Case Report

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Solid Papillary Carcinoma: A Clinicopathological Evaluation of a Rare Variant of Carcinoma Breast

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Abstract

Background: Solid papillary carcinoma (SPC) of the breast is considered a low grade carcinoma with a favorable prognosis. We aimed to describe clinicopathologic features including immunohistochemistry expression profile and to delineate adverse prognostic features, if any.

Methods: Patients diagnosed with SPC between the years 2016–2022 were retrospectively identified from the archives at Kailash Cancer Hospital and Research Centre, Goraj. Microscopic slides and clinical history were reviewed. Immunohistochemical stains were performed.

Results: Of 12 SPCs cases retrieved, 11 (92%) were associated with ductal carcinoma in situ (DCIS). The median tumour size was 1.6cm (range 1.3-7.0cm). All tumors were positive for hormone receptor expression and negative for HER-2Neu. 6 cases (50%) show neuroendocrine differentiation. Lymph node involvement was identified in 4/12 (33.3%) patients. Of 12 patients with outcome data (median follow-up 30 months, range 7-72 months), none (0%) developed local recurrence. No distant metastasis or deaths were observed.

Conclusions: SPCs has excellent prognosis with no local recurrence or distant metastasis in this study. Axillary node metastasis is found to be associated with larger tumor size, however it appears to have no impact on disease free or overall survival.

Keywords: *Solid papillary carcinoma, Breast papillary carcinoma, Neuroendocrine differentiation, Nodal involvement*

Introduction

Papillary neoplasm of breast is rare and accounts for only 1% of total breast carcinoma [1, 2]. It is a broad term and includes diseases from benign to malignant. The spectrum includes benign ductal papilloma, solid papillary carcinoma, encapsulated carcinoma, papillary carcinoma [2, 3]. Among all these, solid papillary carcinoma (SPC) is very rare and least discussed in literature with unique morphological features and has an excellent prognosis [2, 4, 6]. There have been multiple debates on where to put SPC, an in situ carcinoma or invasive carcinoma since decade [1, 5]. Recent WHO has recognized SPC as separate entity as an invasive carcinoma. SPC usually occurs in an older age women (mean age ~63yr). It has a very low rate of (<10%) metastasis and a rare event of local recurrence [17, 19]. We retrieved cases from archive to re-emphasize clinicopathological and immunophenotypic features of this rare entity and to identify any high risk features for regional spread. We also wanted to look at the events of recurrence, if any.

Material and methods

The study was conducted at the department of pathology of Kailash Cancer Hospital and Research Centre, Goraj, Vadodara. This is a retrospective study and includes total 12 cases from January 2016 to February 2022. We selected cases with SPC as an exclusive feature and excluded cases with mixed SPC and infiltrating duct carcinoma variants. The specimen for the histopathological evaluation were preserved in 10% neutral buffered formalin. Sections were processed for paraffin embedded tissue sections. 5-micron thick tissue sections were stained with Harris Hematoxylin and Eosin stain. Immunohistochemical stains were performed on 4 micron thick formalin fixed paraffin embedded sections as per the manufacturer's instructions-estrogen receptor (monoclonal rabbit antibody, EP1, Dako), progesterone receptor (monoclonal mouse antibody, clone PgR636, Dako), Cer-B2 (polyclonal rabbit antibody,

DAKO), synaptophysin (DAKSYNAP/SY38, Dako), chromogranin-A (LK2H10, Biogenix) and MIB1 (Ki67, Dako) were used. For ER and PR IHC interpretation Allred scoring system was used. For CerB2 expression ASCO-CAP 2019 guidelines were used. For neuroendocrine expression immunopositivity of more than 10% was reported as positive.

Aims and objectives: The primary objectives are to study the 1) hormone receptor status (ER and PR) 2) CerB2 expression 3) Neuroendocrine differentiation (Synaptophysin and chromogranin expression) 4) MIB1 proliferation index 5) Mucinous differentiation 6) Tumor stage. The secondary objective is to evaluate impact of above-mentioned features along with other clinicopathological parameters (age, tumor size, mitotic activity, modified R.B score, skin involvement, lymph node status) on prognosis.

Inclusion and exclusion criteria:

The inclusion criteria are Exclusive microscopic features of SPC, Cases with available clinical and histological data, Cases available for follow-up.

The exclusion criteria are any concomitant pattern of IDC along with SPC.

Result

Clinical characteristics

The study consists of 12 cases. All cases were presented as unilateral solitary mass. All patients were female. The mean age was 64years (age range of 47-85 years). Surgical procedures included MRM in 6 patients, simple mastectomy in 3 patients (3 cases with nodal dissection) and lumpectomy in 3 patients (1 case with nodal dissection). Adjuvant radiation therapy was given to 3 patients in view of nodal metastasis. 2 patients received hormone replacement therapy in the form of Letrozole. Rest of the patients didn't opt for any adjuvant therapy.

