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Breast implant associated anaplastic large cell lymphoma: Case report and review

Flávia Zattar Piazera, Pedro Henrique Medeiros Pereira, Luis Henrique Ramos Athaide, Rafael de Sá Vasconcelos

ABSTRACT

Breast implant associated-anaplastic large cell lymphoma (BIA-ALCL) is a recent neoplasia that affects the mammary capsule. In an objective way, data supports that 1 in 6,972 breast implants will evolve annually to BIA-ALCL, which is classified as a rare type of non-Hodgkin lymphoma with no clear physiopathology established. The most common symptoms are preprosthetic late seroma, tumoral mass, lymphadenopathy, and skin alterations. The diagnosis is based on evaluation with imaging, such as ultrasonography and magnetic resonance image (MRI). The gold standard diagnosis is histopathologic analysis of aspirated fluid. Treatment is focused on excision or radiotherapy combined with chemotherapy and immunotherapy, based on the staging of the tumor. We describe a 57-year-old female who developed BIA-ALCL 16 years after bilateral silicone prosthesis implantation with the initial presentation of recurring seroma.

Keywords: Anaplastic large cell lymphoma, Breast implant, Lymphoma, Neoplasms

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INTRODUCTION

Anaplastic large cell lymphoma (ALCL) associated with breast implants is a recent neoplasia. Despite being initially described in 1997, it was only recognized 19 years later by the World Health Association (WHO) [1].

The neoplasia described in this case report is a lesion that affects the mammary capsule. Some epidemiological data suggests an incidence of 2 cases in 1,000,000 women per year [2], with an increase factor varying directly proportional to the patient's age. There is no consensus in relation to epidemiological data, with incidence changing according to different locations. Literature describes incidence ranging from 1/50,000 to 1/3,000,000 in the observed female population [1].

In an objective way, data supports that 1 in 6,972 breast implants will evolve annually to breast implant associated-ALCL (BIA-ALCL) [2]. This lesion is classified as a non-Hodgkin lymphoma without having a clear etiopathogeny. However, there are hypotheses suggesting that its onset is related to the chronic inflammation generated by the breast implant [2], as well as the presence of a bacterial biofilm formed in the prosthesis stimulating the immune system, which culminates in a chronic immune response that would be responsible for the origination of the BIA-ALC.

The main risk factors described are associated with asymmetry of the compromised breast, mostly due to fluid accumulation beneath the skin flaps, commonly called seroma. Late seromas are relatively frequent in patients with prosthesis, being, in most cases, true seromas: transudates with low cell count and low protein content. This is why the cautelous diagnostic investigation is needed in order to rule out BIA-ALCL cases. In the physical exam, besides breast enlargement and temperature difference, some cases may present with a palpable mass in the affected breast [1]. The initial diagnostic suspicion

is made by evaluation signs and symptoms related by the patients associated with physical exam and imaging scans, notably MRI, ultrasonography, and fine-needle aspiration (FNA), but the diagnosis confirmation is only made with cytopathologic fluid analysis associated to immunophenotyping and immunohistochemistry [2, 3].

The objective of this case report is to discuss a patient affected with breast implant associated-anaplastic large cell lymphoma, with the aim of enriching the medical literature and aiding the understanding regarding this rare type of malignization, which has a great importance in a context of growing plastic surgeries. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

CASE REPORT

A 57-year-old female, with a previous history of dyslipidemia and controlled asthma, underwent bilateral silicone prosthesis breast implantation with textured membrane in 2003. In 2017, she suffered a trauma in her left breast, presenting with self-limited localized seroma (Figure 1). In April 2019, she underwent bilateral prosthesis replacement which progressed to recurrent seroma in left breast, refractory to conservative treatments.

Considering the relapsing character, a seroma aspiration was done (Figure 2) and the fluid analysis detected large cell proliferation with abnormal phenotype (CD30+, HLA-DR+, and CD25+), suggesting a BIA-ALCL.

