1].

Surveillance after implant removal and capsulectomy should involve examinations every three–six months, CT of chest, abdomen, and pelvis, or PET/CT scans every six months for the first two years after the surgery [18, 34].

Survival and Mortality

The majority of patients diagnosed with BIA-ALCL can be cured. Complete capsular removal is the most important factor in survival and cure [40]; thus, preoperative planning is mandatory, and the lack of adequate treatment may allow disease progression. The presence of tumor nodules, axillary lymph node involvement, bilateral breast involvement, and infiltrative pattern on capsule histology are correlated with more aggressive behavior [18].

Clemens et al. [41] reported the outcomes after treatment of BIA-ALCL. Both the presence of a mass and the extracapsular disease were associated with increased risks of recurrence and death.

Most deaths related to BIA-ALCL were associated with delayed diagnosis and treatment. Until August 2019, 33 reported deaths have been attributed to BIA-ALCL worldwide (Australia, Brazil, France, the UK, the Netherlands, New Zealand, Sweden, and the USA) [29, 33]. The overall survival and disease-free survival are difficult to determine due to a scarcity of data and proper follow-up.

Patient and Physician Education

Because BIA-ALCL is an indolent disease, which usually takes 8–10 years to develop, and is highly curable in early stages, awareness of this lymphoma is essential for prompt diagnosis and treatment.

It is essential to promote physician education, not only for breast surgeons and plastic surgeons but also primary care physicians and radiologists, as they might be the first doctors to evaluate the patient with symptoms.

Besides physician education, patient education is crucial. ASPS provides plenty of information about BIA-ALCL on its website [24], as well as other medical entities. However, the most effective way to properly educate patients is still through informed consent.

Informed Consent

In 2016, Clemens et al. [42] published a study regarding the importance of the informed consent document, which was followed by a joint statement from the International Society of Aesthetic Plastic Surgery (ISAPS), ASPS, and American Society for Aesthetic Plastic Surgery (ASAPS)

