

Disclosure

- No conflict of interest to disclose

Case history

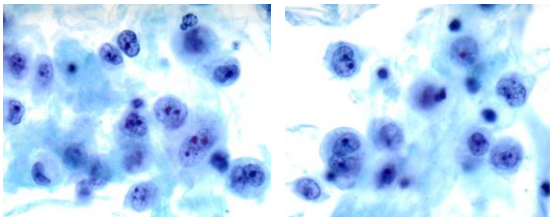
- The patient is a 37 year old female with stage IIA invasive ductal carcinoma of the left breast diagnosed in July 2013.
- After lumpectomy and adjuvant chemotherapy, she underwent bilateral mastectomy and breast reconstruction surgery in February 2014.
- In April 2020, she presented with right breast swelling, and a fine needle aspiration was performed to rule out recurrent disease.

Whole slide digital image - #10

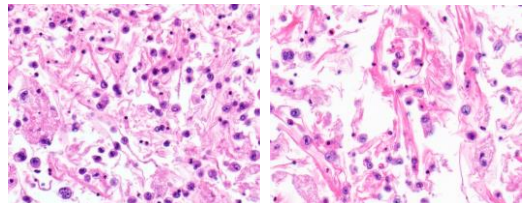
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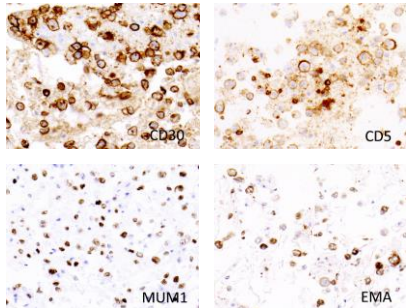
Cytomorphology (PAP stain)



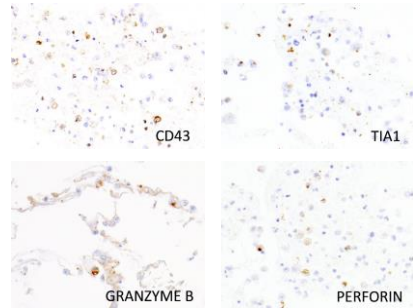
Histomorphology (H&E cell block)



Immunohistochemistry (cell block)



Immunohistochemistry (cell block)



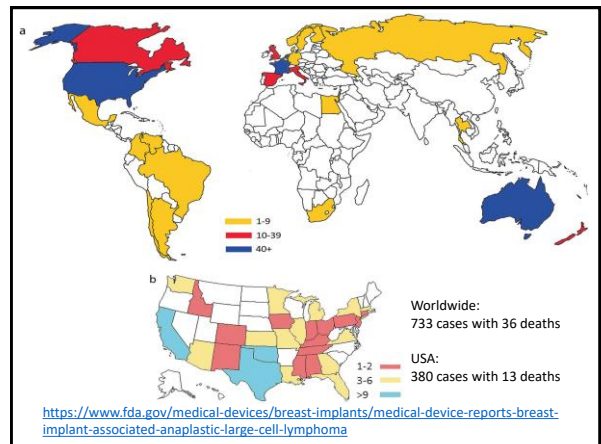
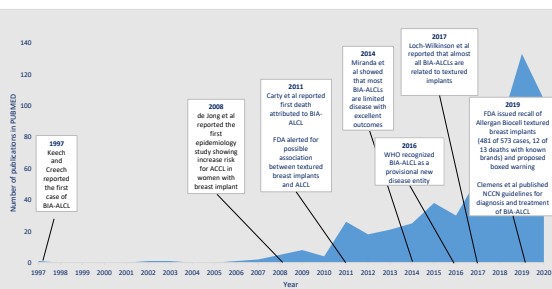
Immunohistochemistry (summary)

- Positive
 - CD30 (strong)
 - MUM1 (strong)
 - CD5 (large subset)
 - EMA (large subset)
 - CD43 (small subset)
 - TIA1 (focal)
 - Perforin (focal)
 - Granzyme B (focal)
- Negative
 - CD2
 - CD3
 - CD4
 - CD7
 - CD8
 - CD20
 - PAX5
 - ALK1
 - CD68
 - Pankeratin
 - HMB45

Diagnosis

- CD30-positive hematolymphoid malignancy consistent with breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)

