OPEN

PRS GLOBAL OPEN

SPECIAL TOPIC
Breast

Prepectoral and Retropectoral Breast-implant–Associated Anaplastic Large-cell Lymphoma

Gonzalo Ziegler-Rodriguez, MD, FACS*†‡
Milko Garces-Ruiz*‡
Gabriel De La Cruz-Ku, MD§¶
Otto Ziegler-Rodriguez, MD, FACS†‡
Otto Ziegler-Gutierrez, MD, FACS†‡
Milko Garces-Castre, MD‡
Jaime Montes-Gil, MD*
Jimena Neira, MD*
Luis Taxa-Rojas, MD*
Rosa Cebrian, MD‖
Abhishek Chatterjee, MD, FACS**

Summary: Breast-implant–associated anaplastic large cell lymphoma (BIA-ALCL) is a non-Hodgkin lymphoma that arises in the space between the surface of a breast implant and the fibrous capsule that grows around the implant. Since its first description 20 years ago, almost 1000 cases of BIA-ALCL have been diagnosed worldwide. Nowadays, guidelines describe the diagnosis, staging, and treatment of this disease. We present the first two cases diagnosed and treated in Peru, demonstrating a wide range of aggressiveness of BIA-ALCL. *(Plast Reconstr Surg Glob Open 2024; 12:e5520; doi: 10.1097/GOX.0000000000005520; Published online 10 January 2024.)*

INTRODUCTION

Breast-implant–associated anaplastic large cell lymphoma (BIA-ALCL) was first described by Keech[1] almost 20 years ago. Since then, almost 1000 patients around the world have been diagnosed with this implant-associated disease. It is considered a non-Hodgkin lymphoma that arises in the space between the surface of a breast implant (aesthetic or reconstructive) and the fibrous capsule that grows around the implant. As a seroma in the majority of cases, this neoplasm presents anaplastic cells that are CD30 positive and ALK negative.[2]

This malignant neoplasm can invade the entire capsule and invade surrounding tissues, including the breast, muscles, or even the chest wall.[2,3] It has been linked to "textured" implant surfaces.[4] The National Comprehensive Cancer Network (NCCN) has published guidelines for the diagnosis, staging, and treatment of BIA-ALCL.[5] Here, we present the first two cases diagnosed and treated in Peru, demonstrating a wide range of aggressiveness of this disease.

*From the *Instituto Nacional de Enfermedades Neoplasicas (INEN), Lima, Peru; †Clinica Ziegler, Lima, Peru; ‡Universidad Peruana de Ciencias Aplicas (UPC), Lima, Peru; §University of Massachusetts Medical School, Worcester, Mass.; ¶Universidad Cientifica del Sur, Lima, Peru; ‖Department of Radiology, Clinical Ricardo Palma, Lima, Peru; and **Division of Plastic and Reconstructive Surgery, Department of Surgery, Tufts Medical Center, Boston, Mass.*

Received for publication August 27, 2023; accepted November 8, 2023.

DOI: 10.1097/GOX.0000000000005520

CASE 1

Late-Stage Case (Retropectoral BIA-ALCL)

A 61-year-old patient presented a history of breast augmentation performed in Venezuela in June 2013. The breast implant was a macrotextured surface type filled with silicone gel (Allergan) in a retro-muscular position with inframammary access. In March 2020, she reported the onset of symptoms that included itching over the operative scar of her right breast. Four months later, she began to experience pain associated with a skin lesion at the operative scar. Asymmetry of the right breast was present with increased volume toward the lower pole in addition to the painful lesion at the surgical scar in the right inframammary groove (Fig. 1). A bilateral breast magnetic resonance imaging study was performed showing the location of the implant, intracapsular liquid, and periprosthetic seroma (Fig. 2).

An ultrasound (US)-guided core needle biopsy of the thickened implant capsule was performed and the result confirmed the diagnosis of BIA-ALCL. Five months after the onset of symptoms, the patient underwent wide local excision of the block, including the scar with the lesion, total capsulectomy, and removal of both the right and left breast implants. A total volume of 300 mL of serous fluid was found in the periprosthetic space and sent for a cytological study. The final pathology report revealed a right-side capsule and fluid indicating BIA-ALCL [IHC: CD 30 (+), ALK (−), CD 3 (+), CD 5 (+), CD 56 (−), PDL–1 (30%), CD 4 (−), Granzyme B (+)]. The breast capsule presented neoplastic infiltration of the whole capsule, pT3. Moreover, the surgeons were unable to excise the mass completely off the chest wall and the surgical

Disclosure statements are at the end of this article, following the correspondence information.

Fig. 1. Clinical image of when the retropectoral breast-implant-associated anaplastic large-cell lymphoma was diagnosed.

