

Surgical Management and Long-Term Outcomes of BIA-ALCL: A Multi-disciplinary Approach

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Background

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is an anaplastic lymphoma kinase (ALK)-negative, T-cell lymphoma that develops around breast implants. Since its first description in a 1997 case report, the medical community has accumulated increased understanding about ALCL. Presently, the best estimates report an incidence of 1:355-1:559 of BIA-ALCL in women with macro-textured implants, and a recent study predicts that prevalence of disease may peak sometime around 2026. In 2016 the World Health Organization recognized breast implant-associated ALCL as a distinct disease entity and soon thereafter, the National Cancer Center Network (NCCN) released its first BIA-ALCL guidance documents.

Updated in 2019, the NCCN documents provide clear guidance regarding the work-up, management, and follow-up of patients with suspected and/or confirmed cases of BIA-ALCL. In those with pathologically-confirmed disease, these guidelines specifically recommend surgical, *en bloc* capsulectomy for the treatment of localized disease and consideration of adjuvant therapies in those with locoregional disease. Follow-up every six months for a minimum of two years is then indicated. A favorable prognosis and acceptably low recurrence rates have been seen when patients with BIA-ALCL are managed according to the NCCN guidelines.

While the outcomes for patients with BIA-ALCL are encouraging, the existing literature to date provides only case series of patients treated by heterogeneous groups of institutions or countries, with different approaches to follow-up or incomplete patient records. The goal of this study is to describe outcomes following the surgical treatment for pathologically-confirmed BIA-ALCL at a single institution using a multi-disciplinary approach.

Methods

- Institutional Review Board approval was obtained, and a retrospective review was performed.
- Pathologically-confirmed BIA-ALCL cases treated at Memorial Sloan-Kettering Cancer Center (MSK) from January 2011 to June 2020 were identified.
 - Patients who completed all surgical +/- medical treatment of their disease under the care of our institutional, multidisciplinary team were subsequently identified and included in the current analysis.
- Patient demographic, diagnostic, treatment, and follow-up information were evaluated
 - Demographic:** age, reason for implant, breast cancer gene (BRCA) mutation, plane of implant insertion, presence of tissue expander, associated breast cancer therapy, history of implant exchange, history of previous implant, and history of implant rupture.
 - Diagnostic:** laterality of disease, years having any implant, years having affected implant, implant fill, texture of implant, implant surface material, implant texture type, time with implant until ALCL diagnosis, duration of symptoms preceding ALCL diagnosis, clinical presentation, lymphadenopathy at presentation, and imaging performed at diagnosis with associated findings.
 - Treatment:** surgical treatment of the affected breast, the contralateral breast, and adjuvant treatments.
 - Follow-up:** duration of follow-up, incidence and rate of recurrence, overall survival years and percentage, proportion of patients continuing to follow-up, and methods of monitoring. Overall and progression-free survival were illustrated using a Kaplan-Meier curve.

Results

Demographics	N	%
Age at Diagnosis (Years)		
Mean	57.9	
Median	57.0	
Standard Deviation	10.3	
Range	35.2-77.3	
Reason for Current Implant		
Cosmetic (n, %)	2	11%
Cancer (n, %)	16	89%
in situ/DCIS	6	38%
Stage 1	4	25%
Stage 2	5	31%
Stage 3	1	6%
Stage 4	0	0%
Stage NA	0	0%
BRCA mutation		
Available (n, %)	9/16	56%
BRCA2	3/9	33%
BRCA1	1/9	11%
Plane of Implant:		
Subglandular	0	0%
Submuscular	17	94%
NA	1	6%
Tissue Expander:		
Yes	16	89%
No	2	11%
Time With Tissue Expander (years):		
Mean	0.45	
Range	0.29-1.00	
Breast Cancer Therapy (x/16 patients)		
Surgery		
Radical Mastectomy	1	6%
Mastectomy	15	94%
Neoadjuvant Chemotherapy	1	6%
Adjuvant Chemotherapy	11	69%
Radiation	3	19%
Breast Implant Exchange After Initial Reconstruction:		
Yes	4	25%
No	12	75%
History of Previous Implant:		
Yes	5	28%
No	13	72%
Reason		
Cosmetic	1	20%
Reconstruct ive	4	80%
History of Implant Rupture		
Yes	2	11%
No	16	89%
Unknown	0	0%

Table 1: Patient Demographics
18 women had their primary surgical treatment of BIA-ALCL by our surgery division, were analyzed in our central pathology, and treated and/or expectantly monitored in our T-cell lymphoma clinic.