Initial staging indicated a localized disease and, in February 2021, the patient underwent prosthesis explanation (Figure 3). Histopathological and immunohistochemistry analysis confirmed the diagnosis of anaplastic T cell lymphoma (CD30+ and ALK-1 negative) in the left mammary capsule as shown in Figure 4, which is an even rarer disease, since the majority of these tumors are located in the fluid. Post-operative staging was Ann Arbor I and surgery was considered curative. The first control positron emission tomography and computed tomography (PET-CT) scan was made 1 month and 20 days after the surgery and evidenced hypermetabolic uptake in a diffuse densification area in deep plan at the left breast (SUV 4,4) and absence of other hypermetabolic suspicious lesions, being interpreted as an inflammatory response. In a new PET-CT, 3 months and 20 days after the surgery, a diffuse densification area in the deep plans of the left breast attached to the pectoral musculature was observed, but without signs of hypermetabolism (Figure 5).

The chosen treatment plan was to maintain the clinical evaluation and laboratorial and imaging reassessment every three months. In an actual exam, one year after surgical treatment, the patient is still in remission by the staging obtained.

DISCUSSION

Breast implant associated large cell anaplastic lymphoma was described for the first time in 1997 [4], standing out only in 2008 when 4 cases of lymphoproliferative disorder of CD30+ T cells associated with silicone implants were reported [5]. Nevertheless, the WHO only recognized it as a new disease in 2016 [6].

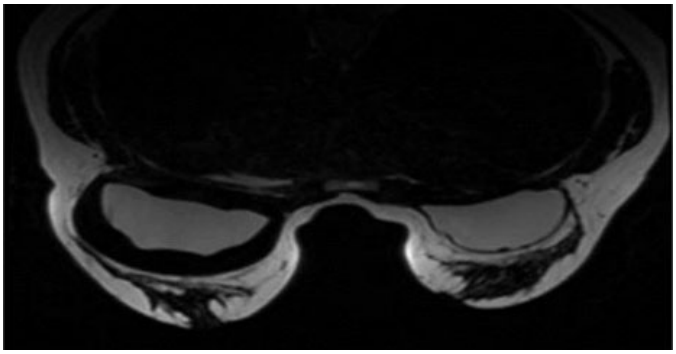

Figure 1: Breast MRI: Bilateral silicone breast implant with pericapsular seroma and capsular enhancement on the left.

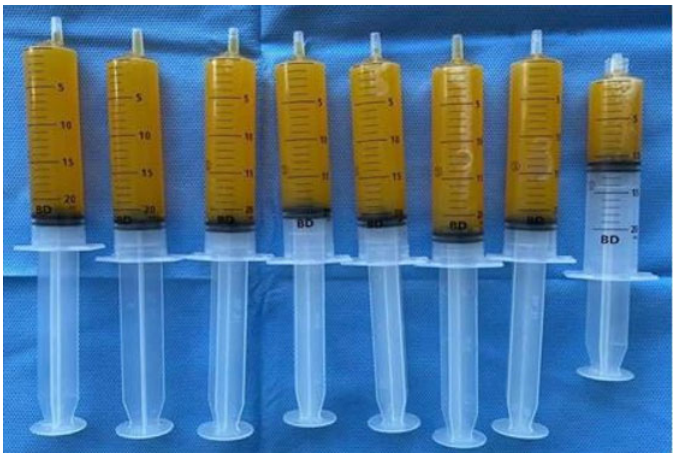

Figure 2: Fluid content from seroma puncture.

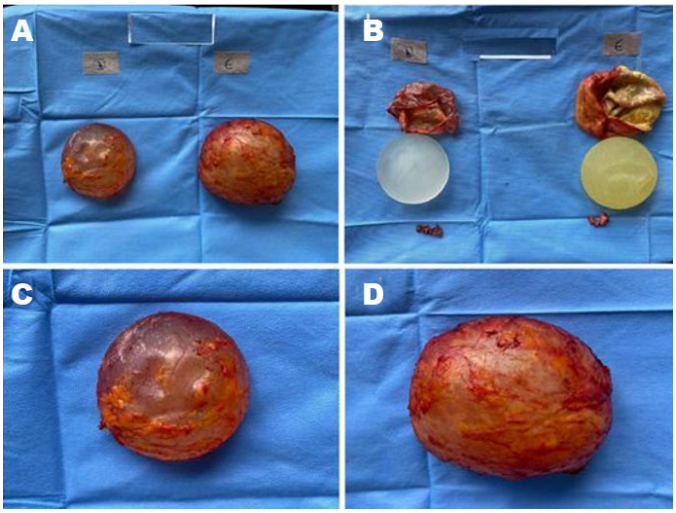

Figure 3: Breast implant explanted prosthesis. On the left (A, C) it is the right capsule, and on the right (B, D), the left capsule.

