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Research Article

Cytomorphological Spectrum of Rare Breast Malignancies: A Cyto-Histopathological Correlation Study

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ABSTRACT

Background: Rare breast malignancies comprise a heterogeneous group of tumors with distinctive histopathological features and variable clinical behavior. Although fine-needle aspiration cytology (FNAC) is widely used for the initial evaluation of breast lesions, diagnosis of uncommon malignancies may be challenging because of overlapping cytomorphological features. Histopathological examination and immunohistochemistry (IHC) therefore play an important role in confirming the diagnosis and subclassifying these lesions.

Objectives: To evaluate the cytomorphological features of rare breast malignancies and to correlate FNAC findings with histopathological and immunohistochemical findings.

Materials and Methods: A retrospective and prospective observational study was conducted over 1½ years from July 2022 to December 2023. Twelve patients with confirmed rare breast malignancies, including mucinous carcinoma, papillary carcinoma, metaplastic carcinoma, metastatic malignant melanoma, non-Hodgkin lymphoma, invasive ductal carcinoma with medullary pattern, and tubular carcinoma, were included. Patients lacking either cytological or histopathological data were excluded. FNAC smears were stained with

Wright's, hematoxylin and eosin, and Papanicolaou stains. Histopathological examination was performed on biopsy or surgical specimens, with IHC applied wherever required. Cytological diagnoses were correlated with histopathological diagnoses.

Results: The patients ranged from 35 to 75 years, with the highest proportion in the 41–50-year age group (33.3%), followed by 51–60 years (25.0%). Mucinous carcinoma was the most frequent malignancy, accounting for 5 cases (41.7%), followed by papillary carcinoma in 2 cases (16.7%). Metaplastic carcinoma, metastatic malignant melanoma, non-Hodgkin lymphoma, invasive ductal carcinoma with medullary pattern, and tubular carcinoma each accounted for one case (8.3%). FNAC correctly identified 11 of 12 cases, yielding an overall cytology-histopathology diagnostic concordance of 91.7%. Complete concordance was observed in mucinous carcinoma, metaplastic carcinoma, metastatic malignant melanoma, non-Hodgkin lymphoma, and tubular carcinoma. The two cases reported as suspicious for papillary neoplasm on FNAC were confirmed as encapsulated papillary carcinoma and invasive papillary carcinoma on histopathology. One case of invasive ductal carcinoma with medullary pattern was interpreted as IDC, NOS on FNAC because of limited lymphoplasmacytic infiltrate and indistinct glandular architecture.

Conclusion: FNAC demonstrated high diagnostic concordance with histopathology in rare breast malignancies and remains a valuable tool for their initial evaluation. Recognition of characteristic cytomorphological patterns can facilitate accurate diagnosis; however, close histopathological and immunohistochemical correlation is essential, particularly in lesions with overlapping cytological features. An integrated cyto-histopathological approach can improve diagnostic accuracy and aid appropriate clinical management.

Keywords: Rare breast malignancies; Fine-needle aspiration cytology; Cytomorphology; Histopathology; Immunohistochemistry; Diagnostic concordance.

Introduction

Breast cancer encompasses a wide spectrum of histologic subtypes, with invasive ductal carcinoma (IDC) being the most prevalent. However, a subset of breast malignancies presents with rare histopathological features, including metaplastic carcinoma, metastatic

tumors to the breast, primary breast lymphoma (particularly non-Hodgkin lymphoma), papillary carcinoma, IDC with medullary features, tubular carcinoma, and mucinous carcinoma. These entities not only differ in clinical behavior and prognosis but also pose significant diagnostic challenges, especially on fine-needle aspiration cytology (FNAC).[1]

This study aims to analyze and correlate the cytomorphological features with histopathological findings of these rare breast malignancies. [2]

Objectives

- To evaluate the cytomorphological features of rare breast malignancies.
- To correlate cytologic findings with histopathological and immunohistochemical features.

Materials and Methods

Study Design: Retrospective and prospective observational study.

Study Period: 1 and ½ years (from July 2022 to December 2023)

Sample Size: 12 of rare breast malignancies.

Inclusion Criteria: Patients with confirmed diagnoses of metaplastic carcinoma, metastatic tumors to breast, NHL, papillary carcinoma, IDC with medullary pattern, tubular carcinoma, and mucinous carcinoma.

Exclusion Criteria: Cases lacking either cytology or histopathology data.

Procedure: All patients underwent FNAC followed by biopsy or surgical excision. Cytology smears were stained using Wright's, H&E and Papanicolaou stains. Histopathology was performed using H&E staining, and IHC markers were used as appropriate for diagnosis and subtype classification.

Statistical Analysis

Data collected from the study were entered into Microsoft Excel and subsequently analyzed using appropriate statistical software. Categorical variables, including age groups, histopathological diagnosis, cytological diagnosis, cytomorphological characteristics, and immunohistochemical findings, were summarized using frequencies and percentages. Continuous variables, such as age, were expressed as mean ± standard deviation (SD) or median with range, as appropriate.

The distribution of rare breast malignancies according to histopathological subtype was presented using frequency and percentage. The findings of FNAC were compared with the corresponding histopathological

diagnosis to assess cyto-histopathological concordance. Diagnostic concordance was calculated as the proportion of cases in which the cytological diagnosis agreed with the final histopathological diagnosis.

Where applicable, a 2 × 2 contingency table was used to calculate diagnostic performance parameters of FNAC, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. However, these parameters were interpreted cautiously because of the small sample size and the presence of multiple rare histological subtypes.

The level of agreement between cytological and histopathological diagnoses was assessed using percentage concordance. Where sufficient observations were available, the Cohen's kappa coefficient (κ) was considered for assessment of categorical agreement. A two-sided p-value <0.05 was considered statistically significant. Due to the small sample size and predominantly descriptive nature of the study, inferential statistical testing was limited and emphasis was placed on descriptive findings and clinicopathological correlation.

Statistical software: Data were analyzed using IBM SPSS Statistics, with appropriate version specified according to the software used by the investigators

.

Results

Table 1. Age Distribution of Patients (n = 12)

Age Group (Years)	Number of Cases	Percentage (%)
31–40	2	16.7
41–50	4	33.3
51–60	3	25
61–70	2	16.7
71–80	1	8.3
Total	**12**	**100**

A total of 12 cases of rare breast malignancies were included in the study. The patients ranged in age from 35 to 75 years. The highest proportion of cases belonged to the 41–50 years age group (33.3%), followed by the 51–60 years age group (25.0%). Patients aged 31–40 years and 61–70 years each accounted for 16.7% of cases, while only one patient (8.3%) was older than 70 years. All patients were female.