Milestones on BIA-ALCL



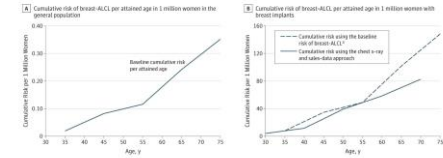
Incidence of BIA-ALCL

Study	Years	#BI-ALCL	Incidence Rate
de Boer et al.	1990-2016	32	8.9 (6.1-12.6)
Wang	1995-2012	2	45.1 (5.6-162)
Largent	1996-2007	3	14.6 (3.0-42.7)
Doren	1996-2015	100	2.0 (1.7-2.5)
Loch-Wilkinson	2017	38	28.2 (20.0-38.8)
Prantl	2002-2018	0	0.0 (0-7.31)
Summary		175	3.2 (2.7-3.7)

Retrospective case-control studies from the Netherlands (de Boer), USA (Largent, Wang and Doren), Australia/New Zealand (Loch-Wilkinson) and Germany (Prantl)

Implant and risk of BIA-ALCL

Figure. Cumulative Risk of Breast ALCL per Attained Age in 1 Million Women in the General Population and With Breast Implants

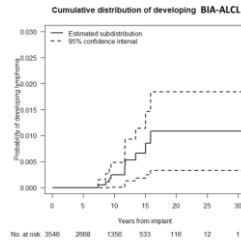


ALCL indicates anaplastic large-cell lymphoma. Cumulative risk of breast ALCL in the general female population was calculated using the number of breast ALCL cases without breast implants from the Nationwide Network and Registry of Histology and Cytopathology in the Netherlands, and the age-specific size of the female Dutch population from 1990 to 2016 per age category.¹¹ Cumulative risk of breast ALCL associated with breast implants was calculated using the number of breast ALCL cases with breast implants and the cumulative

Retrospective case control study from the Netherlands: OR, 421.8 (95% CI, 52.6-3385.2)

De Boer et al, JAMA Oncology (2018)

Implant and risk of BIA-ALCL



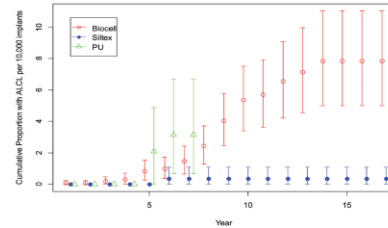
Prospective study from MSK:

- 3546 patients received textured breast implantation
- 10 developed BIA-ALCL
- Medium follow-up 8.1 years
- Overall risk 1/355 women or 0.311 cases per 1000 person-years (95% CI: 0.118-0.503)

Years since textured device insertion	Cumulative risk of developing BIA-ALCL
5	0.000
10	0.0024
15	0.0055
20	0.0109

Cordeiro PG et al, J Plastic Reconstr Aesthetic Surg (2020)

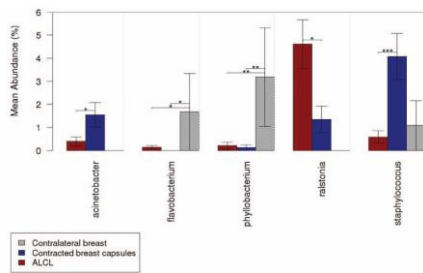
Implant and risk of BIA-ALCL



Implant	Surface Area (mm ²) ^a
Polyurethane (Siluxed)	146.7
Bio-cell	27.9
Silux	12.4
Smooth (Mentor)	1.0

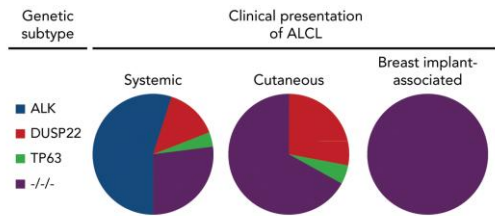
Loch-Wilkinson A et al, Plast Reconstr Surg (2017) and Aesthetic Surg J (2020)

Microbiome and BIA-ALCL



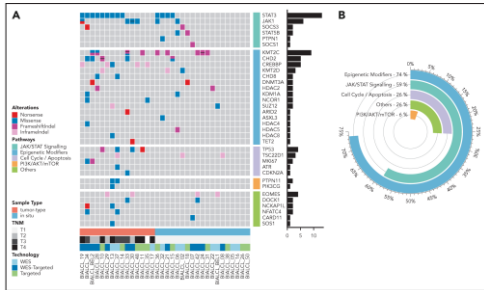
Hu H et al, Plast Reconstr Surg (2015)

Genetics of BIA-ALCL



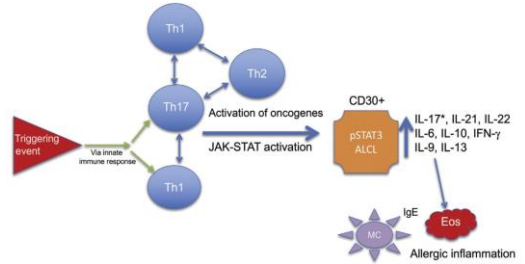
Oishi N et al, Blood (2018)