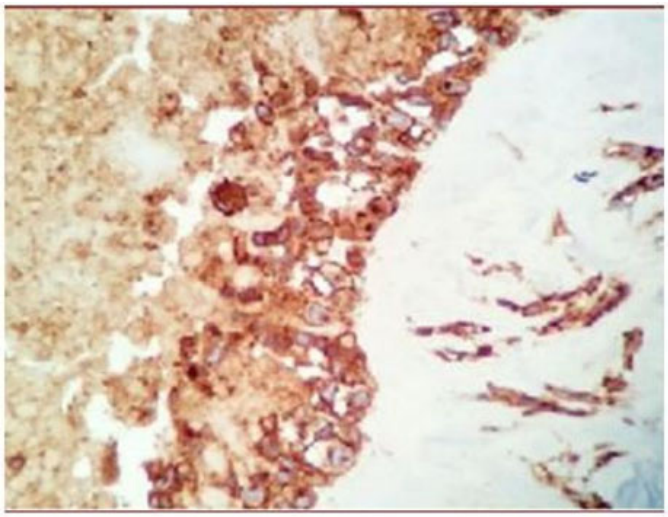

Figure 4: Left breast capsule with histological and immunohistochemistry profile consistent with BIA-ALCL with infiltration of 50% of the capsular wall. CD68+, CD30+, ALK–. Pathological staging p13pNx.

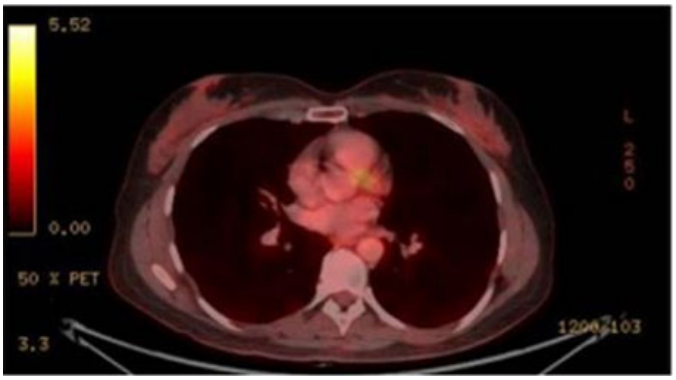

Figure 5: PET-CT May 2021: chest images evidence diffuse densification areas in the deep plans of the left breast, attached to the pectoral musculature, without hypermetabolism (previous SUV of 4,4).

Breast implant associated-anaplastic large cell lymphoma is a rare type of non-Hodgkin lymphoma, with approximately 573 reported cases since its first record until 2019, with 33 associated deaths [2, 7]. The prognosis is favorable, with the diagnosis of 85% of patients in stage 1, which is related to higher probability of cure.

The most common symptoms of BIA-ALCL are periprosthetic seroma or tumoral mass, sometimes with local temperature increase. The clinical signs are overwhelmingly unilateral [1]. Seroma is classified as a late seroma, once it appears over a year after the implantation (with mean time of appearance between 8 and 10 years after the initial surgery), which is characterized as a unilateral fluid accumulation, with high volumes between the prosthesis and the fibrous capsule [1, 2]. The tumoral mass is present in 30% of cases and it is defined as a palpable unilateral mass that may or may not be associated with pain. Other possible manifestations are adenopathy and capsular contracture, besides skin alterations [2]. Lymphadenopathies may occur in 20% of cases, most commonly being found in axillary, infraclavicular, or supraclavicular chains.

The initial investigation exam is the ultrasonography for evaluation of the presence of periprosthetic fluid or mass. The MRI complements the investigation by assessing the presence of tumor or lymph nodes alterations. The histopathologic analysis of aspirated fluid and flow cytometry is the confirmation exam, which shows the effusion containing liquefactive necrotic lymphomatous cells with high protein content associated to the positivity of lymphocytes cell markers in the immunohistochemistry analysis [8]. When the diagnosis is established, the recommendation coincides with all lymphoproliferative disorders, with the need of a PET-CT or tomography exam for staging definition.

