Evaluation of Breast Implant-Associated Anaplastic Large Cell Lymphoma with Whole Exome and Genome Sequencing

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Background

- Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a subtype of T-cell lymphoma with much of its pathogenesis poorly understood.
- JAK/STAT pathway mutations[1] and copy number aberrations (CNAs) have been identified in previous studies[2]
- Genetic analysis of BIA-ALCL thus far have not shown re-arrangements in DUSP22 or TP63[3]
- A more discrete characterization is vital to identify those with a germline predisposition to develop BIA-ALCL, and to identify targets for precision anti-BIA-ALCL therapeutics.

Objective

To determine if there are recurrent gene mutations in BIA-ALCL patients in a cohort at a single institution

Materials & Methods

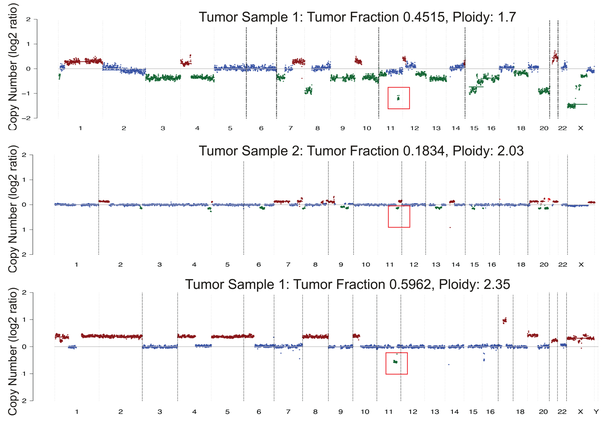
- 10 patients were included that were diagnosed with BIA-ALCL between April 2015 and May 2020
  - Patients were included if they have a biopsy proven diagnosis of BIA-ALCL
- 7 tumor samples were included for whole exome sequencing (WES) from tumors of 6 patients
- Whole genome sequencing (WGS) was performed on 3 BIA-ALCL seroma fluid samples.
- Samples were sequenced on an Illumina NovaSeq 6000. Data was analyzed using the Illumina DRAGEN Bio-IT Platform v3.8 workflow.
- All tissue was collected under an IRB approved lymphoma tissue banking protocol

Results

Table 1

Case number	Diagnosis	Age	Stage (TNM)	Reason for Implant	Time: Last Implant to Diagnosis (months)	Length of follow-up (mo)	Overall survival (D vs. NED)
1	BIA-ALCL	58	IA	Cancer reconstruction	32 (4)	16	NED
2	BIA-ALCL	47	IA	Cosmetic	24 (12)	12	NED
3	BIA-ALCL	55	IB	Cosmetic	35 (24)	15	NED
4	BIA-ALCL	67	3	Cosmetic	96 (32)	9	D
5	BIA-ALCL	66	IA	Contralateral	132 (20)	22	NED
6	BIA-ALCL	45	I	Cosmetic	36 (8)	2	NED
7	BIA-ALCL	56	IA	Cancer reconstruction	96 (8)	61	NED
8	BIA-ALCL	43	IA	Cosmetic	84 (7)	5	NED
9	BIA-ALCL	64	IB	Contralateral reconstruction	12 (6)	6	NED
10	BIA-ALCL	56	IA	Contralateral reconstruction	60 (9)	3	NED

Figure 1



Acknowledgements

This study was funded by the Aesthetic Surgery Education and Research Foundation

Results

Figure 2

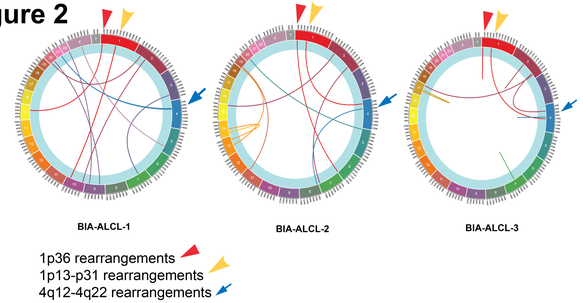


Figure 3

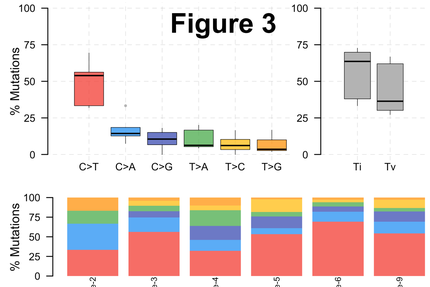


Figure 4

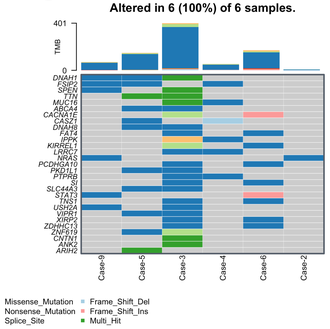
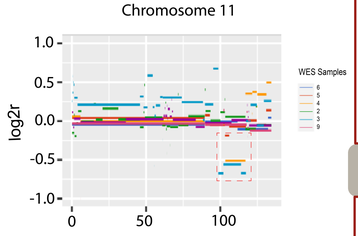


Figure 5



Summary

- WGS showed a critically deleted 7Mb region on chromosome 11 at 11q22.3 region in all 3 samples evaluated (Figure 1)
- WGS showed chromosomal re-arrangements in all 3 cases, notably 1p36, 1p13-p31 and 4q12-4q22 rearrangements (Figure 2)
- WES showed missense mutations in large genes with predominantly C to T transitions. (Figure 3)
- Two WES cases had STAT3 mutations (Figure 4)
- Copy number analysis revealed evidence of 11q22.3 deletion in two cases (figure 5)
- Pathseq GATK pipeline was unable to detect reads mapped to any pathogenic microbial genome

Discussion

- We identified recurrent STAT3 mutations, consistent with prior studies
- 11q22.3 deletions were consistent in WGS cases and present in some exomes, this corresponds to the ATM gene, heterozygous deletions lead to increased tumors in mouse models
- Significant copy number alterations were not seen in this cohort, in contrast to prior studies
- Given the small sample size and rarity of the disease, genomic evaluation of a larger cohort is necessary to confirm these findings

References

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