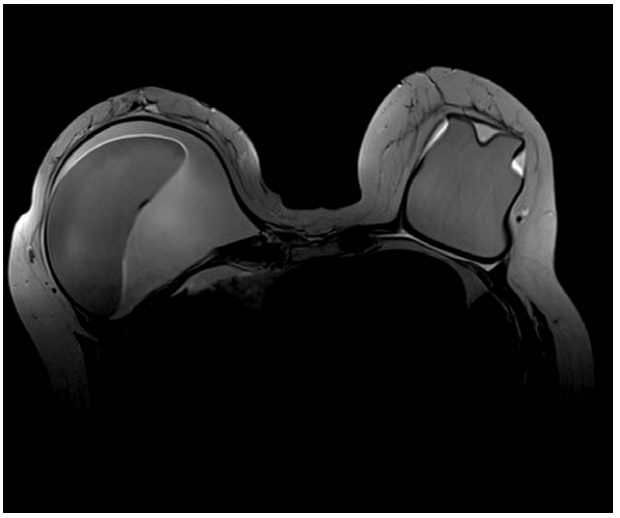

Fig. 2. Preoperative T2-weighted contrast enhanced magnetic resonance image of the diagnosis of retropectoral breast-implant-associated anaplastic large-cell lymphoma.

margins of the capsulectomy were positive for lymphoma. Two weeks later, the patient felt a lump in her right rib cage toward the internal quadrants at the para-sternal level (Fig. 3). She was re-admitted to the National Cancer Center on September 2020, where she was initially classified as having a T-lineage lymphoproliferative syndrome. Bone marrow aspiration and biopsy were performed, with no evidence of distant disease. Imaging studies such as US and computed tomography (CT) scans were performed at that time and found a subsolid tissue in the right breast measuring 1.7×1.6 cm, considered to be residual disease

Takeaways

Question: Management and outcomes of different stages and clinical presentations according to location of the tumor in breast-implant-associated anaplastic large-cell lymphoma (BIA-ALCL).

Findings: BIA-ALCL is a complex and rare disease that should be treated in specialized breast cancer centers. The appropriate diagnosis, characteristics of the implant, and location of the disease are crucial for its management. This disease is treatable in early stages, but challenging when advanced due to deeper invasion.

Meaning: BIA-ALCL is a challenging diagnosis. It must be considered and discussed in a multidisciplinary fashion. Following specific guidelines is key. Treatment requires surgical explantation and en-bloc total capsulectomy in a cancer center. Effectiveness of adjuvant treatment for advanced disease is scarce.

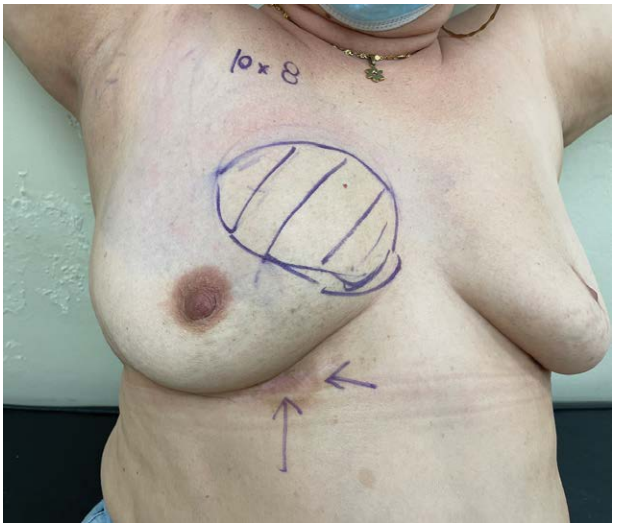

Fig. 3. Clinical image showing residual disease with fistula 2 weeks after surgical intervention.

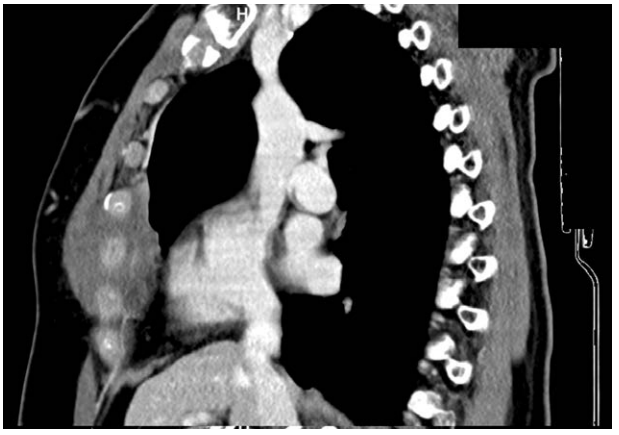

Fig. 4. Coronal computerized tomography image showing the residual disease after surgical intervention.