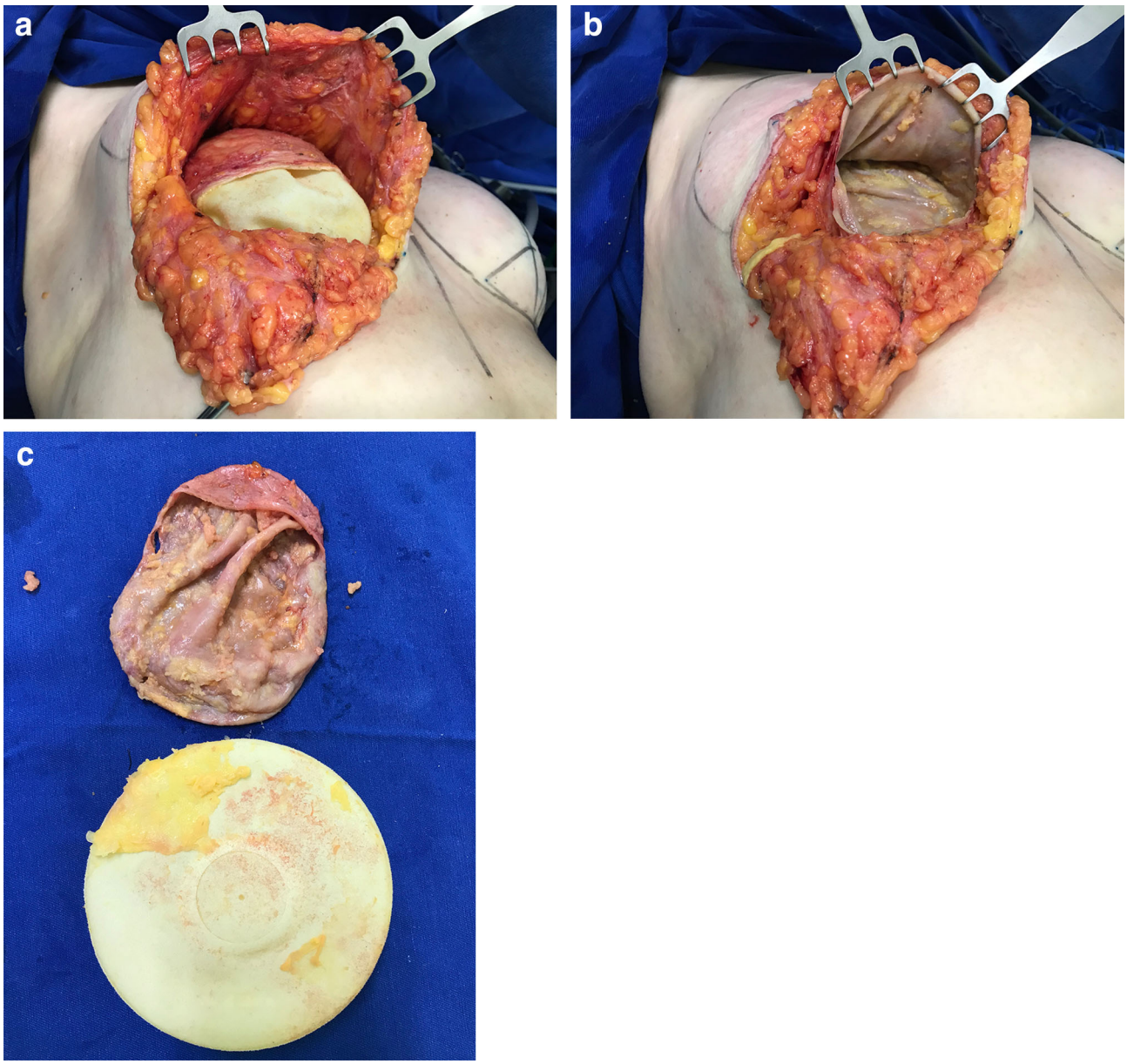

Fig. 8 Surgical treatment of BIA-ALCL. Subglandular polyurethane implant in place and removed. Total capsulectomy and explantation (from the authors)

[43], which resulted in the inclusion of information about BIA-ALCL risk in the informed consent document, as well as other suggestions of best practices.

The informed consent document must contain data regarding risk disclosure for development of BIA-ALCL, with the main objectives of making the patient aware of the disease, to educate the patient about the possible symptoms of the disease, particularly late seroma, and to instruct the patient to follow up with the plastic surgeon annually.

As of 2019, no patient should have been submitted to breast implant procedures without a clear preoperative discussion about BIA-ALCL and a regularly updated risk-wise informed consent.

Prevention

As increasing evidence connects the role of sustained T-cell response to implant bacteria/biofilm in the growth of BIA-ALCL, reducing the number of bacteria around implants is an essential step for prevention. Studies showed that methods to decrease the number of bacteria around implants reduced the incidence of capsular contracture to

