Review Article

Breast Implant-Associated Anaplastic Large Cell Lymphoma: Where Hematology and Plastic Surgery Meet

Maria Magdalena Joks, Krystian Czernikiewicz, Łukasz Mazurkiewicz, Monika Joks, Andrzej Balcerzak, Renata Kroll-Balcerzak, Joanna Rupa-Matysek

Abstract

Breast implant insertion for breast reconstruction or breast augmentation is a developing procedure, with high demand worldwide—being the second most common plastic surgery in the US as of 2022. Breast—implant-associated anaplastic large cell lymphoma (BIA-ALCL) is T-cell, non-Hodgkin lymphoma, typically CD30+, ALK-, presenting with fluid collection in the inner aspect of the peri-implant capsule in most patients, with the onset exceeding 1-year after implantation. The mean time between breast implant insertion and BIA-ALCL development is 7-10 years. The main risk factor is the use of textured implants because of their susceptibility to triggering local inflammation and immune stimulation finally leading to lymphoproliferation. Genetic predispositions to hereditary breast cancer increase the risk of disease development as well. BIA-ALCL seems to be underestimated in many countries and the initial symptom–seroma might be overlooked and misdiagnosed. Despite its rarity, the awareness of the disease should be improved among patients and medical professionals. This paper summarizes epidemiology, etiopathogenesis, differential diagnosis, and treatment—both surgical and hematological approaches.

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Introduction

Breast implants are used for breast reconstruction following mastectomy and for breast augmentation. According to literature, globally up to 1.5 million women have been receiving breast implants each year. Following liposuction, breast augmentation is ranked second most common plastic surgery procedure in the US as of 2022.[1,2] The number of breast augmentations/reconstructions recorded by the American Society of Plastic Surgeons (ASPS) plummeted in 2020 probably due to the COVID-19 pandemic although recent years have shown that demand for this procedure is high.[2-4] Breast implants can be classified in several ways depending on their content, shape, and texture. Content-wise implants can be classified as saline-filled or silicone gel-filled. Different shapes of implants are available: anatomical or round. Regarding the texture smooth and textured implants are available.[5,6]

In 1997 the first case of BIA-ALCL was described.[7] Due to its unique etiology, risk factors, and clinical presentation, this type of lymphoma has been listed in the updated World Health Organization's classification of lymphoid malignancies in 2016.[8,9] In the following years, progress in the understanding of the disease has been made, resulting in the first treatment guidelines in 2017 and an update in 2019.[10,11] As of January 2024, 1355 cases have been confirmed globally and 428 suspected or confirmed just in the United States of America.[12]

According to reports on medical device use ASPS silicone-filled implants made up 84% of all implants used in 2020.[2] The 2023 FDA Medical Device Reports on BIA-ALCL points to a more frequent occurrence when textured (73% of cases) and silicone-filled (66% of cases) devices were used.[13]

Epidemiology

Great efforts have been made to estimate the BIA-ALCL incidence in the European population. A study by Santanelli di Pompeo et al. based on data collected by the European Association of Plastic Surgeons and Committee on Device Safety and Development shows that the mean prevalence for 28 European countries is 1:13 745 patients with textured implants with the lowest recorded prevalence in Romania (1:1:222 498) and highest in the Nether-

