



Original Research Article

Observational study to compare histologically confirmed benign and malignant papillary neoplasm with demographic parameters and features of neoplasm

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ABSTRACT

Background: Papillary lesions of the breast encompass a wide spectrum of benign and malignant entities. Cytological interpretation of these is difficult and they top the list of conditions with a risk of false-positive diagnosis. Understanding the correlation of histologically confirmed benign and malignant papillary neoplasm with demographic parameters and features of neoplasm will help to distinguish the different lesions.

Aims and Objectives: To compare histologically confirmed benign and malignant papillary neoplasm with demographic parameters and features of neoplasm

Materials and Methods: A retrospective study was performed from January 2010 to December 2015 in the cytology section, Department of Pathology of a tertiary care and referral hospital including patients diagnosed as papillary lesion on FNAC. Histopathological follow-up was available for total 44 cases. A total of 44 breast aspirates and their corresponding histology were reviewed.

Results: Majority of the patients with benign and malignant neoplasm had age between 41-50 years (33%) and 51-60 years. All patients with benign neoplasm were women whereas among patients with malignant neoplasm 12 were women and one was a man. Benign papilloma, 36.3% cases showed cellular smear, followed by 27.2% showed moderate cellularity. Malignant papillary lesions, cases showed both cellular and moderate cellularity.

Conclusion: Papillary carcinoma is an infrequent histologic subtype of breast carcinoma. Cytological diagnosis of the lesion is difficult due to overlap with benign entity and other mimics.

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1. Introduction

There are two types of papillary lesions of the breast which are benign called as duct papilloma (DP) and malignant known as papillary carcinoma (PC).¹ Both types are characterized by the presence of fibro-vascular cores (FVC) which are lined by epithelial proliferation with varying degrees of atypia.^{2,3}

Excision biopsy can be performed for the definite diagnosis of the nature of tumour. However, clear difference cannot be made on aspiration cytology. This occurs due to

the overlapping of cytological features among both benign and malignant papillary lesions.⁴

Previous authors have tried to differentiate the cytological features of both benign and malignant papillary breast lesions.^{4,5} Among the malignant lesion high cellularity, complex branching papillary fragments and single atypical intact cells are the common features.⁴ However, these features have not been found to be restricted to the malignant tumours.⁶ Hence a certain diagnosis of papillary breast carcinoma on aspiration cytology is usually not possible. That's why it is important to understand different features of both types of lesion and its correlation with different demographic and clinical parameters.

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Hence, present study is planned to compare histologically confirmed benign and malignant papillary neoplasm with demographic parameters and features of neoplasm.

2. Materials and Methods

The present study was undertaken retrospectively from January 2010 to December 2015 in the cytology section, Department of Pathology of a tertiary care and referral hospital.

2.1. Inclusion criteria

All the case which have been diagnosed as papillary lesion on FNAC and also all the lesions which are diagnosed as papillary lesions of breast on histopathology, which have not been diagnosed as papillary lesion on FNAC. So false negative test would not be missed.

2.2. Exclusion criteria

Lesions diagnosed as non-papillary lesions on both FNAC and histopathology.

Total 84 cases were found. Which includes 44 cases which had histopathology follow-up, 36 cases which didn't had follow-up. 4 cases were removed because of non-availability of slides. Thus, a total of 44 breast aspirates and their corresponding histology were reviewed.

Age, sex, clinical feature, site, location, size wise distribution done on total 60 cases diagnosed as papillary lesion on cytology but didn't have follow up and cases confirmed as papillary lesion on histopathology, and also the cases which had confirmed papillary lesion on histopathology. All the observations were done on total 44 cases.

Final age, sex, clinical features and cytological feature were compared between total 24 cases which include true positive and false negative cases.

Data sheet was completed for each patient. Data sheet contained various identification details of patient, clinical presentation (breast lump, pain, nipple discharge etc.), radiological findings, local examination, microscopic (Cytology) findings, final Impression, histopathology diagnosis and review cytopathology and histopathology diagnosis.