Diagnosis	N
Side	
Right	8
Left	10
Bilateral	0
Implant Fill Material	
Silicone	9
Saline	9
Texture of Implant	
Smooth	0
Textured	17
Unknown	1
Implant Surface Material	
Silicone	18
Polyurethane	0
Implant Type	
Biocell	17
Siltext	0
Sientra	0
Smooth	0
Unknown (textured)	1
Time With Implant Until ALCL Diagnosis (years)	
Mean	12.47
Median	11.32
Standard Deviation	5.98
Range	6.7-32.6
Years Having Affected Implant	
Mean	10.55
Median	10.54
Standard Deviation	3.19
Range	6.28-19.9
Time From Symptoms to ALCL Diagnosis (months)	
Mean	5.28
Median	1.32
Range	0.12-19.2
Standard Deviation	7.8
Clinical Presentation	
Effusion	Yes 14
	No 4
Mass	Yes 4
	No 14
Tumor Size (cm)	Mean 3.03
	STDEV 0.90

Table 2: Diagnostic Data of Women Presenting and Treated for BIA-ALCL at MSKCC
Patients were diagnosed with BIA-ALCL after being symptomatic for an average of 5.28 months and a mean of 12.47 years following initial implantation. 14/18 patients presented with effusion and 4/18 patients had a mass. 83% of patients presented with disease confined to the capsule (Stage 1). One patient had unclassifiable disease localized to an internal mammary lymph node with no capsular involvement. Imaging employed for diagnosis included ultrasound (83%), MRI (39%), and PET/CT before surgery (83%).

Treatment	N	% of Total
Surgical Treatment At Initial Presentation		
Capsulectomy	17	94%
Mastectomy	0	0%
Lymph Node Dissection	1	6%
None	0	0%
Removal of Contralateral Implant		
Yes	15	83%
No	0	0%
NA (uni recon)	3	17%
Adjuvant Treatment		
Radiation Therapy Alone	1/18	6%
Chemo+XRT	1/18	6%

Table 3: BIA-ALCL Treatment
All patients with disease confined to capsule were treated with *en bloc* capsulectomy. A single patient with extra-capsular internal mammary nodal ALCL was treated with VATS lymphadenectomy. One patient had lymph node dissection for stage 3 (T4, N0, M0) disease and received chemo and radiotherapy. A second patient received radiotherapy for disease that was initially presumed to be B-cell lymphoma but was later identified to be BIA-ALCL.

Diagnosis (cont)	N	%
Patients Presenting With Symptoms		
Yes	17/18	94%
Other Presenting Symptoms		
Rash	3/18	17%
Pain	4/18	22%
Swelling/Asymmetry	17/18	94%
Capsule Contracture	6/18	33%
Lymphadenopathy (axillary or mammary internal)		
Yes	3/18	17%
*Stage of Disease at Presentation		
1a	8/18	44%
1b	7/18	39%
2	1/18	6%
3	1/18	6%
4	0/18	0%
Unclassifiable (disease localized in single PET+ internal mammary LN, no seroma/capsule involvement)	1/18	6%
Imaging at Presentation		
Imaging Performed		
Breast US	15/18	83%
Breast MRI	7/18	39%
PET/CT (pre-surgery)	15/18	83%
Ultrasound Findings		
Peri-Prosthetic Fluid	12/15	80%
Capsular Nodules	1/15	6%
Mass	4/15	26%
Lymphadenopathy	2/15	13%
MRI Findings		
Peri-Prosthetic Fluid	4/7	57%
Thickened Capsule	3/7	43%
Capsular Nodules	1/7	14%
Mass	4/7	57%
Lymphadenopathy	2/7	28%
PET Findings		
All FDG-avid	9/15	60%
Mild uptake in fluid, uptake in LN	1/9	11%
Mild FDG avid mass	2/9	22%
Mild uptake only in one LN	1/9	11%
Mild uptake at periphery of fluid collection	5/9	56%

Follow-Up/Outcome	N	%
Follow Up Years		
Mean	3.14	
Median	2.91	
Standard Deviation	2.49	
Range	0.08-10.5	
Recurrence		
Yes	0	0%
No	18	100%
Overall Survival Years		
No Mass		
Median	1.47	
Mean	2.17	
With Mass		
Median	1.81	
Mean	2.27	
Total		
Median	1.59	
Mean	2.19	
Survival (%)		
With Mass		
3 year	2/2	100%
5 year	1/1	100%
Without Mass		
3 year	5/6	83%
5 year	4/5	80%
Total		
3 year	7/8	88%
5 year	5/6	83%
Proportion of Patients Continuing to Follow Up (%)		
	15/18	83%
Method of Monitoring		
Total:		
Clinical Exam	18	100%
PET-CT	16	89%
MRI	4	22%
U/S	2	11%
With Mass:		
Clinical Exam	4	100%
PET-CT	3	75%
MRI	1	25%
U/S	1	25%
Mortality		
*Only one patient is deceased: died of metastatic breast cancer		