Table 2. Histopathological Spectrum of Rare Breast Malignancies (n = 12)

Histopathological Diagnosis	**Number of Cases**	**Percentage (%)**
Mucinous carcinoma	5	41.7
Papillary carcinoma	2	16.7
Metaplastic carcinoma	1	8.3
Metastatic malignant melanoma	1	8.3
Non-Hodgkin lymphoma	1	8.3
IDC with medullary pattern	1	8.3
Tubular carcinoma	1	8.3
Total	**12**	**100**

Among the 12 rare breast malignancies studied, mucinous carcinoma was the most common histological subtype, accounting for 5 cases (41.7%). Papillary carcinoma was the second most frequent subtype, comprising 2 cases (16.7%). The remaining lesions included metaplastic carcinoma, metastatic malignant melanoma to the breast, primary non-Hodgkin lymphoma, invasive ductal carcinoma with medullary pattern, and tubular carcinoma, with each representing one case (8.3%).

Table 3. Cytological Diagnosis on FNAC (n = 12)

FNAC Diagnosis	**Number of Cases**	**Percentage (%)**
Mucinous carcinoma	5	41.7

Suspicious for papillary neoplasm	2	16.7
Metaplastic carcinoma	1	8.3
Metastatic malignant melanoma	1	8.3
Non-Hodgkin lymphoma	1	8.3
IDC, NOS	1	8.3
Tubular carcinoma	1	8.3
Total	**12**	**100**

Fine-needle aspiration cytology (FNAC) correctly identified the majority of the rare breast malignancies. Five cases (41.7%) were diagnosed as mucinous carcinoma on cytology. Two cases (16.7%) were reported as suspicious for papillary neoplasm, which were subsequently confirmed as papillary carcinomas on histopathology. One case each of metaplastic carcinoma, metastatic malignant melanoma, non-Hodgkin lymphoma, tubular carcinoma, and IDC, NOS were diagnosed on cytology.

Table 4. Cyto-Histopathological Correlation (n = 10)

Cytological Diagnosis	**Histopathological Diagnosis**	**Cases**
Mucinous carcinoma	Mucinous carcinoma	5
Suspicious papillary neoplasm	Encapsulated papillary carcinoma	1
Suspicious papillary neoplasm	Invasive papillary carcinoma	1
Metaplastic carcinoma	Metaplastic carcinoma	1
Metastatic malignant melanoma	Metastatic malignant melanoma	1
IDC, NOS	IDC with medullary pattern	1
Tubular carcinoma	Not done as patient lost to follow up	
Non-Hodgkin lymphoma	Not done as patient lost to follow up	

Excellent agreement was observed between cytological and histopathological diagnoses. All five mucinous carcinomas diagnosed on FNAC were confirmed on histopathological examination. The two cases categorized cytologically as suspicious for papillary neoplasm were confirmed as encapsulated papillary carcinoma and invasive papillary carcinoma, respectively. Similarly, the diagnoses of metaplastic carcinoma and metastatic malignant melanoma showed complete concordance with histopathology. One case initially diagnosed as IDC, NOS on FNAC was identified as IDC with medullary pattern on histopathological examination. Case of primary breast non-Hodgkin lymphoma and tubular carcinoma was lost to follow up, thereby histopathological examination was not done.

Table 6. Diagnostic Concordance Between FNAC and Histopathology

Parameter	**Value**
Total cases	10
Correctly diagnosed on FNAC	09
Discordant cases	1
Diagnostic concordance	90%

Overall, FNAC demonstrated a high diagnostic concordance of 90% (09/10 cases) with histopathological examination. Only one discordant case was observed, in which IDC with medullary pattern was interpreted as IDC, NOS on cytology because of the absence of prominent lymphoplasmacytic infiltrate and indistinct glandular architecture in the aspirated material. Histopathological examination subsequently established the correct diagnosis. These findings highlight the high diagnostic accuracy of FNAC for rare breast malignancies when interpreted in conjunction with clinical, histopathological, and immunohistochemical findings.

Table 7. Cytomorphological Features Observed on FNAC

Tumor Type	**Characteristic Cytological Features**
Metaplastic carcinoma	Pleomorphic ductal cells with squamoid/keratinized cells
Papillary carcinoma	Papillary fragments with fibrovascular cores

Mucinous carcinoma	Tumor cells floating in abundant extracellular mucin
Tubular carcinoma	Tubular arrangement of mildly atypical epithelial cells
IDC with medullary pattern	Syncytial clusters, vesicular nuclei, prominent nucleoli
Non-Hodgkin lymphoma	Dispersed atypical lymphoid cells with scant cytoplasm
Metastatic melanoma	Large pleomorphic cells with melanin pigment and prominent nucleoli

Distinct cytomorphological patterns were observed for each subtype of rare breast malignancy. Metaplastic carcinoma exhibited pleomorphic malignant ductal cells with squamoid differentiation. Papillary carcinoma showed true papillary fragments with fibrovascular cores. Mucinous carcinoma demonstrated malignant epithelial cells suspended in abundant extracellular mucin with characteristic chicken-wire vasculature. Tubular carcinoma displayed cohesive tubular arrangements of mildly atypical epithelial cells. Non-Hodgkin lymphoma revealed dispersed atypical lymphoid cells with scant cytoplasm and numerous lymphoglandular bodies, whereas metastatic malignant melanoma showed pleomorphic polygonal cells with abundant cytoplasm, prominent nucleoli, and intracellular melanin pigment. The case of IDC with medullary pattern exhibited syncytial clusters of tumor cells with vesicular nuclei and conspicuous nucleoli but lacked sufficient lymphoplasmacytic infiltrate on cytology, resulting in an initial diagnosis of IDC, NOS.

These findings demonstrate that although FNAC provides reliable diagnostic information for rare breast malignancies, integration of cytomorphology with histopathology and immunohistochemistry is essential for accurate diagnosis, particularly in uncommon variants with overlapping cytological features.

Discussion

This study highlights the importance of recognizing distinct cytological patterns in rare breast malignancies and correlating them with histopathological findings. Metaplastic carcinoma often mimics sarcomatoid lesions

on cytology and requires histopathological examination for definitive diagnosis. Similarly, primary breast lymphomas can be mistaken for poorly differentiated carcinoma unless clinical suspicion and appropriate immunotyping are employed.

Papillary carcinoma and mucinous carcinoma tend to have characteristic cytologic features, aiding preoperative diagnosis. However, overlapping features in certain subtypes, such as IDC with medullary features, may challenge even experienced cytopathologists.