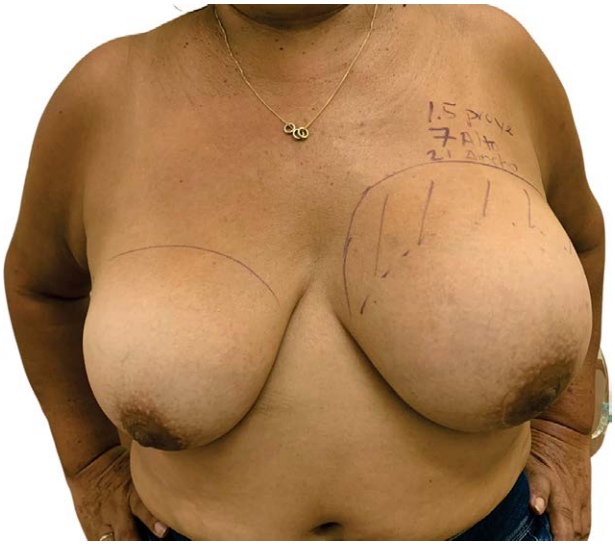

Fig. 5. Clinical images of the patient with seroma when the pre-pectoral breast-implant-associated anaplastic large-cell lymphoma was initially diagnosed.

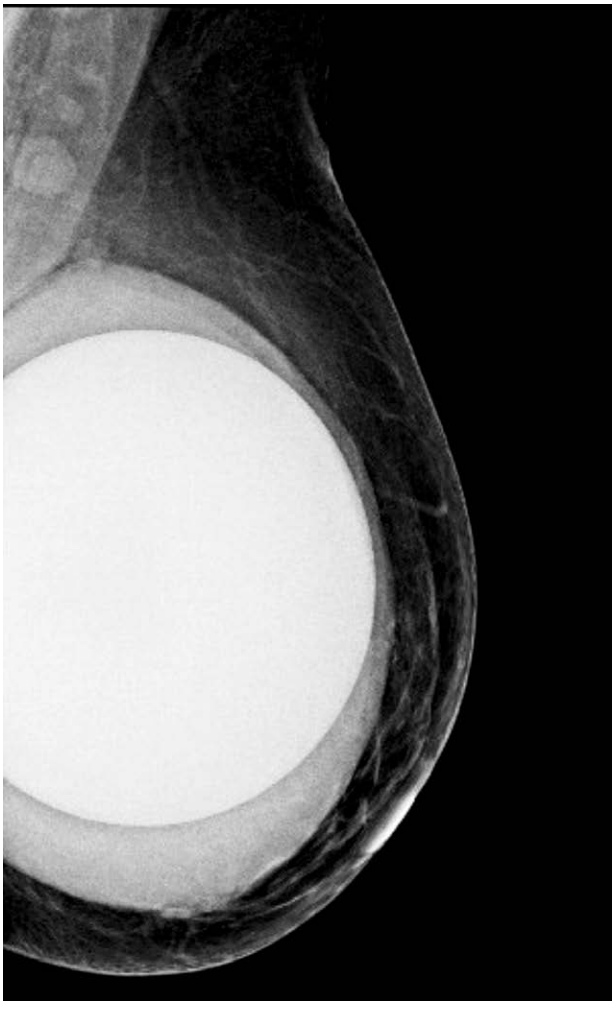

Fig. 6. Preoperative mediolateral oblique mammography with seroma and prothesis.

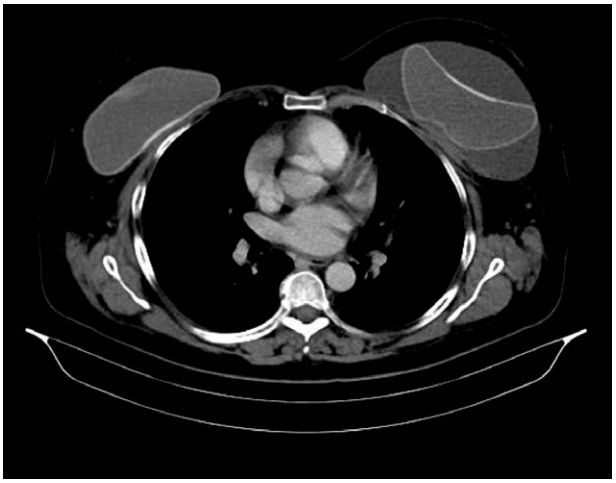

Fig. 7. Axial computerized tomography image showing the prothesis and the seroma.