Pathological characteristics

All 12 cases were morphologically diagnosed as SPC with no other concomitant pattern of IDC. Average tumor size was 2.5cm (ranging from 1.3cm-7.0cm). Microscopically these tumors showed multinodular configuration with individual nodules having a jig saw puzzle like arrangement of tumor nests or islands in solid configuration. There was no tubular differentiation. These tumor nests showed entrapment of fibrovascular stroma within, giving a papillary configuration to the nests. The tumor cells were of medium sized having round to short spindle-shaped morphology. Nuclear palisading and pseudo rosette formation around entrapped fibrovascular cores were seen. The tumor cells possessed round to oval mild to moderately pleomorphic nuclei with fine chromatin and inconspicuous nucleoli. 11 cases also showed DCIS of solid and cribriform type with low to intermediate nuclear grade. Comedonecrosis was absent. Tumors were negative for extensive intraductal carcinoma (EIC). 7 cases showed mucinous differentiation in the form of pools of extra-cellular mucin (range: 5%-40%). However, intracytoplasmic mucin was not evident. Majority of the cases had modified Bloom Richardson score of 6. Average mitotic activity was 9/10HPF. (Range: 7-18). Two cases showed lymphovascular tumor emboli. Overlying skin was free in all patients except in 1 patient (Case 4). Case 4 showed deep dermal involvement by the tumor without ulceration. The base of resection and circumferential soft tissue resection margins were free of tumor in all the cases. 10 cases had nodal dissection (including 4 cases with sentinel node evaluation), out of which 3 patients showed lymph node metastasis with extranodal extension. All these cases were of stage pN1a.

Immunohistochemical features

All 12 cases were ER positive, PR positive and Her2 negative. 6 cases showed neuroendocrine differentiation with synaptophysin positivity along with 4 cases showed chromogranin positivity. All cases had low proliferation rate (<10%) except two cases.

Follow up details

At the last follow up visit (mean follow up 30 months, range 7-72 months), all women were free of disease. There is no event in the form of locoregional recurrence/distant metastasis or cancer related deaths in any patient.

Discussion

Solid papillary carcinoma (SPC) is a rare subtype of papillary carcinoma of breast with distinct morphological features with excellent prognosis [1, 16]. In this study we report clinical-pathological features and results of 12 cases. The mean age is ~64years, in keeping with the literature [1, 3, 8, 9, 15]. All cases are of female patients, other studies have also described rare cases of SPC in men. [1, 10, 19]. Surgical treatment wise 6 patients underwent MRM, 3 patients had lumpectomy and rest of the 3 cases had simple mastectomy. Most authors suggest complete excision of the lesion either by BCS or mastectomy with nodal dissection, preferably sentinel node evaluation. [1,17]

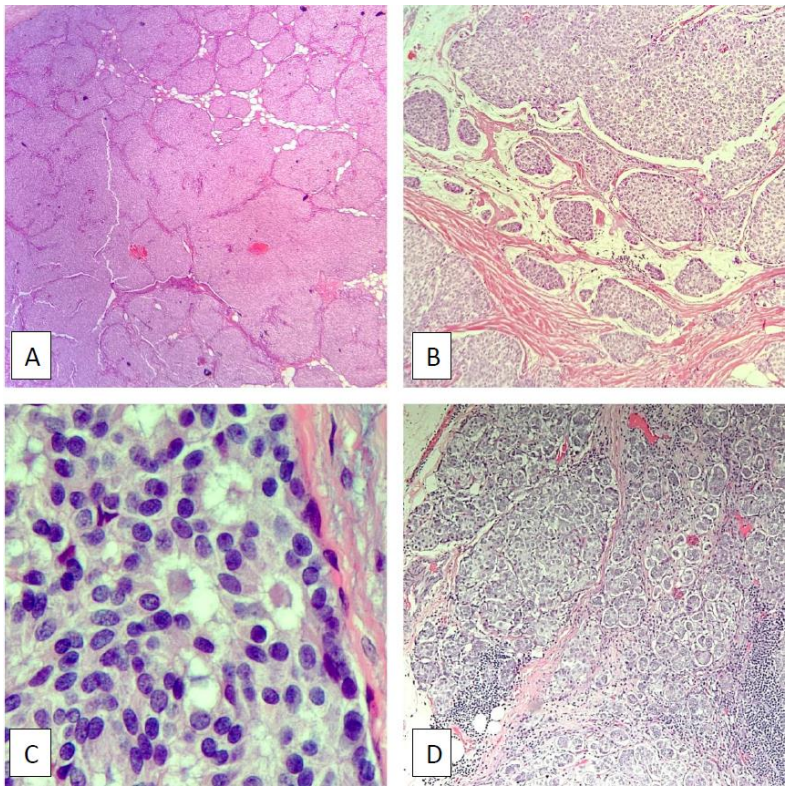

Figure 1: Histopathological features A) Classic SPC with jig saw like arrangement of tumor nests (H&E X100) B) Case with extracellular mucin (H&E X100) C) Case with neuroendocrine differentiation (H&E X400) D) Case with extranodal extension (H&E X100)

