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Case report

Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) in a young transgender woman: A case report

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ABSTRACT

Introduction: Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) is a rare T-cell lymphoma occurring after breast implant procedures. As gender confirmation therapy (GCT) in male-to-female transgender (FT), up to 60–70 % of patients require breast augmentation and are at risk for BIA-ALCL. Hence, we report the youngest BIA-ALCL case in the Italian population and the first early-stage BIA-ALCL occurred in FT patients.
Case presentation: A 27-years-old FT was admitted to outpatients' clinics due to swollen left breast. The patient underwent GCT with a macrotextured implant four years before. Clinical examination revealed swollen left breast. Ultrasound and magnetic resonance imaging confirmed left breast periprosthetic effusion. Positron emission tomography-computed tomography scan did not reveal any focal pathological uptake. Fine needle aspiration cytology confirmed BIA-ALCL suspect. The patient underwent bilateral *en bloc* breast implant removal and periprosthetic capsulectomy. Due to the early stage, adjuvant chemotherapy was omitted. Postoperative follow-up was unremarkable.
Clinical discussion: BIA-ALCL is a rare, emergent clinical concern after breast implant surgery. GCT leads to improved body satisfaction and quality of life in FT individuals. As for non-trans patients undergoing breast reconstruction or breast augmentation, this clinical case once again demonstrates that FT patients undergoing breast implant surgery are at risk of BIA-ALCL.
Conclusion: Physicians should promote awareness among patients' GCT and tailored postoperative follow-up.

1. Introduction

Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) is a rare T-cell Non-Hodgkin lymphoma that occurs after breast implant procedure [1]. Firstly, described in the 1997 and officially classified in the 2016 nomenclature of the World Health Organization, a total of 434 cases have been reported. Due to the rarity of the disease, optimal diagnostic workup and therapeutic procedures are still debated in literature for patients undergoing breast prosthetic reconstruction or augmentation [2].

Gender affirmation surgery is a cornerstone of the multidisciplinary approach to gender dysphoria (GD). Up to 60–70 % of male-to-female transgender (FT) patients require breast augmentation procedure in addition to hormonal therapy for feminization of the chest [3]. Moreover, with the rise in the number of patients referred to gender identity clinics for GD, clinicians should be aware of the risk of BIA-ALCL after breast augmentation [4].

In order to raise awareness among physicians, we report the youngest BIAL-ALCL case in the Italian population, it occurred to 27-year-old FT after breast augmentation surgery. This work is reported by following the surgical case report (SCARE) guidelines [5].

2. Case report

A 27-years-old Italian Caucasian no smoker transgender woman was admitted, in February 2021, to the Oncoplastic Interdepartmental Unit

Abbreviation: BIA-ALCL, Breast Implant-Associated Anaplastic Large Cell Lymphoma; GCT, gender confirmation treatment; GD, gender dysphoria; FT, male-to-female transgender; US, ultrasound; FNAC, fine needle aspiration cytology; MRI, magnetic resonance imaging; FDG PET-CT, 2-[Fluorine-18]fluoro-2-deoxy-D-glucose Positron emission tomography-computed tomography.

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of National Cancer Institute - Naples, after evidence of swollen left breast. Family history was negative for oncological disease. The medical history of the patient includes hypothyroidism in treatment with thyroxine and she was on hormonal treatment for sexual transition with estrogen and anti-androgen (cyproterone acetate). BMI was 26,7. The patient underwent in November 2017 pre-pectoral bilateral breast augmentation surgery with periareolar incision and macrotextured implants (N-TSF485, Natrelle™ Inspira, Allergan, Irvine, CA, USA). The postoperative course was uneventful (Fig. 1).

During the admission visit, the patient reported that she had been suffering from swelling in her left breast for 6 months. The patient stated that she had not undergone a visit earlier, due to the pandemic. Clinical examination revealed left breast enlargement with redness of the left breast skin without any suspicious lump bilaterally. Breast ultrasound (US) showed left breast periprosthetic effusion without intracapsular and extracapsular signs of implant rupture. The US was unremarkable in the right breast and the axilla bilaterally.

Subsequently, the patient underwent a Magnetic resonance imaging (MRI) in March 2021, that confirmed left breast periprosthetic effusion with some areas of hypointense signals and left implant collapse. Contrast enhancement sequences revealed left periprosthetic gadolinium uptake, without evidence of periprosthetic mass (Fig. 2).

