BENHA MEDICAL JOURNAL bmj
Print ISSN 1110-208X.
Online ISSN 2357-0016

Original article

Diagnostic Significance of Immunohistochemistry in Papillary Breast Neoplasms

Omneya Y. Bassyoni [a], Zeinab I. Elshawarby [a], Ahmed M. Abostate [b]

[a] Pathology Department, Faculty of Medicine Benha University, Egypt.

[b] General Surgery Department, Faculty of Medicine Benha University, Egypt.

Corresponding to:
Dr. Omneya Y. Bassyoni.
Pathology Department, Faculty of Medicine Benha University, Egypt.

Email:
omneyayoussef2015@gmail.com

Received: 17 July 2023

Accepted: 26 August 2023

Abstract:

Background: Papillary breast neoplasms are heterogenous group of breast diseases consisting of wide range of benign, atypical and malignant lesions. Evaluation of such papillary neoplasms is considered one of the most problematic issues in diagnosis of breast pathology depending on H&E only as they need different interventional treatment modalities. Aim of study: To differentiate papillary breast lesions depending on immunohistochemical staining of P63, SMA, CK14, chromogranin and ER. **Materials and Methods:** An Immunohistochemical study of P63, SMA, CK14, chromogranin and ER were conducted on 75 cases of different papillary breast neoplasms; papilloma (20 cases) , DCIS (25 cases) , solid papillary carcinoma (12 cases), intracystic papillary carcinoma (11cases) and invasive micropapillary carcinoma (7 cases) . **Results:** Out of 75 cases, all cases of duct papillomas were positive to SMA, P63. Ninety percent (90 %) of them were positive to CK14 in comparison to malignant papillary: DCIS, intracystic papillary carcinomas. solid papillary carcinomas neoplasms which were negative (84.0%, 92.3 %, 90.0% & 100.0%, respectively). Ninety -two percentage (92 %) of DCIS cases, 92.3% intracystic papillary carcinomas, 90.0% solid papillary carcinomas and all cases of invasive micropapillary carcinomas- showed homogenous positivity for ER compared to papillomas that showed focal heterogenous expression with statistical significant ($p<0.01$). Solid papillary carcinoma cases were diffusely positive for chromgranin. P63 was more specific than SMA and CK14 in diagnosis of ductal papilloma (100% Specificity). chromogranin was more specific in discriminating solid papillary carcinoma (95.0% Specificity) .ER was the most sensitive marker in diagnosis of malignant papillary lesions (92.7 % sensitivity). **Conclusion:** A combined panel of markers consisting of P63, SMA, CK14, chromogranin and ER- could be helpful in differentiating begin, atypical and malignant papillary breast lesions which need different interventional treatment modalities. A wider scale study on different variants of malignant papillary lesions is recommended.

Keywords: Breast, Papilloma, Carcinoma.

Introduction

Breast cancer is a leading health problem among women wordwide [1]. It remains the most common type of female cancer in Egypt represents 32.4%. [2]. Benign papillary breast lesions constitute less than 10 % of breast lesions [3]. Papillary carcinoma of the breast is considered a rare subtype of breast cancer, as it compromises nearly 1% of cases [4].

Papillary breast lesions comprise a heterogeneous group of breast diseases that exhibit clinical, histological, and biological variability. Their diagnostic hallmark is the presence of branched papillae with prominent fibrovascular connective tissue core [5].

They include a wide variety of diseases, ranging from intraductal papilloma to papilloma with atypical ductal hyper-plasia (ADH) or ductal carcinoma in situ (DCIS), papillary DCIS, debatable in situ or invasive papillary lesion (intracystic papillary carcinoma and solid papillary carcinoma) and invasive papillary carcinoma [6].

Unlike normal papillae, micropapillae has no fibrovascular core .Although the presence of micropapillae in breast lesions is uncommon ,it is also of practical importance as a micropapillary pattern could be associated with various lesions such as usual ductal hyperplasia, DCIS, and invasive carcinoma [7].

Evaluation of papillary breast neoplasms is considered one of the most difficult problems in diagnosis of breast pathology [8]. The accurate identification of papillary lesions obtained via core needle biopsy or vacuum assisted biopsy may be challenging [9].

Distinguishing benign from malignant papillary breast lesion depending on both the presence or absence of myoepithelial cells and the appearance of the epithelial component has been previously studied [10].

P63 is a myoepithelial marker that belongs to the p53 gene family, but is clearly not a tumor suppressor gene, encoding at least 6 different proteins with different biological functions that influence epithelial organs growth and development [11].

Smooth muscle actin (SMA), one of the myoeptithelial marker, is a common 43000 kDa protein present in all cells and are responsible for cell motility and the maintenance of the cytoskeleton of the cell [12].

Cytokeratin 14 (CK14) is a type I acidic high molecular weight keratin expressed in mitotically active basal cells of stratified epithelium. CK14+ tumors are defined as a basal subtype of DCIS or invasive breast carcinoma [13].

Chromogranin is a neuroendocrine marker commonly used to diagnose papillary breast lesions with neuroendocrine differentiation such as solid papillary carcinoma [14].

The estrogen receptors (ERs) are made up of two subtypes: ERα and ERβ .ERα is evaluated in breast cancer classification, prognosis and treatment. ERα is expressed in breast epithelium and is expressed in over 70% of all breast cancers [15].

The aim of this work is to study the immunohistochemical expression of P63, SMA, CK14, chromogranin and ER in differentiating the benign from variety of malignant papillary breast lesions as they need different interventional treatment modalities.

Materials and Methods

Patients and clinical data: -

This retrospective study was carried out in the Pathology departments, and Early Cancer Detection Unit, Benha University Hospital, Egypt in the period from July 2015 to September 2022, after approval of the Ethical Committee No (M.S.5.6.2023). The study comprised the selected 75 cases of papillary breast lesions.

