# **EDITORIAL**





# 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

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Received: 13 March 2018/Accepted: 28 April 2018/Published online: 16 May 2018 © Springer Science+Business Media, LLC, part of Springer Nature and International Society of Aesthetic Plastic Surgery 2018

#### **Abstract**

Introduction Anaplastic large cell lymphoma associated with breast implants is receiving increased attention. Most cases have been reported in Europe, North America (USA and Canada), Australia and New Zealand. Fewer cases have been reported in Latin America (including Mexico), Africa and Asia.

Methods This report was delivered during our national plastic surgery meeting in Cancun in May 2017. Before the meeting, two participants reviewed the literature. The review was performed using the following information sources: PubMed, Embase, Cochrane, Fisterra, Google Scholar and LILACS, with entries from 1980 to August

2015 in several languages (English, Spanish, French and Portuguese). The results were revealed during the meeting to the other participants. The consensus was divided into two parts. The first part included an open-ended question regarding the incidence and prevalence of the problem. The second part included clinical scenarios with different items that were rated by the participants. After this activity, accordance among the responses was evaluated.

Results Seven cases were reported during the meeting (3 from Mexico, 3 from Chile and 1 from Argentina). Fifty percent of the participants reported consulting with guidelines and clinical centers to help with potential cases. Most agreed that further studies must be done in cases of chronic seroma where the capsule plays an important role.

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Discussion A current debate exists about the incidence of this problem in Latin America because we did not report the same number of cases as Europe, Australia or North America. More studies are required to determine the differences among reports in Latin America.

Conclusion Most representatives agreed that further studies must be done. Concern is increasing, and the problem is known. Other factors involved may be considered, and the problem must not be ignored.

*No Level Assigned* 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 implant · Anaplastic large cell lymphoma · ALCL · Adverse event

# Introduction

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) should be suspected in any patient with breast implants and chronic seroma [1–4]. Most cases have been reported from North America, Europe or Oceania [5–7]. In Mexico and Latin America, there is a concern of this pathology.

We reported the first case in Latin America, which was a Mexican patient with a previous history of breast augmentation and liposuction 8 years before the appearance of breast asymmetry due to chronic seroma [8]. The diagnosis was confirmed by the pathologist after several samples without specific diagnoses. At that moment, we did not find any reports of BIA-ALCL from Central or South America.

Brazil and Mexico are important in the world market of texturized breast implants. For this reason, we organized a meeting with the presidents of different plastic surgery societies to discuss this pathology in the region.

## Methods

A consensus was achieved with representatives from different plastic surgery societies of the region during our national meeting in Cancun. We had representatives from Argentina, Chile, Colombia, Costa Rica, Guatemala, Mexico, Nicaragua, Panama, Paraguay, Peru, Dominican Republic and Venezuela (Fig. 1).

Two participants reviewed the literature before the event. The review was performed using the following information sources: PubMed, Embase, Cochrane, Fisterra, Google Scholar and LILACS. We evaluated articles

published from 1980 to August 2015, in several languages (English, Spanish, French and Portuguese).

The MESH language was used to identify keywords in our research. The following keywords were used: lymphoma or non-Hodgkin's lymphoma or anaplastic large cell lymphoma or ALCL or BIA-ALCL and breast implant or breast prostheses, breast implants or silicones or silicone gel and adverse effects. Article selection: Two researchers reviewed the publications and selected articles based on inclusion and exclusion criteria. The inclusion criteria were cases or a series of cases with at least six of the following variables: age, breast implants, time since implantation and onset of symptoms, implant brand, implant cover characteristics (texturized, non-texturized or polyurethane), biopsy or histopathological study that confirmed the lymphoma diagnosis, markers that were used to perform the diagnosis, surgical treatment, chemotherapy, radiotherapy, follow-up and mortality due to lymphoma associated with breast implants. The exclusion criteria were studies that provided incomplete information or duplicate data for their cases. The results were reported to the participants.

We divided the consensus into two parts. The first part consisted of an open-ended question:

- Do you know any cases of BIA-ALCL in your country?
- 2. If the answer is yes, how many confirmed cases do you have?
- 3. In your country, do you use any medical guidelines to approach any possible cases of BIA-ALCL?
- 4. Do you have pathologists with enough experience to diagnose these cases in your country?
- 5. Do you have a reference center for any possible cases in your country?

The second part consisted of clinical scenarios, each scenario with questions and answers numbered from 1 to 10 with scores of 1–3 indicating disagreement, 4–7 uncertainty and 8–10 agreement. Each question had a final grade rating.

The main questions from the clinical scenarios were as follows:

- At the time of removing or changing breast implants in an asymptomatic patient with chronic seroma, what is the importance of sending samples to laboratory and pathology? Nothing, culture, histochemistry, pap smear, pathology sample, markers.
- A patient with history of breast implants (placed more than 1 year ago) comes to the clinic for an increase in breast tissue volume. What will be the clinical findings that you will investigate? Breast asymmetry, nodes, inflammation.