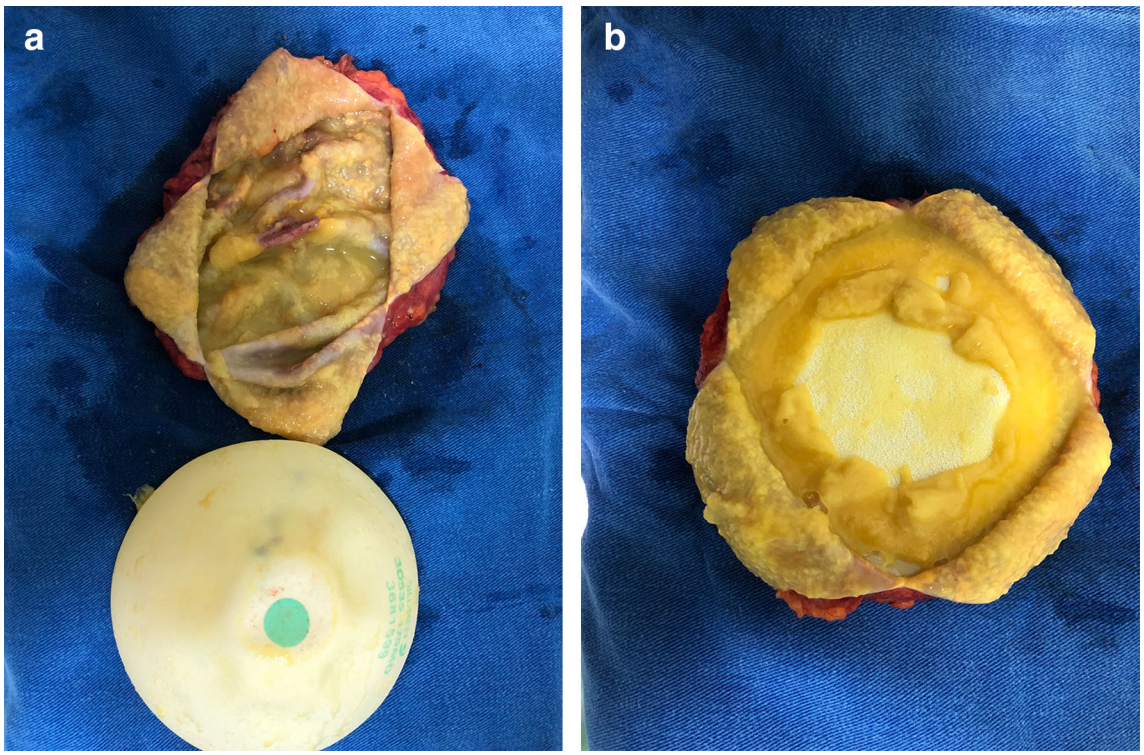

Fig. 9 Surgical treatment of BIA-ALCL on Subglandular Silimed polyurethane implant. Total capsulectomy. Capsular incision showing the aspect of the seroma (from the authors)

less than 1% [9, 18, 47]. As formerly noticed, BIA-ALCL is hypothesized to undergo a process similar to that of capsular contracture. Consequently, the same techniques that reduce bacterial contamination around implants will likely reduce the risk of implant-associated ALCL. Adams et al. [9] suggested a 14-point plan to reduce the risk of BIA-ALCL, as follows: (1) use of intravenous antibiotic prophylaxis at the time of anesthetic induction; (2) avoid periareolar/transaxillary incision; (3) use of nipple shields to prevent spillage of bacteria into the pocket; (4) conduct careful atraumatic dissection to minimize devascularized tissue; (5) perform careful prospective hemostasis; (6) avoid dissection into the breast parenchyma; (7) use a dual-plane pocket; (8) perform pocket irrigation with proven betadine triple-antibiotic solution, non-betadine triple or 50% solution (1:1 dilution povidone–iodine or stronger); (9) minimize skin contamination; (10) minimize implant open time and replacement of implant or sizers; (11) change surgical gloves before handling and use new or cleaned instruments and drapes; (12) avoid using a drain (augmentation); (13) use a layered closure; and (14) use antibiotic prophylaxis to cover subsequent procedures that breach skin or mucosa. By adopting this strategy in 42,000 macrotextured implants, Adams et al. [9] had no recorded cases of BIA-ALCL.

Swanson [45], however, refuted almost all of the 14 points and pointed out that they focus on blaming plastic surgeons for failing to observe adequate surgical sterility rather than analyzing the device itself for fault. He recommended banning textured devices, which are, according to him, the only factor known to be unambiguously associated with BIA-ALCL [46].

The Crisis of Textured Implants

As mentioned above, the development of BIA-ALCL seems to be associated with at least three factors: a textured breast implant, bacterial biofilm, and individual genetic predisposition [5].

In December 2018, the French Agency for the Safety of Health Products (ANSM) declined to renew the CE mark for Biocell and Microcell implants (Allergan, Dublin, Ireland), removing the products from 37 countries [47]. In April 2019, the ANSM banned all macrotextured or polyurethane-coated breast implants, thus impacting Sebbin, Polytech, Nagor, Eurosilicone, Arion, and Allergan [40]. However, after an advisory meeting on breast implant safety, the FDA issued a letter in May 2019 stating that "at this time FDA does not believe that, based on all the available data, any device meets the banning standard" [48]. In July 2019, the FDA-updated database reported 573 cases of BIA-ALCS, with 116 new cases and 24 new deaths worldwide since the previous communication in

March 2019 and recommended a voluntary recall of Biocell products in the USA. Allergan responded by issuing a global recall. Microcell and smooth implants were not subjected to the recommendation [49].