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lands (1:2969).[14,15] As of today, the highest recorded prevalence in breast reconstruction patients -1:355 - was recorded by Cordeiro et al. at Memorial Sloan Kettering Cancer Center (MSKCC),[16] whereas the highest reported BIA-ALCL prevalence in aesthetic breast surgery patients was described by Kolasinski et al. and reached 1:300.[17] Recent studies on large cohorts of US citizens have been conducted to estimate the risk of BIA-ALCL. The highest risk of BIA-ALCL development ranged from 1:559 to 1:355 depending on the implant type, with the overall incidence up to 2.81 per 1000 textured implant patients. 1 in 559 risk was linked to a cohort of 9737 patients in which 11 patients developed BIA-ALCL. 1 in 355 risk was estimated in a cohort of 3546 patients in which 10 patients developed lymphoma. It is worth noting, that in both cohorts all cases were linked exclusively to textured implants. Both studies report long exposure to textured implants as a risk factor in BIA-ALCL development. Median time to the BIA-ALCL diagnosis ranges between 10.3 and 11.5 years.[16,18] The texturization and the surface area of the implants remain the main risk factor, and the influence of the genetic predisposition is being investigated. De Boer et al. investigated 49 cases of BIA-ALCL of which 6 patients were the carriers of BRCA1/BRCA2 mutation. They estimated the absolute risk of developing BIA ALCL with the BRCA1/BRCA2 mutation carriers under the age of 75 at the level of 1 in 1551 in comparison to noncarriers—1 in 7507.[19] There have been reported cases of the BIA-ALCL in women with Li-Fraumeni syndrome.[20] Overall, patients carrying germline mutations with higher susceptibility to hereditary breast cancer seem to develop BIA-ALCL more often and sooner when compared to noncarriers. Nevertheless, according to current postoperative surveillance protocols, this subgroup of patients is not being distinguished as each patient is included in close follow-up programs after breast implant augmentation (ultrasound or magnetic resonance imaging 5 years after the surgery and then every 3 years thereafter).[21,22] Moreover, the presence of the mutation itself is not a contraindication to the implant augmentation or autologous reconstruction.

Etiopathogenesis and Histopathology

BIA-ALCL is of T-cell origin, non-Hodgkin lymphoma, CD30(+), ALK(-), and included in the fifth edition of the World Health Organization classification of Tumors of Hematopoietic and lymphoid tissue in 2016.[8,23] The risk of developing BIA-ALCL in breast-transplant patients is higher than that of primary breast ALCL in nonimplanted persons, but the survival prognosis of BIA-ALCL is better than in systemic ALCL.[24] Etiopathogenesis includes a complex immune stimulation, as well as chronic inflammation leading to capsule formation, which may be the result of bacterial infiltration or associated with textured surfaces and materials of some kinds of breast implants.[23-25] The innate and adaptive immunity factors infiltrate close to the foreign material and produce cytokines—like IL-4 and IL-13,[24,26] with immune reaction leading further to the Il-1 secretion of IL-1 and the other interleukins, finally leading to the specific microenvironment formation[24-26] resulting in the possibility of pericapsular fibrous tissue involvement.[24,27] Molecular findings in BIA-ALCL include the activation of the JAK/STAT signalizing pathway, and the dysregulation of TP53 and MYC.[14,24] In BIA-ALCL, the STAT3 phosphorylation is a common cause of activation of the JAK/STAT signalizing pathway. It can be induced by STAT3 S614R mutation (67% of all cases) or JAK1 G1097V mutation. The JAK3 V722I mutation is considered a predisposing factor for BIA-ALCL. It is noteworthy, that JAK/STAT signalizing pathway activation might be induced by high IL-6 levels.[24] Other specific findings in BIA-ALCL include the triple-negativity in the context of ALK, DUSP22, and TP63, which distinguishes this entity from systemic and primary cutaneous ALCLs. ALK-positivity or the presence of DUSP22 or TP63 rearrangements suggests non-BIA origin of ALCL.[27] A useful tool in the diagnostic procedure, which refers to the microenvironment of the lymphoma, includes carbonic-anhydrase-9—a hypoxia biomarker, which is upregulated in BIA-ALCL. It can be immunohistochemically assessed, however serum CA9 assessment should be evaluated as potential diagnostic biomarker.[14,28,29] Moreover, BIA-ALCL coincidence with Li-Fraumeni syndrome as well as BRCA1/2 mutation has been reported. Both mutations have a well-documented predisposition to neoplasm development. However, since the data on genetic predisposition is scarce further investigation is required.[15,19,20,30]

