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ROLE OF SCRAPE CYTOLOGY IN THE DIAGNOSIS OF BREAST TUMOUR IN RESOURCE LIMITED SETTING

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Abstract

Objectives

To evaluate role of scrape cytology in the diagnosis of breast malignancy so as to establish scrape cytology techniques as a procedure for diagnosis before routine processing of surgical specimens by comparing scrape cytology findings with histopathological diagnosis (Gold Standard)

Material & Methods

A cross sectional study was conduct on 88 cases of Breast Cancer Tumours association was evaluated between scrape cytology and histopathology examination diagnosis. Statistical analysis was done using SPSS v.21.0

Results

The total number of specimen that we received from organ system breast and were incorporated in study is 125. Apart from these 10 specimen that were over-fixed and hence could not be the part of this study therefore were excluded. The percentage of malignant tumours in our study was 33.60% which includes; 1) Ductal Carcinoma Breast (24), 2) Medullary Carcinoma Breast (6), 3) Metaplastic Carcinoma Breast (3), 4) Lobular Carcinoma Breast (9), While 66.40% were benign lesions which includes; 1) Fibroadenoma (42), 2) Phyllode (16), 3) Benign Breast Lesions (25). We observed that 98.40% cases of breast lesions affect female gender. In benign lesions we got a concordance of 98.80% when scrape cytology was compared with Histopathology. In malignant lesions concordance was 95.24% when scrape cytology was compared with histopathology.

Table: Total Number of Breast Tumours

TUMOURS	CASES	PERCENTAGE
Benign	83	66.40%
Malignant	42	33.6%
Total	**125**	**100%**

Table :Ratio of Breast Tumours

BENIGN VS MALIGNANT RATIO OF BREAST TUMOURS	
Benign	Malignant
2	1

Table : Gender Distribution of Breast Tumours

GENDER	TOTAL	PERCENTAGE
Male	2	1.6%
Female	123	98.4%

Table : Scrape vs Histopathology: Benign Breast Tumours

RESULTS	CASES	PERCENTAGE
Concordant	82	98.8%
Discordant	1	1.2%
Total	**83**	**100%**

Discordance was seen in 1 case which amounts to 1.2% which was misdiagnosed as Phyllodes tumor on scrape cytology but on histopathologic examination it was found to be a case of malignant phyllodes tumor.

Table : Scrape vs Histopathology: Malignant Breast Tumours

RESULTS	CASES	PERCENTAGE
Concordant	40	95.24%
Discordant	2	4.76%
Total	**42**	**100%**

Two cases of sclerosingadenosis (HPE diagnosis) were overdiagnosed as invasive breast carcinoma (scrape cytology diagnosis), bringing our discordance percentage in diagnosing malignant breast lesions to 4.76%.

Discussion

crape cytology is an effective, quick and efficient method which has been used as an adjunct or replacement for frozen section and intra-operative consultation.(36)The turn around time in providing a diagnosis has been significantly reduced with this technique. Modification of imprint cytology has resulted in this technique. The diagnostic accuracy was 98.4% and the false positive rate was 0.4%. This diagnostic accuracy was better than reported for imprint cytology or frozen sections alone. Hence scrape cytology can be an excellent adjunct to frozen section technique.(37)

Many studies done prior to our study have concluded that cytology has the advantage of being much less time consuming, easy to adapt, reliable and does not require special equipment's or set ups.(38–40)

The concept of cytology as a method of intra-operative pathological evaluation was given as early as 1927 by Dudgeon and Patrick. Scraping of the cut surface prior to smearing facilitates harvesting of cells. Hence scrape cytology could be prefferd over touch preparation/ imprint cytology as the former technique would yield much more material than the latter.(38)

In a study by Mair et al it was found that the turnaround time for intra-operative cytology was only 2 minutes whereas frozen section takes at least 10 minutes to confirm diagnosis rapidly.(41)

Scucchi LF et al studied the diagnostic accuracy of frozen section and intra-operative cytology. In their study they found that overall accuracy for frozen section was 94.9% whereas that for intra-operative cytology was 96%.(36)

Wakely PE et al concluded that intra-operative cytology serves as a useful supplement in frozen section diagnosis and also can replace (especially when tissue is limited) histologic frozen section examination.(42) As compared to frozen section intra-operative cytology is a simple, fast, easy, reliable, inexpensive technique with excellent preservation of cellular details, does not require special instrument (cryostat) nor any loss of tissue as occurs with cryostat sections and can be interpreted in the light of gross findings.(43)

There are several advantages of intraoperative cytology over frozen sections which have been attested by various authors.(44–47) They are: 1. Rapidity of preparation which is not at the cost of accuracy 2. Simple and inexpensive method 3. Excellent preservation of cellular

details without freezing artifacts 4. No loss of tissue as with cryostat 5. Possibility of identifying focal macroscopically undetectable neoplastic lesions in large tissue fragments 6. Possibility of examining adipose, necrotic and calcified tissue 7. Diagnosis of malignancy when tissue is limited in quantity 8. Avoidance of contamination and safe handling.(48)

In a study done to differentiate malignant from non-malignant lesions sensitivity of detection of malignancy was 96.9%, specificity was 94.1%. Two false positive diagnosis (5.9%) and three false negative (3.12%) were made with a positive predictive value of 97.9% and negative predictive value of 91.4%.(43)

In another study conducted in our country it was seen that for surgical specimen studied by scrape cytology the diagnostic accuracy rate was 93.49%. Out of 169 cases studied 158 were correctly diagnosed as benign or malignant lesions.(49)

