

Primary Squamous Cell Carcinomas of the Breast: A Report of six Cases and review of literature

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Abstract

Primary squamous cell carcinoma of the breast (SCCB) is a rare and aggressive breast malignancy; its management is still not well established.

This was a retrospective study of patients diagnosed and treated at our hospital for a primary squamous cell carcinoma of the Breast from January 2014 to January 2019.

We identified 6 patients with SCCB during this period. The median age at presentation was 52.3 years. 4 patients were negative for hormone receptors as well as human epidermal growth factor receptor-2 (HER-2), they underwent a modified radical mastectomy while the two others had a breast conserving surgery, all patients received adjuvant chemotherapy, 4 patients received radiation therapy and endocrine therapy was prescribed for 2 patients. One patient succumbed to disease progression 3 months after the diagnosis, another patient was lost to follow-up after the radiotherapy and none of the 4 other patients experienced disease recurrence.

SCCB is a rare subtype of breast cancer, often treatment-refractory. Therefore, an innovative therapy needs to be explored to improve therapeutic approach and patient outcome.

Key words: Primary squamous cell carcinoma of the breast, aggressive breast cancer .

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I. INTRODUCTION

Primary squamous cell carcinoma of the breast (SCCB) is a very rare entity. It represents less than 0.1 % of all breast carcinomas (1). The World Health Organization Classification of tumors (2012) includes the squamous cell carcinoma as a subtype of metaplastic breast cancer. Most of SCCB are negative for hormone receptor and human epidermal growth factor receptor-2 (HER-2), the treatment does not differ from other histological types of breast cancer, however, this subtype has often been considered to be more aggressive with a poorer prognosis but this finding remains controversial with recent data reporting a similar prognosis to poorly differentiated adenocarcinoma of breast. We report here 6 cases of this rare breast malignancy.

II. METHODS:

We conducted a retrospective study of patients treated at our hospital for a primary squamous cell carcinoma of the Breast from January 2014 to January 2019.

Only SCCB with following criteria were included:

- Predominance of areas with SCC at histologic examination
- Absence of skin involvement
- Absence of an associated primary SCC in a second site

6 patients with SCCB were identified among 4254 breast cancer patients treated at our hospital during this period. All clinical, histological, radiological and therapeutic data were collected.

III. RESULTS

1- Clinical and pathological characteristics

The median age was 52.3 years (range 42-73), four patients of six were premenopausal at the time of diagnosis.

All of SCCB cases were first diagnosed with palpable breast masses, the interval between symptom onset and the first medical consultation was 4 months (range 1-7 months).

Primary Squamous Cell Carcinomas of the Breast: A Report of six Cases and review of literature

Concerning the histopathological part, the average size of breast tumors was 3.8cm, the scarf-Bloom-Richardson (SBR) grading was between II and III (respectively 66% and 34%), lymphovascular invasion was present in 2 patients and 4 patients had axillary lymph node metastasis.

4 patients had a negative immunohistochemistry (IHC) for estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER2), one patient was hormone receptors (HR) and HER2 positive, the other one was HR positive and HER 2 negative

The clinical and pathological characteristics have been shown in Table 1

Patient No	1	2	3	4	5	6
AGE(years)	47	60	73	43	49	42
MENOPAUSE	NO	YES	YES	NO	NO	NO
SIZE(cm)	7	3	5	3.5	2.3	2.5
LNM	3N+/11N	10N-/10N	2N+/10N	4N-/4N	1N+/10N	2N+/8N
LVI	YES	NO	YES	NO	NO	NO
SBR	II	III	II	II	II	III
STAGE	IIIA	IIA	IIIA	IIA	IIB	IIB
HR/HER	TNBC	TBNC	TBNC	TNBC	RH+/HER-	RH+/HER2+

LNM : Lymph node metastasis, **LVI**: lymphovascular invasion, **SBR**: scarf-Bloom-Richardson **HR**: hormone receptors, **HER2**: human epidermal growth factor receptor-2, **TNBC**: triple negative breast cancer

2- Treatment

4 patients underwent a modified radical mastectomy while the two others had a breast conserving surgery , all patients received Anthracycline and Taxane-Based adjuvant chemotherapy , local radiation therapy was given in 4 of the 6 patients since one patient refused it and the other one presented lung and liver metastases during the adjuvant chemotherapy, she died 3 months later.

One patient was lost to follow-up after the radiotherapy, none of the 4 other patients experienced disease recurrence.

