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(CASE REPORT)

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The importance of a correct diagnosis in breast implant-associated anaplastic large cell lymphoma: Case report

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Abstract

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare neoplasm responsible for 0.04% to 0.5% of all cases of breast disease. It occurs in patients with a previous history of breast implants that generally progress without complications during the first years of post-operatory and is mainly associated with macro-textured implants. Due to its low incidence, it does not represent the first probable diagnosis in patients with a breast tumor. This article reports the case of a patient with BIA-ALCL initially treated as a Hodgkin's lymphoma. We emphasize the importance of a correct and complete diagnosis by immunohistochemistry before imaging in patients that develop a breast tumor associated with the prosthetic capsule after breast implant surgery and its adequate treatment, including surgery.

Keywords: BIA-LCL; Immunohistochemistry; CD30; ALK

1 Introduction

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) ALK-negative is a rare non-Hodgkin T-cell lymphoma primarily associated with textured breast implants. The majority of the cases are present in patients with a prior breast augmentation with macro-textured implants that progress without complications in the first years after surgery.[1] T-cell lymphomas account for 9% of all the cases of lymphomas in Mexico, and BIA-ALCL ALK-negative represents around 44% of these neoplasms[2]. By June 2022, the American Society of Plastic Surgeons recognized and confirmed 1,216 cases worldwide, of which 389 were presented in the United States[3]. The immunohistochemistry of BIA-ALCL demonstrated homogenous positivity for CD30 on the membrane and was negative for the Anaplastic Lymphoma Kinase (ALK). The pathogenesis of BIA-ALCL is not yet well understood; nevertheless, it has been postulated that the presence of the implant in the breast is associated with a sustained inflammation caused by the microtrauma of the capsule of the implant and related to Gram-negative bacteria and a non-bacterial infection that promote the continuous expression of Th1/Th17 lymphocytes, its consequent clonal expansion, and probable malignancies[4]. The appropriate treatment of this neoplasm represents a challenge since it requires a precise diagnosis, which must include an imaging study that shows the presence of a tumor associated with the prosthetic capsule, in addition to a corroboration pathological study of the aspiration biopsy of seroma that exhibits the lipomatous infiltration, associated with the implant capsule in addition to being CD30-positive. It has been defined that the main clinical presentations in this etiology are the presence of a late seroma in the capsular space and ipsilateral enlarged axillary nodes in addition to focal erythema, pain, and rash on the breast skin [5].

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According to the severity and stage of disease, in accordance with the TNM staging system, BIA-ALCL can be classified by the extension of the tumor as T1-T4, by the affection of lymph node(s) N0 - N2, and according to the metastasis as M0 - M1 (Table 1 & 2)[6].

Table 1 TNM classification for breast cancer

TNM Classification	
T= Tumor spread	
T1	Confined to the effusion or inner surface of the seroma
T2	Infiltration of the capsule by isolated cells
T3	Group of cells or mantles infiltrating the capsule
T4	Infiltration beyond the capsule
N: Lymph node	
N0	No infiltration
N1	An infiltrated regional lymph node
N2	Multiple infiltrated lymph nodes
M: Metastasis	
M0	No remote extension
M1	With extension to distant organs

Table 2 TNM staging of breast cancer according to its classification

TNM Stage	
IA	T1 -N0 -M0
IB	T2 – N0 – M0
IIA	T3 – N0 – M0
IIB	T1-T3 – N0 – M0
III	T4 – N1 -N2 – M0
IV	M1

Objective

This article exposes the case report of a patient carrier of a BCL-ALCL, inicially treated as a Hodgkin lymphoma patient due to the low incidence in the presentation of the mentioned pathology. Later, with the help of immunohistochemistry it was correctly diagnosed and treated. It aims to propose the BCL-ALCL as a differential diagnosis in patients with prior breast augmentation with macro-textured implants that develop a breast tumor in the following postoperative years, as the importance of a correct diagnosis by immunohistochemistry study. The presence of a tumor associated with the prosthetic capsule is highlighted, and its surgical management and adequate treatment are prioritized, intentionally ensuring a better prognosis in patients.

