

Breast Implant-Associated Anaplastic Large Cell Lymphoma: Two Distinct Clinical Presentations



Linfoma Anaplásico de Grandes Células Associado aos Implantes Mamários: Duas Apresentações Clínicas Distintas

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ABSTRACT

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare CD30 positive T cell lymphoma whose incidence has recently increased. Until 2020, 733 cases of BIA-ALCL and 36 deaths have been reported around the world, with only one confirmed case in Portugal. The authors describe two clinical cases of BIA-ALCL after breast cancer reconstruction using macrotextured implants. Case 1: A 45-year-old patient, who presented with a typical late-onset seroma five years after breast reconstruction and underwent capsulectomy, confirming localized disease to the capsule. Case 2: A 43-year-old patient presented with an atypical presentation of pleural effusion and tumor mass, 14 years after reconstruction. She underwent implant removal and chemotherapy, due to metastatic disease. These clinical cases illustrate two very distinct clinical presentations of BIA-ALCL. Early diagnosis of this entity allows for effective treatment of the disease, which should be approached in a multidisciplinary setting.

Keywords: Breast Implants; Breast Neoplasms; Lymphoma, Large-Cell, Anaplastic; Portugal

RESUMO

O linfoma anaplásico de grandes células associado aos implantes mamários é um linfoma T CD30 positivo raro, cuja incidência tem aumentado recentemente. Até 2020, estavam registados 733 casos de BIA-ALCL e 36 mortes, em todo o mundo e apenas um caso confirmado em Portugal. Os autores descrevem dois casos de BIA-ALCL, após reconstrução mamária por cancro de mama, com próteses macrotexturadas. Caso 1: Doente com 45 anos, que se apresentou com a manifestação típica de seroma tardio, cinco anos após a colocação da prótese, tendo sido submetida a capsulectomia, que confirmou doença localizada à cápsula. Caso 2: Doente de 43 anos, que se manifestou de forma atípica com derrame pleural e massa tumoral, 14 anos após a colocação da prótese. A doente foi submetida a remoção de prótese e quimioterapia, tendo em conta a doença metastática. Os casos clínicos descritos ilustram duas formas distintas de apresentação clínica de BIA-ALCL. O diagnóstico precoce desta patologia possibilita o seu tratamento de forma eficaz e deve ser abordado em equipa multidisciplinar.

Palavras-chave: Implantes Mamários; Linfoma Anaplásico Cutâneo Primário de Células Grandes; Neoplasias da Mama; Portugal

INTRODUCTION

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare CD30 positive T-cell non-Hodgkin lymphoma. The first case report was published in 1997 by Keech and Creech¹ and was acknowledged by the World Health Organization as a distinct entity in 2016.² Doren *et al* estimated the incidence of BIA-ALCL to be 1:30 000 women with textured implants.³ However, in recent years, the number of cases reported in the literature has noticeably increased, suggesting that this disease was previously underdiagnosed. Until 2020, 733 cases of BIA-ALCL and 36 deaths had been reported by the US Food and Drug Administration (FDA) around the world,⁴ with only one confirmed case in Portugal by the National Authority of Medicines and Health Products (Infarméd).

We present two cases of BIA-ALCL with distinct clinical presentations and treatment.

underwent mastectomy with immediate breast reconstruction using *latissimus dorsi* flap and Silimed® macrotexturated implant placement, followed by adjuvant chemotherapy (ChT) and tamoxifen. Five years later, she presented with right breast swelling, with no fever nor history of trauma. Asymmetry of the breast was noted, without inflammatory signs (Fig. 1). Periprosthetic fluid drainage was negative for neoplastic cells and bacterial culture revealed a *Staphylococcus warneri*. She was treated with levofloxacin for one week, but the effusion relapsed. Magnetic resonance imaging (MRI) showed periprosthetic fluid, without evidence of lymphadenopathy or any suspicious mass in the capsule (Fig. 2). A second fine-needle aspiration was performed and revealed atypical cells that stained positive for CD30 (strong and diffuse), CD4, TIA, Granzina B and negative for ALK, CD3, CD2, CD5 and CD8. The diagnosis was BIA-ALCL. A positron emission tomography (PET) scan excluded distant disease and a bone marrow biopsy was normal. The multidisciplinary team decided to perform a capsulectomy which was made through the periareolar previous incision,

