GATA3 Expression Profile in Invasive Breast Carcinoma Post Neo-Adjuvant Systemic Chemotherapy

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Introduction

- Immunohistochemistry for GATA3, a transcription factor, is a new marker for the diagnosis of breast carcinoma
- Large studies have shown that between 84.5 and 94% of breast carcinomas are positive for GATA3
- GATA3 is also expressed in:
  - Urothelial carcinoma
  - Salivary gland neoplasms
  - Cutaneous tumours: Basal cell carcinoma, squamous cell carcinoma (SCC) and adnexal tumours
  - Others: Non-cutaneous SCC, mesothelioma, and renal chromophobe
- GATA3 has been previously demonstrated to be positive in all metastatic breast carcinomas that have GATA3 positive primaries
- GATA3 expression is positively linked to estrogen receptor (ER) expression.
- ER positive breast carcinoma potentially loses ER expression post neo-adjuvant systemic chemotherapy
- To date, there have been no studies examining how systemic chemotherapy affects expression of GATA3

Materials and Methods

- All cases of post neo-adjuvant breast carcinoma surgically resected at The Ottawa Hospital between June 2010 and September 2013 were reviewed
- 77 cases were identified that had paraffin embedded tissue blocks for both pre-treatment biopsies and post-treatment resections available
- All cases had ER status recorded previously
- Each specimen was reacted with antibodies for GATA3 and reactivity was recorded for pre-treatment and post-treatment specimens
- Each GATA3 immunohistochemistry was reviewed, blinded to ER status, by one senior resident and one staff breast pathologist
- Expression profiles were created for each paired biopsy and resection for GATA3 and ER
- GATA3 expression was graded according to the Allred Score to aid in consistency and reproducibility
  - Each Allred Score was stratified into 0, 1+, 2+ and 3+
    - Scores 0 (1,2), 1+: Allred scores 3-4, 2+: Allred scores 5 and 6, 3+: Allred scores 7 and 8

Results

Post-Chemotherapy Retained ER/GATA3

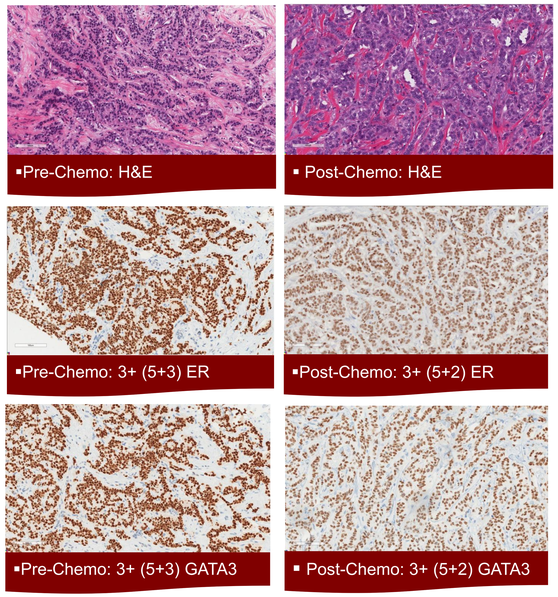

Figure 1: Paired biopsy and post chemotherapy H&E, ER and GATA3 profile demonstrating retention of ER and GATA3 (20x, Allred scoring)

Post-Chemotherapy Loss of ER/GATA3

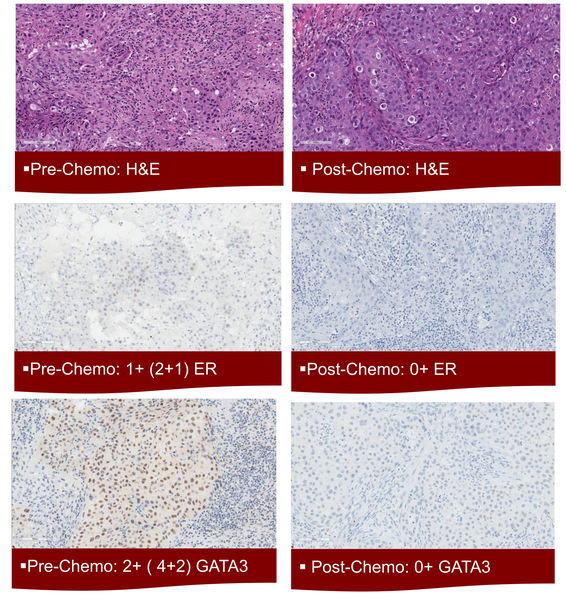

Figure 2: Paired biopsy and post chemotherapy H&E, ER and GATA3 profile demonstrating loss of ER and GATA3 (20x, Allred scoring)

Table 1: Expression profiles of paired cases that demonstrated loss or decreased expression of ER post-chemotherapy.

	Biopsy:		Resection:	
Cases (N=18):	ER	GATA3	ER	GATA3
3	3+	3+	1+	3+/2+
1	3+	3+	0	1+
1	3+	2+	0	2+
1	1+	3+	0	2+
1	1+	2+	0	0
1	1+	1+	0	0
1	0	2+	1+	2+
2	0	3+/2+	0	2+
1	0	3+	0	0
2	0	3+	0	1+
1	0	2+	0	1+
1	0	1+	0	1+
1	0	0	0	2+
1	0	0	0	0

Table 2: Breast carcinomas in this study by histological subtype.

Subtype:	Cases:
Ductal NOS	61
Lobular	8
Pleomorphic Lobular	3
Micropapillary	2
Ductal with lobular features	2
Apocrine	1

Table 3: Overall ER and GATA3 status pre and post chemotherapy.

	Pre-Chemo Positive:	Post-Chemo Positive:
ER	67 (87%)	63 (82%)
GATA3	75 (97%)	73 (95%)

Results

- Expression Status Consistent Pre-and Post Chemotherapy:
  - The majority of cases, 59 cases (77%), were 3+ for ER pre and post chemotherapy with:
    - All cases 3+ for GATA3 on biopsy
    - 49 cases (83%) being 3+ for GATA3 post-chemotherapy
    - 10 cases (17%) being 2+ for GATA3 post-chemotherapy
  - 10 cases (13%) were negative for ER prior to treatment
  - ER expression was decreased in 3 cases (4% of total cases) with moderate (2+) to weak (1+) reactivity
- Expression Status Deviations Post Chemotherapy:
  - ER expression was lost in 5 cases (6.5% of total cases)
  - GATA3 expression was lost (0+) 2 cases (40% of ER loss cases)
  - GATA3 expression was weak (1+) in 1 case (20% of ER loss cases)
  - Of ER negative breast carcinomas (10) that had moderate to strong (2+/3+) reactivity for GATA3 pre-chemotherapy:
    - 1 case (10%) lost GATA3 reactivity
    - 2 cases (10%) had weak GATA3 (1+) staining
- Histological subtypes:
  - Weak staining for GATA3 was noted for the single case of apocrine carcinoma, no other associations were noted

Conclusions

The IHC profile for GATA3 and ER in tumour bed status post chemotherapy is as follows:

- The majority of cases will retain GATA3 reactivity
- GATA3 reactivity is potentially weak or absent in ER negative breast carcinomas
- Histological subtype does not appear to affect GATA3 expression
- GATA3 is useful for identifying breast carcinoma metastases post-chemotherapy, but should be used with caution with ER negative carcinomas

References

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