2 Case presentation

We present the case of a 45-year-old woman with a prior history of breast augmentation with macro-textured, round subglandular implants in 2007 without any immediate or mediate complications and who did not receive appropriate annual medical checkups (clinical or imagenology). In March 2021, she presented with a focal right breast rash, erythema, and mastalgia of moderate intensity on mammography. She presented an electrical impedance mammography which reported as a right breast tumor, localized in the superior and inferior external quadrants

categorized as BI-RADS 3. Additionally, a magnetic resonance study of both breasts was performed and reported segmental enhancement of 33x14mm in the upper-inner quadrant of the right breast, with a neoplastic appearance, type 2 perfusion curvature, heterogeneous collection between the enhancement and the implant, as well as right axillary lymphadenopathies with loss of fatty hilum, categorized as BI-RADS 4. Subsequently, an excisional biopsy of the right breast node and resection of the right axillary lymph nodes were performed, with a definitive histopathological diagnosis of classical Hodgkin's lymphoma of the nodular sclerosis type. Additionally, 1 of 6 right axillary lymph nodes were reported as a classical Hodgkin's lymphoma of the nodular sclerosis type, with the following immunohistochemistry results: CD30 +, CD15 +, LMP-1 +, and PAX-5 +. Management was complemented with a PET/CT demonstrating the presence of hypermetabolic lymph nodes in the right axilla and infraclavicular region, corresponding to a stage I Hodgkin lymphoma. The patient was managed with high-spectrum antibiotics and anti-inflammatories; however, the symptomatology persisted, and the pain became incapacitated, with associated erythema, edema, and moderate desquamation in the dermis of the right breast. In June 2021, due to the persistence of the clinical symptoms, a histopathological reassessment of the prior biopsy of breast tissue and axillary lymph nodes was requested **(Figure 1).**

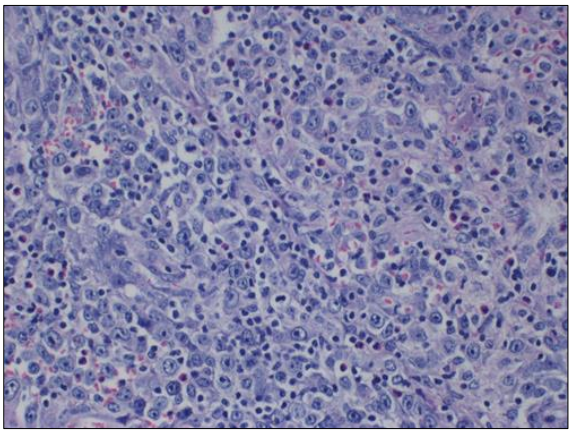

Figure 1 Histologically study where large and pleomorphic cells with variegated nuclei are seen

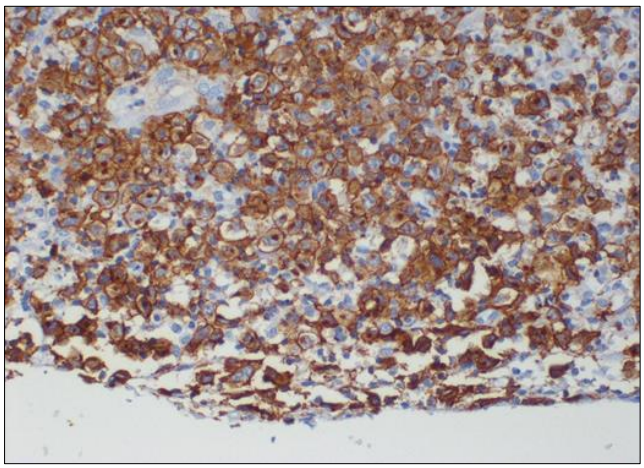

Figure 2 Pathological study of biopsy of neoplastic cells with immunohistochemistry of CD30 + in the cytoplasm and plasma membrane

The final report demonstrated T-cell anaplastic large cell subtype non-Hodgkin lymphoma associated with breast implants, ALK-1 negative, immunophenotype CD30+/CD43+/CD45+/EMA+/CD4+/CD45RO+/TIA-1+FOCAL **(Figure 2 and 3)** with a proliferation index of 70%. Surgical treatment was proposed and realized in conjunction with oncological and plastic surgery. Complete resection of breast implants and total bilateral capsulectomy were performed without complications. Surgical specimens were sent for a definitive histopathological study, corroborating a diagnosis of large cell anaplastic subtype T-cell Hodgkin's lymphoma associated with breast implants. A postoperative control PET scan

was performed, which when compared to the previous study, evidenced a nodular lesion in the right breast as well as an increase in the number, size, and metabolism of cervical and mediastinal nodes with Lugano stage 2 classification. For this reason, complementary surgical treatment was performed, and adjuvant chemotherapy was indicated. The chemotherapy regimen included: cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone (CHOP), in addition to immunotherapy with brentuximab. A new control PET scan was performed in September 2021, with data on the partial metabolic response to treatment. She remains under periodic surveillance with a good prognosis and is clinically asymptomatic.

