Assessment of Outcomes in Rare Subtype of Breast Cancer: Metaplastic Breast Cancer and Novel Immune Markers

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Introduction

- Metaplastic breast cancer (MBC) is a very rare type of invasive breast cancer (TNBC) that accounts for <1-5% of all breast cancers.
- The majority of MBC are triple negative cancers; however the prognosis of MBC is generally worse than other triple negative breast cancers on average[1].
- We aimed to compare disease free and overall survival between patients with MBC and those with non-metaplastic TNBC at OSUCCC - James.
- In addition, we assessed expression of immune markers in the primary tumor and correlated with clinical outcomes.

Methods

- We retrospectively reviewed the clinical charts of 382 patients seen at OSUCCC – James between January 1, 1994 and December 31, 2014.
- Patients with MBC (n=44) were matched, using a 1 to 3 ratio, with non-metaplastic TNBC controls (n=130) by stage and age at diagnosis.
- Demographics and treatments were compared between MBC and TNBC controls, and multivariate analysis was performed to assess disease free survival (DFS) and overall survival (OS) outcomes between groups.
- Observation time was defined as the time from diagnosis to death or censoring.
- Samples from a small cohort of TNBC patients (n=119) and MBC patients (n=27) were used to assess immune marker staining.

Results

- Median observation time was 2.8 years with only 8 patients followed for more than ten years.
- Taxane therapies were used less frequently for the treatment of MBC compared to TNBC patients (70.5% vs 85.4%, p=0.0411).
- Rates of disease free (p=0.35) and overall survival (p=0.32) were similar between MBC and TNBC patients.
- Risk of disease recurrence (HR=1.64, 95% CI=0.75-3.58, p=0.22) and death (HR=1.64, 95% CI=0.69-3.90, p=0.26) were also similar between MBC and TNBC patients
- Fewer MBC samples were positive for CD8 in tumor cells than TNBC samples (18.5% vs. 44.5%, p=0.0158).
- More MBC samples were positive for CD163 in stroma cells (96.3% vs. 79.8%, p=0.0468) and PD-L1 in tumor cells (29.6% vs. 10.1%, p=0.0133) than the TNBC samples.

Table 1: Demographics Characteristics

Variable	Level	Triple negative n=130	Metaplastic n=44	Total	P-value
Age at diagnosis	Mean (SD)	54.6 (12.8)	55.4 (13.9)	54.8 (13.0) [n=174]	0.7495
Weight at diagnosis	Mean (SD)	170.3 (38.8)	166.8 (31.3)	169.4 (37.0) [n=171]	0.5977
Race	White	108 (83.1%)	40 (90.9%)	148 (85.1%)	0.2451
	Black	14 (10.8%)	4 (9.1%)	18 (10.3%)	
	Other	8 (6.2%)	0 (0.0%)	8 (4.6%)	
Hispanic ethnicity	Yes	3 (2.3%)	0 (0.0%)	3 (1.8%)	1.0000
Positive nodes	Yes	60 (46.2%)	13 (29.5%)	73 (42.0%)	0.0765
Stage at diagnosis	1	16 (12.3%)	6 (13.6%)	22 (12.6%)	0.9812
	2	96 (73.8%)	32 (72.7%)	128 (73.6%)	
	3	15 (11.5%)	5 (11.4%)	20 (11.5%)	
	4	3 (2.3%)	1 (2.3%)	4 (2.3%)	
Surgery and radiation	None	4 (3.1%)	1 (2.3%)	5 (2.9%)	0.8203
	Comp Mast only	33 (25.4%)	15 (34.1%)	48 (27.6%)	
	Lump only	2 (1.5%)	1 (2.3%)	3 (1.7%)	
	RT only	2 (1.5%)	0 (0.0%)	2 (1.1%)	
	Comp Mast + RT	37 (28.5%)	13 (29.5%)	50 (28.7%)	
	Lump + RT	52 (40.0%)	14 (31.8%)	66 (37.9%)	
Radiation	Yes	91 (70.0%)	27 (61.4%)	118 (67.8%)	0.3509
Breast conserving surgery	Yes	54 (41.5%)	15 (34.1%)	69 (39.7%)	0.4763

Table 2: Chemotherapy Characteristics

Variable	Triple negative n=130	Metaplastic n=44	Total	P-value
Chemotherapy first year following diagnosis	119 (91.5%)	38 (86.4%)	157 (90.2%)	0.3782
Doxorubicin + Cyclo	101 (77.7%)	31 (70.5%)	132 (75.9%)	0.4149
Docetaxel + Cyclo	9 (6.9%)	2 (4.5%)	11 (6.3%)	0.7322
Paclitaxel + Carbo	15 (11.5%)	6 (13.6%)	21 (12.1%)	0.7895
Paclitaxel	80 (61.5%)	21 (47.7%)	101 (58.0%)	0.1157
Anthracycline therapy	104 (80.0%)	34 (77.3%)	138 (79.3%)	0.6731
Platinum therapy	17 (13.1%)	6 (13.6%)	23 (13.2%)	1.0000
Taxane therapy	111 (85.4%)	31 (70.5%)	142 (81.6%)	0.0411