Parameters that will be used to determine utility of FNAC for diagnosing papillary lesions of breast included background (blood, calcification, single scattered columnar cells, hemosiderin laden macrophages), cellular features (cellularity, dissociation, nuclear atypia (focal and diffuse-mild (1+), moderate (2+), severe (3+), cell morphology, e.g., apocrine, columnar), and tissue fragments (long finger-like branching fragment (complex vs. simple branching, presence of fibro-vascular cores), complex fragments, other than papillary, cellular balls, single detached papillae).

Sampling was performed by the pathologist using FNAC. Ultrasound guided FNACs was performed for non-palpable and small lump. Cytology slides were prepared and stained. Clinical history and notes were obtained from cytology section in Department of Pathology and Medical record department. All these cytology slides were retrieved and reviewed whenever possible.

All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was performed to prepare the tables. The statistical calculations were based on histopathological outcome and sensitivity and specificity was calculated.

3. Results

Majority of the patients with benign neoplasm had age between 41-50 years (33%) which ranged from 14 to 60 years whereas majority of the patients with malignant neoplasm had age between 51-60 years which ranged from 37 to 80 years.

All patients with benign neoplasm were women whereas among patients with malignant neoplasm 12 were women and one was a man. This indicate that in male malignancy is more common than benign papillary lesions. In benign and malignant both most common presentation was breast lump, nipple discharge was more common in benign lesions as compared to malignant.

Most of the benign tumours were located in upper outer quadrant (UOQ) region. Most of the malignant tumours were located in central region.

The benign tumours ranged in size from 1 to 3 cm, with an average maximal diameter of 1.4 cm. The malignant tumours ranged in size from 1-8 cm. Maximum number of cases size was more than 2 cm.

4. Discussion

In present study benign papillary lesion were found in the age group of 14-60 years (average 43 year), which was similar to the study conducted by Jeffery et al where age ranged from 23-69 years (average 43 year).⁷ In the study conducted by Gomez et al mean age of benign papillary lesions was 49 years.⁸

In present study malignant papillary lesion were found in the age group of 37-80 years which is in line with the study conducted by Jeffery et al where age ranged from 37-81years.⁷ In the study conducted by Gomez et al average age of malignant papillary lesions was 66 years.⁸

In our study all benign papillary lesion patients were female which is in line with the study done by Jeffery et al (6 cases).⁷ In our study almost all malignant papillary lesions were present in female only one lesion was seen in male. In the study done by Jeffery et al one malignant papillary lesion was seen in a male patient (5 cases).⁷

Table 1: Comparison of benign and malignant cases

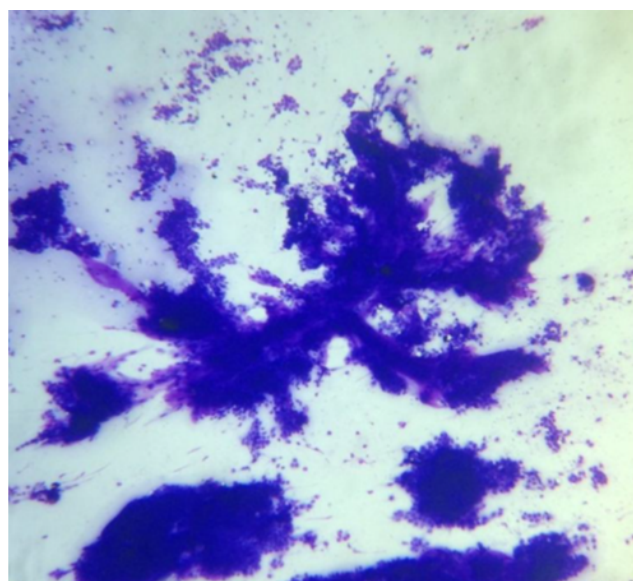
Features	Benign (n=11)	Malignant (n=13)
Cellular (3+)	4 (36.3%)	6 (46.1%)
Moderately cellular(2+)	3 (27.2%)	4 (30.76%)
Pauci-cellular (1+)	4 (36.3%)	0 (0%)
True papillae/Fibrovascular core	7/8 (63.6/72.7%)	9 (69.2%)
Papillaroid fragment-Simple branching	6 (55.5%)	0 (0%)
Papillaroid fragment-Complex branching	1 (9.1%)	9 (69.2%)
Complex sheet	7 (63.6%)	4 (30.76%)
Cell ball	1 (9.1%)	2 (15.38%)
Dis-cohesion	1 (9.1%)	10 (76.9%)
Single cell atypia	0 (0%)	7 (53.8%)
Columnar cell	5 (45.4%)	7 (53.8%)
Fibrovascular core-Thick	7 (63.6%)	1 (7.6%)
Fibrovascular core-Thin	1 (9.1%)	8 (61.5%)
Stromal fragment	0 (0%)	0 (0%)
Cyst macrophages	4 (36.3%)	2 (15.38%)
Atypia- 3+	0 (0%)	8 (61.5%)
2+	1 (9.1%)	2 (15.38%)
1+	1 (9.1%)	1 (7.6%)
Focal/ Degenerative atypia	4/1 (36.3/9.1%)	0/0 (0%)