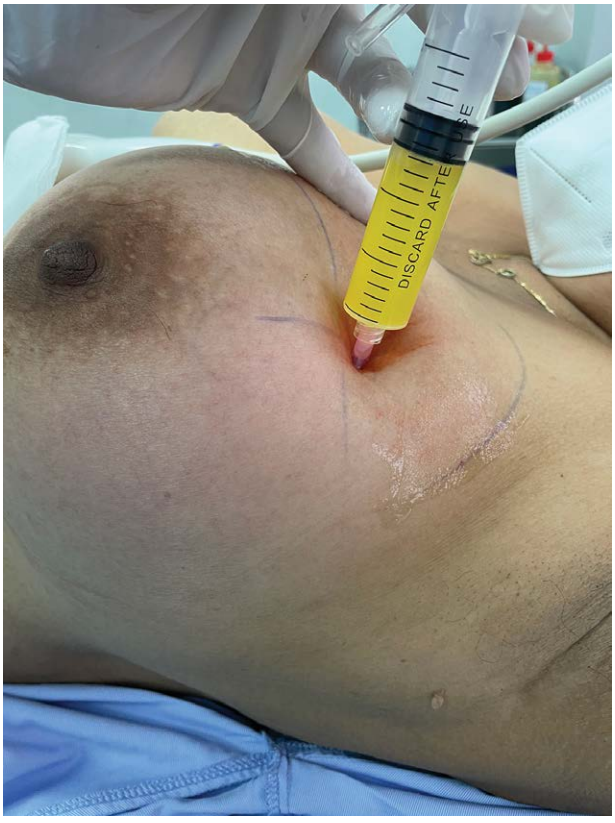

Fig. 8. Clinical image showing fine needle aspiration of the peri-prosthetic seroma.

(Fig. 4). Therefore, due to the persistence of a tumoral mass, medical oncology recommended adjuvant chemotherapy with a CHOP regimen, which started the month after hospitalization. A multidisciplinary board meeting was held in November 2020, which concluded that surgery was not further indicated due to the extent of the disease, and chemotherapy and radiotherapy should continue. The mass was then re-evaluated by medical

oncology; etoposide was added to the CHOP regimen. Later, 3 months after the hospitalization, the patient had a physical evaluation at breast surgery, showing a palpable immobile mass of 8×7 cm in the internal quadrants of the right breast. The rest of the breast tissue was not involved, except for the skin at the scar at the inframammary fold, which was considered part of the original disease process, concerning for progression of disease. Chemotherapy was continued, and 6 months after the beginning of chemotherapy, the patient underwent a US-guided needle core biopsy of the implant capsule, which confirmed viable BIA-ALCL. The patient was unfortunately lost to follow-up 9 months after the hospitalization, after having been considered untreatable by surgery and the inability to access brentuximab vedontin in our health system.

CASE 2

Early-stage Case (Prepectoral BIA-ALCL)

This patient was a 52-year-old woman with a history of aesthetic prosthesis breast augmentation performed 7 years earlier. The breast implant had a macrotextured surface type filled with silicone gel (Eurosilicone) in retroglandular space with peri-areolar access. On physical examination, no bulk or lymphadenopathy was found, but left upper pole asymmetry was present secondary to a seroma (Fig. 5). The CT scan showed no lymph node involvement,

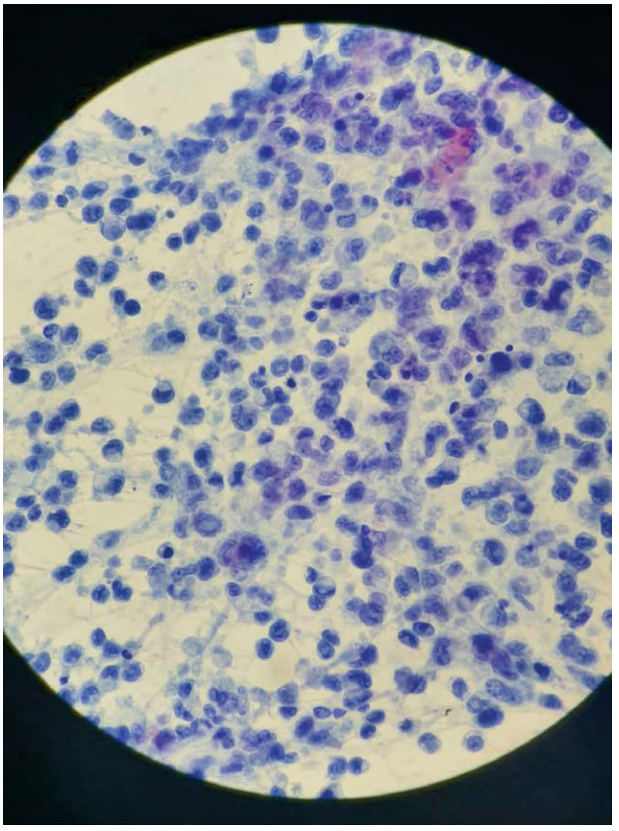

Fig. 9. Image of effusion cytology (4×) showing breast-implant-associated anaplastic large-cell lymphoma.