A total of 20 benign and 55 malignant papillary lesions of the breast were included in the testing cohort. All 20 benign cases were papilloma. Of the 55 malignant lesions ;25 cases of DCIS, 10

cases of solid papillary carcinoma, 13 cases of intracystic papillary carcinoma and 7 cases of invasive micropapillary carcinoma.

Ten cases were true cut biopsy, 15 of incisional biopsy, 43 lumpectomy and 7 cases were mastectomy specimens. Six cases of normal breast tissue were included as control.

Inclusion criteria: All breast true cut biopsy, incisional biopsy, lumpectomy and mastectomy specimens of patients with neoplastic diagnosis with sufficient available tissue in the block- were included in the study. In the category of malignant lesions, only the histopathologically proven cases of breast carcinoma- were included.

Exclusion criteria: Patients with a previous history of receiving any chemo-therapeutic agents or radiation- were excluded.

All specimens were fixed in formalin and embedded in paraffin-wax, the blocks were cut at thin sections (4-5 microns) and stained with routine Hematoxylin & Eosin stain to revise the microscopic diagnosis of the tumors.

Immunohistochemistry

For immunohistochemical analysis, streptavidin-biotin technique was used following the manufacturer's instructions (Neomarker, LABVISION, USA, CA 94538-7310. Data concerning antibodies, antigen retrieval and positive controls are shown in Table (1). The sections were stained with 0.02% diaminobenzidine (DAB) solution. Finally, sections were counterstained with hematoxylin then dehydrated and mounted. Negative controls were performed by omitting the primary antibody. For interpretation of immunohistochemical staining of all used markers, the percentage staining of each marker was assessed followed by previous study (16).

Statistical Analysis:

Results were analyzed using IBM SPSS Statistics for Windows, Version 22.0 (SPSS Inc., Chicago, IL, USA) as follow: P >.05 is non-significant, P <.05 is significant and P ≤ .01 is highly significant.

Table (1): Data for using P63, SMA CK14, ER and chromogranin antibodies.

Antibody	Type	Cat. No	Dilution	Positive control	incubation	Antigen retrieval
P63	Rabbit Monoclonal	Thermo Fisher Scientific, Cat. No. 703809	1:100	prostate	30 minutes	Citrate buffer, pH 7.2
SMA	Mouse Monoclonal	Thermo Fisher Scientific, Cat. No. PA5-85070	1:100	Spleen	30 minutes	Citrate buffer, pH 7.2
Ck14	Rabbit Polyclonal	Thermo Fisher Scientific, PA5-28002	1:100	Lung cancer	30 minutes	Citrate buffer, pH 7
Chromogranin	Rabbit Polyclonal	Thermo Fisher Scientific, Cat. No.PA5-77917	1:100	Pancreas	30 minutes	Citrate buffer, pH 7
ER	Rabbit	Thermo Fisher Scientific, Cat. No. MA5-14501	1:200	Breast carcinoma	30 minutes	Citrate buffer pH 7.2

SMA: smooth muscle action, CK14: cytokeratin 14, ER: estrogen receptor.

Results

The mean age in studied cases was 45.6 ±12.3 years (range 11–81) and 58.0 ± 13.7 years (range 30–81) for benign and malignant lesions. There was a statstically significant difference in age between benign and malignant breast lesions (P < 0.001).

Expression of the studied markers among benign and malignant papillary breast lesions.The expression of three groups of biomarkers, myoepithelial markers [p63, SMA and CK14] hormone receptor (ER) and neuroendocrine marker (chromogranin)- were evaluated in the papillary breast lesions as shown in Table (2) .

Table (2): Expression of the studied markers (P63, SMA, CK14, Chromogranin and ER) among the benign and malignant papillary breast lesions.

Studied groups	Total	SMA		P V	P63		P V	CK14		P V	CG		P v	ER		P v
		+ve	-ve		+ve	-ve		+ve	-ve		+ve	-ve		+ve	-ve	
papilloma	20 26.7%	19 95.0%	1 5.0%	<0.01	20 100.0%	0 0.0%	<0.01	18 90.0%	2 10.0%	<0.01	1 5.0%	19 95.0%	<0.01	2 10.0%	18 90.0%	<0.01
DCIS	25 33.3%	15 60.0%	10 40.0%		12 48.0%	13 52.0%		4 16.0%	21 84.0%		5 20.0%	20 80.0%		23 92.0%	2 8.0%	
intracystic papillary carcinoma	13 17.3%	3 23.1%	10 76.9%		0 0%	13 100%		1 7.7%	12 92.3%		1 7.7%	12 92.3%		12 92.3%	1 7.7%	
solid papillary carcinoma	10 13.3%	2 20%	8 80%		0 0%	10 100%		1 10.0%	9 90.0%		9 90.0%%	1 10.0%		9 90.0%	1 10.0%	
invasive micro papillary carcinoma	7 9.3%	0 0.0%	7 100.0%		0 0.0%	7 100.0 %		0 0.0%	7 100.0 %		1 14.0%	6 86.0%		7 100.0%	0 0.0%	
Total	75 100.0 %	39 52.0%	36 48.0%		32 42.7%	43 57.3%		24 32.0%	51 68.0%		17 22.7%	58 77.3%		53 70.7%	22 29.3%	

The positive expression rates for myoepithelial markers (P63 & SMA) and CK14 were found in 100 % all cases of benign lesion compared to malignant neoplasms with statistically significant positive correlation (P< .001). There was a diffuse, continuous staining of the peripheral rim with P63 and SMA in 100 % of papillomas. Also, the intraluminal portion of the benign papillomas showed an intact, continuous myoepithelial layer expressed positively for both P63 Figure (1, A) and SMA Figure (2, A).