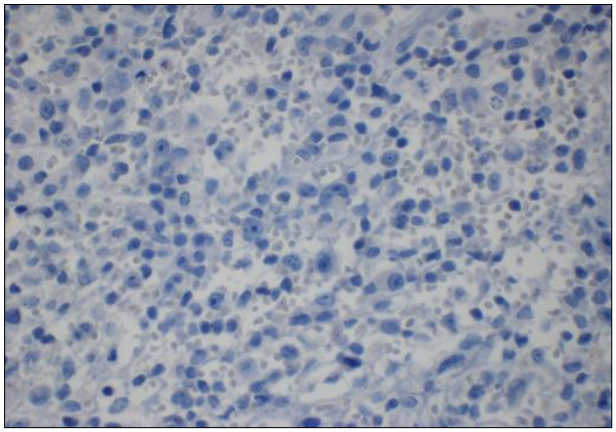

Figure 3 Pathological study of biopsy of neoplastic cells with negative immunohistochemistry for lymphoma protein kinase (ALK)

3 Discussion

BCL-ALCL is a rare infrequent neoplasm primarily present in patients with prior breast augmentation with macro-textured implants in which the lymphoma is directly related to the prosthetic capsule of the implant. It usually develops between 2 and 32 years after the surgery, with an average of 9 years. It accounts for 0.04%-0.5% of the malignant neoplasms of the breast, 1.7%-2.2% of the extranodal lymphomas, and is responsible for 0.38%-0.7% of the non-Hodgkin lymphomas. Due to its low prevalence, the appropriate diagnosis represents a clinical challenge in patients that develop this disease[7].

The physiopathology of this entity is not yet well known; nevertheless, the most accepted one is a chronic inflammation caused by the stimulation of the implant in the breast, and the presence of Gram-negative bacteria or non-bacterial infection creates chronic inflammation. This inflammation is mediated by the continuous activation and proliferation of T-cells, CD30, and its consequent malignant expression. Therefore, the correct diagnosis when suspecting malignant neoplasm requires surgical management and confirmatory immunohistochemistry study of the biopsy which will demonstrate the positivity of CD30/CD43/CD4/TIA1/CD45/EMA/Bcl2 and negativity of ALK/CD20/Pax/CD79a/CD8/CD68[7] markers. (Table 3)

Once the diagnosis is assured, treatment must be completed with a bilateral capsulotomy, guaranteeing up to a 98% survival rate in surgeries that progress without complications.

Due to its low incidence, the BCL-ALCL is not the first suspected diagnosis in patients with a possible malignant breast neoplasm; nevertheless, it is important to consider this entity as a differential diagnosis in patients with prior breast augmentation that develop a late seroma in the capsular space, ipsilateral enlarged axillary nodes followed by focal erythema, pain, and rash on the breast skin. However, it is important to recognize Hodgkin lymphoma, B-cell associated lymphomas or other T-cell associated lymphomas as other possible causes of a breast tumor in young patients with a history of breast implants[2]

Table 3 Immunohistochemical markers for ALK-negative ALCL neoplastic cells.

Primary Antibody	Case D203763	Tester
CD7	Negative in neoplastic cells	Appropriate
CD20	Negative in neoplastic cells	Appropriate
CD4	Positive in neoplastic cells	Appropriate
EMA	Positive in patches in neoplastic cells	Appropriate
ALK1	Negative in neoplastic cells	Appropriate
CD3	Negative in neoplastic cells	Appropriate
LMP-1	Negative in neoplastic cells	Appropriate
Ki-67	Positive at 50%	Appropriate
CD30	Positive in neoplastic cells	Appropriate
PAX-5	Negative in neoplastic cells	Appropriate
EBER-ISH	Negative	
CD8	Negative in neoplastic cells	Appropriate
CD7	Negative in neoplastic cells	Appropriate
TIA1	Negative in neoplastic cells	Appropriate
ALK	Negative in neoplastic cells	Appropriate
Fascina	Positive in neoplastic cells	Appropriate

4 Conclusion

BIA-ALCL is a rare infrequent neoplasm associated with T-cell malignant proliferation in which patients develop a late seroma in the capsular space, ipsilateral enlarged axillary nodes, focal erythema, pain, and rash on the breast skin. It is primarily associated with macro-textured breast implants; therefore, it must be considered a possible diagnosis in patients with breast tumors and prior breast augmentation. Its surgical management, which includes a complete ipsilateral capsulectomy followed by immunohistochemistry, must be performed and is mainly highlighted in this article.

We thank the multidisciplinary medical team for their dedication, care, and commitment to the good prognosis of this patient!

Compliance with ethical standards

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Disclosure of conflict of interest

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Statement of ethical approval

- **Protection of people and animals.** No experiments have been performed on humans or animals.

- **Data confidentiality.** The authors declare that they have followed the protocols of their work center on the publication of patient data.
- **Right to privacy and informed consent.** The authors have obtained the informed consent of the patient referred to in the article. This document is in the possession of the corresponding author.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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