Clinical Manifestation

BIA-ALCL symptoms are seen over 1 year postoperation, with an average of 7-10 years.[11,31] Due to the fact, that the pathologic process most commonly (up to 85%) originates from the luminal aspect of the peri-implant capsule the most common clinical presentation is unilateral seroma, manifesting with breast swelling and asymmetry, as periprosthetic fluid accumulation. About 33% of patients present additional signs such as pain. Erythema is rare, but the literature suggests it occurs in 14% of cases.[1,31-34] Rarely, cutaneous infiltration or axillar, supraclavicular, internal mammary chain mediastinal lymphadenopathy is detected. A palpable mass is associated with a more advanced stage at the diagnosis and might be accompanied by fluid.[31-33] Systemic "B" signs (fevers, night sweats, and unexplained weight loss) are reportedly present in 9% of cases.[32]

Chest-wall infiltration is a negative prognostic factor for overall survival, reducing the possibilities of surgical excisions of the tumor.[35]

Given that late seroma is a rare and mostly benign complication of breast implant placement (0.1%) it is worth mentioning, that 10% of seromas might be associated with BIA-ALCL.[32]

BIA-ALCL differential diagnosis is presented in Table 1.

Radiological Diagnostics

Ultrasound

Ultrasound imaging (US) is the most available imaging method and is regarded as a first-step method of choice in BIA-ALCL diagnostics, superior over mammography. It should be performed in the contralateral implant as well.[31-33] The sensitivity of the US is 84% and the specificity is less than 50%.[32,38] According to Adrada et al.,[39] the sensitivity of the US is 84% in effusion testing and 46% sufficient in mass testing and has a specificity of 75% in effusion testing and 100% in mass testing. The US findings are described as homogeneous peri-implant effusion, with inflammatory features, sometimes with irregular capsule contours, or as an oval hypoechoic

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Table 1 Differential Diagnosis of BIA-ALCL

Medical Condition	Findings	Diagnostic Procedures
Implant rupture	(1) Capsular contracture, pain, lump, change of the shape[36] (2) No increase in overall breast volume[31]	US, MRI[36]
Trauma	(1) Mechanical injury (2) Chronic inflammation (3) Drug administration	US, MRI[37]
Infection	(1) Acute symptoms—fever, nausea, vomiting (2) Subacute symptoms—indolent, chronic symptoms and pain	CBC, US, FNA microbiology
Primary breast cancer (PBC)	(1) PBC in relatives (2) Familial and genetic risk factors[32]	Mammography: MRI[38] histopathology
Other lymphomas	(1) T-cell markers—CD2 (+); CD3 (+); CD4 (+); CD5 (+); CD7 (+); CD8 (+) (2) B-cell markers—CD20 (+); CD79a (+); PAX5 (+) (3) t(2;5), FISH	Cytology, immunophenotyping IHC[11] FISH TCR rearrangement

Abbreviations: CBC = complete blood count; CD = cluster of differentiation; FISH = fluorescence in situ hybridization; FNA = fine needle aspiration; IHC = immunohistochemistry; TCR = T-cell receptor rearrangement.

and well-circumscribed solid mass with negative hypervascularity in Doppler US.[32,39]

Mammography

Though mammography is desirable in breast cancer screening programs, it is not recommended for BIA-ALCL detection due to its inaccuracy in identifying effusions and mass components in BIA-ALCL. It is useless in biopsy guidance as well.[38] Though mammography is less specific in BIA-ALCL, it may help distinguish other probable breast malignancies in patients > 40 years of age.[32] Detailed medical history contributes to more precise differentiation between BIA-ALCL and PBC. Patients with a family history of breast malignancies are more likely to develop familiar breast cancer, especially with the presence of BRCA1, BRCA2, and TP53 mutations.[32,40] Carriers of BRCA1 and BRCA2 mutations between the ages of 40-69 should remain under annual mammography surveillance, and annual MRI surveillance is recommended for 30-49-years-old carriers of BRCA1 and BRCA2 mutations and 20-69-year-old carriers of TP53 mutation.[40]

Magnetic Resonance Imaging

At the point of diagnosis establishment, when US findings are uncertain or insufficient for accurate determination of the lesion, MRI should be performed because of its high sensitivity in detecting effusions around breast implants.[11,39] Moreover, an MRI needs to be performed to evaluate the BIA-ALCL local extent and plan surgical treatment after diagnosis.[32,38] No-contrast sequences show implant membrane ruptures, pericapsular effusions and signs of gel bleed, and dynamic contrast-enhanced sequences can assess capsular enhancement and masses undetectable in the US.[32]