P63 which expressed in 48% of cases as discontinuous or incomplete nuclear positivity in the periphery of the papillary growth in Figure (1, B) as well as SMA which showed positivity in 60% cases of DCIS expressed only in the outer peripheral myoepithelial layer Figure (2, B)

Malignant papillary neoplasms: solid papillary carcinoma in Figure (1, C) intracystic Figure (1, D) and invasive micropapillary carcinoma Figure (1, E) - showed absent myoepithelial cell layer with no staining of the central portion of the lesions for p63.

SMA showed lower positivity in solid papillary carcinoma as shown in Figure (2, C) and intracystic papillary carcinoma in Figure (2, D) in (20 % and 23.1 %, respectively) but negative in all cases of invasive micropapillary carcinoma in Figure (2, E)

For the expression rates of CK14, it was in 90 %papilloma Figure (3, A) compared to the respective rates of its expression in 16%, 7 %, 10% in malignant lesions, DCIS Figure (3, B), solid papillary carcinoma Figure (3, C), intracystic papillary carcinoma Figure (3, D), respectively) but negative in all cases of invasive micropapillary carcinoma Figure (3, E).

Papilloma showed significantly lower expression rates for neuroendocrine markers (CG), (P >.05) and hormone receptors (ER), (P <.01) than malignant lesions. For neuroendocrine marker, Chromogranin (CG) expression were negative in 95% of papilloma illustrated in Figure (4, A) but in 7 of 10 solid papillary carcinoma (70%) as shown in Figure (4, D) and 22 of 55 (40%) of malignant cases including DCIS Figure (4, B), intracystic papillary carcinoma Figure

(4, C) and invasive micropapillary carcinoma in Figure (4, E) -were negative. The expression rate of ER in papilloma were 10% Figure (5, A) but was (92%, 90 % , 92.3 % and 100 %) in malignant lesions (DCIS , solid papillary carcinoma , intracystic papillary carcinoma and invasive micropapillary carcinoma respectively as shown in Figure (5, B ,C,D and E ,respectively).

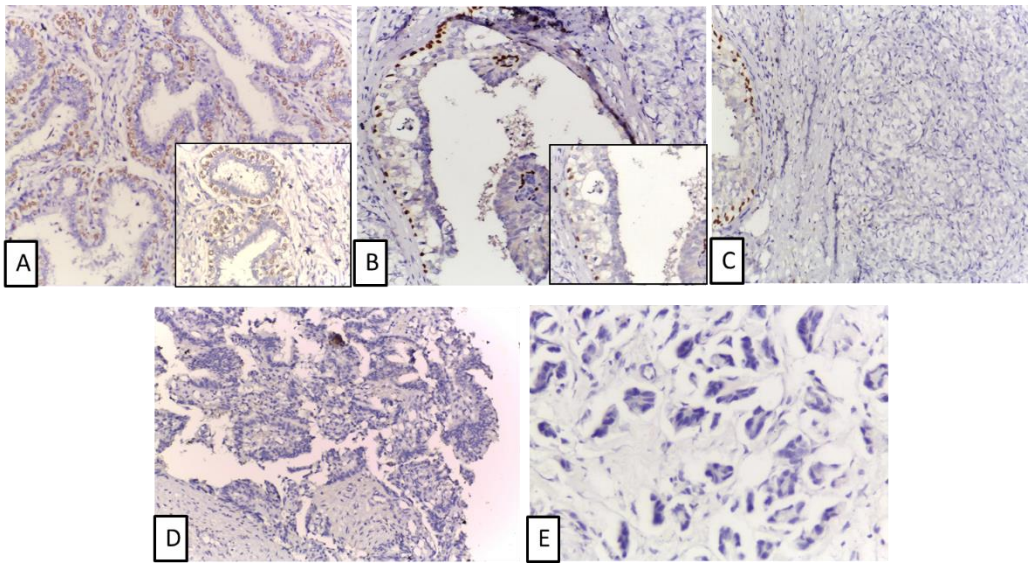


Figure (1): P63 expression in papillary breast neoplasms: (A)intraduct papilloma showing complete nuclear p63 expression inside the papillea (IHC, 200x), inset (IHC,400x). (B) DCIS and micropapillary DCIS with positive nuclear p63 as incomplete dot like nuclear expression in the periphery (IHC, 200x), inset (IHC ,400x). (C) Solid papillary carcinoma, (D) intracystic Papillary Carcinoma and (E) invasive micropapillary carcinoma showing negative nuclear p63 staining for myoepithelial layer both inside and outside the papillary lesion (in D ,left area of showing positive control) (IHC, 200x)