There seems to be a cyclic pattern of breast implant crises [50, 51] with implant brands being approved and then removed from the market, considerably harming patients that were already submitted to psychological stress and revision/removal surgeries [50]. The first crisis involved Dow Corning in 1982 [50] after reports that breast implants were related to autoimmune diseases. The second crisis, in 2010, occurred after investigations showed that Poly Implant Prothèse (PIP) implants contained a cheap, nonapproved industrial-grade silicone [50]. Over 600,000 patients were affected in 65 countries. It seems that the third crisis is currently affecting textured implants due to BIA-ALCL. Nonetheless, how can we avoid the next crisis? We believe it is possible to prevent such crises, but only if we start a mandatory worldwide collection of breast implant data and strengthen their registry.

Breast Implants Registry

Due to the rarity of BIA-ALCL, collecting case reports in shared databases represents the only available method to obtain data about this lymphoma [36]. Several efforts have been made in this direction [52]. Australia [53], New Zealand, Italy, the Netherlands, and the USA have created consistent breast implant registries. In the USA, a registry named PROFILE (Patient Registry and Outcomes For breast Implants and anaplastic large cell Lymphoma Etiology and Epidemiology) has also been created. Italy's Ministry of Health created the DISPOVIGILANCE [54], a dedicated online database to notify cases of BIA-ALCL. However, in most countries, there are no registry systems for breast implants. The Brazilian breast implant market is the second largest in the world, with several manufacturers and almost exclusively textured implants, and yet there are no more than a dozen reported cases [55]. Ramos-Gallardo [35] reported seven cases at the 2017 Mexican plastic surgery annual meeting, questioning the lower number of reported cases in Latin America, as there is a significant mismatch of incidence compared to Australia or the USA, which leads to the question whether there are actual differences between populations or Latin American physicians simply are not ready to identify BIA-ALCL cases. We know many locations in Latin America do not have access to laboratories with flow cytometry, so the diagnosis relies only on pathological analysis, sometimes resulting in false negatives [35]. Notification of BIA-ALCL in Brazil is not well structured, leading to underreporting. Teixeira [55] reported 11 confirmed cases in Brazil. Breast and plastic surgeons must work together to improve the registry of breast implants. Such an effort would allow the collection of detailed and robust data that could be shared internationally [56], contributing to the assessment of the safety of breast implants and elucidation of breast implant-associated disorders, including BIA-ALCL. The International Collaboration of Breast Registry Activities (ICOBRA^{TM}) was proposed as an intermediary mechanism to align the breast implant registries worldwide and, if successful, may bring some aspired answers.

What We Know So Far

Because it was only after 2016 that BIA-ALCL was recognized as an independent disease by the WHO, new data have been intensively published covering many aspects of the lymphoma.

What is known, so far, is that this is a type of cancer related to textured breast implants—not a strict sense breast cancer [9]—that are placed for reconstructive or cosmetic reasons, it usually appears 9 years after insertion and, if diagnosed early, it has a chance of cure with surgery alone [57].

Conclusions

The highest priority in breast surgery is the patient's safety and quality of life. We need to be aware and also make patients aware of this disease. We also need to facilitate early diagnoses because this is the key to the cure of BIA-ALCL [7].

Although the occurrence of BIA-ALCL has pointed out some important safety questions and brought some degree of uncertainty, we must keep in mind that it is an uncommon disease with good prognosis after implant removal and capsulectomy [56]. BIA-ALCL research will continue, and current theories will evolve. We need robust data to determine the real risk, but, based on findings available today, no data support the discouragement of the use of breast implants. With the more robust breast registries around the world, new data may or may not support the use of textured implants in the future. In markets where the vast majority of breast implants used are textured, such as the Brazilian market, the industry must start offering smooth implants as well.

The Allergan recall in July 2019 [49] with the worldwide removal of Biocell implants has created a crisis and some panic, but it is our obligation as doctors to analyze the data and numbers as they become available, besides using the scientific method for doing so. There are no recommendations for textured implant removal by any

regulatory agency or medical society to this day [49]; however, as mentioned above, new data are becoming available, and further studies are underway to assess the specific risk associated with textured implants [12]. Thus, we should continue to collect data regarding BIA-ALCL, besides exploring and considering all benefits and risks with the available breast devices, so that optimal and safe patient outcomes can be achieved [7].