CASE REPORT

Case 1

A 45-year-old woman was diagnosed with right-sided breast cancer in 2005. At the time of diagnosis, the patient

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Figure 1 – Right breast asymmetry



Figure 2 – Breast MRI, T2 axial: right-side periprosthetic fluid (red arrow), with no lymphadenopathy or any suspicious mass at the capsule

without post-operative complications (Fig. 3). The pathological examination of the surgical specimen confirmed BIA-ALCL – Stage IA by tumor, lymph node, metastasis (TNM)

solid tumor staging system. The patient continued regular follow-up.

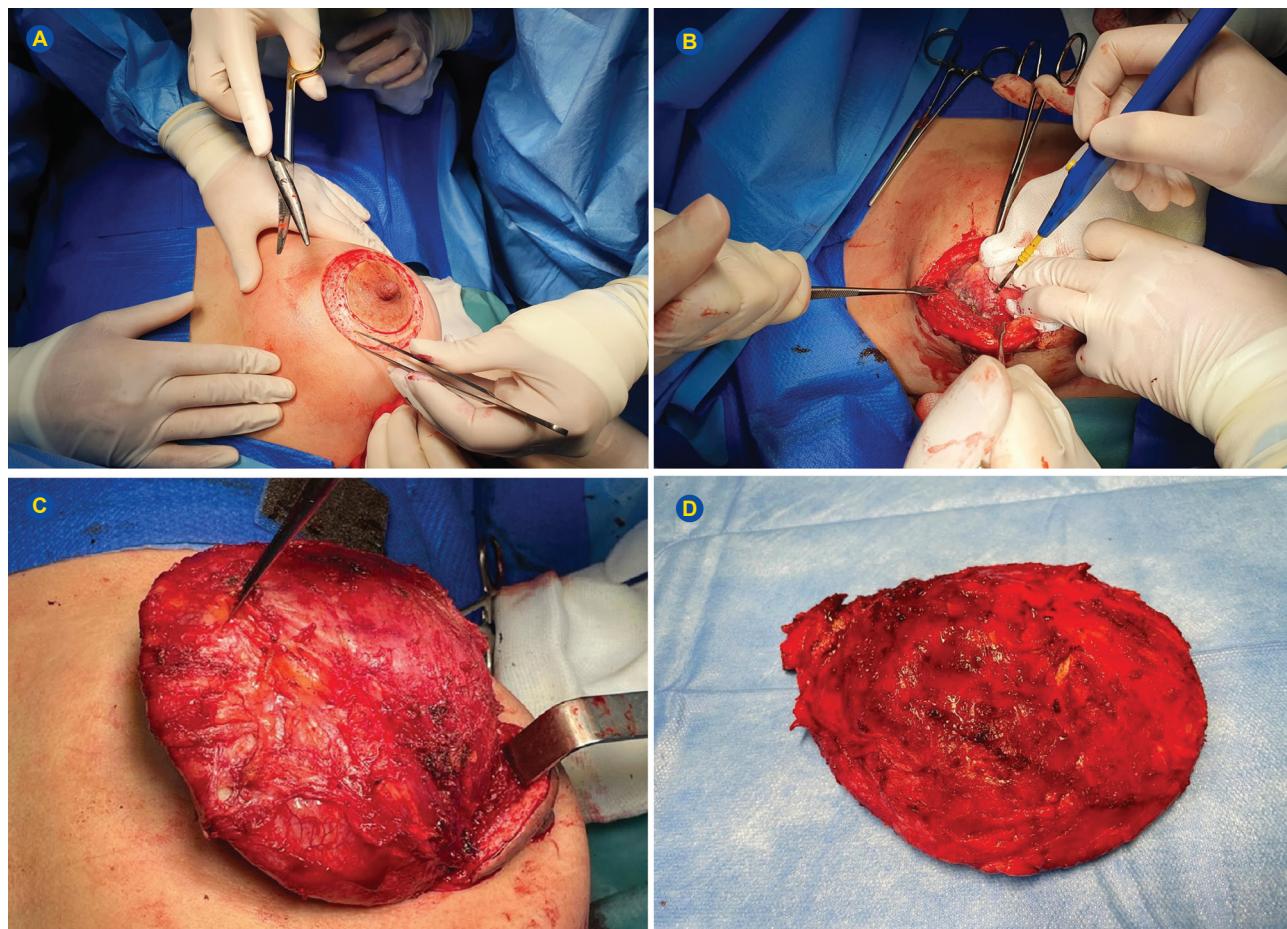


Figure 3 – Surgical procedure: complete capsulectomy by periareolar incision (A: Periareolar incision; B: Dissection of capsular plan; C: Implant extrusion within integral capsule; D: Surgical specimen)