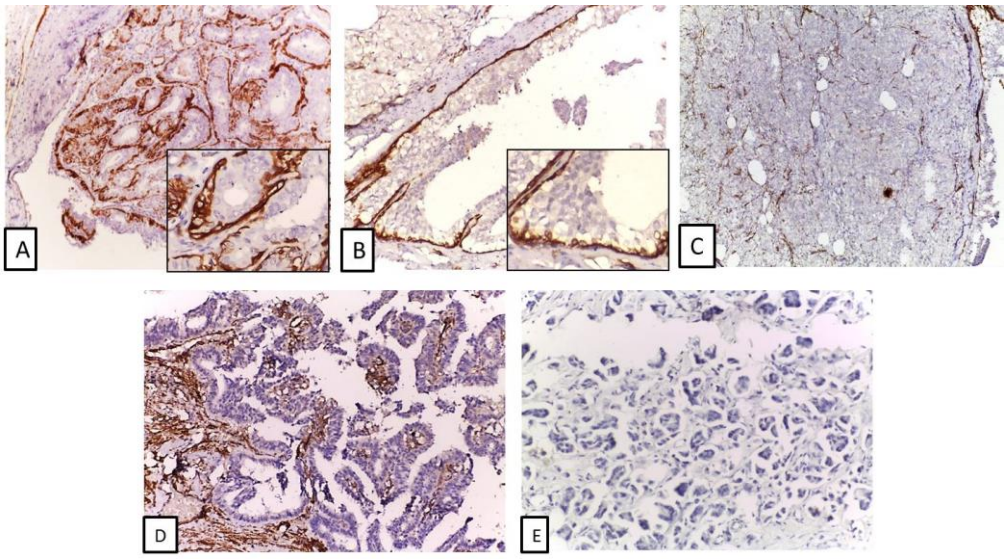


Figure (2): SMA expression in papillary breast neoplasms :(A) Positive cytoplasmic expression of SMA in myoepithelial cells in papilloma (IHC, 200x), inset (IHC,400x). (B) DCIS showing positive cytoplasmic staining in the periphery of the lesion, inset (IHCX400). (C) &(D) focal cytoplasmic positivity for SMA in solid papillary carcinoma, intracystic papillary carcinoma. (E) Negative expression of SMA in invasive micropapillary carcinoma (IHC, 200x).

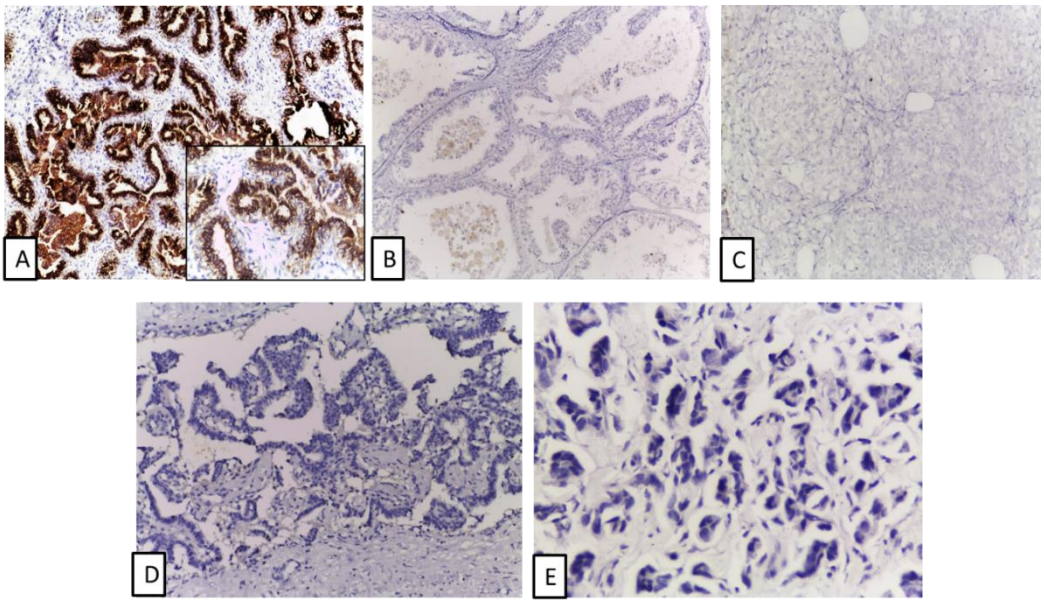


Figure (3):CK14 expression in papillary breast neoplasms : (A)positive cytoplasmic staining of epithelial cells in papilloma for CK14 ,inset(IHCX400) . (B) , (C) , (D) & (E) Negative staining of the epithelial cells component by cytokeratin 14 in DCIS, solid papillary carcinoma . intracystic papillary carcinoma and invasive micropapillary carcinoma. (IHC, 200x).

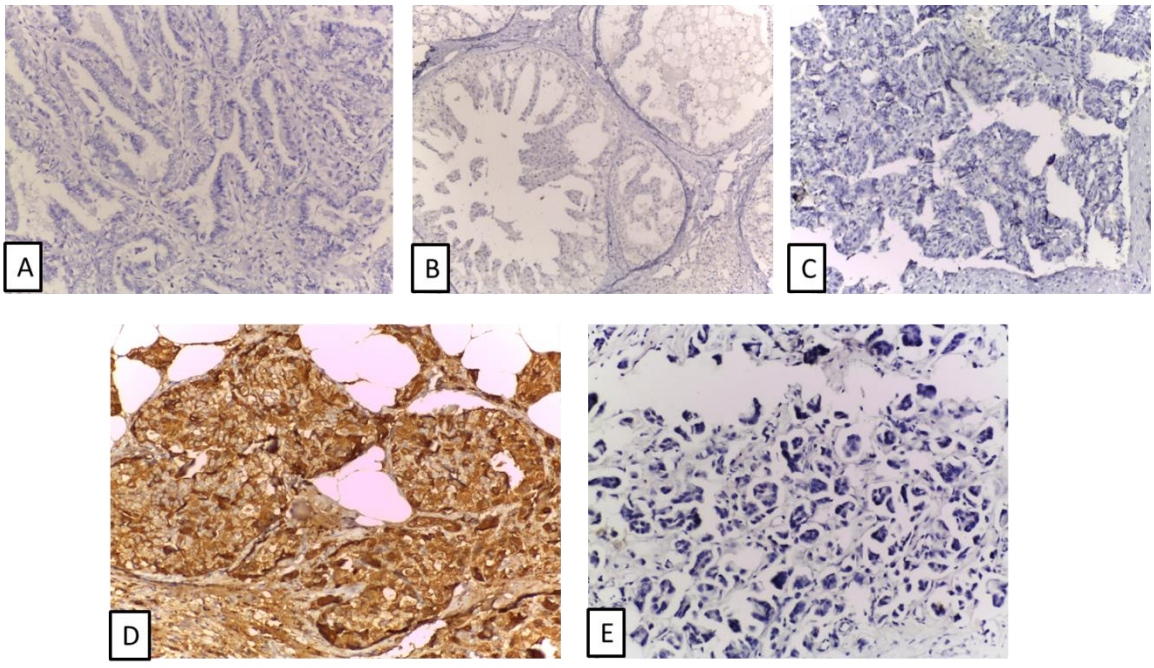


Figure (4): Chromogranin expression in papillary breast neoplasms. (A), (B) , (C) &(E) Negative staining For chromogranin in papilloma, in DCIS, , intracystic papillary carcinoma and invasive micropapillary carcinoma . (D) Diffuse strong granular cytoplasmic expression in solid papillary carcinoma. (IHC, 200x).