PET/CT

A PET/CT scan should be performed before treatment planning to evaluate the extent of the disease before and after treatment—it enables accurate lesion characterization and the assessment of treatment response.[11,31,32,38] However, in PET/CT, it is difficult to see, whether the effusion is benign or malignant and if the marker uptake is elevated due to normal inflammatory activity around the implant capsule, resulting in false-negative and false-positive interpretations respectively.[38] It is not recommended to conduct PET-CT scans after surgical interventions, though after surgery natural inflammation may give a false view of extracapsular or nodal involvement.[32]

Cytological/Histopathological Diagnosis

Primary Assessment

In the presence of effusion, the fine needle aspiration (FNA) of the entire volume of peri-implant fluid (minimum 50 ml) is indicated.[11,32] Repetitive, or small-volume aspirations are at greater risk of receiving false-negative results. Each implant will likely have a small amount of surrounding fluid, however, if the quantity of fluid exceeds 5-10 mL, it requires further diagnostics to exclude malignancy.[11] The fluid samples undergo centrifugation to isolate cells.[32] Cytological evaluation of choice consists of air-dried Wright–Giemsa stain smears and hematoxylin and eosin (H and E) stained cell blocks.[41,42] Giemsa, Papanicolaou or Romanowsky stains are useful too.[41]

Atypical cells with irregular nuclei, vesicular chromatin, prominent nucleoli, and moderately abundant cytoplasm are treated as a gold-standard prerequisite for BIA-ALCL diagnosis.[32,41] For the samples containing inflammatory cells, or in the absence of cells further analysis is not required. If the sample does not bring suspicion of malignancy, a follow–up after 3 months is recommended.[32] When a palpable mass is detected—the core biopsy of the associated capsular mass or pathological lymph node is indicated.[11] Flow cytometry is recommended in the final assessment (Figure 1).

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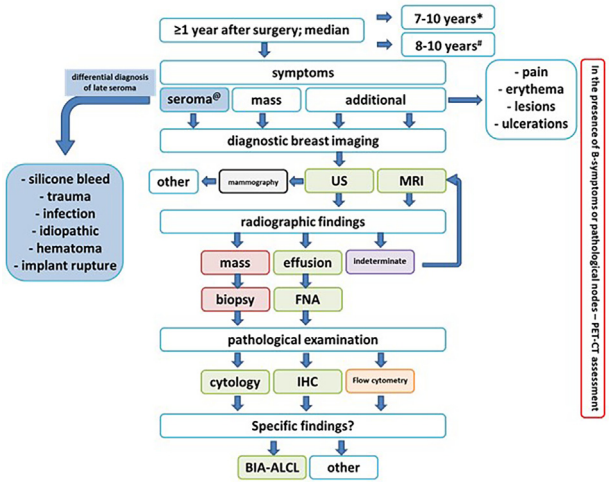
Figure 1 Diagnostic algorithm of BIA-ALCL. First-choice procedures are marked green. Exceptions marked red. Performed flow cytometry should be interpreted in the context of cytological assessment (detection of CD30+ cells may lead to false-positive results). Mammography may help distinguish other probable breast malignancies in patients > 40 years old.*NCCN guidelines; #UK guidelines; @late seroma—occurring > 12 months postoperatively. This algorithm is based on Turton et al.[32]



Final Assessment

Next diagnostic steps include cytology, immunohistochemistry, and flow cytometry.[11,14,32,33,41,43] Immunostaining is a key procedure leading to confirmation of BIA-ALCL in the differential diagnosis through the confirmation of the origin of the cells (Table 1). CD30 antigen positivity and ALK negativity are distinctive factors in the BIA-ALCL diagnosis and should be sought.[11,31,44] However, neither CD30 positivity nor ALK negativity is pathognomonic for BIA-ALCL.[11,14,31,44]

Additionally, markers specific for T-cell lymphocytes are searched—CD2, CD3, CD4, and CD8. To exclude Diffuse Large B-cell lymphomas (DLBCL), the B-cell panel is being investigated as well.[32]

In aberrant phenotypes, the tumor cells might not contain T-cell antigens on the surface. PCR for T-cell receptor gene rearrangements is required to confirm the clonality of T cells (Figure 2).