CASE 2

A 43-year-old woman was diagnosed with left-sided breast cancer in 2001. At the time of diagnosis, the patient underwent modified radical mastectomy with immediate breast reconstruction with saline-implant (unknown brand) followed by chemotherapy. Four years later, the saline-implant had been changed to the Allergan Biocell® macrotextured silicone implant with capsulectomy, and the pathological examination was negative for neoplastic cells. Fourteen years later she presented with thoracic pain and a pleural effusion was diagnosed by computed tomography (CT)-scan. The thoracocentesis fluid at that time was negative for neoplastic cells. She underwent a PET scan, which revealed a large left pleural effusion, with peripheral hypermetabolic foci extending from the base of the breast implant with a standardized uptake value (SUV) of 4.7, to the chest wall (SUV 9.1) (Fig. 4). There were also two left pleural nodules (SUV 4.7 and SUV 3.7), multiples nodules in the right lung (SUV 3.1) and an increased uptake by the right adrenal gland (SUV 10). A MRI was also performed and confirmed a locally advanced disease with periprosthetic fluid, capsular enhancement and mass-forming component, which invaded beyond the capsule and extensively infiltrated the homolateral chest wall with axillary and internal mammary chain lymphadenopathies (Fig. 5). A chest wall biopsy showed

large CD30 positive atypical cells but the complete immunohistochemical study could not be carried out because of insufficient material. Therefore, we performed an incisional biopsy of the capsule, fluid aspiration and excision of suspicious axillary nodes under local anesthetic. The pathological examination revealed a large cell anaplastic lymphoma, CD30 positive/ALK negative, present in the axillary (extranodal) soft tissues, in the serous effusion and in the luminal side of the capsule, which was compatible with BIA-ALCL clinically stage IV (T4N2M1). The implant was removed, and the multidisciplinary team decided to proceed with complete chemotherapy with cyclophosphamide, etoposide, vincristine and prednisolone (CEOP).

DISCUSSION

Although the pathogenesis of BIA-ALCL is still unknown, the role of textured implants is well documented, as there are no cases of BIA-ALCL with smooth implants only.⁴ Both saline and silicone-filled implants have been reported in association with BIA-ALCL without a statistically significant difference in frequency.⁷ The problem seems to be the prosthetic shell, with the highest risk for macrotextured implants, as reported in described cases (Silimed and Allergan Biocell).⁸ Several mechanisms have been proposed: chronic T cell inflammation; the expression of Th17/Th1