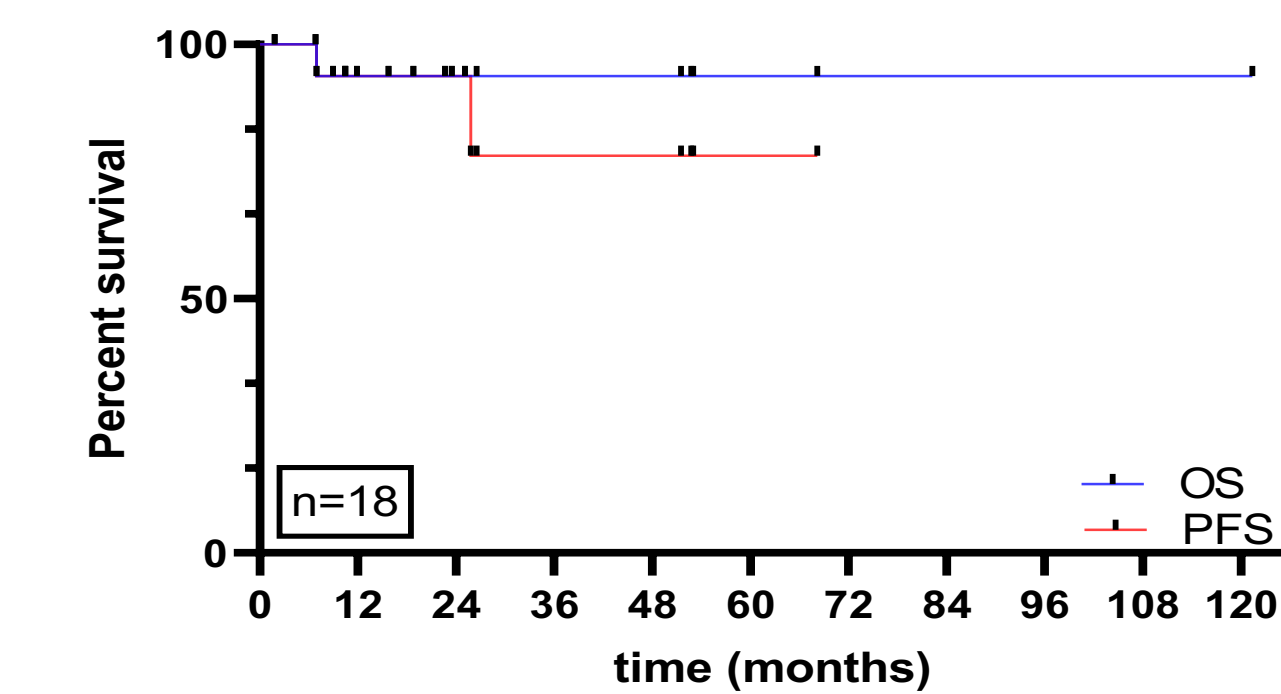


Table 4: Follow-up/Survival Data of BIA-ALCL Patients
Mean follow-up in our cohort was 3.14 years (median 2.91 years). No patients in our population had recurrent disease and the 5-year survival rate was 83%, with the lone patient succumbing to metastatic breast cancer. All patients were monitored by clinical exam, with 89% also receiving PET/CT.

Strengths/Limitations

- Strengths:
 - Complete Data:
 - All patients were diagnosed and treated entirely at a single institution with continued follow-up
 - All patients had complete demographic and implant data
 - Long follow-up time to provide stronger information about disease-free survival
 - 3.14 years of mean follow-up (median=2.91 years) exceeds NCCN recommended follow-up interval
- Weaknesses:
 - Cosmetic augmentation patients under-represented in the study population
 - Subglandular/prepectoral population under-represented in the study population

Conclusions

Our data on this cohort of patients with BIA-ALCL surgically treated and followed at a single institution confirm the importance and efficacy of *en bloc* capsulectomy in patients presenting with confirmed ALCL. The complete follow-up data described here reinforces the high rates of progression-free and overall survival when diagnosis is identified early and treatment provided to those with limited stage disease.

Key References

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