



Case Report

Ductal papilloma with atypical ductal hyperplasia – Understanding the importance of immunohistochemistry- A case report

Nisarga Rani R^{1,*}, Anuradha C K Rao², Siddhartha Biswas¹, Madan K¹

¹Dept. of Oncopathology, Yenepoya Medical College, Mangalore, Karnataka, India

²Dept. of Pathology, Yenepoya Medical College, Mangalore, Karnataka, India



ARTICLE INFO

Article history:

Received 12-01-2022

Accepted 21-01-2022

Available online 28-02-2022

Keywords:

Ductal papilloma

ADH

Proliferative breast disease

ABSTRACT

Solitary intraductal papilloma of the breast is a common benign mammary proliferative disease and is the most common neoplasm associated with nipple discharge in women. Women with solitary papillomas have 1.5-2.0 times increased risk of developing invasive carcinoma. The papillary lesions of the breast include a broad spectrum of disorders from benign papilloma, atypical papilloma to papillary carcinoma. Benign papilloma on core needle biopsy has been found to have concurrent malignancy in about 3–5% of cases at excision. Solid papillomas commonly pose a diagnostic dilemma due to similarities with other ominous papillary lesions. The presence of ADH within a papilloma and/or in the surrounding breast is associated with an increased risk of recurrence or invasive carcinoma. The present study undertakes to fully describe the morphological changes occurring within the epithelial component of central papillomas and to search for factors of prognostic significance concerning recurrence, progression and differentiation of atypical ductal hyperplasia.

This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprint@ipinnovative.com

1. Introduction

Solitary intraductal papilloma of the breast is a common benign mammary proliferative disease and is the most common neoplasm associated with nipple discharge in women. Women with solitary papillomas have 1.5-2.0 times increased risk of developing invasive carcinoma.¹

The papillary lesions of the breast include a broad spectrum of disorders from benign papilloma, atypical papilloma to papillary carcinoma. Benign papilloma on core needle biopsy has been found to have concurrent malignancy in about 3–5% of cases at excision.²

Solid papillomas commonly pose a diagnostic dilemma due to similarities with other ominous papillary lesions.

The presence of ADH within a papilloma and/or in the surrounding breast is associated with an increased risk of

recurrence or invasive carcinoma.

The present study undertakes to fully describe the morphological changes occurring within the epithelial component of central papillomas and to search for factors of prognostic significance concerning recurrence, progression and differentiation of atypical ductal hyperplasia.³

2. Case Presentation

A 32 year female came with complaints of nipple discharge and mass in retroareolar region since 6 months. On examination 2x2 cm mass was noted in retroareolar region with pale yellow serous nipple discharge on squeezing. FNAC done suggested benign proliferative breast disease. Patient underwent microdocheotomy procedure.

Specimen received for histopathological examination measured 4x3x2.5cm with an irregular external surface and adjoining adipose tissue. Cut surface showed a

* Corresponding author.

E-mail address: nisarga.rani91@gmail.com (N. Rani R).

circumscribed, lobulated tumour measuring 2x1.5x1.5cm. The lesion was solid, pale white, lobulated and firm in consistency. Sections were given, processed and stained with H&E.

On microscopy multiple sections studied from the breast tumour showed a large dilated duct filled with an intraluminal papillary lesion with multiple small solid foci. Adjacent multiple smaller dilated ducts with focal luminal papillary lesions were noted. The papillary lesion were lined by bilayered epithelium, outer myoepithelial and inner luminal cells with focal myoepithelial proliferation, apical snouts and apocrine change. Also noted in the largest lesion were focal solid areas comprising cells with variable amount of cytoplasm along with myoepithelial cells, suggestive of usual ductal hyperplasia. Within these were small foci of atypical ductal hyperplasia comprising of solid sheets with monomorphic cells and showing mild atypia. Final impression given as Papillary lesion of breast- Papilloma with usual ductal hyperplasia.