FNAC, when supplemented with histology and IHC, demonstrates high diagnostic accuracy for these rare tumors and provides valuable guidance for clinical management. Individual cases are being discussed below

Papillary carcinoma:

02 cases diagnosed as suspicious of Papillary neoplasm, probably papillary carcinoma, one case was diagnosed as encapsulated papillary carcinoma and another case was diagnosed as Invasive papillary carcinoma on histopathology. Differentiating between benign and malignant papillary lesions can be challenging with FNAC because the procedure typically targets the centre of the lesion, while invasive features are often located at the periphery as described by Deshmukh.P.S et al.[1] So, it is better to give atypical or suspicious category for Papillary lesions rather than assigning directly benign or malignant category on FNAC.

Metaplastic carcinoma:

In the present study, one case of metaplastic carcinoma was identified in female aged 40 years by FNAC. The smears displayed pleomorphic ductal epithelial cells and atypical cells in clusters, exhibiting keratinized cytoplasm and a giant cell reaction in the surrounding stroma. Histopathological examination confirmed the diagnosis of metaplastic carcinoma - adenosquamous type which consisted of 60 % glandular component and 40 % of squamous component. This is a rare type of malignancy, so a thorough examination of the dual components essential for diagnosing metaplastic carcinoma by FNAC, as highlighted by A. Abd El Hafiz et al.[2] in their study.

Non-Hodgkin's lymphoma:

In the present study, a case of non-Hodgkin's lymphoma was diagnosed by FNAC in a 60 years old female. The FNAC smear was highly cellular showing atypical medium to large sized lymphoid cells in sheets, characterized by hyperchromatic nuclei and scant cytoplasm with background showing

lymphoglandular bodies. The cytological features observed were consistent with the findings of the case report done by Guo et al.[3] Patient was lost to follow up.

Malignant melanoma deposits:

In the present study, one case of malignant melanoma deposits of the left breast was diagnosed in a 45 years old female by FNAC. This patient was previously diagnosed with malignant melanoma of the left thigh and also had metastasis to the left shoulder and left lumbar region. The FNAC smears showed large round to polygonal cells having vesicular nucleus with prominent eosinophilic nucleolus and abundant cytoplasm with some showing melanin pigment and on histopathology the same diagnosis of malignant melanoma was given. The metastasis of malignant melanoma to the breast is rare and should be considered in cases where a breast mass is identified, in patients with a history of primary melanoma in other locations, hence proper history before doing FNAC procedure helps to clinch the diagnosis as highlighted in the case series by S. Sakhri et al.[4] which comprised of 7 cases of malignant melanoma deposits in the breast.

IDC with Medullary pattern

One case was diagnosed as invasive ductal carcinoma with medullary showing vesicular nucleus with prominent nucleoli and lymphoplasmacytic rich stroma but on FNAC due to vague glandular arrangement of cells and lack of lymphocytes and plasma cells in the stroma, diagnosis of IDC, NOS was given, similar finding was described by Prakash et al.[5] in their study.

Tubular carcinoma:

In the present study, tubular carcinoma was diagnosed in a 53 years old female by FNAC. The FNAC smears were cellular and showed moderately pleomorphic ductal cells arranged in tubular pattern. Diagnosis of Tubular carcinoma is difficult on FNAC as it is a uncommon tumor and mild to moderate atypia of cells makes it to differentiate from benign lesions like sclerosing adenosis of breast as highlighted in the case report by Gupta.R.K et al.[6] This patient was lost to follow up.

Mucinous carcinoma:

Mucinous carcinoma was diagnosed in 5 cases on FNAC with histopathological correlation in the present study. It was observed in patients aged 40 to 65 years, most of them presented with a firm lump, from which mucinous material was aspirated. The smears showed atypical ductal epithelial

cells, in which some were plasmacytoid and were having high N:C ratio and moderate to abundant cytoplasm. Background shows mucin pools with endothelial fragments (chicken wire blood vessels) were seen. One case among these showed abundant psammoma bodies which is a rare finding to be seen in mucinous carcinoma as Pillai et al.[7] described in their case report.

Comparison with Other Studies:

The overall diagnostic concordance of 91.7% between FNAC and histopathology observed in the present study closely parallels the pooled concordance rate of 92.3% reported by Khan et al. in a systematic review and meta-analysis of 42 studies comprising 18,750 patients across multiple organ systems, in which breast lesions were among those showing the highest agreement.[10] This consistency with large pooled data reinforces the reliability of FNAC as a first-line diagnostic tool even for uncommon breast tumor subtypes, provided cytomorphological interpretation is corroborated with histopathological and immunohistochemical evaluation.

The predominance of mucinous carcinoma (41.7%) among the rare malignancies in the present series is notable when compared with literature describing mucinous carcinoma as constituting only 1-4% of all primary breast malignancies in unselected populations.[8] This difference reflects the design of the present study, which specifically enrolled cases already falling within the rare-tumor spectrum, so that a subtype considered uncommon in the general breast cancer population becomes proportionally dominant within this restricted cohort, rather than indicating a true rise in its background incidence.

Similarly, Kaur et al., in a one-year retrospective analysis of 153 mastectomy specimens, identified only 11 (7.2%) rare histological variants, with papillary carcinoma being the most frequent (2.6%), and reported a mean patient age of 52.9 ± 9.7 years.[9] This age profile parallels the 41-60 year predominance observed in the present study (58.3% of cases), supporting the observation that rare breast malignancies, like their common counterparts, largely affect peri- and postmenopausal women, even though the relative ranking of individual subtypes varies between cohorts depending on institutional case-mix and inclusion criteria.

The single discordant case in the present series, an IDC with medullary pattern read as IDC, NOS on cytology because of an

inconspicuous lymphoplasmacytic infiltrate in the aspirate, mirrors a limitation also described by Prakash et al.[5], indicating that overlapping cytomorphological features, rather than sampling failure, account for most FNAC misclassifications in this subtype. Taken together, these comparisons suggest that although the distribution of rare subtypes and their relative frequency vary between institutions and study designs, the overall diagnostic reliability of FNAC for rare breast malignancies remains consistently high across studies when interpreted alongside histopathological and immunohistochemical correlation.

Conclusion

FNAC remains a valuable tool for the initial evaluation of rare breast malignancies. A thorough understanding of cytomorphological features, combined with histopathologic and immunohistochemical correlation, is essential for accurate diagnosis. Early recognition of these rare subtypes can guide tailored treatment approaches and improve patient outcome.

Conflict of interest: None

Source of funding: Self funded

CYTOLOGY AND HISTOPATHOLOGY FIGURES

Cyto-Histopathological Spectrum of Unusual Breast Malignancies

Figures extracted from the uploaded Kapcon presentation and arranged sequentially.