Fig. 1 Banner of the event

- 3. In the same patient, what type of breast imaging will you propose? Nothing, ultrasound, CT scan, MRI.
- 4. What will be your treatment if fluid (seroma) is found in the studied breast? Wait for spontaneous resolution, antibiotic and anti-inflammatory drugs, puncture-guided surgical aspiration.
- 5. Once the fluid has been aspirated, what type of study will you order? Nothing, culture, pap smear, immunomarkers, immunohistochemistry.
- Do you agree to order the following test to identify possible bacteria or biofilm? Sonication, normal culture, anaerobe culture, mycobacteria, PCR for mycobacteria.
- 7. If after seroma aspiration, the patient returns because of persistence of the problem, what will be your approach? Implant removal of the affected side, implant removal both sides, exchange implant, fluid aspiration, capsulectomy, nodes exploration.
- 8. What type of study will you order for the capsule? None, culture, histopathology, immunomarkers.
- 9. Once the implant is removed, what findings will you look for in the implant? Integrity, site of rupture, opacity, type of implant (silicone, saline), type of

- coverage (smooth and texture), brand, timing of implantation.
- 10. In cases of suspected BIA-ALCL, in addition to the pathology report, what type of clinical findings will you record? Age, race, location of pocket, past history of drains, antibiotics, past history of seroma, type of incision.

# **Results**

In total, 172 publications were identified; according to the inclusion and exclusion criteria, information from 42 articles was discussed with the panelists [8–49] including representatives of plastic surgery societies from Argentina, Colombia, Costa Rica, Guatemala, Mexico, Nicaragua, Panama, Paraguay, Peru, Dominican Republic and Venezuela.

Representatives from three societies confirmed at least one case of BIA-ALCL (Chile 3, Mexico 3 and Argentina 1). Fifty percent of the representatives reported that they would consult with a center to follow guidelines for approach and treatment. All participants were informed about the relationship between BIA-ALCL and chronic



Table 1 Results of the second part of the study

	Disagree	Uncertain	Agree	
At the time to remove or exchange breast in send samples to laboratory and pathology		patient, if additional findir	ng is chronic seroma, who	at is the importance t
Nothing	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	1.53
Culture	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.9
Histochemistry	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.5
Pap smear	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	6.6
Pathology	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.75
Markers	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8
If female with breast implant comes to clinic will be the clinical findings that you will		volume of breast tissue (im	plants were placed more	than 1 year ago), who
Breast asymmetry	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.23
Nodes	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.52
Inflammation	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.62
In the same patient what type of breast ima	ge will you propose?			
Nothing	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	1.07
Ultrasound	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.5
CT scan	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	5.68
MRI	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.7
In the breast image study if the final report	comes with fluid (seron	na), what will be your treati	ment?	
Waiting expontaneous resolution	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	3.1
Antibiotic and anti-inflammatory	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	5.9
Puncture guided	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	6.2
Surgical aspiration	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.4
Once the fluid has been aspirated, what type	e of study will you orde	r?		
Nothing	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	2.25
Culture	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.83
Pap smear	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.72
Immunomarkers	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.33
Immunohistochemistry	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.89
Do you agree to order the following test to	identify possible bacter	ia or biofilm?		
Sonication	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	4.5
Normal culture	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.1
Anaerobes culture	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.18
Mycobacteria	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.46
PCR for mycobacteria	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7
If after seroma aspiration patient came back	with persistence of the	problem, what will be you	r approach?	
Repeat treatment	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	3.1
Consult oncology	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	6.8
Implant removal of the affected side	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.58
Implant removal both sides	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.94
Exchange implant	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	5.76
Fluid aspiration	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.6
Capsulectomy	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.05
Nodes exploration	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	6.5
What type of study will you order to the ca				
None	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	2.25
Culture	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.83
Histopathology	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.72



Table 1 continued

	Disagree	Uncertain	Agree	
Immunomarkers	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.33
Histochemistry	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.89
Once the implant is removed, what type of fir	ndings will you be lookii	ng for in the implant?		
Integrity	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.38
Site of rupture	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.35
Opacity	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.76
Type of implant (silicone or saline)	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.94
Type of coverage (smooth or texture)	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.38
Brand	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.47
Timing implantation	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.7
In case of possible case of lymphoma addition	nal to the pathology repo	ort, what type of clinical fine	dings will you register?	
Age	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	7.88
Race	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.72
Pocket location	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.27
Type of incision	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.31
Use of drains	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.31
Antibiotic	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	8.15
Past history of seroma	(1) (2) (3)	(4) (5) (6) (7)	(8) (9) (10)	9.57

seroma. The subject has been discussed in the meetings in the region.