Compliance with Ethical Standards

Conflict of interest Dr. Groth has received a speaker honorarium from Allergan. The authors received no financial support for the research, authorship, and publication of this article.

Human and Animal Rights This article did not require any studies with human participants or animals performed by any of the authors.

Informed Consent Informed consent is not required for this type of study.

References

1. Clemens MW, Horwitz SM (2017) NCCN consensus guidelines for the diagnosis and management of breast implant-associated anaplastic large cell lymphoma. Aesthet Surg J 37:285–289
2. Aladily TN, Nathwani BN, Miranda RN et al (2012) Extranodal NK/T-cell lymphoma, nasal type, arising in association with saline breast implant: expanding the spectrum of breast implant-associated lymphomas. Am J Surg Pathol 36:1729–1734
3. Keech JA Jr, Creech BJ (1997) Anaplastic T-cell lymphoma in proximity to a saline-filled breast implant. Plast Reconstr Surg 100:554–555
4. Swerdlow SH, Campo E, Pileri SA et al (2016) The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 127:2375–2390
5. Rastogi P, Deva AK, Prince HM (2018) Breast implant-associated anaplastic large cell lymphoma. Curr Hematol Malig Rep 13:516–524
6. Calobrace MB, Capizzi PJ (2014) The biology and evolution of cohesive gel and shaped implants. Plast Reconstr Surg 134:6S–11S
7. Calobrace MB, Schwartz MR, Zeidler KR et al (2017) Long-term safety of textured and smooth breast implants. Aesthet Surg J 38:38–48
8. Randquist C, Gribbe O (2010) Highly cohesive textured form stable gel implants: principles and techniques. In: Hall-Findlay EEG (ed) Aesthetic and reconstructive surgery of the breast. Elsevier, Philadelphia, pp 339–365
9. Adams WP Jr, Culbertson EJ, Deva AK et al (2017) Macrotextured breast implants with defined steps to minimize bacterial contamination around the device: experience in 42,000 implants. Plast Reconstr Surg 140:427–431
10. McGuire P, Reisman NR, Murphy DK (2017) Risk factor analysis for capsular contracture, malposition, and late seroma in subjects receiving Natrelle 410 form-stable silicone breast implants. Plast Reconstr Surg 139:1–9
11. Hall-Findlay EJ (2011) Breast implant complication review: double capsules and late seromas. Plast Reconstr Surg 127:56–66
12. Zingaretti N, Galvano F, Vittorini P et al (2019) Smooth prosthesis: our experience and current state of art in the use of smooth sub-muscular silicone gel breast implants. Aesthetic Plast Surg. https://doi.org/10.1007/s00266-019-01464-9
13. Namnoum JD, Largent J, Kaplan HM et al (2013) Primary breast augmentation clinical trial outcomes stratified by surgical incision, anatomical placement and implant device type. J Plast Reconstr Aesthet Surg 66:1165–1172
14. Jones P, Mempin M, Hu H et al (2018) The functional influence of breast implant outer shell morphology on bacterial attachment and growth. Plast Reconstr Surg 142:837–849
15. Collett DJ, Rakhorst H, Lennox P et al (2019) Current risk estimate of breast implant-associated anaplastic large cell lymphoma in textured breast implants. Plast Reconstr Surg 143:30S–40S