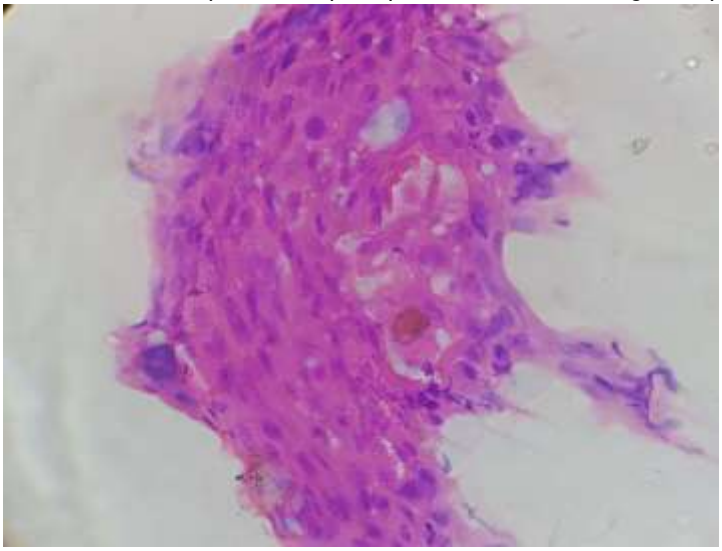

Figure 1. Metaplastic carcinoma – squamous area in adenosquamous type: cytology image.

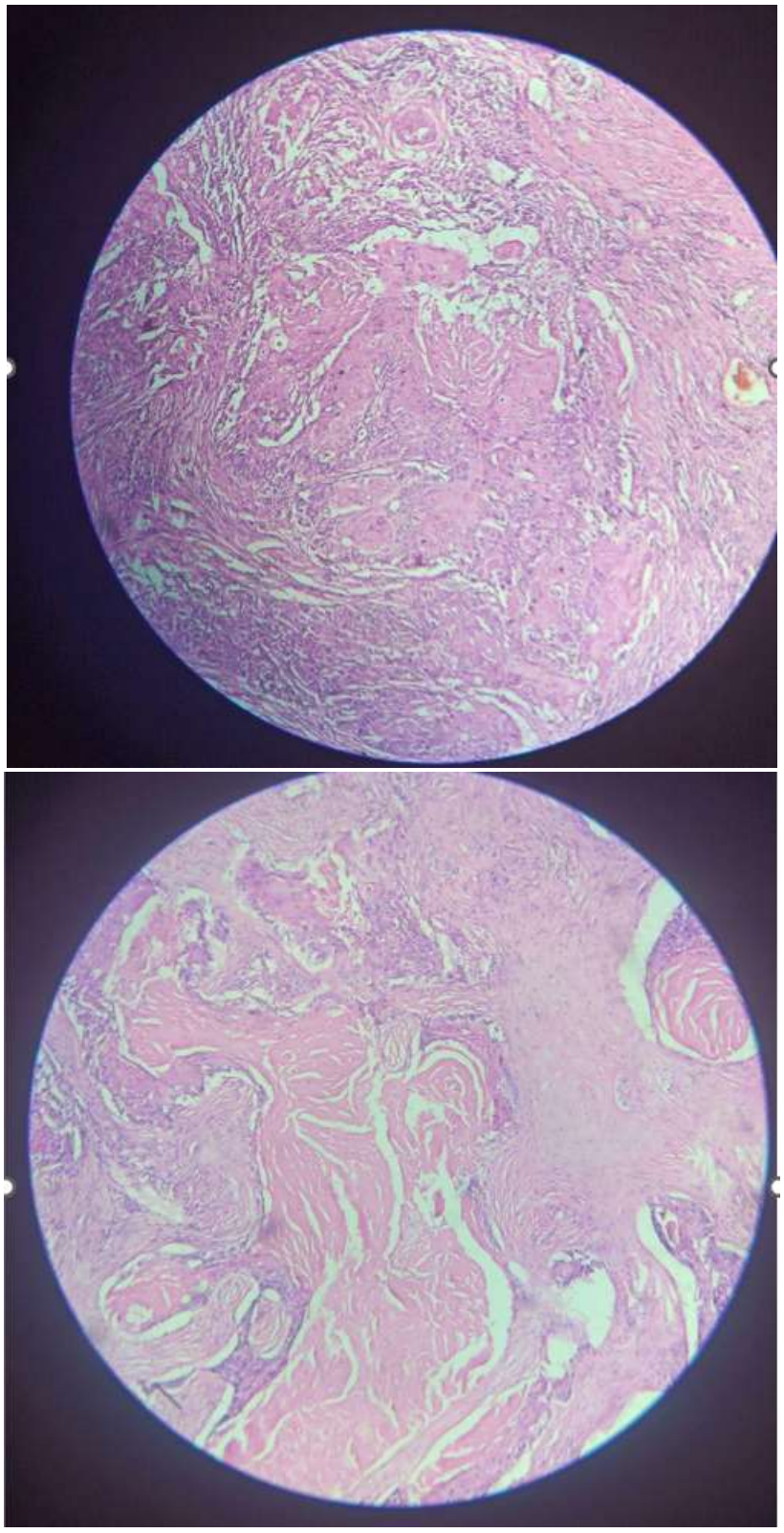

Figure 2. Metaplastic carcinoma – adenosquamous type: histopathology image.

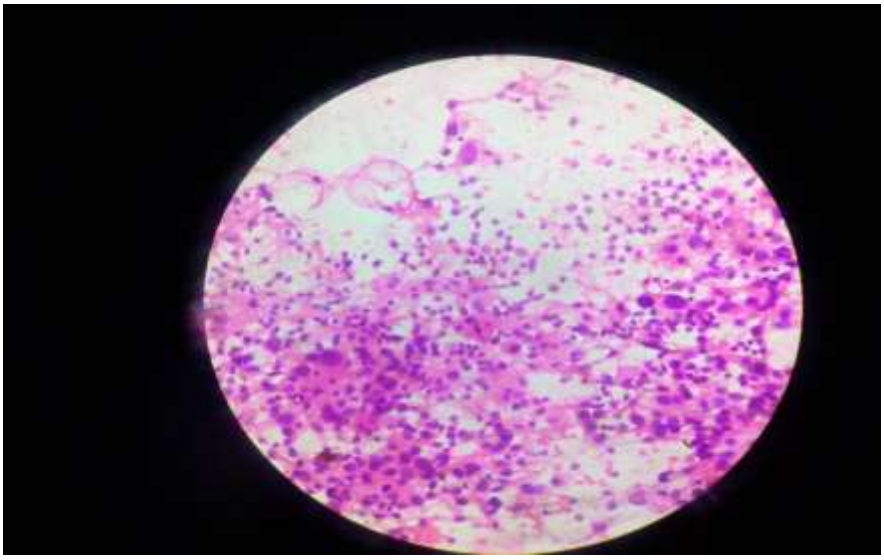

Figure 3. Metastatic malignant melanoma of the breast: cytology image.