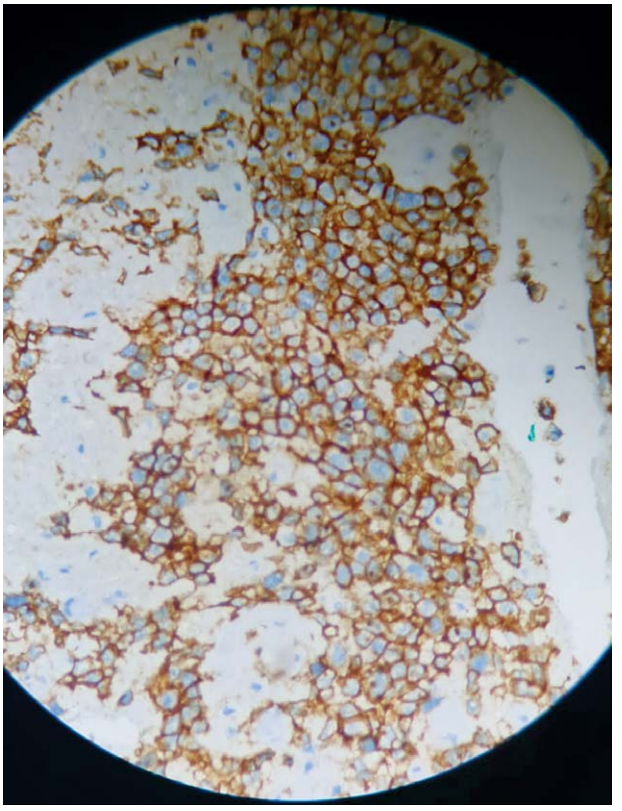

Fig. 10. Cytology showing CD30 expression in the neoplastic cells.

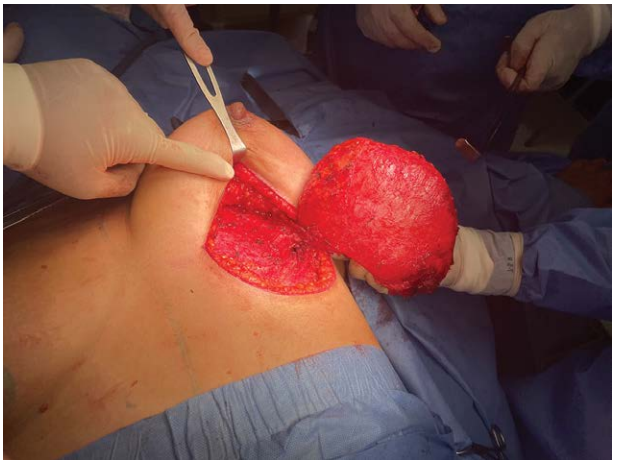

Fig. 11. Surgical intervention for the total capsulectomy with implant.

and the capsule of the left implant was filled with liquid, leading the implant to rotate on its axis (Figs. 6 and 7). The breast surgeon performed US-guided fine needle aspiration of the implant capsule for diagnostic purposes, obtaining a yellow, slightly dense fluid (Fig. 8). Cytological analysis confirmed the presence of atypical cells, CD30 (+) and ALK (−); results confirmed the diagnosis of BIA-ALCL (Figs. 9 and 10). NCCN guidelines were followed for early-stage BIA-ALCL,[5] and the decision to perform surgery was

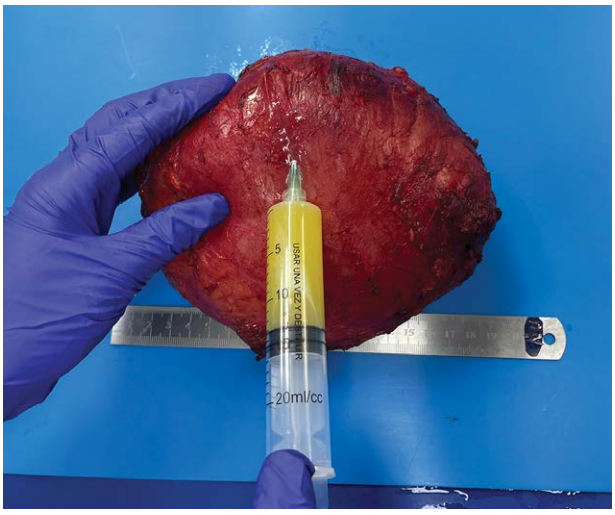

Fig. 12. Specimen with needle aspiration of the periprosthetic seroma.

Fig. 13. Image showing the capsule incised and opened following removal.

made in a multidisciplinary fashion. The surgical team was led by breast surgical oncologists and plastic surgeons. Although a Wise pattern incision was planned, a wide inframammary fold incision was finally performed for total capsulectomy with en bloc breast implant removal (Fig. 11). Caution was taken to avoid capsule damage to prevent leakage of neoplastic liquid. Surgery of the contralateral side was carried out the same day. The capsule surrounding the textured surface implant was found in a prepectoral position (Figs. 12 and 13). Macroscopic examination of the specimen in the pathology laboratory followed specifical guidelines for staging (Figs. 14–17).[6] The final diagnosis was early-stage BIA-ALCL, with partial invasion of the capsule (<50%), T2N0M0. No adjuvant treatment was undertaken. At 6 months postoperative, a CT scan was performed without evidence of disease (Fig. 18). At 24 months postoperative, the clinical examination showed no evidence of disease (Fig. 19).