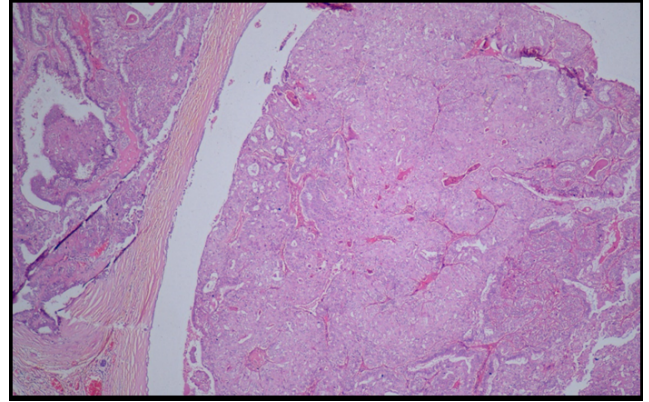


Fig. 3: Ductal papilloma with ductal hyperplasia. (H&E, 100x)

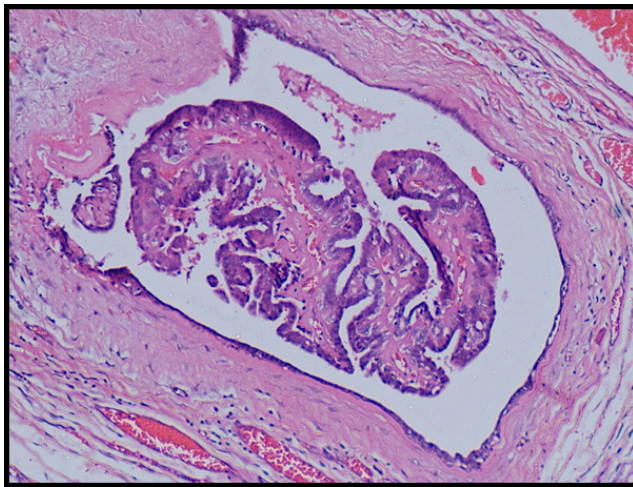


Fig. 1: Duct showing papillary architecture. (H&E, 100x)

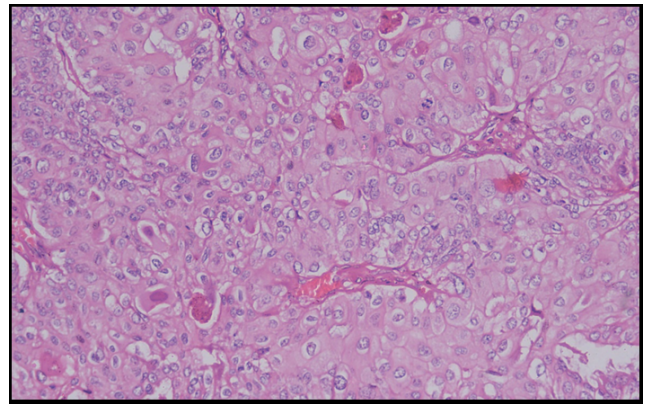


Fig. 4: Papilloma with ductal hyperplasia areas showing absence of myoepithelial cells at places. (H&E, 400x)

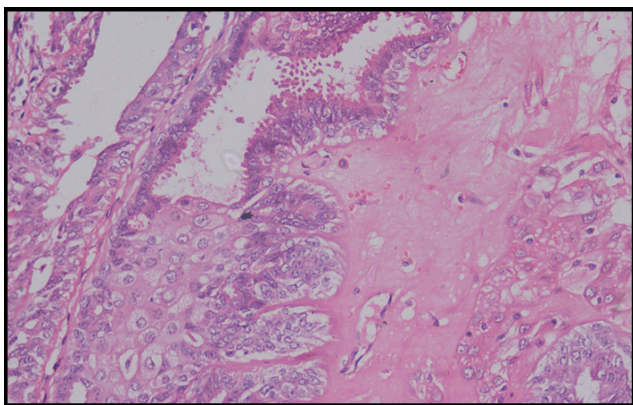


Fig. 2: Duct lined by inner epithelial cells and outer myoepithelial throughout the duct. (H&E, 400x)