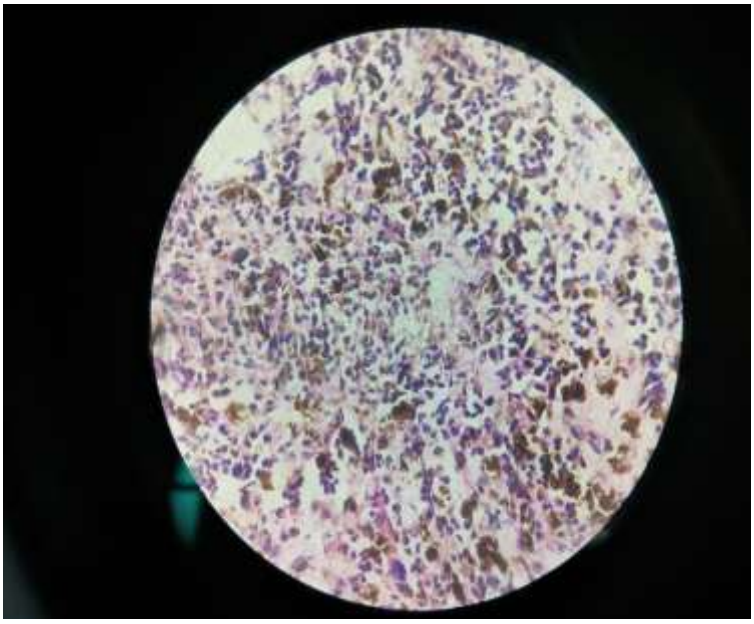

Figure 4. Metastatic malignant melanoma of the breast: histopathology image.

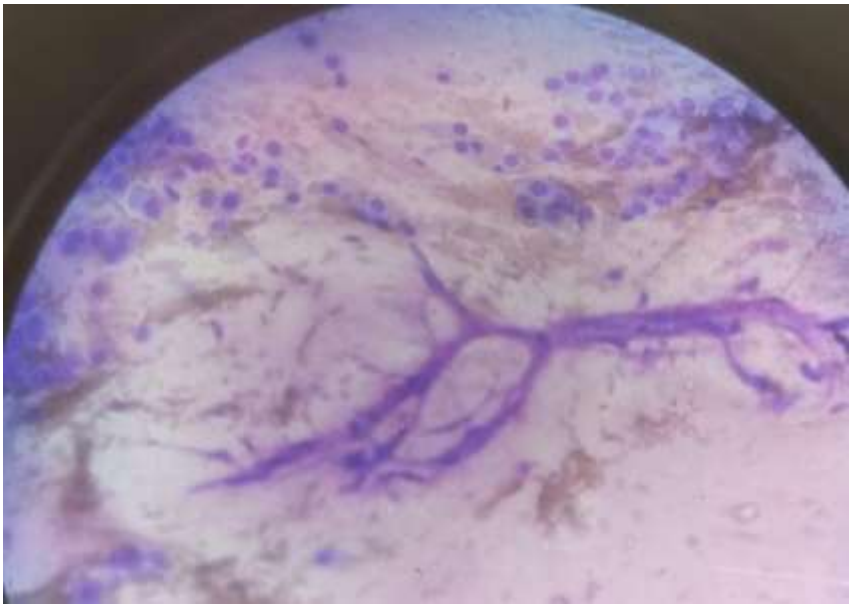

Figure 5. Mucinous carcinoma of the breast: cytology image

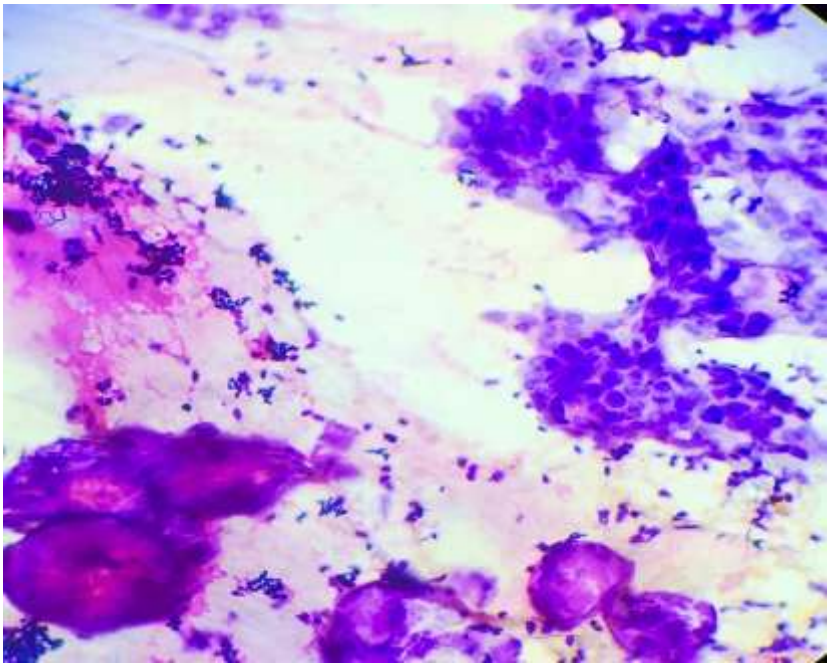

Figure . Mucinous carcinoma of the breast with psammoma bodies: cytology image

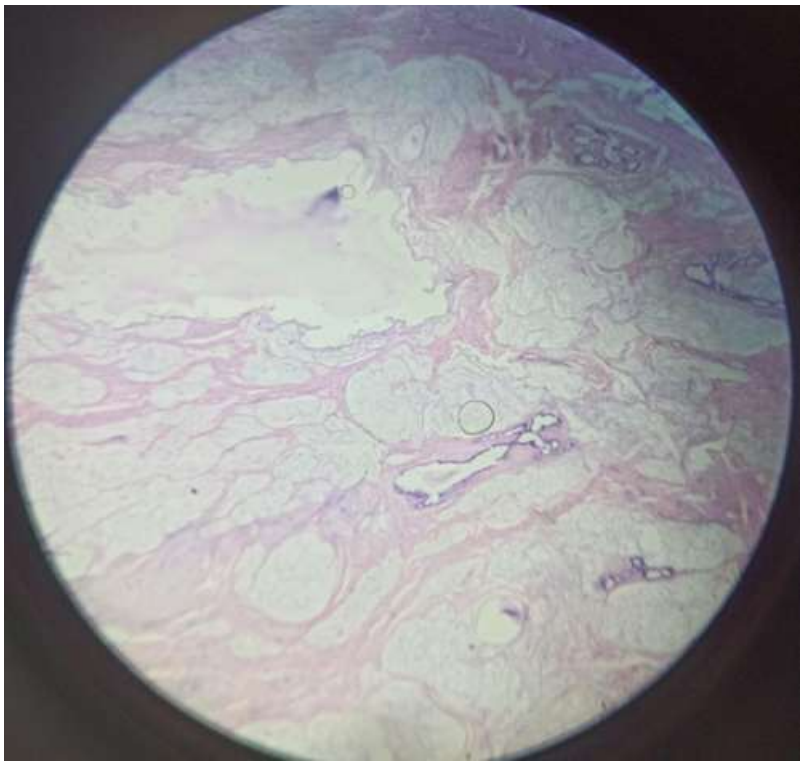

Figure 5. Mucinous carcinoma of the breast: histopathology image.