After the MRI, the patient was subjected to a Fine Needle Aspiration Cytology (FNAC) of fluid effusion that revealed 1000 cm^3 of cloudy yellow serous periprosthetic effusion. The microbiological assessment was negative, while cytological evaluation revealed large-sized atypical CD30+ lymphoid cells, highly suspicious for Anaplastic Large Cell Lymphoma (ALCL). After the cytological diagnosis of a neoplastic disorder, the patient underwent 2-[Fluorine-18]fluoro-2-deoxy-D-glucose Positron emission tomography-computed tomography (FDG PET-CT) scan which did not reveal any focal periprosthetic, locoregional, or distant pathological uptake (cT1N0M0).

The case was discussed at multidisciplinary meeting with oncoplastic breast surgeon, onco-hematologist and psych-oncologist, and the patient was designated for surgery. Before surgery the patient underwent an anesthesiologic, endocrinology and a psych-oncology counseling. Because of an increased risk of thrombosis for anti-androgen and estrogen therapy, the patient was treated with anti-thrombocyte prophylaxis with enoxaparin sodium 12 h before surgery. In May 2021, bilateral *en bloc* breast implant removal and periprosthetic capsulectomy were performed by the oncoplastic surgeon to reduce the risk of intraoperative seeding as much as possible (Fig. 3). The postoperative course was uneventful, and the patient was discharged during the third postoperative day. Due to a decline in psychological and emotional condition, the patient was referred to a psycho-oncology track. Surgical specimen confirmed diagnosis of left breast BIA-ALCL with CD 30+, CD3+, CD2-, CD7- and CD 5- pattern expression with negative surgical margins. Due to the early stage of the disease (Stage 1A as proposed by Clemens et al. [2]) adjuvant chemotherapy was omitted. Postoperative follow up were unremarkable and 12 months after surgery, breast reconstruction with prosthesis was proposed to the patient.

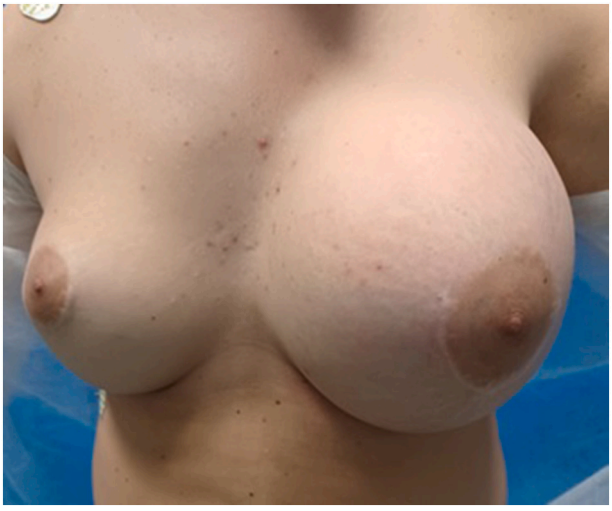

Fig. 1. Preoperative assessment of the chest. Bilateral periareolar incision, left breast redness and left breast swollen.

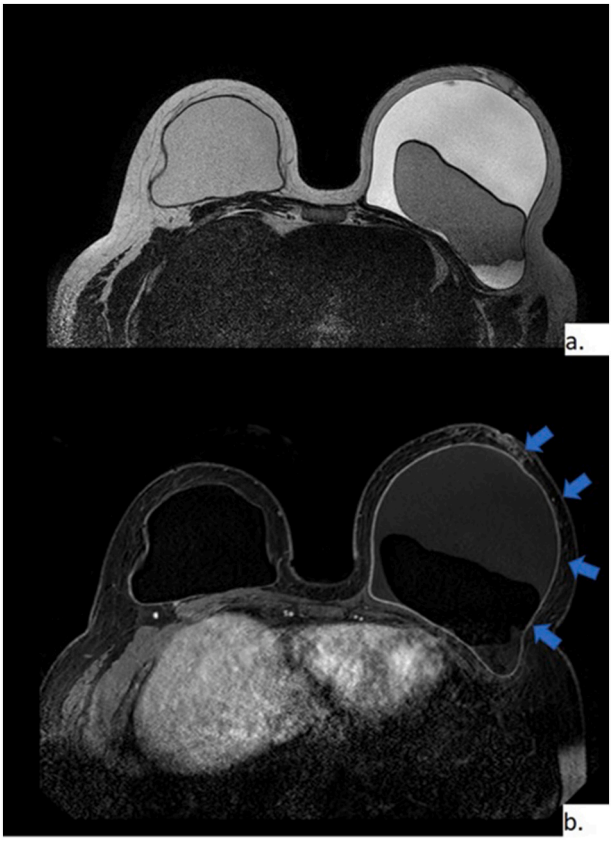

Fig. 2. Bilateral breast MRI. a. Axial T2-weighted image showing an effusion around the intact left breast silicone implant. b. Dyn-eTHRIVE image showing left effusion and capsular enhancement (blue arrows). MRI: Magnetic resonance. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3. Discussion

BIA-ALCL is a rare, emergent clinical concern after breast implant surgery [1]. In the present case report, we present the 5th clinical case known in the literature of BIA-ALCL and the youngest case reported in the Italian population which occurred after gender confirmation treatment (GCT) [6].