Breast implant associated-anaplastic large cell lymphoma neoplastic cells classically express strong and uniformly CD30, but not always express the same way other markers such as CD3 and CD5, which are identified in few cases. The negativity of anaplastic lymphoma kinase (ALK) is also common [8]. In other words, the classic standard for immunohistochemistry markers of this neoplasia is CD30 positive and ALK negative [2].

The standard treatment is based on en bloc surgical excision, maintaining, if possible, the integrity of the capsule and the prosthesis, without opening of the effusion with identification of clear margins. In most cases, the lymphoma is restricted to the effusion fluid; therefore, its correct manipulation is necessary to recover the diagnostic cells and avoid spreading of the neoplasia. If sentinel lymph nodes are positive, a lymph node clearance should be done.

In the case of impossibility of resection due to lesion infiltration, there are coadjutant treatment such as radiotherapy, anthracyclines-based chemotherapy, and immunotherapy with monoclonal antibody targeting CD30, currently represented by Brentuximab vedotin [2].

After resection surgery or alternative treatments, follow-up should be carried out by PET-CT scan in order to assess the local and systemic progression of the disease.

It is very common for the appearance of true seromas—without the presence of lymphomas. In this setting, the non-lymphomatous effusions are hypocellular with rare mature lymphocytes and foam cells. The capsule contains synovial metaplasia with a discrete inflammatory infiltrate without large or atypical cells. As for the immunohistochemistry, there may be sparse isolated positive cells for CD30 (corresponding to normal activated T cells) without the pattern of diffusely positive aggregated cells [3].

Meanwhile, in the ALCL histopathology reflects the cytological findings: cells are enlarged, with loss of cohesion, presence of pleomorphism, and anaplasia. The nucleus appears multilobulated, increased in size, with higher density chromatin, prominent nucleoli, and frequent mitosis [3]. Lymph nodal involvement occurs in a predominantly sinusoidal pattern, but it can also present in a diffuse, perifollicular or interfollicular pattern.

The exact physiopathology of BIA-ALCL is not completely elucidated, but the possibility of the existence of a bacterial biofilm in the breast prosthesis—especially in the textured ones—seems to have a relation with the development of the neoplasia, since the bacterial presence would trigger chronic inflammatory responses, culminating in the formation of aberrant T cells due to continuous antigenic stimulation. Moreover, there are hypotheses regarding the genetic predisposition and time since implantation as possible driving factors [1, 3, 6]. Even though there are some reports that mention the onset of BIA-ALCL in patients with smooth silicone implants, in no case the use of smooth prosthesis was exclusive, all the cases had a textured implant at least once [2, 5, 6].

Theoretically, there is an initial proliferation of isolated neoplastic cells inside of the periprosthetic fluid and cell necrosis, which is converted to the late seroma. Afterward, neoplastic cells adhere and infiltrate the capsule deeply, reaching the breast parenchyma and subsequently involving the lymph nodes with a rare systemic spreading.

CONCLUSION

Breast implant associated-anaplastic large cell lymphoma is a medical condition that is still poorly described in the medical literature; however, it has a substantial importance in the current scenario due to its high resolution and cure if early diagnosed and to its association with the increasing practice of breast implants. Even though it has an indolent clinical course, it remains with an invasive potential toward the adjacent soft tissues, with the possibility to spread to regional lymph nodes and systemically with far worse outcomes. Therefore, the importance of this case report rests in its collaboration to the increase of knowledge about this disease. In addition, the documentation of information on BIA-ALCL will significantly contribute to a more detailed natural history and to a more consistent physiopathological hypothesis. Hence, this increment in the knowledge gathered is crucial for the establishment of more concise and assertive diagnostic and treatment models regarding the health and well-being of the patients, addressing symptomatic relief and the improvement of global survival rate and of quality of life.

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Author Contributions
Flávia Zattar Piazera – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Pedro Henrique Medeiros Pereira – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.