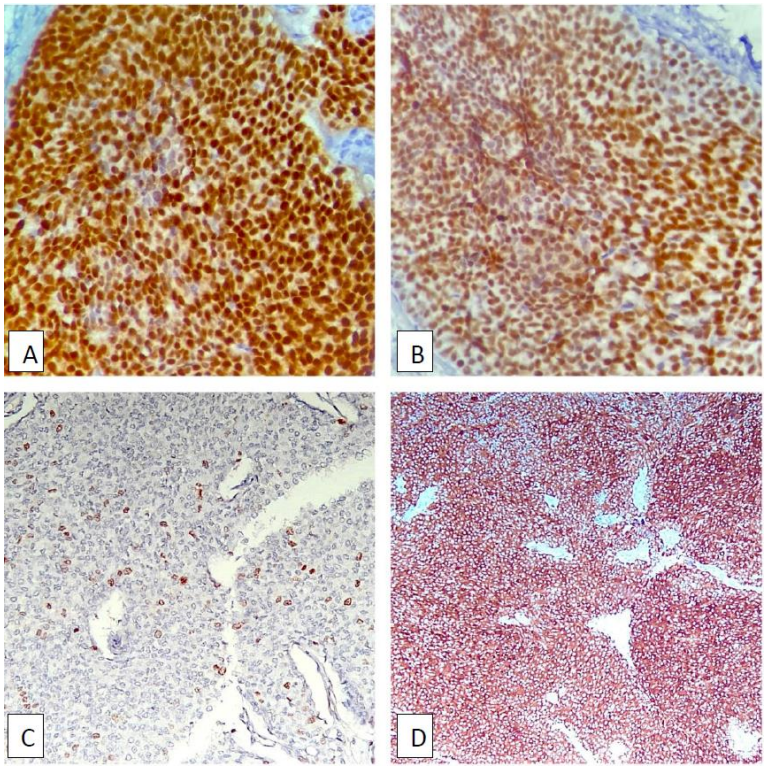

Figure 2: Immunohistochemical features A) ER positivity (X400) B) PR positivity (X400) C) MIB 1 proliferation (X100) D) Synaptophysin positivity (X100)

Table 1: Clinical characteristics

Cases	Age (yr.)	Months of follow-up(months)	Surgery	Adjuvant therapy	Recurrence
Case 1	60	72	MRM	No	No
Case 2	67	56	Simple mastectomy with SNE	No	No
Case 3	52	51	MRM	HRT	No
Case 4	55	46	MRM	No	No
Case 5	62	37	MRM	No	No
Case 6	65	32	Simple mastectomy with SNE	No	No
Case 7	82	27	MRM	No	No
Case 8	60	27	Lumpectomy with SNE	RT	No
Case 9	60	17	Lumpectomy	No	No
Case 10	47	16	MRM	RT	No
Case 11	85	11	Lumpectomy	RT	No
Case 12	74	7	Simple mastectomy with SNE	HRT	No
	Mean age- 64yr	Mean followup-30 months			Recurrence- 0%
MRM- Modified radical mastectomy, SNE- Sentinel node evaluation, RT- Radiotherapy, HRT- Hormone replacement therapy					

Table 2: Pathological characteristics

Cases	Size	Mitotic activity/10HPF	Mucin production	DCIS	Nodal status	RB score	Skin	Pathological Stage	Group stage
Case 1	2.2	8	Absent	Yes	0/10	6	Absent	pT2N0	IIA
Case 2	1.6	10	Absent	Yes	SN (0/2)	6	Absent	T1cN0(sn)	I
Case 3	2.1	9	5%	Yes	0/14	6	Absent	pT2Nx	IIA
Case 4	7.0	9	5%	Yes	2/11 +ENE	6	Involved without ulceration	T3N1a	IIIA
Case 5	4.0	9	Absent	Yes	3/11 +ENE	6	Absent	T2N1a	IIB
Case 6	2.1	7	Absent	No	SN (0/2)	6	Absent	T2N0(sn)	IIA
Case 7	1.3	8	10%	Yes	0/14	6	Absent	T1cN0	I
Case 8	1.8	6	Absent	Yes	SN (0/1)	6	Absent	T1cN0(sn)	I
Case 9	1.5	9	10%	Yes	--	6	Absent	T1cNx	I
Case 10	3.5	18	40%	Yes	3/11 +ENE	7	Absent	T2N1a	IIB
Case 11	2.0	8	5%	Yes	--	6	Absent	T1cNx	I
Case 12	1.8	9	10%	Yes	SN (0/3)	6	Absent	T1cN0(sn)	I
DCIS- Ductal carcinoma in situ, RB score- Modified Bloom Richardson score,									