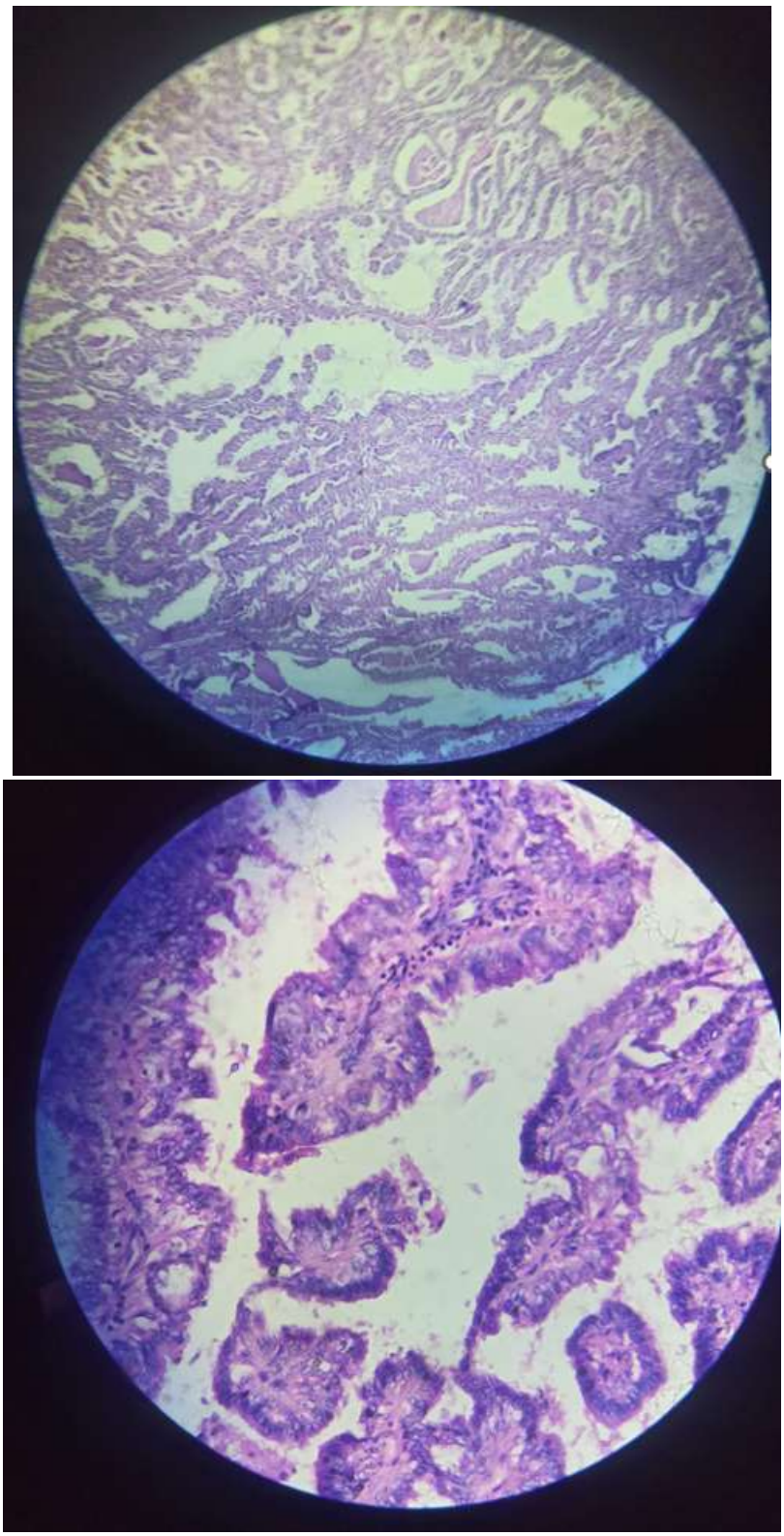

Figure 6. Invasive papillary carcinoma of the breast: histopathology image.

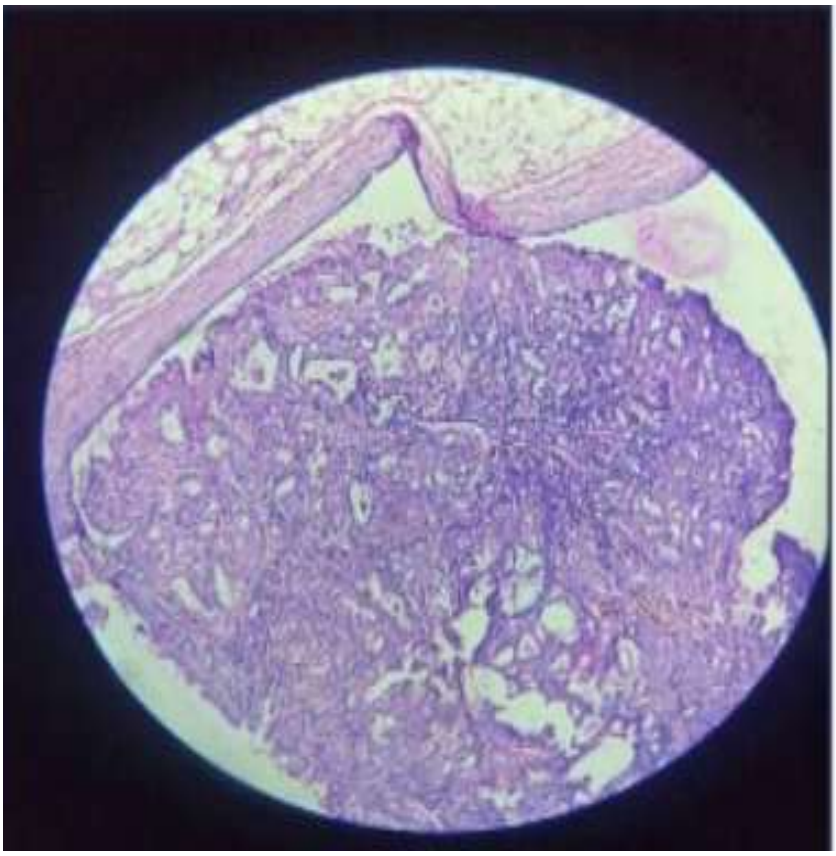

Figure 7. Encapsulated papillary carcinoma of the breast: histopathology image.