16. Hu H, Jacombs A, Vickery K et al (2015) Chronic biofilm infection in breast implants is associated with an increased T-cell lymphocytic infiltrate: implications for breast implant-associated lymphoma. Plast Reconstr Surg 135:319–329
17. Hu H, Johani K, Almatroudi A et al (2016) Bacterial biofilm infection detected in breast implant-associated anaplastic large-cell lymphoma. Plast Reconstr Surg 137:1659–1669
18. Deva AK, Adams WP Jr, Vickery K (2013) The role of bacterial biofilms in device-associated infection. Plast Reconstr Surg 132:1319–1328
19. Loch-Wilkinson A, Beath KJ, Knight RJW et al (2017) Breast implant-associated anaplastic large cell lymphoma in Australia and New Zealand: high-surface-area textured implants are associated with increased risk. Plast Reconstr Surg 140:645–654
20. Leberfinger AN, Behar BJ, Williams NC et al (2017) Breast implant-associated anaplastic large cell lymphoma: a systematic review. JAMA Surg 152:1161–1168
21. Bizjak M, Selmi C, Praprotnik S et al (2015) Silicone implants and lymphoma: the role of inflammation. J Autoimmun 65:64–73
22. Adams WP Jr, Conner WC, Barton FE Jr et al (2000) Optimizing breast pocket irrigation: an in vitro study and clinical implications. Plast Reconstr Surg 105:334–338 **discussion 339-343**
23. Jewell ML, Adams WP Jr (2018) Betadine and breast implants. Aesthet Surg J 38:623–626
24. Blombery P, Thompson E, Ryland GL et al (2018) Frequent activating STAT3 mutations and novel recurrent genomic abnormalities detected in breast implant-associated anaplastic large cell lymphoma. Oncotarget 9:36126–36136
25. Adams WP Jr (2017) Discussion: breast implant-associated anaplastic large cell lymphoma in Australia and New Zealand: high-surface-area textured implants are associated with increased risk. Plast Reconstr Surg 140:663–665
26. American Society of Plastic Surgeons BIA-ALCL Physician Resources. https://www.plasticsurgery.org/for-medical-professionals/health-policy/bia-alcl-physician-resources/by-the-numbers. Accessed 5 Aug 2019
27. Therapeutic Goods Administration (TGA). Breast implants and anaplastic large cell lymphoma. https://www.tga.gov.au/alert/breast-implants-and-anaplastic-large-cell-lymphoma. Accessed 24 Jan 2019
28. Brody GS, Deapen D, Taylor CR et al (2015) Anaplastic large cell lymphoma occurring in women with breast implants: analysis of 173 cases. Plast Reconstr Surg 135:695–705
29. Doren EL, Miranda RN, Selber JC et al (2017) U.S. epidemiology of breast implant-associated anaplastic large cell lymphoma. Plast Reconstr Surg 139:1042–1050
30. Magnusson M, Beath K, Cooter R et al (2019) The epidemiology of breast implant-associated anaplastic large cell lymphoma in Australia and New Zealand confirms the highest risk for grade 4 surface breast implants. Plast Reconstr Surg 143:1285–1292
31. Ruffenach L, Bruant-Rodier C, Goldammer F et al (2019) Thirty-six (36) French cases of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL): What do we know about their