Lateral flow assay (LFA) is believed to be the alternative method which requires less time and equipment in comparison to CD30 ELISA and thus can be performed by nonspecialized personnel making point-of-care testing for BIA-ALCL more available.[42]

Staging

The application of the Ann-Arbor classification regarding BIA-ALCL is limited since the BIA-ALCL develops as an effusion in the implant capsule, then infiltrates the capsule, and finally spreads beyond the capsule to the lymph nodes or extranodal tissues. This fact cleared out the need for a classification based on the degree of capsule infiltration. Initial proposals of BIA-ALCL staging considering capsule infiltration were made by Clemens et al. in 2015. Their classification was adopted by the NCCN in 2019 guidelines.[11,45] BIA-ALCL staging is based on the assessment of the tumor, lymph nodes, and metastasis (Table 2). It is worth noting that BIA-ALCL is classified as aggressive lymphoma at all clinical stages, completely excluding being a benign tumor at any stage.[11,44,45]

Treatment

Surgical Treatment

Surgical intervention proves to be an effective treatment modality for localized disease.[32] In contrast to other lymphomas, the preferred therapeutic approach for early-stage BIA-ALCL does not involve systemic treatment but rather entails complete surgical excision in the majority of cases. This is attributed to the confined malignancy within the capsule surrounding the breast implant.[24,31,45] Patients in advanced stages benefit from a combination of adjuvant chemotherapy, immunotherapy, and radiotherapy. The standard surgical procedure is complete capsulectomy, en-bloc resection of any associated masses, and implant removal.[11,14,33,46] The specimen is extracted as a complex consisting of the implant, effusion fluid, and capsule. In the presence of any additional mass, it should be excised along with the complex. Piercing of the capsule and fluid evacuation should be avoided. In case of a puncture, the wound must be thoroughly irrigated before closure. Sentinel node biopsy is not recommended as part of the surgical approach.[32]

Patients are advised to remain under oncological surveillance every 3-6 months for the subsequent 2 years, and thereafter as deemed necessary according to the stage.[32,46] Furthermore, prophylactic contralateral implant removal and total capsulectomy are recommended to mitigate the risk of BIA-ALCL in the contralateral breast. Existing data implies that in 2%-4.6% of cases, BIA-ALCL develops bilaterally.[14]

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Figure 2 Beige—skin; yellow—adipose and glandular tissue; light blue—pectoral fascia; stripes—effusion/seroma; red—pectoral and intercostal muscles; white ovals—ribs; red triangle—CD30+ antigen; EBER—EBV-encoded small RNAs. When atypical cells are not present, another FNA should be performed after 3 months.