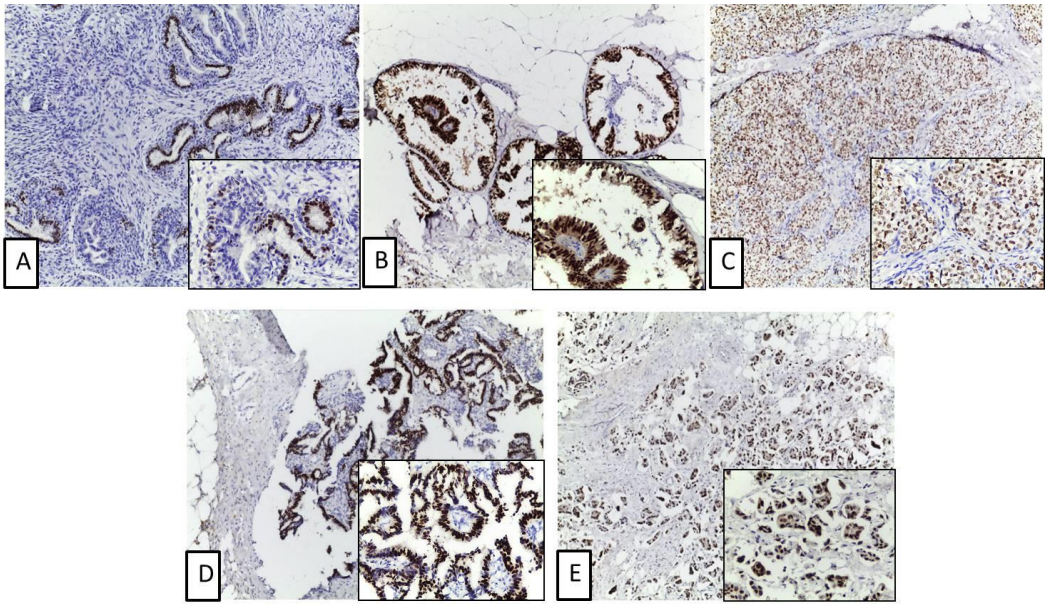


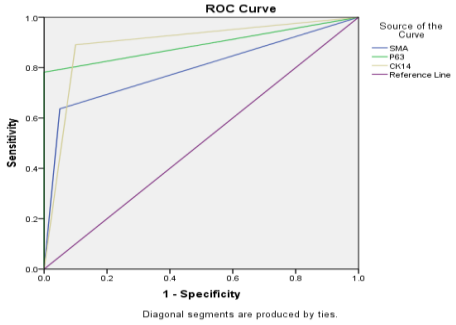
Figure (5):ER expression in papillary breast neoplasms. (A) focal heterogenous nuclear expression for ER in papilloma, inset (IHC,400x). (B), (C), (D) &(E) Diffuse homogenous nuclear staining of ER in DCIS, solid papillary carcinoma, intracystic papillary carcinoma and invasive micropapillary carcinoma (IHC, 200x), inset, (IHC,400x).

ROC curve

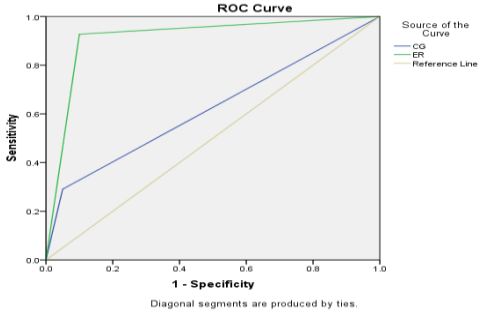
Among the myoepithelial markers, P63 was more sensitive than SMA with specificity in papilloma (100%, 95%, respectively) and sensitivity (78% and 63%, respectively) compared to malignant groups . CK14 is one of the most sensitive basal epithelial markers in this study (90% and 89% in specificity and sensitivity, respectively). Neuroendocrine marker (CG) is the least sensitive immunohistochemical marker showed (95%) specificity in papilloma, sensitivity (29%) for identifying malignant papillary lesions. ER showed. the highest sensitivity among the studied markers in this work (specificity in papilloma 90% and sensitivity 92%) for identifying malignant papillary lesions as illustrated in Figure (6, A&B).

Cominbination of myoepithelial markers (P63, SMA, CK 14) in the studied cases

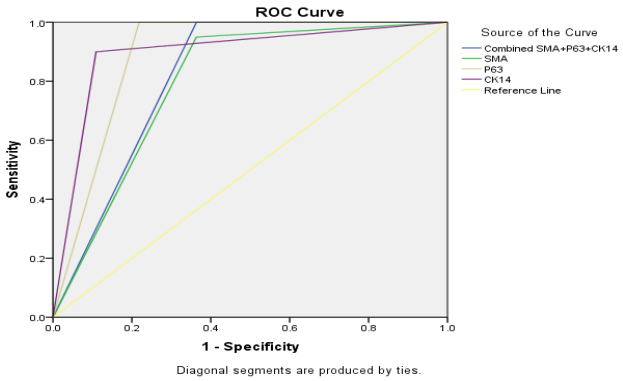
Combined expression of the 3 myepithelial markers (P63, SMA, CK 14) has a high specificity and low sensitivity in diffrentiating benign from malignant papillary breast neoplasms (100% specificty & 63.3% sensitivity) as shown in Figure (6, C).



