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LETTER TO THE EDITOR

Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL): An Open Wound

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Abstract Since 2017, there have been an increasing number of reported cases regarding breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) in the literature. Although significant attention was dispensed for this relevant issue, there is no consensus on what the trigger points for disease development are. BIA-ALCL trigger point speculation includes textured breast implants, bacterial contamination, and genetic factors. However, little attention is given by the literature regarding gel bleeding and the toxicity of polydimethylsiloxane. This opinion-based article aims to report our experience in a prospective study of breast implants and share our knowledge regarding silicone-induced granuloma of breast implant capsule.
Level of Evidence V 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.

Recently, a discussion session regarding BIA-ALCL was published in this journal [1]. All articles report the importance of diagnosis but emphasize the rarity of its frequency: 500 confirmed cases. However, the etiology of BIA-ALCL remains unclear while accepting the possibility of multifactorial origin. There seems to be consensus on the association with textured implants. However, gel bleeding/detrition has little attention to this issue.

Since early 2017, we started a prospective study at our institution to research BIA-ALCL. The research was approved by the ethics committee and registered at Plataforma Brasil. Patients referred for magnetic resonance imaging (BMRI) who had breast implants were included in the study. Breast ultrasound, percutaneous biopsy, or surgical excision consists of further investigation in patients with positive findings. Based on an observational study, we described a new pathology related to breast implants: silicone-induced granuloma of a breast implant capsule (SIGBIC) [2]. For SIGBIC diagnosis, we adopt three restrictive BMRI criteria: black drop signal, late contrast enhancement, and mass with a hyper signal at T2* images, previously published. Since then, we acquired experience regarding implant-related imaging findings, with extensive documentation of images, clinical data, and histopathology [3].

Throughout the study, we observed the high frequency of SIGBIC in our patients, about 30%. Many patients had common symptoms such as joint pain, skin itching/pruritus, and breast hardening/enlargement. All patients referred to percutaneous breast biopsy or surgical capsulectomy confirmed silicone particles in histology. In the same period began a worldwide movement of women reporting complications related to breast implants. They named the disease as breast implant illness (BII). Because of the lack of scientific evidence, Medical Societies handled these reports as myths. However, many of the stories reported by these women were similar to those observed in our study. If we search for breast implant illness in Google images, the number of results is incredible.

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After 3 years of study, we had no case of BIA-ALCL. However, we had 689 confirmed cases of SIGBIC in 1643 patients included in the study (to be published). Of that, only five patients had smooth implants. Interestingly, in many cases, the clinical complaints and imaging findings were very similar to those reported in the articles on BIA-ALCL, which generated publications on the subject [4–6]. Recently, we had the first confirmed BIA-ALCL case.

As we speculated in previous studies, the BIA-ALCL-compromised breast implant showed signs of deterioration of its shell and a change in its internal contents, despite the lack of macroscopic evident rupture. Further documentation of the implant shell was performed with a 1600-magnification fold digital microscope (Koolertron, Hong Kong, China). Although it was a textured implant, we observed changes in both textured and smooth surfaces. Most often, the changes were at the transition zone of the smooth to the textured surface (posterior seal).

Surface deterioration of the silicone shell with signs of permeability loss was the main findings. The presence of oil/lipids inside the implant that reacts with the inside content indicates the permeability loss (Fig. 1a, b).

The substance used in the production of silicone is polydimethylsiloxane (PDMS). Silicone is toxic when found in isolation [7]. In both the smooth and textured areas of the BIA-ALCL implant, we observed the decomposition of silicone with the release of silicone corpuscles. When it comes into contact with the fibrous capsule, it triggers an immune response that may vary in intensity according to the host. The trigger point of this reaction is when the macrophages phagocyte these particles. In the histology, intracellular silicone identified as foamy histiocytes is the main finding. The intensity of the immune response to silicone corpuscles is qualitative rather than quantitative, as discussed in our previous manuscripts. Although it is easy to perform, SIGBIC-diagnosed cases are rare in our practice, mainly due to the lack of knowledge of pathologists and radiologists about this issue. Some reasons could be enumerated: (1) in the histology, xylol washes silicone particles on the slide preparation; (2) for diagnosis, the polarized light microscope has better performance detecting silicone residues; and (3) there is a lack of foamy histiocytes described at the final histology report. For BMRI, the use of contrast media and the knowledge of SIGBIC findings are needed to perform the diagnosis.