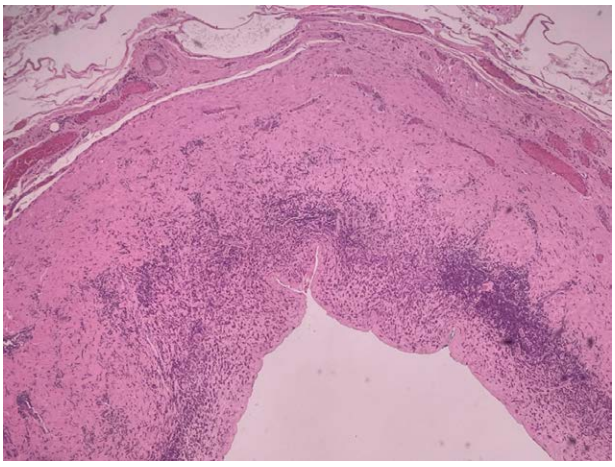

Fig. 14. Pathology images with hematoxylin and eosin staining in 4× magnification showing tumor infiltration of the capsule.

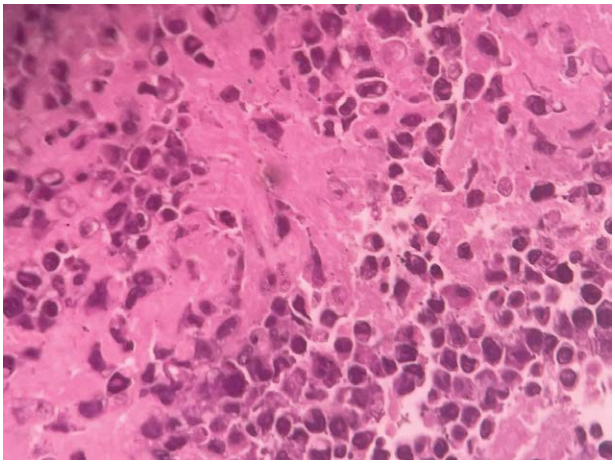

Fig. 15. Pathology images with hematoxylin and eosin staining in 40× magnification showing tumor infiltration of the capsule.

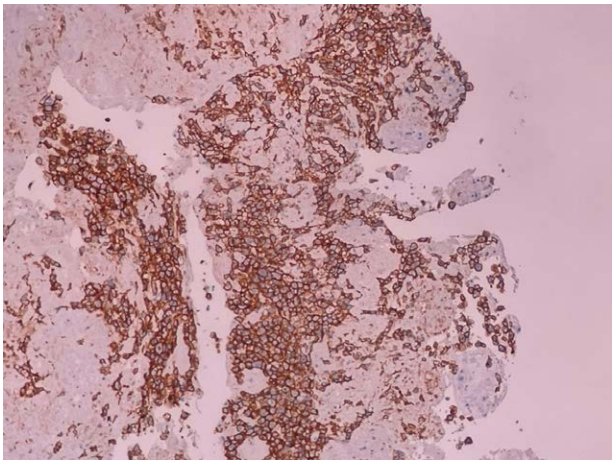

Fig. 16. Pathology images with staining of CD30 in 4× magnification showing positivity of the neoplastic cells.

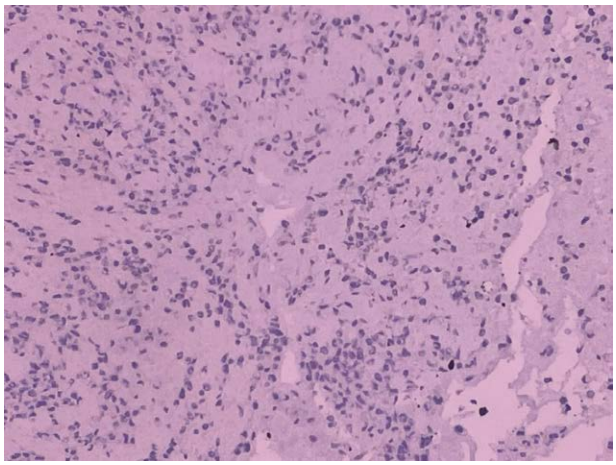

Fig. 17. Pathology images with staining of anaplastic lymphoma kinase 1 in 4× magnification showing negativity of the neoplastic cells.

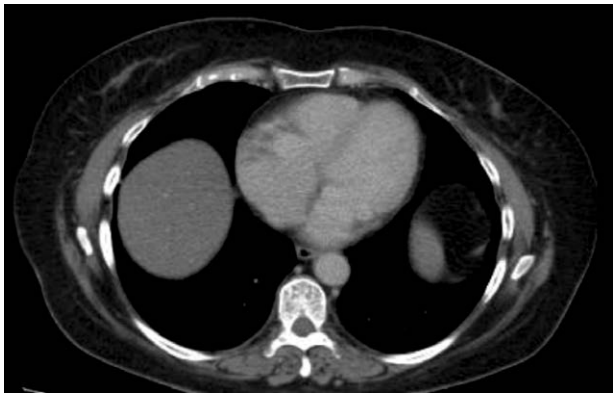

Fig. 18. Axial computerized tomography images showing nonrecurrence of disease 6 months after surgical intervention of the early case of prepectoral breast-implant–associated anaplastic large-cell lymphoma.