A



B



C

Figure (6): Log Rank curve regarding. (A), (B) Performance of p63, SMA and CK14 & chromogranin and ER in discriminating benign from malignant papillary breast lesions. (C) performance of combined markers (P63, SMA, CK14) in differentiating benign from malignant papillary breast neoplasms.

Discussion:

Papillary breast lesions comprise a heterogeneous group of breast diseases that exhibit clinical, histological, and biological variability. The diagnosis of papillary lesions obtained via core needle biopsy can be a complex task, and the appropriate application of immunohistochemical markers in order to achieve an accurate diagnosis is regarded as a challenge for further therapeutic intervention [9].

The present investigation has demonstrated that P63 showed continuous nuclear positivity in 100 % of duct papilloma both in the intraluminal and peripheral outer myoepithelial layers, it exhibited focal positivity in 48 % of DCIS cases, where it was expressed in a discontinuous focal dot like staining pattern in the outer myoepithelial cell layer exclusively differentiating them from papillary carcinomas which were completely negative (P<.01).

Consistent with our investigation, previous studies [7,16] revealed continuous p63 expression within the myoepithelial cell layer of ductal papilloma. In addition, previously conducted studies [17,18] demonstrate the presence of p63 expression in benign lesions, including ductal papilloma, with a 100% detection rate.

Consistent with th), Pndings of previous analysis [19] , all cases of papillomas showed positive immunostaining with P63, SMA which were focally positive in papillary DCIS and totally negative in intracystic papillary carcinoma and invasive papillary carcinoma .In previous study [20] ,P63 nuclear staining for myoepithelial cell layer helped in confirming the benign cases (duct papilloma of the breast) , 40% of malignant cases in their study were of papillary DCIS. , p63 was absent within the papilla but present peripherally around the papillary lesion .In malignant lesions, p63 helped in confirming the absence of myoepithelial cell layer in (solid papillary carcinoma and invasive papillary carcinoma)

According to previous study [21], benign papilloma exhibited continuous p63 expression with a score of 3. Minor neoplastic disorders such as ductal carcinoma in situ exhibited the lowest degree of reactivity with a score of 1, while papillary carcinoma displayed a lack of p63 expression.

The current study findings revealed that SMA exhibited diffuse positivity in 95% of duct papilloma, as well as expression in

60 % of DCIS , 20% of solid papillary carcinoma , 23.1% of intracystic papillary carcinoma , However, all instances of invasive micropapillary carcinoma were negative staining for SMA with statistically significant correlations(P <0.01) .

These outcomes are consistent with the results reported in previous studies [18,19] which also highlighted the presence of cytoplasmic SMA in the myoepithelial cell layer of ductal papilloma, while it was absent in intracystic papillary carcinoma and invasive papillary carcinoma. Moreover, previous study [22] reported that there was a negative expression of SMA in over 70% of solid papillary carcinoma.

We found that the expression rates of CK14 was 90 % in benign breast lesions (papilloma) compared to the respective rates of its expression in 16%, 7 %, 10% in malignant lesions (DCIS, solid papillary carcinoma, intracystic papillary carcinoma, respectively. All cases of invasive micropapillary carcinoma displayed complete negativity.

The result of our study came in line with previous study [16] in which showed that CK14 exhibited a positive expression in 75% cases of benign papillary breast lesions, whereas only 5. 3% of malignant papillary breast lesions exhibited a positive expression.

The findings of our investigation aligned with those of previous study [23] which demonstrated that increased positivity of CK14 in all cases intraductal papilloma while low to negligible expression was observed in all cases of solid papillary carcinoma in situ cases. The findings of previous investigation [24] corroborate with our own results, as CK 14 was found to be positively expressed in over 95% of papillomas but only in 12-20% of ductal carcinoma in situ associated with papillomas.

In contrast to the findings of the current study, previous work [25] reported a lack of high-molecular-weight keratin (CK14) expression in neoplastic epithelial cells of papillary DCIS. However, this discrepancy may be attributed to variations in the scoring system and a relatively small sample size in the current work.

Regarding neuroendocrine markers, Chromogranin (CG) expression -in this study –was seen in only in 5 % of pailloma but in 70% of the solid papillary carcinoma and 40% of remaining malignant lesions. The findings of the study reveal that Papilloma exhibits considerably reduced rates of expression for neuroendocrine markers (CG, P >. 05) as compared to malignant lesions.

This result was in agreement with the former study [24] where it was observed that neuroendocrine markers (chromgranin, synaptophysin) were predominantly negative in benign ductal papilloma. In contrast, a positivity rate of 35% was noted in papillary carcinoma. The papillary carcinoma was subdivided into solid type and non-solid type, the positivity rate for solid type was 67% and for non-solid type was 8%. our findings are consistent with those of a previous study [26] wherein a significant level of chromogranin positivity was detected in solid papillary carcinoma of the breast.

Former investigation [16] found that there was a significantly lower expression of chromogranin for benign papillary breast lesions than malignant papillary breast lesions (P=.05) which came in parallel to the result of our study.

The current investigation reports a significant difference in the expression rate of ER between papilloma and various types of malignant lesions such as DCIS, solid papillary carcinoma, intracystic papillary carcinoma, and invasive micropapillary carcinoma (P <.01). Specifically, ER expression in papilloma were 10%, whereas it was observed to be markedly higher in malignant lesions accounting for 92%, 90%, 92. 3%, and 100% for DCIS, solid papillary carcinoma, intracystic papillary carcinoma, and invasive micropapillary carcinoma, respectively.