Table 1 shows the results of the second part of the study.

#### Discussion

BIA-ALCL is a rare malignancy arising in an effusion or capsule in breast prosthesis.

The causes of this pathology are debatable and include, for example, biofilm due to bacteria, the surface of the or a possible genetic predisposition. [17, 25, 50, 51]. This condition drew our attention because in South America, we observed more reports than those in other countries with smaller populations. It is true that some authorities play an important role in recording cases and providing important information about this pathology, and some others work in close contact with different societies [5]. Specifically, in Mexico, we have organized sessions, meeting and guidelines because we represent an important market for texture implants, and we only have information from three cases, the first of which was reported to the companies 2 years ago [8].

Since the first report, we have seen an increase in the information about this matter [52]. More recent studies in our population will help to clarify the possible causes, including the genetic or demographic factors that may play a role in this pathology. We are working together with other plastic surgery societies including the Global

Network of BIA-ALCL. This is a group of experts from different parts of the world who are joining efforts, knowledge and experience in this subject. As mentioned by Clemens and colleagues, it is extremely important to mention the possibility of this problem in the informed consent [53].

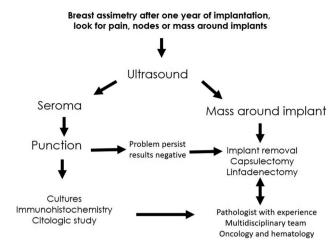
We have instructed plastic surgeons to be aware about the possibility of chronic seroma in any patient with breast asymmetry after 1 year of implantation. Additional findings including nodes, contracture and masses should also be determined [1–4].

It is important to mention that not all the cases of chronic seroma are ALCL, but the most common symptom of ALCL is chronic seroma [54] [56] (Fig. 2). The cases that we know of from our region were diagnosed by persistence of the seroma and high suspicion from the plastic surgeon. Our suggestion in the case of chronic seroma is to take a sample by puncture-guided ultrasound and to work with an experienced pathologist. In cases of high suspicion even after a negative result, we should consider bilateral removal and capsulectomy to help make diagnoses and guide important steps in treatment.

Most of the information comes from other countries, and we are aware of this, so we are making an effort to join all the possible cases with the same group of specialists to provide the same treatment. We should not forget that cancer treatment has changed in recent years. New biological treatments have come into the field [55].

Traditionally, surgery has been the key treatment of many cancers, for example, breast cancer. Currently, new





**Fig. 2** Algorithm for the management of chronic seroma in patients with breast implants. Chronic seroma is defined as one that occurs after 1 year from the placement of breast implants

treatments have come into use. Specific markers, such as Her2, have become important, and trastuzumab has become one of the main treatments in the field [56]. Brentuximab has become a new option to treat BIA-ALCL, and for this reason, it is very important that every society, medical authority and country has a pathologist capable of confirming diagnoses using proper markers such as CD30 and ALK. Immunology is receiving more attention as a promising treatment option to help patients with advanced stage cancer.

BIA-ALCL is not as common as breast cancer, and for this reason, we encourage that in any suspected case of BIA-ALCL, the patient should be oriented to a multidisciplinary treatment approach where the plastic surgeon can help to make right diagnosis [57]. We have seen that it is not common for the pathologist to study this problem. In South and Central America, we know that pathologists are not familiar, so if the problem persists (seroma), we can collaborate to rule out this entity. In Mexico, it was necessary to take more than one sample to rule out this problem in the first case. We also know this is not the same problem as there is in other countries at this moment.

The topic seems to be popular in social media and the news. We need to be careful how we handle this problem and how we inform our patients.

### Conclusion

BIA-ALCL is receiving increased attention among different societies in the region. More efforts to create a multidisciplinary team will improve awareness of this problem. All participants agreed that the manner in which chronic seroma is approached needs to be changed, and efforts to consult with a multidisciplinary team will help to make the correct diagnoses and treatment.

Acknowledgements We want to acknowledge the great effort of Dr. María del Mar Vaquero Pérez. She has contributed to the study of this pathology in the region. She collaborates with different plastic surgery societies in the region. She is an enthusiastic and cooperative surgeon that always offers help to the members of the FILACP (Federación IberoLatinoamericana de Cirugía Plástica). She is an active member of the FILACP and the Sociedad Española de Cirugía Plástica Reparadora y Estética (SECPRE). We want to recognized the work of Rufino Iribarren Moreno, Ernesto Theurel Sangeado and Marco Antonio Kalixto Sánchez if favor of the Safety of the Plastic Surgery. He works has done a lot in favor of the patients.

#### **Compliance with Ethical Standards**

Conflict of interest The authors declare that they have no conflict of interest.

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