Table 3: Immune Markers

Outcome	TNBC (n=119)	MBC (n=27)	Total	P-value
Age at diagnosis: Mean (SD)	51.9 (11.8)	57.8 (15.3)	53.0 (12.7)	0.0281
CD8+ in stroma ≥ 10	94 (79.0%)	21 (77.8%)	115 (78.8%)	1.0000
CD8+ in tumor ≥ 10	53 (44.5%)	5 (18.5%)	58 (39.7%)	0.0158
CD163+ in tumor ≥ 10	55 (46.2%)	13 (48.1%)	68 (46.6%)	1.0000
CD163+ in stroma ≥ 10	95 (79.8%)	26 (96.3%)	121 (82.9%)	0.0468
PD-L1 tumor ≥ 1	12 (10.1%)	8 (29.6%)	20 (13.7%)	0.0133
PD-L1 stroma ≥ 1	87 (73.1%)	16 (59.3%)	103 (70.5%)	0.1665
PD-L1 overall ≥ 1	87 (73.1%)	15 (55.6%)	102 (69.9%)	0.1025

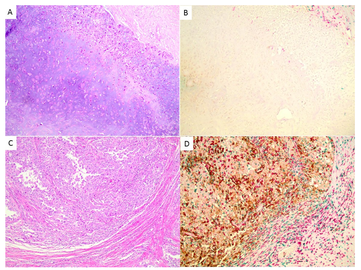

Figure 1: Immune reaction and PD-L1 expressions in two invasive metaplastic breast carcinomas. A, B) No PD-L1 expression, scattered CD163+ cells, and rare CD8+ cytotoxic T-cells in the stroma. C,D) Strong PD-L1 expression in tumor and stromal cells, diffuse CD163+ cells and CD8+ cytotoxic T-cells in stroma. 100x.

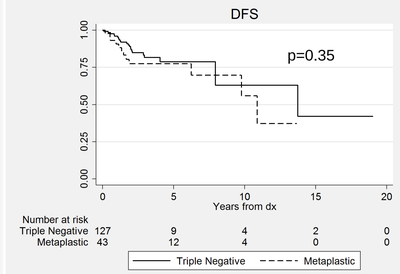

Figure 2: Kaplan-Meier curves for DFS

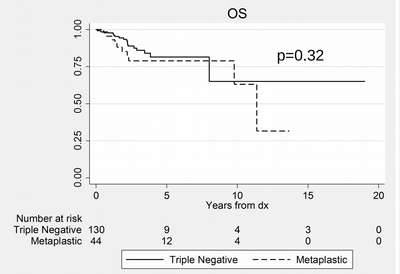

Figure 3: Kaplan-Meier curves for OS

Table 4: Multivariate Cox Model DFS

Variable	HR (95% CI)	P-value
Age at diagnosis	1.01 (0.98, 1.04)	0.6608
Chemotherapy first year following diagnosis	0.42 (0.11, 1.65)	0.2129
Metaplastic diagnosis	1.64 (0.75, 3.58)	0.2159
Positive nodes	4.32 (1.66, 11.29)	0.0028
Radiotherapy given	0.58 (0.23, 1.50)	0.2643
Stage at dx 1	0.33 (0.06, 1.83)	0.0287
Stage at dx 2	0.32 (0.14, 0.74)	
Stage at dx 3	Ref	

Table 5: Multivariate Cox Model OS

Variable	HR (95% CI)	P-value
Age at diagnosis	1.03 (0.99, 1.07)	0.1252
Chemotherapy first year following diagnosis	0.71 (0.16, 3.21)	0.6552
Metaplastic diagnosis	1.64 (0.69, 3.90)	0.2597
Positive nodes	2.62 (0.88, 7.82)	0.0844
Radiotherapy given	0.55 (0.20, 1.49)	0.2384
Stage at dx 1	0.06 (0.01, 0.54)	0.0021
Stage at dx 2	0.24 (0.06, 0.93)	0.0021
Stage at dx 3	0.07 (0.02, 0.28)	0.0021

Discussion

- Contrary to previous publications[2], our data suggests that patients with MBC had similar outcomes to TNBC based on disease free and overall survival.
- Use of taxane and anthracyclines based therapy was more common among our patients with MBC (70.5% and 77.3%) in comparison to other studies[3,4].
- Lower CD8, higher CD163, and higher PD-L1 staining in our MBC samples is comparable to data from previous publications using samples associated with worse prognosis[5,6].
- Future studies are needed to confirm the prognostic role of tumor PD-L1, stromal CD163, and tumor CD8 in MBC, and further research is needed to see if these are potential therapeutic targets.
- Metaplastic breast cancer is a rare disease with a small patient population, so a prospective study will be difficult.
- Our retrospective study gives some hope for patients with MBC, showing that their outcomes can be as good as those with TNBC when treated with appropriate adjuvant therapies.

References

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