This result was in parallel with the result of prior study [24] which found in papillary breast lesions, the benign areas revealed significantly lower expression rates for hormone receptor ER (ER, P=.002) than malignant lesions. And also, our result came in agreement with earlier research [7] which illustrated heterogenous positivity of ER in papilloma and showed strong positivity of ER in DCIS, solid papillary carcinoma, encapsulated papillary carcinoma and invasive micropapillary carcinoma.

The present study has demonstrated that P63, a myoepithelial marker, exhibits 100% specificity and 78% sensitivity in differentiating papillomas from malignant papillary neoplasms. The expression rate of P63 is therefore considered to be a reliable indicator for distinguishing benign and malignant papillary lesions. In contrast, SMA is found to be capable of detecting myoepithelial cells in benign papillary breast lesions with 95% accuracy, but its sensitivity is only 63% in both non-invasive and invasive malignant papillary lesions, which is consistent with the findings of previous studies [27, 28]. The former studies found that SMA was less sensitive than p63 in differentiating benign from malignant papillary breast lesions with considerable stromal cross reactivity.

Consistent with the present study, former investigation [24] reported specificities of 100% and sensitivities ranging from 73-100% for p63 in distinguishing papilloma from papillary carcinoma, whereas SMA exhibited specificities and sensitivities of 65% and 88%, respectively.

P63 is more sensitive than SMA in detection of myoepithelial cells as the latter one stain vascular smooth muscle cells and myofibroblasts making interpretation difficult while p63 expression was in proximity to the epithelium not have cross reactivity and the reported positive staining for stromal cells was 10% [27].

CK14 is one of the basal cytokeratins which could be used in diagnosis of papillary breast lesions. As it was highly expressed in papilloma with 90% specificity and 89% sensitivity. discriminating it from malignant papillary breast neoplasms. This result came partly in parallel to the result of prior study [24] which found specificity rate was 78-100% and sensitivity rate was 92-100% for papilloma in differentiating it from papillary carcinoma.

The present study has determined that myoepithelial markers (SMA & p63) associated with CK14 exhibit significantly higher expression rates in benign lesions in comparison to malignant lesions as evidenced by ($P < .00$), with high specificity (100%) and low sensitivity (63.3%). It is suggested that combined panel of P63, SMA, and CK14 may be utilized as reliable markers for distinguishing between benign and malignant papillary breast lesions.in agreement with previous work [29] which concluded that CK5/p63/CK8/18 antibody cocktail is a useful adjunct to morphology for evaluating breast papillary lesions.

Chromogranin (CG) is of commonly used neuroendocrine markers, it was found to be negatively expressed in papilloma but highly positive in solid papillary carcinoma with more specificity 95% and less sensitivity 29% respectively. This result was partly parallel to one study [24] which found the neuroendocrine marker was negative in benign papilloma but the sensitivity rate in papillary breast carcinoma was 35%.

Estrogen receptor (ER) could be useful in differentiating papillary breast lesions, as the positive expression rate in papilloma was 10% while in malignant papillary breast lesions was 90-100% with specificity 90 % A preceding study [16] showed that in there was a significant lower expression for ER (P=.002) in benign lesions than in malignant lesions with the expression rate in benign lesions was 44.8% and was 84.2% in malignant lesions

Conclusion:

A combined panel of markers consisting of P63, SMA, CK14, chromogranin and ER- could be helpful in differentiating bengin, atypical and malignant papillary breast lesions which need different interventional treatment modalities. A wider scale study on other variant of invasive papillary lesions is recommended.

No conflict of interest

References:

1. Kashyap D, Pal D , Sharma R, Garg VK , Goel N , Koundal D, et al. Global Increase in Breast Cancer Incidence: Risk Factors and Preventive Measures. BioMed Research International Volume 2022, Article ID 9605439, 16 pages https://doi.org/10.1155/2022/9605439
2. Hamdy A. Azim, Hagar Elghazawy, Ramy M. Ghazy, Ahmed H. Abdelaziz, Marwa Abdelsalam, Amira Elzorkany, et al. Clinicopathologic Features of Breast Cancer in Egypt—Contemporary Profile and Future Needs: A Systematic Review and Meta-Analysis JCO Global Oncology 2023 :9
3. Deshpande AK. Efficacy of immunohistochemistry in diagnosing papillary lesions of the breast..DOI: 10.33545/pathol.2020.v3.i1d. 178.
4. Rehman B , Mumtaz A, Sajjad B, Urooj N, Khan SM, Zahid MT, et al. Papillary Carcinoma of Breast: Clinicopathological Characteristics, Management, and Survival. International journal of breast cancer Volume 2022 | Article ID 5427837 | https://doi.org/10.1155/2022/5427837
5. Rakha EA, Badve S, Eusebi V, Reis-Filho JS, Fox SB, Dabbs DJ,Decker T, et al. Breast lesions of uncertain malignant nature and limited metastatic potential: proposals to improve their recognition and clinical management. Histopathology (2016) Jan 68 (1):45–56.
6. Nuñez DL, González FC, Ibargüengoitia MC, Fuentes Corona RE, Hernández Villegas AC, Zubiate ML, et al. Papillary lesions of the breast: a review. Breast cancer management.2020.VOL 9 ,NO 4.
7. Kulka J , Madaras L , Floris G and Lax SF. Papillary lesions of the breast. Virchows Archiv (2022);480(1):65–84 https://doi.org/10.1007/s00428-021-03182-7 .
8. Alexandre A. Vdovenko. Pathology of breast papillary neoplasms: Community hospital experience. Annals of Diagnostic Pathology (2020)Dec ;49,151605, ISSN 1092-9134, https://doi.org/10.1016/j.anndiagpath.2020.151605.
9. Rakha EA and Ellis IO .Diagnostic challenges in papillary lesions of the breast. Pathology (2018)Jan;50(1):100–110.
10. Yunbi Ni and Gary M Ts.Papillary lesions of the breast – review and practical issues. Seminars in Diagnostic Pathology (2022) September ;39(5) : 344-354.
11. Pernick N. p63. PathologyOutlines.com website. ://www.pathologyoutlines.com/topic/stainsp63.html. Accessed February 16th, 2023.
12. Kösemehmetoğlu K and Johnson G. Actin, alpha smooth muscle type. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/stainsalphasmoothmuscleactin.html. Accessed April 24th, 2023.
13. Pernick N. Cytokeratin 14 (CK14, K14). PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/stainsck14.html. Accessed April 24th, 2023.
14. Lin X, Matsumoto Y, Nakakimura T, Ono K, Umeoka S, Torii M, et al. Invasive solid papillary carcinoma with neuroendocrine differentiation of the breast: a case report and literature review. Surg Case Rep. (2020) Jun 19;6(1):143. doi: 10.1186/s40792-020-00905-x. PMID: 32562013; PMCID: PMC7305294.
15. Pernick N. Estrogen receptor. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/stainser.html. Accessed April 24th, 2023.
16. Tse GM, Ni YB, Tsang JY, Shao MM, Huang YH, Luo MH, et al. Immunohistochemistry in the diagnosis of papillary lesions of the breast. Histopathology. (2014) Dec;65(6):839-53. doi: 10.1111/his.12453. Epub 2014 Oct 30. PMID: 24804569.
17. K S, Patil RK, Haravi RM,. Patil P and Anand DR. Expression of p63 in Breast Lesions – A Cross Sectional Study. European Journal of Molecular & Clinical Medicine (EJMCM) (2022);9(6) ISSN: 2515-8260.
18. Rani R, Rao A C K, Biswas S and K M . IP Journal of Diagnostic Pathology and Oncology (2022);7(1):60–63.
19. Rupali Bavikar, Sanjay Deshmukh, Tejal .Spectrum of papillary lesions of breast