The relevance of these findings extends in the explanation of breast implant illness. Today, if a patient is CD30 positive at immunochemistry, she will be diagnosed with BIA-ALCL and adequately treated. If negative, her illness may be considered incidental. We found in our study at least ten severe cases of SIGBIC, CD30 negative. The clinical complaints of these cases were worse than those of the BIA-ALCL case at our institution. They were usually

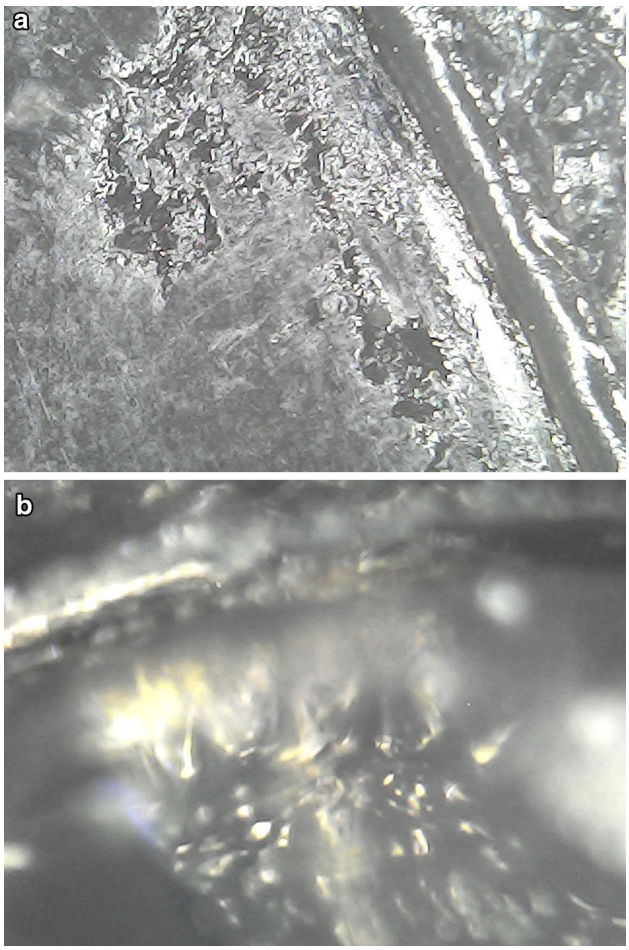

Fig. 1 **a** Digital magnification fold of ×1600. Posterior aspect of breast implant in the area of the transition of smooth to textured surface (seal) in a patient diagnosed with BIA-ALCL. It is possible to see degradation/leakage of the shell at the smooth surface. It is also possible to note color change at the textured surface, from clear to cloudy. **b** Same implant. At the region of the transition, when looking at the interior content, there is fat/ oil in the surface with chemical reaction to the internal content (silicone gel), inferring loss of permeability

from patients referred to our services after the unsuccessful empirical treatment of breast infections. Another issue is that some protocols advocate the use of betadine (50% or higher concentration of povidone-iodine [PI] 10% solution, 1% available iodine) (Purdue Frederick Company, Stamford, CTI) to prevent bacterial infections (*Ralstonia pickettii*). However, as a chemical agent, the safety of this procedure could be compromised since this could react with the shell polymer and speed up the chemical reaction [8].

CD30 is not a tumor marker. It is just a replication activity membrane marker. Its expression should be higher at the acute phase of the inflammatory process. We speculate that if there is high consumption of T lymphocytes in this stage, immature lymphocytes are likely to be recruited.

We believe that many of our patients were CD30 negative due to the remission of the inflammatory process following clinical antibiotic and anti-inflammatory treatments, reducing the replication activity of the membrane [9]. We also classified the severity of SIGBIC according to imaging and histological findings in previous studies [9, 10].

Probably, the relationship between BIA-ALCL and texturized implants is more related to the percentage of this type of implant. In Brazil, smooth implants are rare. However, in our SIGBIC study, we observed silicone corpuscles in all implant types and brands, including the smooth ones.

Possibly, we arrived at a time that the discussion about the safety of breast implants should not be restricted to the presence of BIA-ALCL. Gel bleeding and PDMS toxicity are an issue that our Medical Societies should discuss.

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Compliance with Ethical Standards

Conflict of interest There is no competing interest.

Ethics Approval Waived due to the type of manuscript.

Informed Consent Informed consent was obtained from the patient.

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