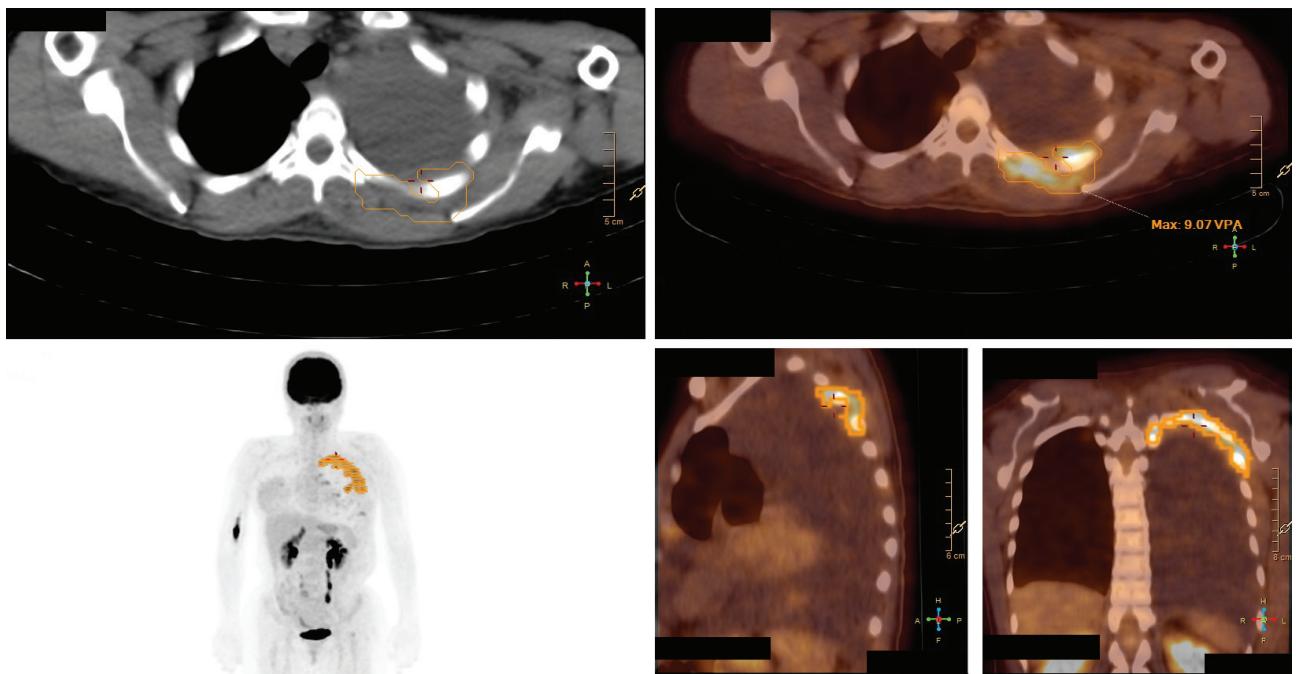


Figure 4 – PET-CT scan: left pleural effusion, with hypermetabolic mass from the base of the breast implant to the chest wall (max. SUV 9.1)



Figure 5 – Breast MRI, T2 axial: left periprosthetic fluid and invasive mass extending through the capsule to the homolateral chest wall

phenotype; somatic mutations with JAK/STAT3 signaling pathway activation; and the biofilm theory proposed by Hu *et al* but not supported by Walker *et al* in 2019.⁹

BIA-ALCL most commonly occurs in patients with a median age of 52 years old and about eight-nine years after breast implant placement. BIA-ALCL may have a bimodal

clinical presentation. The typical one is a 'late seroma' which is a malignant effusion around the implant that occurs in about two thirds of patients and is associated with an indolent course, is usually diagnosed in the early stages and has an excellent prognosis after complete capsulectomy (Case 1). The other one is a tumor mass, with or without

effusion, which has an aggressive clinical course, frequently requiring multimodal therapy (Case 2).¹⁰

The diagnosis of BIA-ALCL is made by aspiration cytology (> 50 mL fluid) with cell block, immunohistochemical study and/or flow cytometry or by mass biopsy showing atypical, large, CD30 (+) and ALK (-) clonal cells.^{11,12}

The American Joint Committee on Cancer (TNM) solid tumor staging system better predicts survival and relapse compared with the Lugano modification of the Ann Arbor System.^{13,14}

Localized disease (\leq IIA) may be treated with surgery alone if complete surgical excision is possible, although a slightly higher rate of recurrence is noted with infiltration beyond the capsule.^{13,14}

Due to the rarity of advanced disease (\geq IIB), treatments are generally extrapolated from the experience of systemic ALK negative anaplastic large cell lymphoma (ALCL). Radiation therapy is suggested for patients with localized residual disease, positive margins, or unresectable disease with chest wall invasion. Systemic therapy is warranted in patients with stage IIB-IV disease with cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) or CEOP when a maximum threshold of anthracycline dosing was reached as in case 2 or, alternatively, a combination with brentuximab vedotin.^{13,14}

These clinical cases illustrate the bimodal clinical presentation of BIA-ALCL, and its recognition may promote the early treatment of this disease. A multidisciplinary approach and prospective data compilation are the mainstay of the management of BIA-ALCL patients.

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AUTHORS CONTRIBUTION

PM: Acquisition of information, draft of the paper, image shooting.

FM, JVM: Critical review of the paper.

CRS: Concept and design of the work, critical review of the paper.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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