Genomics of BIA-ALCL



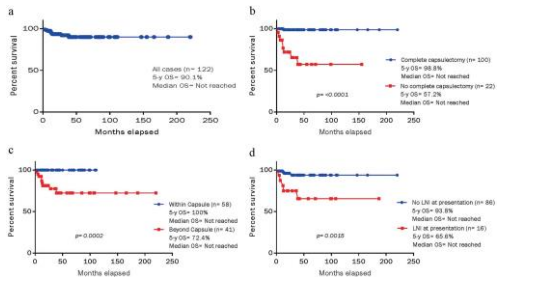
Laurent C et al, Blood (2020)

Pathogenesis of BIA-ALCL



Tumer SD et al, Am J Pathol (2020)

Prognosis of BIA-ALCL

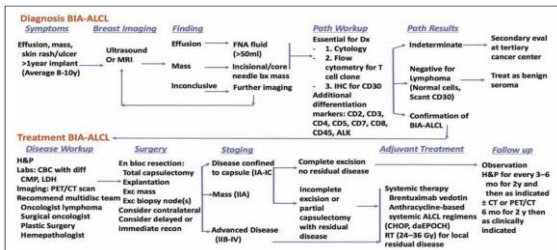


Quesada AE et al, Mod Pathol (2019)

Clinicopathological features

- Mean age at diagnosis – about 50 years
- Interval from implantation to diagnosis varies from 2.2-44 years with a mean of 9 years.
- More frequently associated with textured than smooth shell surface implant
- Physical findings
 - Swelling, asymmetry or pain, usually unilateral
 - Peri-implant effusion or seroma most common (80%)
 - Mass lesion(s) around the implant (10-20%)
 - Loco-regional or systemic lymphadenopathy (rare)
- Genetic and epigenetic driver genes mutations
- Excellent prognosis with appropriate management

NCCN guidelines of BIA-ALCL diagnosis and management

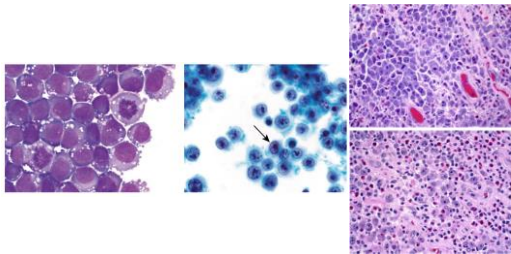


Clemens MW et al, Aesthetic Surgery J (2019)

Pathology workup

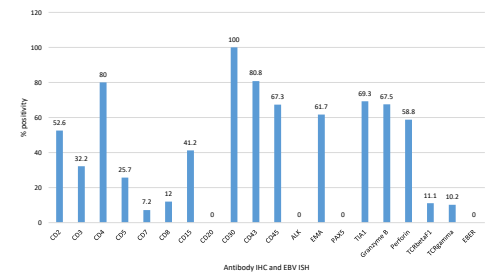
- **Diagnosis**
 - Fine needle aspiration of fluid/effusion
 - Cytomorphology
 - Smear – Papanicolaou and Wright-Giemsa stains
 - Cell block
 - H&E sections
 - Immunohistochemistry
 - Flow cytometry
 - T-cell receptor gene PCR
 - Incisional/needle core biopsy of mass
 - Histomorphology
 - H&E sections
 - Immunohistochemistry
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- **Staging**
 - En bloc resection/total capsulectomy with explantation
 - Excision of extracapsular mass
 - Excision of lymph nodes

Diagnosis - cyto/histomorphology



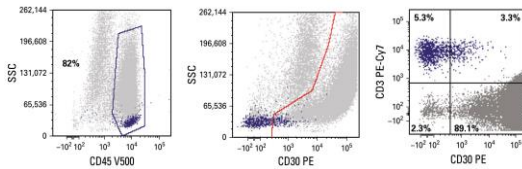
Jaffe ES et al, J Clin Oncol (2020)
Tumer SD et al, Am J Pathol (2020)

Diagnosis - immunohistochemistry



Adapted from Quesada AE et al, Mod Pathol (2019)

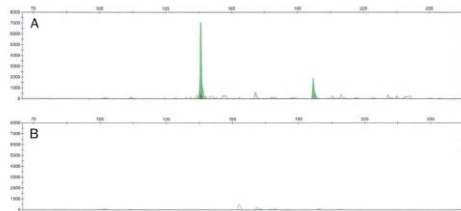
Diagnosis - flow cytometry



Very low success rate due to cell size and low viability. A negative flow does not exclude BIA-ALCL.