DISCUSSION

BIA-ALCL is a rare oncologic disease, the incidence of which is currently increasing. The risk of this disease ranges between one per 355 to one per 86,029, depending on the manufacturer type of textured implant.[3] Here, we have presented two cases. The first involved a retropectoral advanced tumor with deeper invasion that did not respond to surgery and progressed despite chemotherapy. The final tumor board recommendation was to proceed with palliative care without further therapy. The second case involved a retroglandular early-stage tumor, which was successfully managed surgically despite the challenging diagnosis.

To date, textured implants are generally avoided. However, after the peak in the usage of these implants in 2016 and the disease being found almost 10 years later, an increase in incidence during the following years is expected.[7] These types of implants were preferred in Europe compared with those in the United States, although South American[8] countries, such as Brazil and

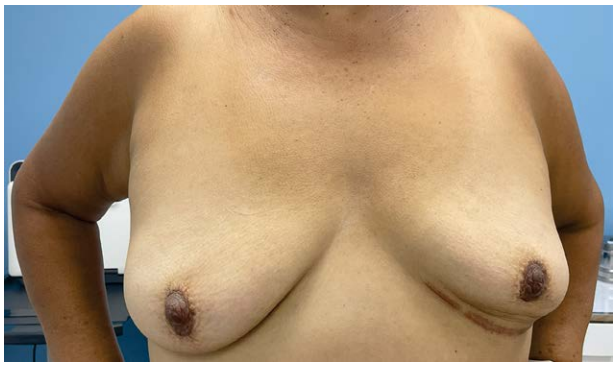

Fig. 19. Clinical image showing nonrecurrence of the disease 2 years after surgical intervention of the early case of prepectoral breast-implant–associated anaplastic large-cell lymphoma.

Colombia, were also among the top countries that eventually used these implants.[9] Hence, it is crucial that plastic and breast surgeons worldwide be aware of the presentation of symptoms for its diagnosis, such as seromas (66%–70%)[10,11] or breast masses (8%).[7]

Although US and mammography are the first tool for diagnosis, magnetic resonance imaging, CT with three-dimensional reconstruction, PET-CT, and diffusion-weighted imaging can be very useful to accurately determine the extension of the disease.[5,12] In a systematic review, Naga et al reported that 73% of patients presented with local disease.[11] However, if a more advanced stage is diagnosed, the main goal is resection with clean margins, which is achieved by en bloc resection performed by multidisciplinary teams, including breast, plastic, and thoracic surgery.[13] The 2017 NCCN guidelines[14] note that these tumors present a better overall survival and event-free survival when complete surgical excision of the breast implant and capsulectomy is performed compared with partial resection with adjuvant treatment.[15]

The location of the implant is important in surgical planning and oncologic terms. Retropectoral implants usually present a higher probability of deep invasion and are more difficult to resect, as shown in our case with advanced stage BIA-ALCL. Moreover, the removal of the contralateral implant should be performed due to a 2%–4% risk of contralateral disease.[5]

Adjuvant chemotherapy is warranted in the setting of advanced BIA-ALCL with stable IIB or higher in a patient who undergoes surgery or incomplete resection with positive margins.[5] Our first patient progressed despite chemotherapy, and the tumor board did not recommend further treatment. The ECHELON-II trial (a comparison of brentuximab vedotin and CHP with standard-of-care CHOP in the treatment of patients with CD30-positive mature T-cell lymphomas) described an improved OS with brentuximab in tumors that are CD30+.[16,17] Access to certain chemotherapy treatments may be limited in some middle- or low-income countries. Additionally, there is a scarcity of strong evidence-based recommendations for tumor progression. Although brentuximab could be started as salvage therapy or other secondary chemotherapy schemes can be pursued, radiotherapy or additional

chest wall resection may be alternative options.[18] New studies and evidence are needed on these complex cases.

Even though reconstruction was not performed in our patients, it may also be feasible in cases of localized disease, especially in patients achieving cure after treatment. Lamaris et al reported that 27% of 66 patients with BIA-ALCL underwent reconstruction, and that this option should be evaluated on a case-by-case basis. For example, reconstruction should be delayed until complete remission is achieved in patients with advanced disease.[19]

CONCLUSIONS

It is important for BIA-ALCL patients to receive treatment at specialized breast centers with a multidisciplinary team able to manage this complex and rare disease. It is essential to have specific details, such as the time from implant surgery, type of surface, and position of the breast implant. BIA-ALCL is a morbid, albeit treatable, disease especially in the early stages. Advanced tumors with progression can be challenging to resect. Adequate diagnosis and surgical excision is crucial; however, retropectoral implants might present a greater probability of deep invasion. Further studies and therapeutic options are needed for cases of advanced BIA-ALCL that do not respond to chemotherapy.