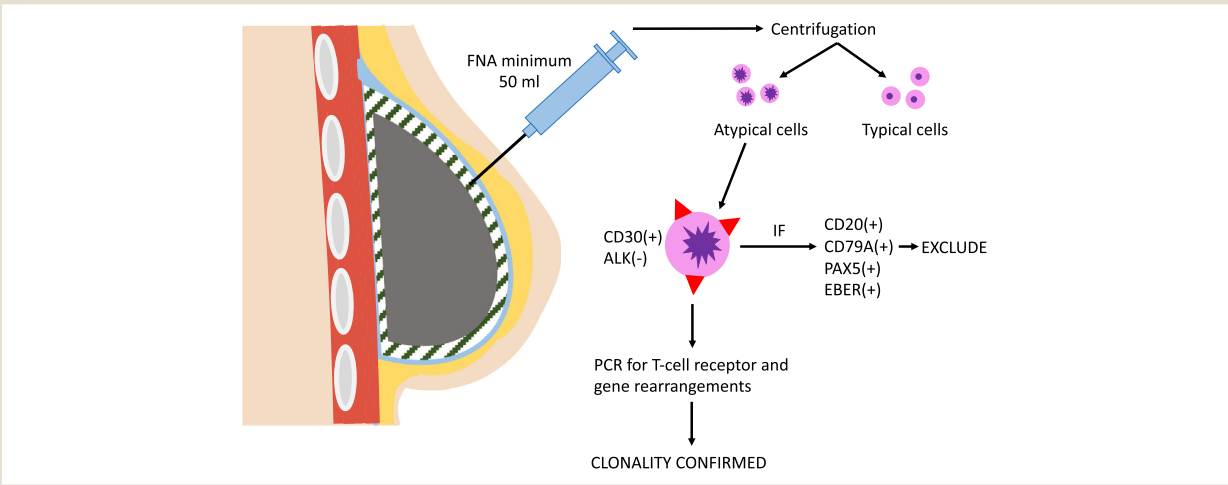

Table 2 BIA-ALCL Staging Based on Clemens MW, Horwitz SM (2017) NCCN Consensus Guidelines for the Diagnosis and Management of Breast Implant-Associated Anaplastic Large Cell Lymphoma[10]

Tumor (T):	
T1	Confined to effusion or a layer on the luminal side of the capsule
T2	Early capsule infiltration
T3	Cell aggregates or sheets infiltrating the capsule
T4	Lymphoma infiltrates beyond the capsule
Lymph node (N):	
N0	No lymph node involvement
N1	One regional lymph node (+)
N2	Multiple regional lymph nodes (+)
Metastasis (M):	
M0	No distant spread
M1	Spread to other organs/distant sites
TNM assessment:	Stage
T1 N0 M0	IA.
T2 N0 M0	IB
T3 N0 M0	IC
T4 N0 M0	IIA
T1-3 N1 M0	IIB
T4 N1-2 M0	III
T_{any} N_{any} M1	IV

Chemotherapy/Radiotherapy

The lymph node involvement indicates the progression of the disease or aggressive clinical course and, according to Ferrufino-Schmidt et al.,[24,47] decreases the 5-year overall survival rate from 97.9% to 75%. Thus, as mentioned before, a PET-CT scan should always be performed if lymphadenopathy or B-symptoms are present. Lymphadenopathy is not always a definitive indicator of malignancy as enlarged lymph nodes may be the result of local reaction to silicone.[32]

For disease stage II–IV, in the case of incomplete tumor excision surgery, or with the biopsy–proven recurrent disease, the adjuvant treatment should be implemented.[31,32] For positive surgical margins or unresectable localized disease, the adjuvant radiotherapy of 24-36 Gy is recommended.[24] The suggested chemotherapeutic choice is extrapolated from the studies regarding the management of systemic ALK(-) ALCL.[32] Currently, NCCN guidelines recommend as a first–line treatment anthracycline–based regimen—CHOP with or without etoposide (cyclophosphamide 750 mg/m^2 iv. day 1,

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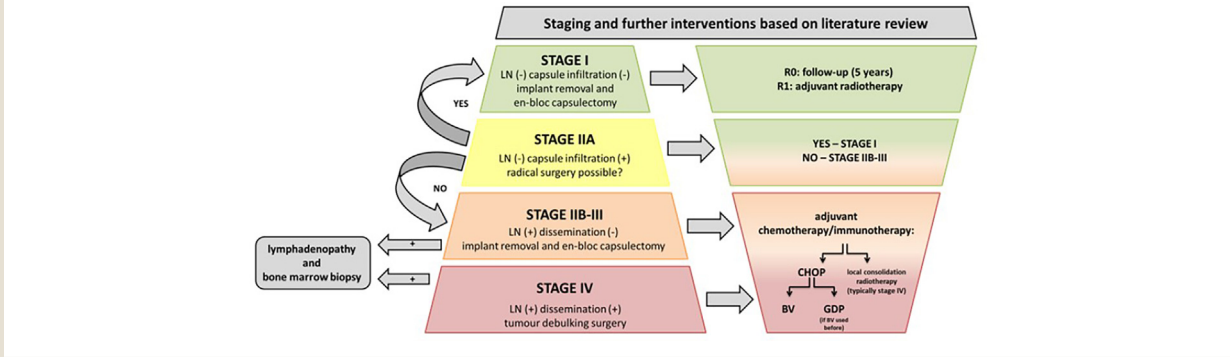
Figure 3 BIA-ALCL treatment algorithm.[31,32] R0 = microscopically margin-negative excision; R1 = microscopically margin-positive excision; LN = lymph node involvement; CHOP = Cyclophosphamide, Doxorubicin, Vincristine, Prednisone; BV = Brentuximab Vedotin; GDP = Gemcitabine, Dexamethasone, Cisplatin.



