HEMATOLOGY, TRANSFUSION AND CELL THERAPY

www.htct.com.br

Case Report

Breast implant-associated – Anaplastic Large Cell Lymphoma: a call for disease awareness

Lara de Holanda Jucá Silveira, *Vanessa Silva de Oliveira*, *Ronald Feitosa Pinheiro* *

Universidade Federal de Ceará (UFC), Fortaleza, CE, Brazil

ARTICLE INFO

Article history:
Received 19 April 2021
Accepted 21 June 2021
Available online 11 September 2021

Introduction

Breast lymphomas are rare non-Hodgkin extranodal lymphomas, mostly B-cell derived, representing less than 1% of breast malignant tumors, being either primary (PBL) or secondary (SBL) neoplasms. Among these, SBLs have slow progression and are associated with breast implants. BIA-ALCL (Breast Implant-Associated – Anaplastic Large Cell Lymphoma) is a CD 30 positive/ALK-negative non-Hodgkin lymphoma usually localized with capsule-restricted initial clinical onset, although capsule invasion and systemic disease are still threatening.

Despite its not well-defined molecular origin, some BIA-ALCL cases have markedly mutated JAK1-STAT3 pathway effectors and epigenetic regulators.[1] Moreover, a Th17/Th1 mediated chronic inflammation surrounding breast implants characterizes its pathogenesis. Clinical findings are usually breast lumps and local swelling in capsule-limited disease (Lugano modified-Ann Arbor IA), the most prevalent form of BIA-ALCL. Even though rare, invasive ALCL can be evident at disease onset, indicating severe systemic disease. However, gray zones of diagnosis should be approached by anatomopathological studies, in which breast implant capsule invasion would support any need for additional chemotherapy.

Whereas BIA-ALCL is a rare type of lymphoma, studies report a peaked incidence of 1:2832 patients.[2] This increasing incidence is possibly due to more widespread disease awareness, better diagnosis, and a rising number of breast implants worldwide. In 2018, Brazil reached second place in the aesthetic procedures global rank, according to the International Society of Aesthetic Plastic Surgery (ISAPS). Breast augmentation was the most performed Brazillian surgery, accounting for over 270 000 procedures in one year. Some companies performed recalls on textured silicone breast implants after an increased associated risk of BIA-ALCL. Nevertheless, there is no mandatory information in surgery agreement terms over the risk of BIA-ALCL in Brazil.

Our study describes a case of BIA-ALCL diagnosed after surgery with breast implant removal and immediate silicon re-implantation. We also discuss the clinical follow-up of breast lymphoma and review treatment approaches for BIA-ALCL.

* Corresponding author at: Cancer Citogenomics Laboratory. Universidade Federal do Ceará (UFC), Rua Coronel Nunes de Melo St, 1000, CEP 60430-275 Fortaleza, Ceará, Brazil.
E-mail address: pinheirorfeitosa@gmail.com (R.F. Pinheiro).

https://doi.org/10.1016/j.htct.2021.06.019

Case report

A 42-year-old female presented persistent left breast pain and edema after routine mammography in 2018. She had a history of breast enhancement with a Silimed silicone implant in 2008. In November 2018, she had progressive left breast edema, confirmed by mammography. She was diagnosed with breast implant rejection by her plastic surgeon in May 2019. Afterward, she proceeded to total capsulectomy and breast prosthesis exchange into a Silimed polyurethane breast implant.

A trained pathologist analyzed the removed en-bloc piece (implant plus surrounding capsule). The immunohistochemistry study was strongly positive for CD5, CD4, CD 30 and focally positive for CD43 and CD15. ALK was negative. We established the diagnosis of capsule-confined BIA-ALCL (Ann Arbor IA, capsule positive). At the hematologist referral after surgery, her physical exam presented edema in the right superior quadrant of the left breast. There was no lymph node enlargement, and other physical exams were otherwise regular.

After surgery, she underwent a PET scan that presented a bilateral and heterogeneous increase in the glycolytic metabolism, especially in the left breast. The medical advice to the patient was the complete removal of her new breast implants as the standard treatment. The patient refused to remove them because of aesthetic loss even after clear medical advice. Due to the maintained implants and the uncertainty surrounding her disease progression, she underwent CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) in June 2019. The patient performed six cycles of CHOP, the last one in October 2019. Fifteen months later, she presented a PET-Scan without periprosthetic glycolytic metabolism or fluid collection.