prosthetic histories, and what conclusions may be drawn? Ann Chir Plast Esthet 64:285–292
32. Clemens MW, Brody GS, Mahabir RC et al (2018) How to diagnose and treat breast implant-associated anaplastic large cell lymphoma. Plast Reconstr Surg 141:586e–599e
33. Di Napoli A, Pepe G, Giarnieri E et al (2017) Cytological diagnostic features of late breast implant seromas: from reactive to anaplastic large cell lymphoma. PLoS ONE 12:e0181097
34. Elswick SM, Nguyen MT (2018) Breast erythema in a patient with breast implant-associated anaplastic large cell lymphoma: a Case Report Discussing Cutaneous Manifestations. Aesthet Surg J 38:NP47–NP52
35. Deva AK (2018) Commentary on: Breast erythema in a patient with breast implant-associated anaplastic large cell lymphoma: a case report discussing cutaneous manifestations. Aesthet Surg J 38:NP53–NP55
36. U.S. Food and Drug Administration (FDA) FDA. Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) Available at: www.fda.gov/medicaldevices/productsandmedicalprocedures/implantsandprosthetics/breastimplants/ucm239995.htm. Aug 5th 2019
37. Clemens MW, Jacobsen ED, Horwitz SM (2019) 2019 NCCN consensus guidelines on the diagnosis and treatment of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). Aesthet Surg J 39:S3–S13
38. Ramos-Gallardo G, Cuenca-Pardo J, Cardenas-Camarena L et al (2018) Is Latin America ready to identify anaplastic large cell lymphoma in breast implants patients? Regional encounter during the national plastic surgery meeting in Cancun, Mexico. Aesthetic Plast Surg 42:1421–1428
39. Nava MB, Adams WP Jr, Botti G et al (2018) MBN 2016 aesthetic breast meeting BIA-ALCL consensus conference report. Plast Reconstr Surg 141:40–48
40. Santanelli di Pompeo F, Laporta R, Sorotos M et al (2015) Breast implant-associated anaplastic large cell lymphoma: proposal for a monitoring protocol. Plast Reconstr Surg 136:144e–151e
41. Alderuccio JP, Desai A, Yepes MM et al (2018) Frontline brentuximab vedotin in breast implant-associated anaplastic large-cell lymphoma. Clin Case Rep 6:634–637
42. Pro B, Advani R, Brice P et al (2012) Brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large-cell lymphoma: results of a phase II study. J Clin Oncol 30:2190–2196
43. Mehta-Shah N, Clemens MW, Horwitz SM (2018) How I treat breast implant-associated anaplastic large cell lymphoma. Blood 132:1889–1898
44. Clemens MW, Medeiros LJ, Butler CE et al (2016) Complete surgical excision is essential for the management of patients with breast implant-associated anaplastic large-cell lymphoma. J Clin Oncol 34:160–168
45. Clemens MW, Miranda RN, Butler CE (2016) Breast implant informed consent should include the risk of anaplastic large cell lymphoma. Plast Reconstr Surg 137:1117–1122
46. Joint ASPS & ASAPS Statement on Breast Implant-Associated ALCL. https://www.surgery.org/sites/default/files/BEST%20PRACTICES_1.pdf. Accessed 23 Jan 2017
47. Giordano S, Peltoniemi H, Lilius P et al (2013) Povidone–iodine combined with antibiotic topical irrigation to reduce capsular contracture in cosmetic breast augmentation: a comparative study. Aesthet Surg J 33:675–680
48. Swanson E (2019) The textured breast implant crisis: a call for action. Ann Plast Surg 82:593–594
49. Swanson E (2017) Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL): why the search for an infectious etiology may be irrelevant. Aesthet Surg J 37:NP118–NP121
50. (ANSM) Andsdmedpds Le marquage CE des implants mammaires texturés de la marque Allergan (Microcell et Biocell) n'a pas été renouvelé par l'organisme notifié GMED - Point d'information. https://ansm.sante.fr/S-informer/Points-d-information-Points-d-information/Le-marquage-CE-des-implants-mammaires-textures-de-la-marque-Allergan-Microcell-et-Biocell-n-a-pas-ete-renouvele-par-l-organisme-notifie-GMED-Point-d-information. Accessed 5 Aug 2018
51. (FDA) USFaDA Statement from FDA Principal Deputy Commissioner Amy Abernethy, M.D., Ph.D., and Jeff Shuren, M.D., J.D., director of the FDA's Center for Devices and Radiological Health on FDA's new efforts to protect women's health and help to ensure the safety of breast implants. https://www.fda.gov/news-events/press-announcements/statement-fda-principal-deputy-commissioner-amy-abernethy-md-phd-and-jeff-shuren-md-jd-director-fdas. Accessed 5 Aug 2019
52. (FDA) USFaDA FDA. Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). https://www.fda.gov/medical-devices/safety-communications/fda-requests-allergan-voluntarily-recall-natrelle-biocell-textured-breast-implants-and-tissue. Accessed 5 Aug 2019
53. Deva AK, Cuss A, Magnusson M et al (2019) The "Game of Implants": a perspective on the crisis-prone history of breast implants. Aesthet Surg J 39:S55–S65
54. Deva AK (2019) A perspective on the never-ending cycle of breast implant crises. Aesthet Surg J 39:NP85–NP86
55. Hopper I, Ahern S, Nguyen TQ et al (2018) Breast implant registries: a call to action. Aesthet Surg J 38:807–810
56. Australian Breast Device Registry. https://dica.nl. https://www.abdr.org.au. Accessed 20 Jan 2019
57. Campanale A, Boldrini R, Marletta M (2018) 22 cases of breast implant-associated ALCL: awareness and outcome tracking from the Italian Ministry of Health. Plast Reconstr Surg 141:11e–19e
58. Teixeira BN (2018) Anaplasic large cells lymphoma associated with breast implants. Mastology 28:67–68
59. Young-Afat DA (2018) Risk of breast implant-associated anaplastic large cell lymphoma. JAMA Oncol 4:1434–1435
60. Deva AK (2017) Discussion: U.S. Epidemiology of Breast Implant-associated anaplastic large-cell lymphoma. Plast Reconstr Surg 139:1051–1052