vincristine 1.4 mg/m^2 iv. day 1, doxorubicin 50 mg/m^2 iv. day 1, prednisone 100 mg p.o. days 1-5).[32,48] Brentuximab – Vedotin (BV)—anti-CD30 antibody combined with monomethyloauristatine is the regimen that significantly improved the patient's prognosis.[49] The ECHELON 2 trial revealed that BV-CHP improved the overall survival and prolonged the progression-free survival when compared with CHOP treatment in patients with peripheral T-cell lymphomas.[24,50] Pro et al.[49] report, that in patients with systemic ALCL or recurrent disease and at least 1 previous line of treatment who have been receiving BV 1.8 mg/kg every 3 weeks, objective response and complete response rates were 86% and 57% respectively. In the case of disease relapse, if the patient has already received BV or is intolerant, platinum-based chemotherapeutics such as GDP are recommended.[32,48] Autologous stem cell transplantation (auto-HSCT) was performed in some cases, however, the role of auto-HSCT in the BIA-ALCL treatment has not been established until now.[32,51] The BIA-ALCL treatment algorithm is summarized in Figure 3.

New Drugs

Current research considers interleukin—targeted therapy as a potential treatment alternative, however further studies are needed.[24] Cyclin D2 (CCND2) is strongly expressed in BIA-ALCL—it has the function to regulate cyclin-dependent kinases 4 and 6 (CDK4/6) leading to regulation of the G1/S cell cycle phase transition. Retinoblastoma protein (RB) is phosphorylated by these kinases, further being a subject of other steps, finally inducing the expression of genes, which are responsible for cell growth.[52] A recent study by Nagel et al. demonstrated, that implementing a palbociclib a CDK4/6 inhibitor counteracts this process and favors cell cycle arrest in G1. The same study suggests that PI3K/AKT inhibitor downregulates CCND2 protein and reduces phosphorylation of RB, favoring cell cycle arrest in G1.[52] Furthermore, discovering molecular aspects underlying the disease, some targeted therapies, like JAK/STAT inhibitors or PD1/PD-L1 inhibitors may also be the future, although more clinical studies are required.[27]

Prognosis

Between 1 January, 2008 and 30 June 2023, FDA received the total number of 9458 Medical Device Reports (MDR) that were following the breast surgery using implants. A total number of 1264 MDR was the diagnosis of BIA-ALCL. Among them, 63 cases resulted in death.[13] Thus, FDA prepared a safety note regarding the risk of potential adverse outcomes that constitute an immediate danger to patient's health and safety. With the absence of complications, the removal of implants is unnecessary, nevertheless, patients are obliged to monitor their health and be aware of numerous side effects, including malignancies.[13]

The prognosis depends mostly on the possibility of en-bloc capsulectomy performance - patients with BIA-ALCL have excellent prognosis overall when the disease is confined to the capsule (5 OS 100% when compared to 72.4% in cases of extension beyond the capsule).[44] Another crucial prognostic factor is chest wall infiltration and lymph node involvement (LNI) (5-year OS 97.9% for patients without LNI and 75% for patients with LNI).[47]