Discussion

BIA-ALCL is a rare non-Hodgkin lymphoma which overall treatment is controversial in advanced and particular cases. We reported a BIA-ALCL diagnosed after prosthetic removal and substitution for a new product, followed by the denial to remove her silicone implant. According to the NCCN Consensus Guidelines on the Diagnosis and Treatment of Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) for clinical management and follow-up, most cases are indolent and limited to the prosthetic capsule while the survival rate for ALK-negative ALCL can be less than 50% in 5 years.[3]

According to a 2018 survey on breast implants in Brazil, 52.89% of plastic surgeons affirmed to prefer textured breast implants. These prosthetics offer advantages over smooth implants because of better breast positioning and lower risk of capsule contracture, a common cause of corrective breast reconstruction (49.8%).[4] BIA-ALCL is mainly present in textured breast implants, although polyurethane and smooth breast implants are also associated with BIA-ALCL. The implant texture represents an increased risk of BIA-ALCL depend on higher grades of roughness and surface area. See Table 1 for the most common BIA-ALCL clinical features, tumor stage, and associated implant types.

In December 2019, the FDA urged a class I recall to Allergan over its Biocell textured breast implants owing to increased BIA-ALCL risk. This decision occurred nearly a year after the diagnosis of BIA-ALCL in our patient. Among the 573 BIA-ALCL cases reported at that time, 481 patients had Allergan/Biocell prosthetics and 12 died shortly after the diagnosis. Allergan products accounted for nearly 90% of European and Australian markets, reaching 34.97% of Brazilian breast implants in 2018.[4] Another serious concern is polyurethane products, as they have high roughness and surface area (grade 4). An Australian survey indicated that the polyurethane Silimed breast implant had a 23.4 times higher risk of BIA-ALCL than Biocell (Allergan),[5] a finding compatible with its grade 4 surface type.

Our case describes a 42-year-old female who underwent immediate breast implant exchange and refused to remove her new breast implant after the BIA-ALCL diagnosis. Even though this patient had a localized BIA-ALCL with total capsulectomy performed, she remained at risk of incomplete disease excision and exposure to polyurethane implant. These polyurethane foam-coated silicone implants were also previously linked to BIA-ALCL with grade 4 surface type.[6] Our patient's decision to refuse medical advice set her at a maintained risk of disease. Thus, we decided to proceed with a six-cycle CHOP regimen, an anthracycline-based systemic therapy. See Table 2 for a summary of BIA-ALCL main reports on treatment, most common chemotherapy regimen, and clinical outcomes.

Table 1 – BIA-ALCL clinical presentation and related implants.

Article	Number of cases	Mean exposure time	Clinical presentation	Tumor stage (TNM/Ann Arbor)	Implant Type
Loch-Wilkinson et al [11]	55	7.46 years	Seroma only (76.4%)	Stage IA (58.2%)	Silicone textured (58.7%)
Miranda et al[10]	60	10.9 years	Seroma only (70%)	Stage I (83%)	Silicone (45.09%) Textured (35%), others unknown
Clemens et al [7]	87	8 years	Seroma only (59.8%)	Stage I (35.6%)	Silicone (49.4%) Textured (93.7%)
Adrada et al [8]	44	10 years	Seroma only (47.7%)	Stage I (72.7%)	Silicone (43.1%)
Brody et al [12]	52	–	Seroma only (69.2%)	Stage IA	Textured (78.8%), others unknown
Srinivasa et al [9]	363	–	–	–	Textured (50%), Smooth (4.3%)
Doren et al [13]	100	10.7 years	–	–	Textured (51%), unknown (49%) Salt-loss (43%)

Table 2 – Overview of BIA-ALCL treatment approaches.