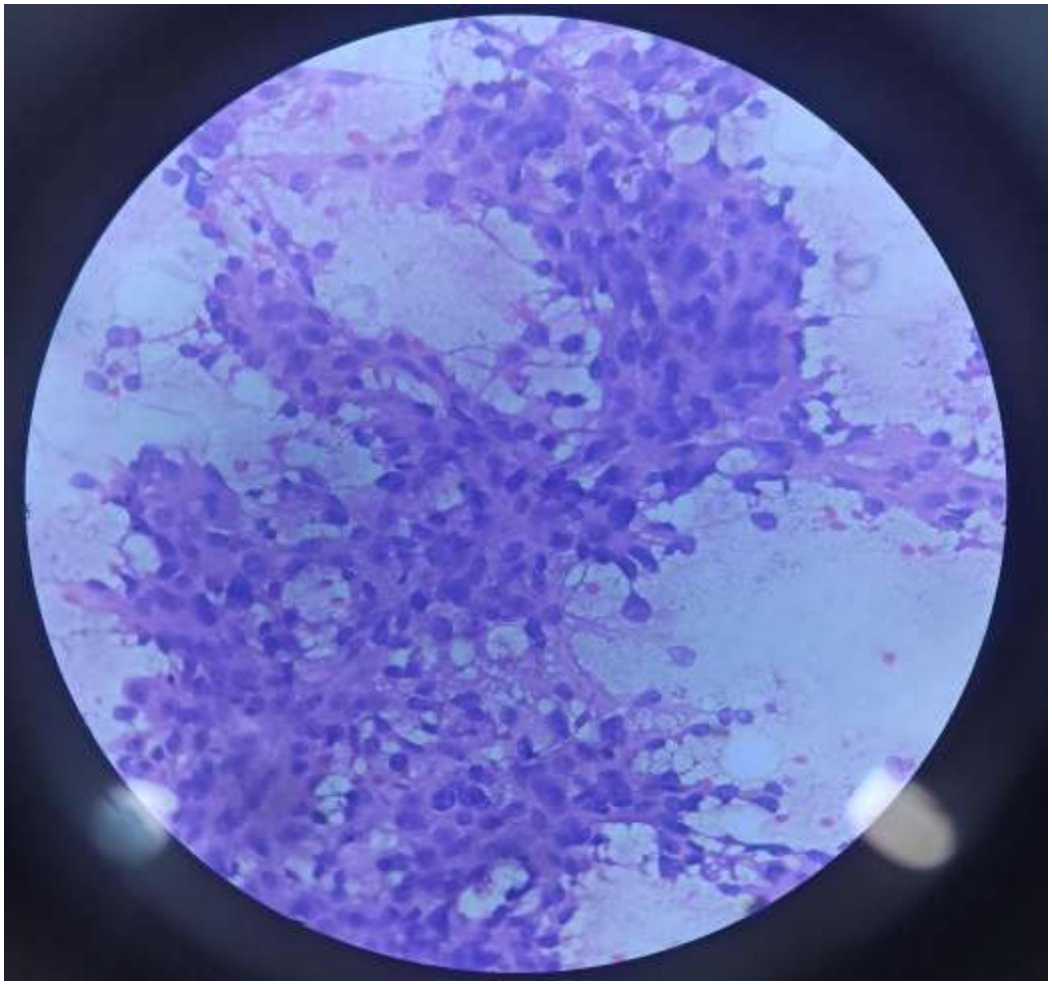

Figure 8. Invasive ductal carcinoma with medullary pattern: cytology image

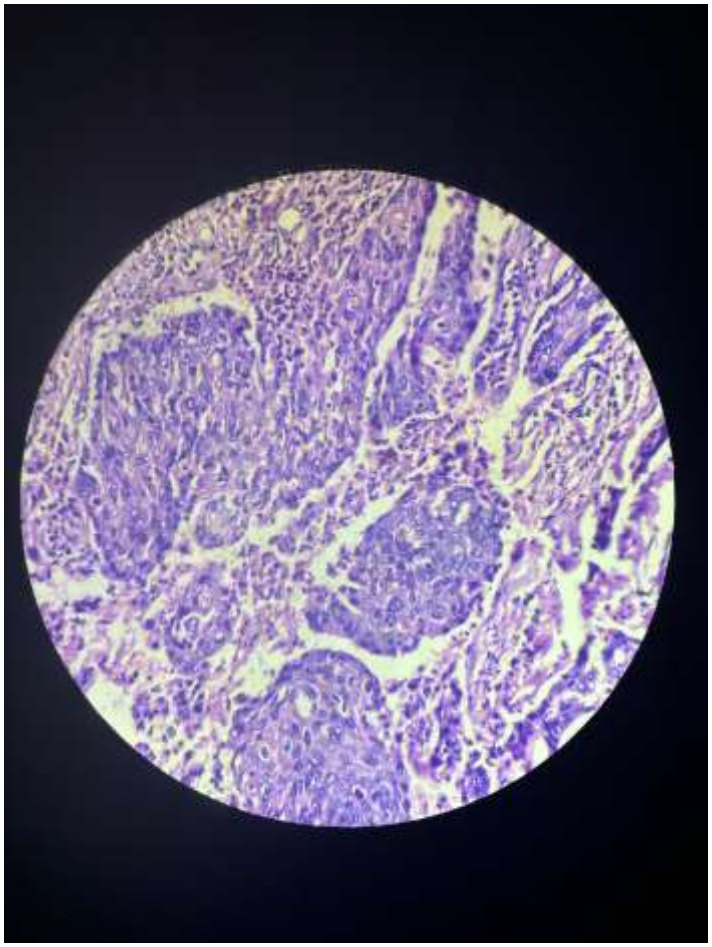

Figure 9. Invasive ductal carcinoma with medullary pattern: histopathology image.