In our study, we found that benign papillary lesions were located in peripheral area. Malignant papillary tumours were located in central region. However, reports of Jeffery et al are not in line with the findings of present study.⁷

In present study the benign papillary tumours ranged in size from 1 to 3 cm, with an average diameter of 1.4 cm. In the study conducted by Jeffery et al the benign papillary tumours ranged in size from 1 to 2 cm, with an average diameter of 1.5 cm.⁷ In the study conducted by Gomez et al the average size of benign papillary tumours was 1.3 cm.⁸ which are in line with the present study findings. The malignant papillary tumours ranged in size from 1 to 8 cm, with an average diameter of 4.5 cm. In the study conducted by Jeffery et al the malignant papillary tumours ranged in size from 3 to 10 cm, with an average diameter of 5 cm.⁷ Similarly in the study conducted by Gomez et al the average diameter of tumours was 3.5 cm.⁸

Thick fibro-vascular core (Figure 1) was seen in benign papillary lesions and thin fibrovascular core (Figure 2) in malignant papillary lesions. In benign papillary lesion simple branching papillae were seen in comparison with malignant papillary lesions which showed complex branching papillae (Figure 3). Study done by Michael and Buschmann also shows similar features.⁹

In our study 72% benign papillary lesions show true papillae. In 3 cases where papillae were not seen, cellularity was scanty (sampling error). Study done by Gita Jayaram, 94.7% benign cases showed papillary pattern. Author did not mention whether these were true papillae or they were papillaroid fragments.¹⁰ In our study 69% (9/13 cases) of malignant papillary lesions showed true papillae. Out of 4 cases of malignant papillary lesions which did not show true papillae, 2 cases were micro-papillary carcinoma and

**Fig. 1:** Papilla with thick fibro-vascular core (Giemsa 10x)

two cases showed sampling error (scanty cellularity). Gita Jayaram reported that 100% cases showed papillary pattern. True papillae are specific features in diagnosis of papillary lesions.¹⁰

In our study, as well as in the study by Gita Jayaram columnar cells were seen in benign and malignant papillary lesions and also in duct carcinoma and fibroadenoma. Our study showed higher percentage of cases with columnar cells in comparison to the study by Gita Jayaram.¹⁰

Gita Jayaram in her study has said that the presence of columnar epithelial cells is not a distinguishing feature in

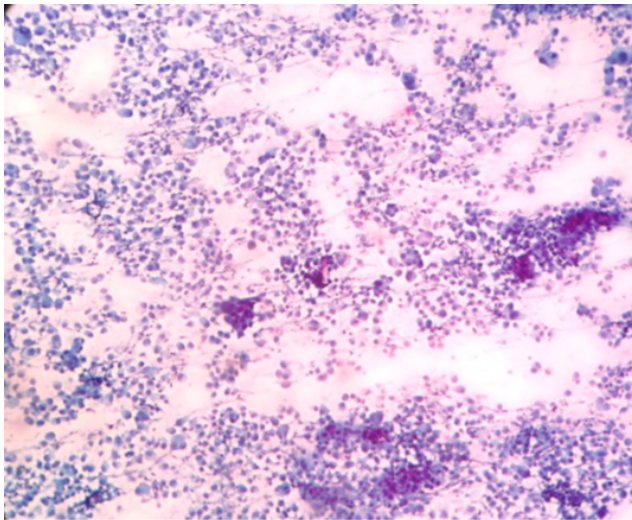


Fig. 4: Dis-cohesion with diffuse atypia (Pap 10X)