Gonzalo Ziegler-Rodriguez, MD, FACS
Surgical Oncologist, Mastologist
Instituto Nacional de Enfermedades Neoplasicas (INEN)
Av. Angamos 2520, Surquillo
Lima, Peru
email: dr.gonzaloziegler@gmail.com

DISCLOSURES

Dr. Chatterjee is a consultant for 3M and De Royal, Molnylcke, Hologic and Dilon. All the authors have no financial interest to declare in relation to the content of this article.

ACKNOWLEDGMENTS

The authors thank the Instituto Nacional de Enfermedades Neoplasicas for all the support to facilitate management of our patients, and the Universidad Cientifica del Sur for their support in the publication of this research/project. Special thanks to mentors Roberto Miranda, MD and Scott Spear, MD.

ETHICAL APPROVAL

This study did not require ethical approval in the setting of reporting individual cases.

REFERENCES

1. Keech JA, Jr, Creech BJ. Anaplastic T-CELL lymphoma in proximity to a saline-filled breast implant. *Plast Reconstr Surg.* 1997;100:554–555.
2. Miranda RN, Medeiros LJ, Ferrufino-Schmidt MC, et al. Pioneers of breast implant-associated anaplastic large cell lymphoma: history from case report to global recognition. *Plast Reconstr Surg.* 2019;143(3S):7S–14S.
3. Clemens MW. BIA-ALCL Resources. By the numbers, and what they mean. Paper presented at: ASPS Spring Meeting 2019. Available at https://www.plasticsurgery.org/for-medical-professionals/health-policy/bia-alcl-physician-resources/by-the-numbers. Updated October 1, 2020. Accessed June 4, 2023.
4. Rastogi P, Riordan E, Moon D, et al. Theories of etiopathogenesis of breast implant-associated anaplastic large cell lymphoma. *Plast Reconstr Surg.* 2019;143(3S A Review of Breast Implant-Associated Anaplastic Large Cell Lymphoma):23S–29S.
5. Clemens MW, Jacobsen ED, Horwitz SM. 2019 NCCN consensus guidelines on the diagnosis and treatment of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). *Aesthet Surg J.* 2019;39:S3–S13.
6. Quesada AE, Medeiros LJ, Clemens MW, et al. Breast implant-associated anaplastic large cell lymphoma: a review. *Mod Pathol.* 2019;32:166–188.
7. Matros E, Shamsunder MG, Rubenstein RN, et al. Textured and smooth implant use reported in the tracking operations and outcomes for plastic surgeons database: epidemiologic implications for BIA-ALCL. *Plast Reconstr Surg Global Open.* 2021;9:e3499.
8. Jalalabadi F, Doval AF, Neese V, et al. Breast implant utilization trends in USA versus Europe and the impact of BIA-ALCL publications. *Plast Reconstr Surg Global Open.* 2021;9:e3449.
9. Ossa Gomez CA, Robledo Abad JF, Duque A, et al. Breast implant-associated anaplastic large cell lymphoma in Colombia: report of a multidisciplinary national registry. *Plast Reconstr Surg Global Open.* 2020;8:e3013.
10. Leberfinger AN, Behar BJ, Williams NC, et al. Breast Implant-associated anaplastic large cell lymphoma: a systematic review. *JAMA Surg.* 2017;152:1161–1168.
11. Naga HI, Mellia JA, Basta MN, et al. Breast implant-associated anaplastic large-cell lymphoma: updated systematic review and analysis of treatment strategies. *Plast Reconstr Surg.* 2022;150:762–769.
12. Sharma B, Jurgensen-Rauch A, Pace E, et al. Breast implant–associated anaplastic large cell lymphoma: review and multiparametric imaging paradigms. *Radiographics.* 2020;40:609–628.
13. Kim DH, Webster TK, Bartolacci JG, et al. Use of needle localization in the surgical management of non-seroma, mass-forming BIA-ALCL. *Plast Reconstr Surg Global open.* 2022;10:e4286.
14. National Comprehensive Cancer Network. T-Cell Lymphoma: NCCN; 2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed June 4, 2023.
15. 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. *J Clin Oncol.* 2016;34:160–168.
16. Horwitz S, O'Connor OA, Pro B, et al. The ECHELON-2 trial: 5-year results of a randomized, phase III study of brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma. *Ann Oncol.* 2022;33:288–298.
17. Pro B, Advani R, Brice P, et al. Brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large-cell lymphoma: results of a phase II study. *J Clin Oncol.* 2012;30:2190–2196.
18. Alotaibi S, Hamadani M, Al-Mansour M, et al. Breast implant-associated anaplastic large cell lymphoma. *Clin Lymphoma Myeloma Leuk.* 2021;21:e272–e276.
19. Lamaris GA, Butler CE, Deva AK, et al. Breast reconstruction following breast implant-associated anaplastic large cell lymphoma. *Plast Reconstr Surg.* 2019;143(3S):51S–58S.