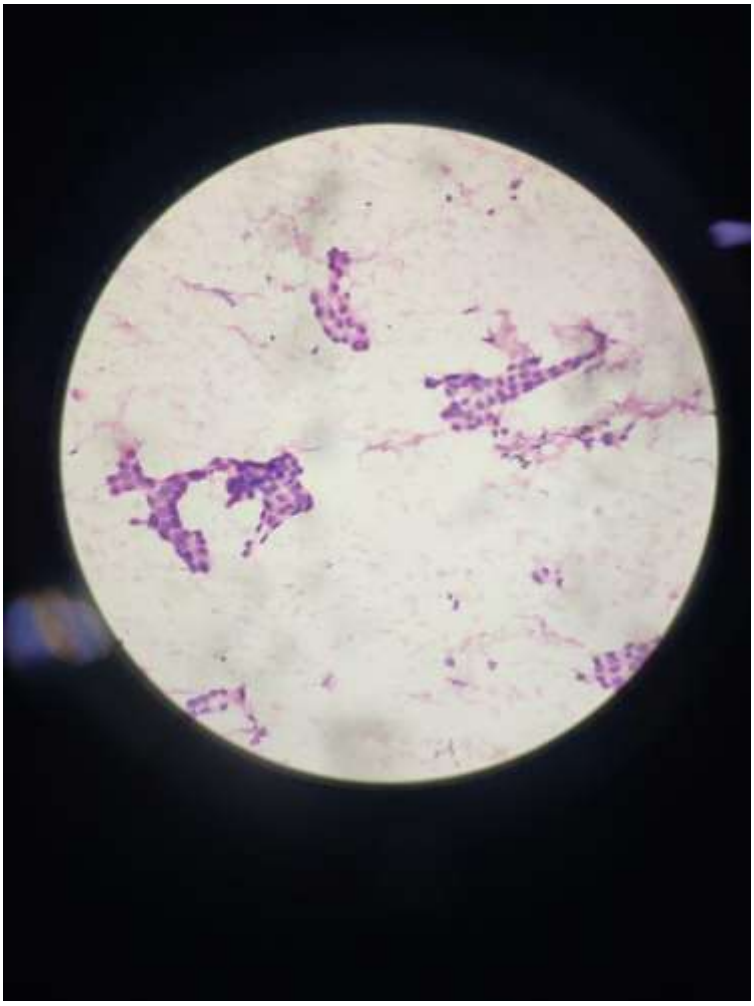

Figure 10. Tubular carcinoma of the breast: Cytology image

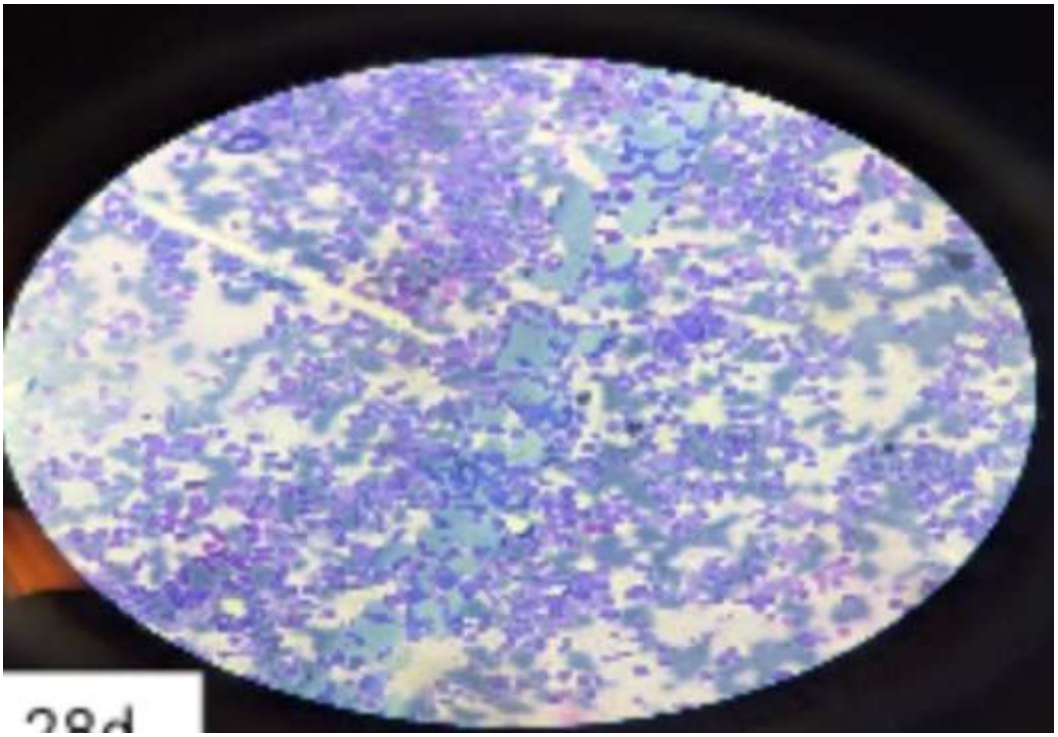

Figure 11. Non Hodgkins Lymphoma of the breast: Cytology image

References

1. Deshmukh S.P. Papillary Carcinoma of the Breast- Case Reports and Review of Literature Regarding Management Guidelines. Indian J Surg (November–December 2012) 74(6):510–512.DOI 10.1007/s12262-012-0524-6.
2. A. Abd El hafez and A.A. Shawky. Analysis of metaplastic breast carcinoma: FNAC; histopathology and immunohistochemistry are complementary for diagnosis ;FNAC, Histopathology and Immunohistochemistry of MBC. Breast Disease 34 (2012/2013) 67–75 DOI 10.3233/BD-130353.
3. Guo M, Liu J, Gilmore R, et al. Primary breast diffuse large B cell lymphoma. BMJ Case Rep 2022;15:e250478. doi:10.1136/bcr-2022250478.
4. Sakhri.S et al; METASTATIC MELANOMA IN THE BREAST: A

REPORT OF 7 CASES. Int J Gynecol Cancer 2020;30(Suppl 3):A1–A2101136/ijgc-2020-IGCS.78 on 13 November 2020.

5. Prakash D, Puvvala ORK, Nuguri VK, Venkatapathappa P. Advantages of the cell block technique over the FNAC and correlation with histopathology of most prevalent breast lesions in the community at the tertiary care center. Indian J Pathol Oncol 2022;9(4):312-317.
6. Gupta R.K. et. al; Fine-needle aspiration cytology of tubular carcinoma of the breast in a young woman.https://doi.org/10.1002/dc.2840070119.
7. Pillai et. al, Mucinous Carcinoma of Breast with Abundant Psammoma Bodies in Fine-Needle Aspiration Cytology: A Case Report. Diagnostic Cytopathology Vol 35, No 4, DOI 10.1002/dc.
8. Kuzmiak C.M., Calhoun B.C. Pure Mucinous Carcinoma of the Breast: Radiologic-Pathologic Correlation. J Breast Imaging. 2023;5(2):180-187. DOI 10.1093/jbi/wbac084.
9. Kaur M., Tiwana K.K., Singla N. Rare breast malignancy subtypes: A cytological, histological, and immunohistochemical correlation. Niger J Surg. 2019;25(1):70-75. DOI 10.4103/njs.NJS_27_18.
10. Khan N., Khan S., Rathore D., Upadhyay S., Vinita. Concordance Between Fine Needle Aspiration Cytology and Histopathology Across Organ Systems: A Systematic Review and Meta-Analysis. Int J Med Pharm Res. 2026;7(2):418-425.