GCT leads to improved body satisfaction in FT individuals [7]. GD is linked with a high level of body image dissatisfaction and distress, resulting in a higher rate of restrained eating, bulimic behavior, weight, and shape concerns in FT individuals [8]. Moreover, body dissatisfaction and poor body image have been linked to other disorders, such as chronic depression, substance abuse, affective spectrum disorders, and somatic disorders [8]. As for non-trans patients undergoing breast reconstruction or breast augmentation, this clinical case once again demonstrates that FT patients that underwent breast implant surgery are at risk of BIA-ALCL.

A recent literature review regarding BIA-ALCL development in the FT population analyzed the 4 previous clinical cases presented [3]. Data evaluation revealed how the mean time from initial symptoms was 5 years, and the mean time to presentation was 12 years [3]. Interestingly,

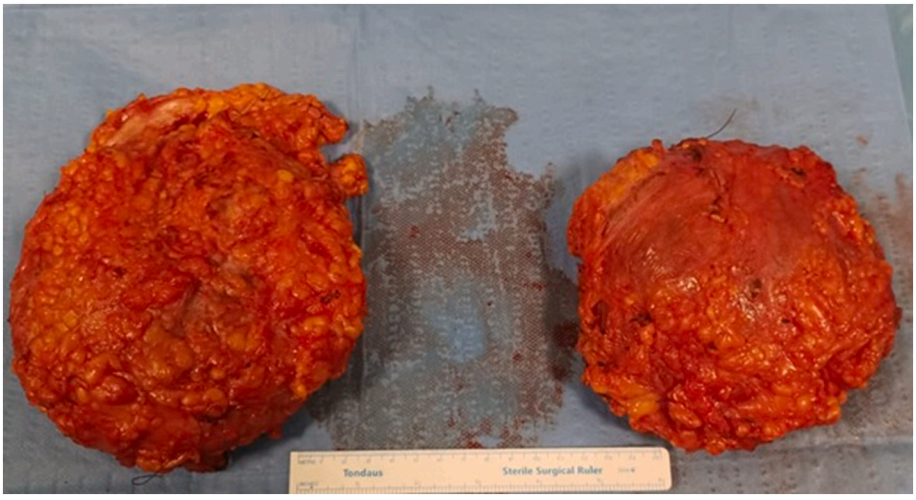

Fig. 3. Breast periprosthetic tissue and implant specimen. Left specimen is swollen and bigger when compared with the right specimen. Histologic examination revealed left CD 30+, CD3+, CD2-, CD7- and CD 5- lymphoid cells and BIA-ALCL diagnosis was established. Right specimen did not revealed any abnormality. BIA-ALCL: Breast implant associated anaplastic large cell lymphoma.

the time from initial symptoms was similar in our clinical case and the previous case series, but shorter when compared with the cis-gender population, which is usually 7 years [3]. A shorter period between breast implant procedure and BIA-ALCL clinical onset stresses the importance of a postoperative follow-up after GCT. Moreover, unlike breast cancer patients who are enrolled in structured follow-up, patients who perform GCT or breast augmentation are less likely to routinely perform postoperative follow-up with an intrinsic risk of delayed diagnosis [3,6]. Moreover, despite the putative protective role of estrogen in lymphoid neoplasm and the complex crosstalk between the immune and reproductive system [9,10], the impact of hormonal treatment in BIA-ALCL is still unknown. The physician should be aware that due to the rise of adolescents with GD which required GCS, preoperative awareness and postoperative structured follow-up should be offered in patients undergoing breast implant procedures. Notably, BIA-ALCL awareness is even more urgent in this period due to coronavirus pandemic restriction and patients' delayed self-referral [11].

Regarding clinical presentation, all 4 previous cases of BIA-ALCL occurring in the FT population could be considered at a late stage, experiencing palpable periprosthetic mass, while our patient clinical presentation was cold seroma [3]. Cold seroma occurring several years after breast implant surgery is the most common symptom among the BIA-ALCL population. However, late cold seroma is not pathognomonic and BIA-ALCL accounts only for 9 % of the unselected late peri-implant breast effusions [12]. Breast palpable mass or regional lymph node involvement are late symptoms accounting for up to 10 % of patients [1,13].