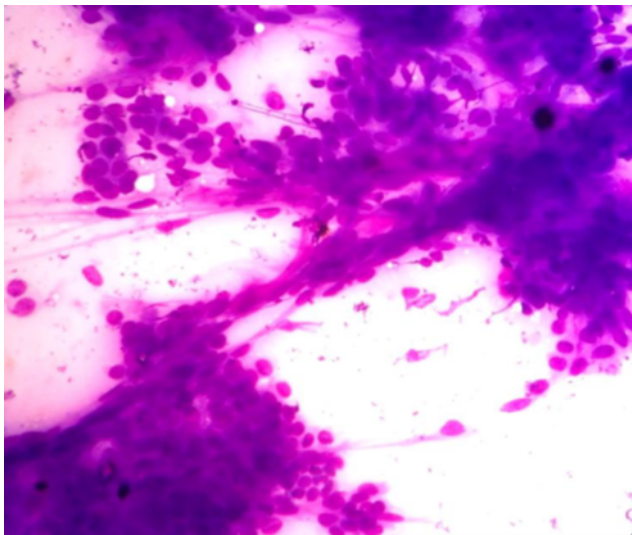


Fig. 2: Papilla with thin fibro-vascular core (Giemsa 40x)

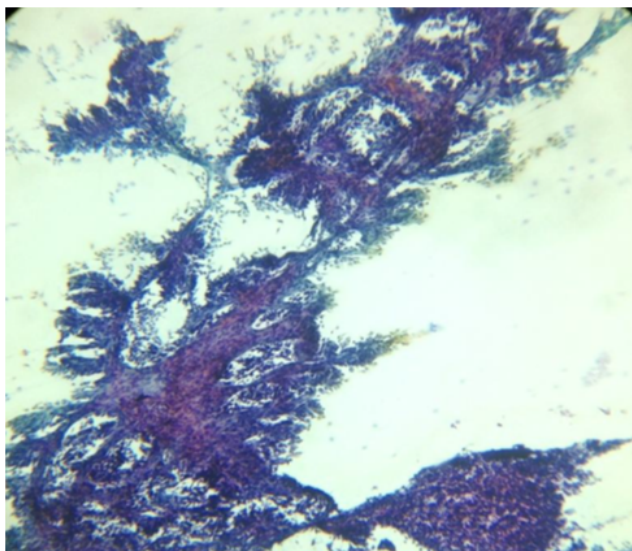


Fig. 3: Complex branching papillae (Pap 40x)

differentiating benign from malignant papillary lesions. We want to point out that columnar cells are seen in papillary as well as non-papillary lesions and their presence or absence does not help in differentiating benign papillary lesions from malignant papillary lesions.¹⁰ Presence of columnar cell is not a specific feature for diagnosis of papillary lesions of breast on FNAC.

In our study 75% cases of malignant papillary lesions showed both dis-cohesion and diffuse atypia (Figure 4). Cases of DP also showed atypia but it was focal and if diffuse it was mild and some cases also showed degenerative atypia. We found that prominent cell dis-cohesion and diffuse (2+ and 3+) atypia is an important distinguishing feature in differentiating PC from DP. Cellularity is not a useful feature to differentiate malignant papillary lesions from benign papillary lesions. The overall incidence of false positive was 25% and false negative was 13.75%. Sensitivity of FNAC to diagnose papillary lesions was 54.1%.

Being a cross sectional nature of the study, present study findings cannot be applied to large population, there is a need of a large randomized clinical trial to provide strength to present study findings.

5. Conclusion

Based on the present study findings we can conclude that papillary carcinoma is an infrequent histologic subtype of breast carcinoma. Cytological diagnosis of the lesion is difficult due to overlap with benign entity and other mimics. Hence, cytopathologists need to be aware of the features helpful in distinction between benign and malignant papillary lesions.

6. Source of Funding

None.

7. Conflict of Interest

None.

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