The table 2 summarizes all treatment outcomes :

	1	2	3	4	5	6
SURGERY	MRM	MRM	MRM	MRM	BCS	BCS
CT	YES	YES	YES	YES	YES	YES
RT	NO **	YES	NO	YES	YES	YES
ET	NO	NO	NO	NO	YES	YES
RECURRENCE	NO	NO	YES	-	NO	NO
DISEASE-FREE INTERVAL	Disease-free at 48 months	Disease-free at 26 months	2 months	-	Disease-free at 60 months	Disease-free at 43 months
DEATH	NO	NO	YES	-	NO	NO

MRM: modified radical mastectomy, **BCS**: Breast conserving surgery,

CT: chemotherapy, **RT** radiotherapy **ET** endocrine therapy,

** refused by the patient

IV. DISCUSSION

Pure primary squamous cell carcinoma of the breast (SCCB) is a rare malignancy representing around 0.1% of breast carcinomas (1) it was first described by Troell in 1908 (3). The etiology and pathogenesis of this breast cancer subtype are not well understood.

Yadav et al confirmed in the largest series of SCCB reported to date with 445 patients, that it is a rare and aggressive tumor with a cumulative incidence of 0.62 cases per 1,000,000 per year (4). The incidence tends to be higher in Blacks compared to Whites or other races (4).

SCCB is a special type of cancer accompanied by squamous metaplasia with keratinization and/or intercellular bridges. Pure SCCB is defined as a lesion in which more than 90% of the tumor is comprised of squamous carcinoma or its variant without glandular features, and it must be independent of the overlying skin or nipple without any other primary epidermoid tumors present in the other sites (oral cavity bronchus, esophagus, renal pelvis, bladder, ovary, and cervix) (5)

Salient features of five large series have been described in Table 3.

The median age at presentation of SCCB was reported to be 54 years in old studies (6-7), but recently, larger studies have indicated a median age of 65 years with a clear predominance in postmenopausal patients.

Imaging features are unspecific and similar to those used in invasive ductal carcinoma, the most consistent feature of SCCB on mammogram is the lack of microcalcifications (8) .

Most studies on SCC of the breast reported less frequent involvement of axillary lymph nodes than invasive ductal carcinoma (IDC) (7,9) and similar to prior series, the majority of our patients were ER, PR and HER 2 negative, indeed, over 90% of SCCB are estrogen and progesterone receptor negative, and cases of Her2/neu positive SCCB are few (10-11) which is generally expected as most SCC of the breast has the basal-like molecular subtype (12-13). A high frequency of EGFR positivity in SCCB was also reported by Hennessy et al (7).

Due to its rarity, the management of SCCB is still unclear and usually meets that of invasive ductal carcinoma; many studies suggest that mastectomy would be the best option to offer to these patients given the locally advanced and aggressive nature of the tumor (2,7, 14-17).

Additionally, it is possible to perform sentinel lymph node resection to address any involvement of the axillary lymph nodes (14).

Regarding the adjuvant treatment, chemotherapeutic agents commonly used in invasive ductal carcinoma (cyclophosphamide, methotrexate, 5-fluorouracil and doxorubicin) seem to be not effective in SCCB (7,15,18), however, some limited activity with drugs such as S-1, CDDP, and eribulin has been reported (19-22), clinical trials testing platin based regimen or targeted therapies such as EGFR inhibitors given the high EGFR expression, are needed for a better management of these patients. Besides of their chemoresistance, these tumors also seem to be relatively radioresistant because of their tendency for locoregional relapse (7). However, patients who have received adjuvant chemotherapy and radiotherapy have demonstrated a better survival rate than those who did not (7,23-24). Endocrine therapy is rarely prescribed since most tumors are negative for hormone receptors. Yadav and al reported in the largest retrospective study to date a 5-year cause-specific survival of 63.5%. (4)

Table 3: Features of five large series

Characteristics	Hennessy et al. 2005 (7) MD Anderson	Hennessy et al 2005 (7) SEER 1988 -2001	Grabowski, et al. 2009 (9)	Zhang et al. 2016 (25)	Yadav et al 2017 (4)
N° of patients	33	137	177	30	445
Age, years (range)	52 (32–71)	-	64(24-79)	50 (28–87)	73 (26-99)
Race/ethnicity					
White	21(64 %)	119 (87%)			358 (80.4%)
Hispanic	5 (15 %)	NR	NA	NA	NR
Black	7 (21%)	11 (8%)			66 (14.8%)
Other	-	7 (5%)			16 (3.6%)
Unknown	-	-			5 (1.1%)
T stage at diagnosis					
T1	5 (15%)	37 (27%)	NA	T1–2 :24 (80%)	88 (19.8%)
T2	20 (61 %)	62 (45%)			157 (35.3%)
T3	4 (12%)	33 (24%)		T3–4 : 6 (20%)	62 (13.9%)
T4	4 (12%)	-			53 (11.9%)
Unknown	—	5 (4%)			85 (19.1%)
N stage at diagnosis					
N0	16 (49%)	89 (65%)		18 (60%)	285 (64.0%)
N1	13 (39 %)	27 (20%)	NA	9 (30%)	70 (15.7%)