Jaffe ES et al, J Clin Oncol (2020)

Diagnosis - T-cell receptor gene PCR



TCRgamma: 26/34 (76.5%)
TCRbeta: 5/12 (41.7%)

Lee A et al, IJCEP (2010); Quesada AE et al, Mod Pathol (2019)

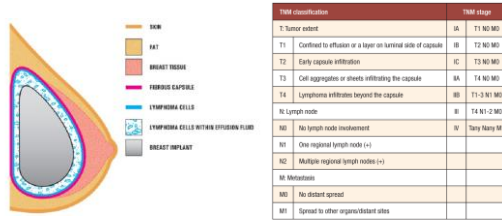
Differential diagnosis

- Hematolymphoid malignancies
 - Systemic ALCL - ALK-positive and ALK-negative
 - Primary cutaneous ALCL
 - Extranodal NK/T cell lymphoma
 - Plasmablastic lymphoma
 - (Extracavitary) Primary effusion lymphoma
 - Diffuse large B-cell lymphoma
- Non-hematolymphoid malignancies
 - Metastatic carcinoma
 - Metastatic melanoma
 - Sarcoma

Pathology workup

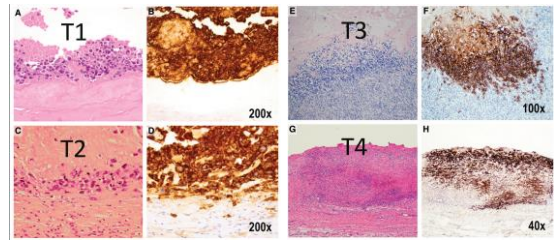
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Staging of BIA-ALCL



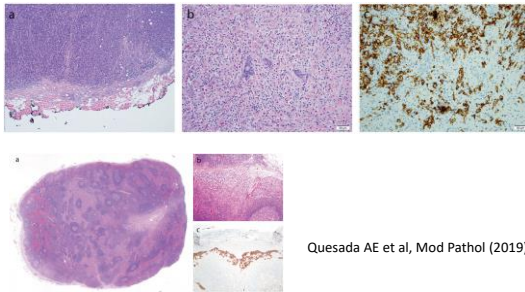
Mehta-Shah N et al, Blood (2018)

Staging of BIA-ALCL



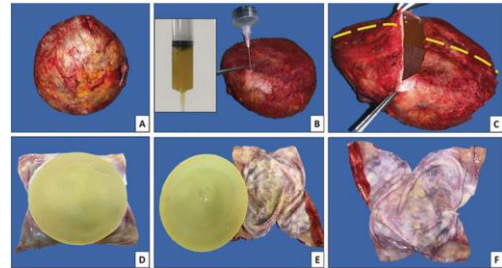
Jaffe ES et al, J Clin Oncol (2020)

Staging of BIA-ALCL



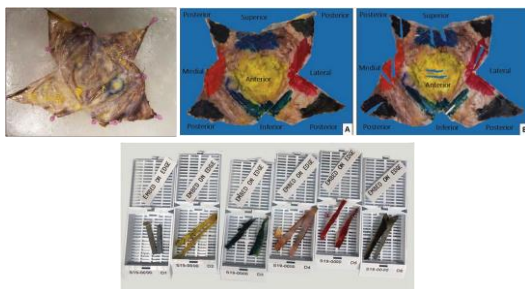
Quesada AE et al, Mod Pathol (2019)

Pathologic processing of total capsulectomy specimen



Lyapichev KA et al, Mod Pathol (2020)

Pathologic processing of total capsulectomy specimen



Lyapichev KA et al, Mod Pathol (2020)

Patient follow-up

- Bilateral capsulectomy with implant removal (no residual lymphoma, stage 1A) and re-construction in May 2020.
- PET from skull to abdomen shows s/p bilateral mastectomy with breast implants in place and low level homogenous activity around the implants
- No evidence of disease recurrence at her last clinic visit on July 17, 2020.




Other seroma-associated ALCL

- Tibial implant-associated ALCL
- Dental implant-associated ALCL/MCU
- Chest port-associated ALCL
- Bariatric implant-associated ALCL
- Gluteal implant-associated ALCL

Palraj B et al, J Foot Ankle Surg (2010); Yoon HJ et al, USP (2015); Engberg A et al, J Clin Oncol (2013); Kellogg B et al, Ann Plastic Sur (2013); Umakanthan JM et al, J Oncol Practice (2017); Mendes J et al, Plast Reconstr Surg (2019)

Selective references

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Breast Implant-associated Anaplastic Large Cell Lymphoma

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