The development of BIA-ALCL is a complex cascade that takes years until the expansion of a monoclonal neoplastic T-cell lymphocyte. Current BIA-ALCL pathogenetic theories suggest that genetic instability and tumor progression might be caused by several factors, including textured breast implant surface, genetic predisposition, periprosthetic microbiome, biofilm formation, and the release of silicone particles leading to chronic subclinical inflammation [14–18]. In the present clinical case, the patient underwent surgery with macrotexured breast implants, which were retired from the market in 2018, due to the higher risk of BIA-ALCL development [1].

Regarding diagnostic evaluation, current guidelines encompass bilateral breast and axilla US, FNAC, breast MRI, Mammography, and FDG PET-CT. the US represents the first choice in case of pain, swelling, or a mass related to a breast implant. Despite US quality being operator dependent and subjective to interpretive error, US sensitivity is over 80 % for detecting a peri-implant collection [19], and breast US is the preferred first-line imaging to assess any breast implant alteration. Additionally, the US could detect axillary lymphadenopathy, periprosthetic solid, or mixed cystic/solid masses and it is the preferred guidance to perform FNAC. In patients over 40 years old, a breast mammogram should be performed to rule out any potential sign of in situ or invasive primary breast malignancy (breast mass, microcalcification) [2]. Breast MRI is commonly considered second-level imaging when the US is inconclusive and it is extremely useful to identify implant rupture, the exact extent of fluid effusion, and any potential mass or local lymphadenopathy [1,2].

Besides breast imaging procedures, FNAC represents the cornerstone of the diagnosis of BIA-ALCL [2]. Recent work by Di Napoli et al. confirmed its role in late breast implant effusion assessment and with a cytological pattern consistent with the histology of the corresponding capsules [12]. In fact, despite late implant seroma is considered an early and specific BIA-ALCL clinical presentation, >90 % of this symptom could be addressed to other disorders such as infection (even subclinical), implant rupture, and mechanical shearing [12]. Peri-implant fluid aspiration allows obtaining a specimen for cytological and microbiological assessment. Microbiological samples are usually set up to exclude peri-prosthetic infections and to assess antimicrobial susceptibility. An adequate sample with >50 ml or whole effusion aspiration reduces the false-negative rate [2] because CD 30 + expression pattern is not specific to lymphomatous cells, and it can be present on activated B and T lymphocytes. Therefore, FNAC diagnosis requires a careful clinico-pathologic correlation with relevant clinical history to aid pathologists [2,12].

Once a cytological suspect is established, the local and distant stage disease is performed with whole-body FGD PET-CT. For any confirmed BIA-ALCL case, preoperative FGD PET-CT is the preferred imaging to detect pathological masses, locoregional lymphadenopathy, chest wall involvement, and distant disease [2]. Any BIA-ALCL patient should be addressed to FGD PET-CT to identify metastases and evaluate the response after the administration of systemic therapy. Moreover, FGD PET-CT and breast MRI are extremely useful for surgical planning [1,2,20].

Once established diagnosis, surgery when feasible with clear oncological margins demonstrated improved overall survival and event-free survival, and adjuvant systemic therapy is indicated in cases of distant disease, lymph node involvement, or locally advanced neoplasm with cells that infiltrate beyond the capsule [2]. In the case of distant disease, primary medical therapy is usually offered with combined chemotherapy as cyclophosphamide, doxorubicin, vincristine, prednisone

(CHOP), or other anthracycline-based chemotherapy [2].

4. Conclusion

BIA-ALCL is a rare lymphoma, which occurs after breast implant procedures. Recent evidence demonstrates how FT subjects after gender affirmation surgery with breast implant augmentation are at risk of BIA-ALCL development. Despite the diagnostic delay related to the COVID-19 pandemic, our case represents the first diagnosed BIA-ALCL in FT population at an early stage. Due to the increasing number of FT patients requiring breast implant surgery, specialists should promote both awareness among these patients of the risks they run when undergoing surgery and a tailored postoperative follow-up.

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Ethical approval

For this study, ethical and ethnical approval are not required.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Marco Materazzo: Writing - Original Draft, Conceptualization; Gianluca Vanni: Methodology, Formal analysis; Maurizio Rho: Term, Resources, Investigation; Emanuela Morra: Validation; Chiara Buonomo: Writing - Review & Editing. Stefano Mori: Supervision. All authors read and approved the final manuscript.

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Declaration of competing interest

None.

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