with immunohistochem and review of literature .Indian Journal of Pathology and Oncology. (2017) January-March;4(1):52-55.

20. Hemrajani Deepika , Hemrajani Deepika , Nehra Pritika , Choudhary Nikita, Harsh Anita . Diagnostic Evaluation of the Papillary Lesions of the Breast. Saudi J Pathol Microbiology. (2021);6(10): 329-336.
21. K S, Patil RK, Haravi RM,. Patil P and Anand DR. Expression of p63 in Breast Lesions – A Cross Sectional Study. European Journal of Molecular & Clinical Medicine (EJMCM) (2022);9(6) ISSN: 2515-8260.
22. Nicolas MM, Wu Y, Middleton LP and Gilcrease MZ. Loss of myoepithelium is variable in solid papillary carcinoma of the breast. Histopathology. (2007)Nov;51(5):657-65. doi: 10.1111/j.1365-2559.2007.02849.x. PMID: 17927587.
23. Maeda I, Tajima S, Kanemaki Y, Tsugawa K and Takagi M. Use of immunohistochemical analysis of CK5/6, CK14, and CK34betaE12 in the differential diagnosis of solid papillary carcinoma in situ from intraductal papilloma with usual ductal hyperplasia of the breast. SAGE Open Med. (2018) Nov 9;6:2050312118811542. doi: 10.1177/2050312118811542. PMID: 30455948; PMCID: PMC6236862.
24. Tse GM, Tan PH, Moriya T. The role of immunohistochemistry in the differential diagnosis of papillary lesions of the breast. J Clin Pathol. 2009 May;62(5):407-13. doi: 10.1136/jcp.2008.063016. Epub 2009 Jan 6. PMID: 19126567.
25. Tan PH, Aw MY, Yip G, Bay BH, Sii LH, Murugaya S, et al. Cytokeratins in papillary lesions of the breast: is there a role in distinguishing intraductal papilloma from papillary ductal carcinoma in situ? Am J Surg Pathol. (2005) May;29(5):625-32. doi: 10.1097/01.pas.0000157941.88161.39. PMID: 15832086.
26. Jadhav T, Prasad SS, Guleria B, Tevatia MS and Guleria P. Solid papillary carcinoma of the breast. Autops Case Rep. (2022) Jan 13;12:e2021352. doi: 10.4322/acr.2021.352. PMID: 35096664; PMCID: PMC8796863
27. Tse GM, Tan PH, Lui PC, Gilks CB, Poon CS, Ma TK, et al. The role of immunohistochemistry for smooth-muscle actin, p63, CD10 and cytokeratin 14 in the differential diagnosis of papillary lesions of the breast. J Clin Pathol. (2007) Mar;60(3):315-20. doi: 10.1136/jcp.2006.036830. Epub 2006 May 12. PMID: 16698948; PMCID: PMC1860581.
28. Ichihara S, Fujimoto T, Hashimoto K, Moritani S, Hasegawa S and Yokoi T. Double immunostaining with P63 and high-molecular-weight cytokeratins distinguishes borderline papillary lesions of the breast. Pathol Int (2007)Mar;57(3):126-132.
29. Emily S. Reisenbichler, ,Amy L. Adams, Omar Hameed .The Predictive Ability of a CK5/p63/CK8/18 Antibody Cocktail in Stratifying Breast Papillary Lesions on Needle Biopsy. Am J Clin Pathol (2013);140:767-779

To cite this article: Omneya Y. Bassyoni, Zeinab I. Elshawarby , Ahmed M. Abostate. Diagnostic Significance of Immunohistochemistry in Papillary Breast Neoplasms. BMFJ 2023; 40(2): 516-527.