Table 3: Immunohistochemical features

Cases	ER (Allred score)	PR (Allred score)	Her2	Synaptophysin	Chromogranin A	MIB 1
Case 1	Positive (8)	Positive (8)	Negative	Positive	Positive	9.3%
Case 2	Positive (8)	Positive (8)	Negative	Negative	Negative	4.6%
Case 3	Positive (8)	Positive (8)	Negative	Positive	Positive	13.8%
Case 4	Positive (8)	Positive (8)	Negative	Positive	Positive	1.8%
Case 5	Positive (8)	Positive (8)	Negative	N/A	N/A	N/A
Case 6	Positive (8)	Positive (8)	Negative	Negative	Negative	10.2%
Case 7	Positive (8)	Positive (8)	Negative	Negative	Negative	0.9%
Case 8	Positive (8)	Weak positive (5)	Negative	Positive	Positive	1.2%
Case 9	Positive (8)	Positive (8)	Negative	Negative	Negative	1.5%
Case 10	Positive (8)	Positive (8)	Negative	N/A	N/A	N/A
Case 11	Positive (8)	Positive (8)	Negative	Positive	Negative	4.2%
Case 12	Positive (8)	Positive (8)	Negative	Positive	Positive	3.5%
ER- Estrogen receptor, PR- Progesterone receptor, N/A- Not available						

DCIS component was present in 11 cases (92%), is higher in our study compared to the available literature. In Morgan S. study the association of DCIS with invasive SPC was 17.4% [1]. In Leena J.B. study the in situ component was 32.7% [15]. Average size of the tumor is ~2.5cm, with 6 having tumor size </=2cm (i.e. pT1c stage). The largest tumor size in our study was 7cm, only case with pT3 stage. In Morgan et al study the average size of the tumor was ~1.6cm. [17]. As with other types of breast carcinoma, our study of SPC cases also show trend of smaller sized tumor (<2.3cm) with negative nodal metastasis status. Although sample size in our study is small, all 3 tumors with size >3.5cm were associated with axillary node metastasis with extra-nodal extension (25%). In Morgan et al study, 26 patients who underwent sentinel node biopsy, nodal involvement was identified in 3 cases (11.5%) [17]. In Rakha and Inno A. studies the nodal metastasis varied from 3-5% [9, 21]. Sentinel node evaluation ranges from 30%-100% in the literature [1, 3, 21]. These studies re-emphasize the role of sentinel node evaluation in breast carcinoma patients to reduce the morbidity associated with complete axillary nodal dissection. We suggest the association of larger tumour size and nodal involvement also applies to the SPC cases, however it seems the nodal involvement does not impact disease free and overall survival, which needs further research. Extracellular mucin production is frequent in SPC and in our study it was present in 7 cases (58%) and the extracellular mucinous component ranged from 5%-40%. In Nassar H. study the extravasated mucin component associated with SPC was 8.6% [12]. Although the percentage of the mucin component differs in every study, it doesn't impact the prognosis. All cases except one were grade II with modified RB score 6. Thus it is a low grade carcinoma.

All tumors in our study were strong positive for hormone receptors. All cases were Cer-B2 negative. The findings are similar to the available literature [17, 22]. 6 cases (50%) showed synaptophysin positivity along with 4 cases with chromogranin-A positivity, compared to Maluf study in which they found endocrine differentiation by using chromogranin marker in 57% cases [14], though this does not appear to have clinical significance.

In our study, local recurrence and distant metastasis was absent in all the cases with a follow up range of 7-72 months. Maluf and Koerner described a case in which lung metastasis occurred without evidence of axillary lymph node involvement [14]. One study showed 6.5% cases with distant metastasis in SPC [17]. Although some of our patients did not went through ideal therapy in adjuvant setting in the form of chemotherapy and/or HRT, none of them suffered loco regional recurrence or distant metastasis in the span of mean follow up of 30 months, with a range extending up to 6 years, which suggests that tumor biology is favourable even in cases with surgery alone as a treatment. Larger study with extended follow up is suggested for cases with SPC to consolidate these findings, which will save patients from unnecessary morbidity associated with adjuvant therapies.

Conclusion

Solid papillary carcinoma (SPC) is a unique type of papillary carcinoma of breast with distinct morphological and immunophenotypic features. This entity has excellent prognosis with no local recurrence or distant metastasis in this study. Axillary node metastasis is found to be associated with larger tumor size, however it appears to have no impact on disease free or overall survival.

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