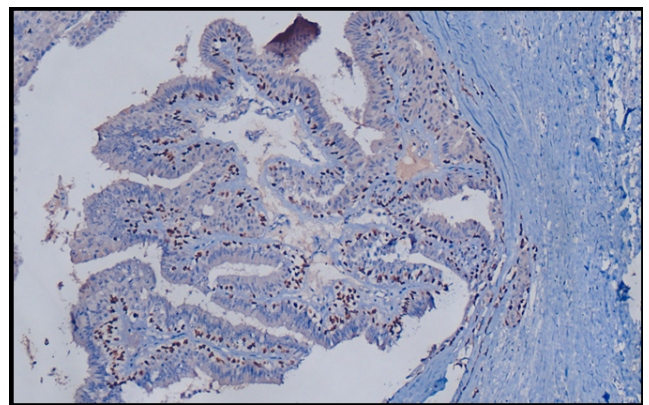


Fig. 5: p63 nuclear positive myoepithelial cells throughout the papillary structure. (100x)

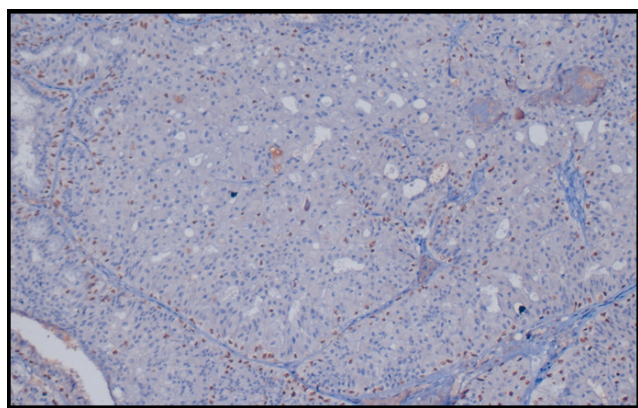


Fig. 6: Immunohistochemistry, in the areas of ductal hyperplasia expression of p63 is absent at places. (100x)

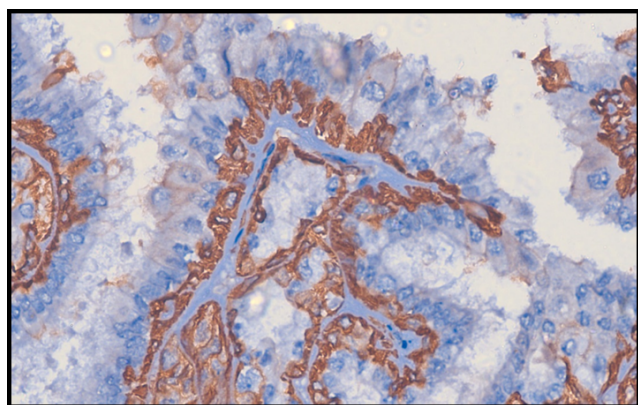


Fig. 7: Immunohistochemistry, diffusely cytoplasmic expression of SMA noted in myoepithelial cells.(400x)

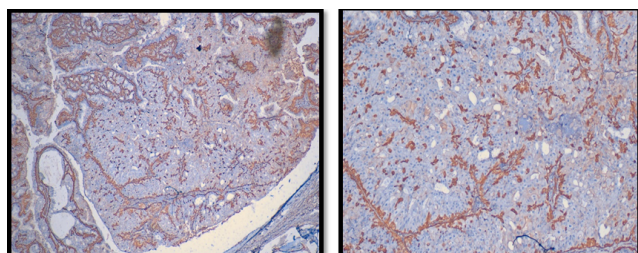


Fig. 8: Immunohistochemistry, absence of SMA expression at places in the areas of ductal hyperplasia is noted.(100x)

For confirmation immunohistochemistry p63 and SMA were done. Both were diffusely positive in myoepithelial cells. Estrogen receptor (ER) was also performed. The foci corresponding to ADH on H&E showed fewer p63 positive myoepithelial cells and a higher concentration of ER positive cells (Allred score 8), confirming the presence of microfoci of ADH (Figures 1, 2, 3, 4, 5, 6, 7 and 8). The diagnosis was subsequently revised to include microfoci of ADH.