Article	Surgery (capsulectomy/ complete excision)	Adjuvant	Chemotherapy type	Other	Clinical outcome
Loch-Wilkinson et al[11]	100%	Chemotherapy (31.7%) Radiotherapy (16.3%)	Not available	Stem-cell transplantation (1.8%)	Survival (92.7%)
Miranda et al [10]	93.3%	Chemotherapy (65%) Radiotherapy (55.35%)	CHOP (50%)/ 6 cycles (78.5%)	Stem-cell transplantation (13.3%)	Survival (92%)
	-	Chemotherapy + Radiotherapy (43.3%)	–	–	–
Clemens et al [7]	85%	Chemotherapy (58.6%) Radiotherapy (20.6%)	CHOP (86.3%)/ 6 cycles (63.6%)	–	Survival (86.5%)
Adrada et al [8]	93%	Chemotherapy (68%) Radiotherapy (51%)	–	–	Complete remission (89%)
Srinivasa et al [9]	91.9 %	Chemotherapy (30.8%) Radiotherapy (18.4%)	–	Stem-cell transplantation (6.6%)	Survival (98.6%)

Conclusion

An increase in disease awareness and correct diagnosis may reveal a more accurate incidence and risk of BIA-ALCL over time. Patients, clinicians, and surgeons must be aware of this entity to share better decisions about procedures and breast implants. We should also consider avoiding textured or polyurethane prosthetics for breast reconstruction after BIA-ALCL.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Financial Support

We declare no financial support in this work.

REFERENCES

1. Turner SD, Inghirami G, Miranda RN, Kadin ME. Cell of origin and immunologic events in the pathogenesis of breast implant-associated anaplastic large-cell lymphoma. Am J Pathol. 2020;190:2–10.
2. Laurent C, Nicolae A, Laurent C, Le Bras F, Haioun C, Fataccioli V, et al. Gene alterations in epigenetic modifiers and JAK-STAT signaling are frequent in breast implant-associated ALCL. Blood. 2020;135:360–70.
3. Cordeiro PG, Ghione P, Ni A, Hu Q, Ganesan N, Galasso N, et al. Risk of breast implant associated anaplastic large cell lymphoma (BIA-ALCL) in a cohort of 3546 women prospectively followed long term after reconstruction with textured breast implants. J Plast Reconstr Aesthet Surg. 2020;73:841–6.
4. Parrilla Castellar ER, Jaffe ES, Said JW, Swerdlow SH, Ketterling RP, Knudson RA, et al. ALK-negative anaplastic large cell lymphoma is a genetically heterogeneous disease with widely disparate clinical outcomes. Blood. 2014;124:1473–80.
5. Charles-De-Sá L, Gontijo-De-Amorim NF, Albelaez JP, Leal PR. Profile of breast augmentation surgery in Brazil. Rev Bras Cirurgia Plást (RBCP) Braz J Plast Sug. 2019;34:174–86.
6. Magnusson M, Beath K, Cooter R, Locke M, Prince HM, Elder E, et al. 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. 2019;143:1285–92.
7. Clemens MW, Medeiros LJ, Butler CE, Hunt KK, Fanale MA, Horwitz S, et al. Complete surgical excision is essential for the management of patients with breast implant-associated anaplastic large-cell lymphoma. J Clin Oncol. 2016;34:160–8.
8. 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 Res Treat. 2014;147:1–14.
9. Srinivasa DR, Miranda RN, Kaura A, Francis AM, Campanale A, Boldrini R, et al. Global adverse event reports of breast implant-associated ALCL: an international review of 40 government authority databases. Plast Reconstr Surg. 2017;139:1029–39.
10. Miranda RN, Aladily TN, Prince HM, Kanagal-Shamanna R, de Jong D, Fayad LE, et al. Breast implant-associated anaplastic large-cell lymphoma: long-term follow-up of 60 patients. J Clin Oncol Off J Am Soc Clin Oncol. 2014;32(2):114–20.
11. Loch-Wilkinson A, Beath KJ, Knight RJW, Wessels WLF, Magnusson M, Papadopoulos T, et al. 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. 2017 Oct;140(4):645–54.
12. Brody GS, Deapen D, Taylor CR, Pinter-Brown L, House-Lightner SR, Andersen JS, et al. Anaplastic large cell lymphoma occurring in women with breast implants: analysis of 173 cases. Plast Reconstr Surg. 2015;135(3):695–705.
13. Doren EL, Miranda RN, Selber JC, Garvey PB, Liu J, Medeiros LJ, et al. U.S. epidemiology of breast implant-associated anaplastic large cell lymphoma. Plast Reconstr Surg. 2017 May;139(5):1042–50.