Primary Squamous Cell Carcinomas of the Breast: A Report of six Cases and review of literature

N2	4 (12%)	-		3 (10%)	24 (5.4%)
N3	-	-		-	17 (3.8%)
Unknown	-	21 (15%)		-	49 (11.0)
M stage at diagnosis					
M0	31 (94 %)	125 (91%)	162 (91.5%)	37 (100%)	NA
M1	2 (6%)	12 (9%)	15 (8.5%)	0 (0%)	43 (9.7%)
Unknown	-	-	-	-	NA
Stage at diagnosis					
Stage I	2 (6%)	34 (25%)	Localized	5 (16.7%)	76 (17.1%)
Stage II	23 (69%)	71 (52%)	93 (52.5%)	18 (60%)	197 (44.3%)
Stage III	6 (18%)	20(14%)	Regional	7 (23.3%)	87 (19.6%)
Stage IV	2 (6%)	12 (9%)	56 (31.6%).	-	43 (9.7%)
Unknown			Distant		42 (9.4)
			15 (8.5%)		
			Unknown		
			13 (7.3%)		
Grade					
I/II	2 (6%)	41 (30%)	NA		147 (33.1%)
III	31 (94%)	65 (47%)			205 (46.1%)
IV					13 (2.9%)
Unknown	—	31(23%)			80 (18.0%)
ER status					
Positive	4 (12%)	12 (9%)	NA	2 (6.5%)	71 (16%)
Negative	28(85%)	81 (59%)		16 (54.8%)	256 (57.5%)
Unknown	1 (3%)	44 (32%)		12 (38.7%)	118 (26.5%)
PR status					
Positive	3 (9 %)	9 (7%)	NA	1 (3.3%)	45(10%)
Negative	29 (88%)	82 (60%)		16 (54.8%)	282 (63.5%)
Unknown	1 (3%)	46 (34%)		13 (41.9%)	118 (26.5%)
HER2/neu status					
Positive	2 (6%)		NA	5 (16.1%)	NA
Negative	23 (70%)	NA	NA	9 (32.3%)	
Unknown	8 (24%)			16 (51.6)	
Surgery					
BCS/AD	13 (39%)	46 (34%)	NA	5 (16.7%)	149 (33.5)
MRM/AD	19 (58%)	80 (58%)		21 (70%)	212 (47.6)
Lumpectomy	-	-		4 (13.3%)	-
Bilateral mastectomy	-	-		-	63 (14.2)
None	1 (3%)	11 (8%)		-	21 (4.7)
Adjuvant RT					
Adjuvant	19 (61%)	48 (35%)	NA	6 (20%)	152 (34.2%)
None	12 (39%)	86 (63%)		24 (80%)	275 (61.8%)
Unknown	—	3 (2%)			18 (4.0%)
Adjuvant CT					
Neoadjuvant	5 (16%)		NA	5 (17%)	NA
Adjuvant	19 (61%)	NA	NA	21(70%)	
None	7 (23%)			4(13%)	
Adjuvant ET					
Adjuvant	4 (13%)	NA	NA	NA	NA
None	27 (87%)				
5year OS Stage (%)					
I	100	88	NA	50	92.4
II	45	60		67.5	
III	0	39		51.4	
IV	50	33		-	11.5
5year OS rate	40	64	68.1	67.2	63.5

ER: Estrogen-receptor **PR:** Progesterone-receptor

NA: Not available, **MRM:** modified radical mastectomy, **BCS:** Breast conserving surgery, **AD:** axillary dissection. **CT:**chemotherapy, **RT** radiotherapy **ET** endocrine therapy,

V. CONCLUSION

SCCB is a rare and extremely aggressive breast malignancy, the lack of an established method of treatment and the poor response of the tumor to standard chemotherapeutic regimens should lead to multidisciplinary clinical trials in order to find a better systemic therapy to improve patient outcomes.

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