3. Discussion

Most solitary papillomas occur centrally in the large subareolar ducts. The consensus opinion of the College of American Pathologists is that solitary papillomas are associated with a slightly increased risk of breast carcinoma, but this relationship remains controversial.¹

Nipple discharge of less than 6 months' duration as seen in the present case is the most common and dominant clinical sign associated with breast papillomas, and is seen in 64-88% of patients. Typically this discharge is sanguineous, but various studies have shown that a significant percentage (29-48%) of patients have only serous discharge.¹

Papillomas are typically not seen on mammograms because of their small size, lack of associated calcification or fibrosis, and intraductal location. Mammographic findings that may be present include benign-appearing circumscribed masses of various sizes (typically retroareolar in location), a solitary dilated retroareolar duct, and rarely, calcifications. Mammographically identified calcifications within a papilloma may be rounded, crescentic, or eggshell like but can have other appearances indistinguishable from clustered microcalcifications seen in malignant lesions.¹

MRI was reported to have a higher sensitivity in defining the number and the extent of the papillary lesions than mammography and ultrasound.⁴

Breast intraductal papilloma is characterized by a finger-like fibrovascular core lined by epithelial and myoepithelial cells either occurring within the epithelial component of an otherwise benign papilloma or in adjacent foci. An intraductal papilloma can be subject to a spectrum of morphological changes ranging from metaplasia to usual ductal hyperplasia (UDH), atypical hyperplasia (ADH) or could co exist with similar lesions in adjoining in the breast across the broad spectrum of benign, high risk and malignant lesions.¹

Benign papilloma with or without benign proliferative lesions is managed conservatively with close observation. In contrast, papilloma with malignant lesions warrants complete surgical excision. Papilloma with high-risk lesions, which is associated with a significant risk of breast cancer, is also recommended for complete surgical excision. Therefore, it is essential to differentiate between benign papilloma and papilloma with high-risk or malignant lesions.⁴

Immunohistochemistry is essential in distinguishing small foci of ADH from UDH in intraductal papilloma, necessitated as ADH falls into the high risk category. UDH shows high expression of basal (CK 5/6), myoepithelial (p63) and absent ER, focally/ weakly expressed in ADH/DCIS. Estrogen receptor (ER) further aids in this differentiation, as clonal cell expansion in ADH/DCIS causes a diffuse often strong expression, whereas it

is scattered in UDH reflecting the normal breast ER expression.⁵

The present case showed foci of strong expression of ER, typically representing areas of ADH in a background showing dispersed and variable ER expression.

4. Conclusion

Intraductal papilloma is the commonest amongst the broad spectrum of mammary gland papillary lesions. The morphological spectrum of changes that can often occur within this lesion requires a careful scrutiny of multiple sections. Applications of basal markers and estrogen receptor by immunohistochemistry aid substantially in conclusive and confirmatory diagnosis of high risk foci, as evidenced in this case.

5. Conflict of Interest

The authors declare that there is no conflict of interest.

6. Source of Funding

None.

References

1. Woods ER, Helvie MA, Ikeda DM, Mandell SH, Chapel KL, Adler DD, et al. Solitary breast papilloma: Comparison of mammographic, galactographic and pathologic findings. *AJR Am J Roentgenol.* 1992;159(3):487–91. doi:10.2214/ajr.159.3.1503011.
2. Moon HJ, Jung I, Kim MJ, Kim EK. Breast papilloma without atypia and risk of breast carcinoma. *Breast J.* 2014;20(5):525–33. doi:10.1111/tbj.12309.
3. Grogan MC, Tavassoli FA. Central atypical papillomas of the breast: a clinicopathological study of 119 cases. *Virchow Arch.* 2203;443(5):609–17. doi:10.1007/s00428-003-0888-x.
4. Wang LJ, Wu P, Li XX, Luo R, Wang DB, Guan WB, et al. Magnetic resonance imaging features for differentiating breast papilloma with high risk or malignant lesions from benign papilloma: a retrospective study on 158 patients. *World J Surg Oncol.* 2018;16(1):234. doi:10.1186/s12957-018-1537-9.
5. Liu H. Application of Immunohistochemistry in Breast Pathology: A Review and Update. *Arch Pathol Lab Med.* 2014;138(12):1629–42. doi:10.5858/arpa.2014-0094-RA.

Author biography

Nisarga Rani R, Fellow

Anuradha C K Rao, Professor

Siddhartha Biswas, Professor and HOD

Madan K, Assistant Professor

Cite this article: Rani R N, Rao ACK, Biswas S, Madan K. Ductal papilloma with atypical ductal hyperplasia – Understanding the importance of immunohistochemistry- A case report. *IP J Diagn Pathol Oncol* 2022;7(1):60-63.