Discussion

Apart from BIA-ALCL, in the past decade awareness of implant-associated diseases and their possible correlation with hematological neoplasms have been described, including numerous cases of ALCL localized in gluteal implants, pacemakers, or orthopedic implants.[46,53,54] However, no BIA-ALCL has been registered with a clear history of only smooth implants, thus texturization is believed to be a significant risk factor triggering chronic inflammation finally leading to lymphomagenesis. Hence, there are suggestions that the term Rough Implant Associated-Anaplastic Large Cell Lymphoma (RIA-ALCL) would be more suitable.[54] Rising awareness of BIA-ALCL and the link between implant type and disease has raised doubt regarding the use of specific breast implant types in modern reconstructive surgery eventually putting an end to the use of textured breast implants in France in 2018 and in South Korea in 2019.[6,15] By refusing the certification of textured implants from Allergan, France blocked their sale in other countries that require CE mark.[15,55] In 2019 Allergan recalled BIOCELL devices

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worldwide due to FDA intervention, whereas other companies were mandated to add special health warnings on rough-texture implant packaging. As of 2022 textured breast implants are still available in Europe.[14,41,56]

As mentioned above, BIA-ALCL is strongly associated with prolonged exposure to macro-textured devices. Textured tissue expanders (TE) are used in 2-stage breast reconstruction. Initially, textured TEs were used more often than smooth TEs due to the lower risk of malposition and need for reoperation, but the current approach mandated by the association of textured devices with BIA-ALCL implies the use of smooth TEs.[6,57] In recent years temporary textured TEs use has raised concerns due to their textured surface and scarce information concerning their oncological safety in literature.[6,18] Additionally, there is a reported case of a patient developing BIA-ALCL with a history of smooth breast implants and textured TEs beforehand.[14]

Despite possible complications such as malposition of TEs, Di Valerio et al. and McLaughlin et al. who have researched textured TEs and their correlation with BIA-ALCL postulate that the choice of smooth TEs for breast reconstruction might be beneficial due to lower risk of BIA-ALCL development and no significant impact on reconstructive timeline owing to possible complications increasing the overall patient safety.[6,57]

Aside from the texturization of the device, the disease might be triggered by situations of immune disreactivity in a course of autoimmune diseases or the treatment with antitumor necrosis factor agents.[58] There are described numerous cases of lymphomas potentially triggered by adalimumab treatment.[58,59] Additionally, women with BRCA1/2 and TP53 mutations are believed to be at increased risk of developing BIA-ALCL,[19,20,30] which raises the question of the safety of breast reconstruction surgeries after breast cancer or prophylactic mastectomies. In this group, alternative procedures such as autologous breast reconstruction should be taken into consideration.[25]

As mentioned before, the treatment of choice in BIA-ALCL is implant removal. However, several authors modified their approaches concerning BIA-ALCL. Alderuccio et al.[60] reported successful BV use in the treatment of BIA-ALCL stage IIB—with the presence of mass lesions and right axillary lymphadenopathy. In the course of treatment, no adverse effects were noticed and the patient achieved CR which, according to the follow-up, currently has lasted 3 years. It was the first reported use of BV in BIA-ALCL treatment and it offered the possibility to consider BV as a potential therapeutic choice, especially for advanced or unresectable lymphoma.[61] Allchin et al.[62] also described a successful treatment of a 65-year-old woman using anti-CD30 agent BV in monotherapy.

To conclude—the frequency of breast implant surgeries rises, leading to an improvement of the quality of life in women implanted for aesthetic or reconstructive reasons. BIA-ALCL is a rare, late implant complication. Taking into account the risk of BIA-ALCL, it seems that aesthetic implant surgeries should be carefully discussed with the patient.

Treatment prognosis is generally good when BIA-ALCL is diagnosed in the early stage, so the awareness among health professionals like general practitioners, gynecologists, hematologists, and plastic surgeons should be spread constantly.[34] The first symptoms of BIA-ALCL may be easily recognized as well as simply explained to the patients and finally accurately diagnosed and successfully treated.

Disclosure

None.

CRediT authorship contribution statement

Maria Magdalena Joks: Conceptualization, Writing – original draft. **Krystian Czernikiewicz:** Conceptualization, Writing – original draft. **Łukasz Mazurkiewicz:** Visualization, Writing – original draft. **Monika Joks:** Supervision, Writing – review & editing. **Andrzej Balcerzak:** Conceptualization. **Renata Kroll-Balcerzak:** Conceptualization. **Joanna Rupa-Matysek:** Supervision, Writing – review & editing.

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