Scrapings of the cut surface prior to fixation facilitates the harvesting of cells hence scrape cytology could be preferred over touch/ imprint cytology as the material yeilded from scrape would yield much more material than touch/ imprint.(50) In scrape preparations, cut surface of the specimen is scraped with the edge of the glass slide. Relevant clinical data and gross morphological features are valuable information for evaluating the cytological smears.(49)

It was found that smears prepared after scrapings of tumor yielded uniformly cellular smears and that scrape smears being more cellular than touch preparation.(51,52) Since intra-operative cytology increases diagnostic accuracy of frozen sections for the confirmation of various lesions, scrape cytology can be an excellent adjunct to frozen section technique.(53,54)

In our present study which was done over a period of 18 months i.e. May 2021 to October 2022 in the Department of Pathology, Government Medical College, Srinagar we have studied the diagnostic accuracy of scrape cytology in determining whether the scrape cytology diagnosis is correlating with the diagnosis on histopathological examination and identifying malignant lesions. Also we have tried to incorporate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic value of this procedure.

In our study 125 breast specimen were processed for scrape cytology. Apart from these 10 specimen were over fixed and hence could not be part of the study therefore were excluded. Majority of the breast lesions (123) were found in females (98.40%) while 2 cases (1.6%) were found in males.

Overall the ratio between benign to malignant breast lesions was 2:1. The percentage of benign Tumours in our study was 66.40% with a concordance of 98.80% when correlated with histopathological examination. Discordance was seen in 1 case which amounts to 1.2%

which was misdiagnosed as Phyllodes tumor on scrape cytology but on histopathologic examination it was found to be a case of malignant phyllodes tumor.

The remaining 33.60% malignant lesions showed a concordance of 95.24% when scrape cytology was compared with histopathological examination. Two cases of sclerosingadenosis (HPE diagnosis) were misdiagnosed as invasive breast carcinoma (scrape cytology diagnosis), bringing our discordance percentage in diagnosing malignant breast lesions to 4.76%. This was because in our study, the cytologic features that lead to an over interpretation included the cohesive epithelial groups/tubules, especially those having an angulated configuration or pointed ends, discohesive cell clusters, few or no myoepithelial cells and nuclear atypia.

Jayaram and Gupta reported a case in which SclerosingAdenosis was misdiagnosed as invasive lobular carcinoma where the cytologic features included high cellularity and small clusters of monomorphic cells with mild nuclear pleomorphism.(55)

Gal R studied cases of breast carcinoma in which only lumpectomy was performed. Here scrape cytology was used as a method for examination of lumpectomy margins. Good cytological and histopathological correlation was found.(39)

100% accuracy in diagnosing benign or malignant lesions of breast was acheived in a study conducted by Sadhana et al.(49)

Issam et al showed sensitivity, specificity and accuracy for intra-operative scrape cytology were 95.8%, 100%, 96.8% respectively.(56)Bukhari et al showed sensitivity, specificity, accuracy, PPV, NPV, for intra operative scrape cytology were 91.30%, 100%, 95%, 100%, 89%, respectively.(57)

Hiregoudar et al showed that sensitivity, specificity, PPV, NPV and accuracy for IOSC were 95.24%, 100%, 100%, 95%, 97.5% respectively.(58)

Jackin RK et al did a study in which they concluded that Fine-needle aspiration (FNA) has a generally high false-negative rate in the diagnosis of phyllodesTumours with an average sensitivity of 63%.(59)

Conclusion

The present study was conducted in the department of pathology from SMHS and associated hospitals over the period of eighteen months May 2021 to October 2022 were studied. We received a total number of cases which consisted of Breast (125), and we came to the following conclusion:

1. Scrape cytology is rapid, safe, simple and inexpensive method to diagnose suspicious malignant lesions.
2. If scrape is positive, we can chart out next level of management (if needed).
3. Scrape can be used in a resource limited areas and promote early diagnosis and refer to higher centres to a specialist care.
4. This method of diagnosing can allay anxiety due to shorter duration in diagnosis and aids in quick decision making.
5. It is highly sensitive, hence can be used as rapid screening test.
6. It can be used intra-operatively in case of malignancies.
7. It is compatible to HPE reports 96.9% of cases hence can be used as a valuable tool in PHCs and district hospitals.
8. Minimal cellular distortion provides crisp cytological details

Introduction

Breast cancer is a leading health concern among women due to its high mortality and morbidity rate. The five-year survival rate in metastatic breast cancer is less than 30%, even with adjuvant chemotherapy.(1) Recent GLOBOCAN 2018 data produced by the IARC (International Agency for Research on Cancer) from 185 countries reported 2.3 million new cases (11.7%) of breast cancer and a mortality rate of 6.9%.(2) Breast cancer incidence is more common in highincome countries (571/100 000) than in low-income counties (95/10 000), reflecting the association with globalization. Breast cancer is usually called a group of disease (>100) due to the presence of various biological subtypes reflecting distinct molecular profile and clinic pathological features.(2,3)Other than histological subtypes, gene expression profiling has classified breast cancer into different molecular subtypes, i.e., receptor-positive (Luminal A, Luminal B, Normal like, and HER-2 (Human epidermal growth factor receptor 2 positive) and receptor-negative (TNBC (Triple negative breast cancer)) or Basal like)(4–6) Lehmann et al. further identified the different groups named in TNBC subtypes Basal like-1, Basal like, Immunomodulatory, Mesenchymal, Mesenchymal Stem Cell like, and Luminal Androgen depending upon expression of distinct genes.(7) The overall collective data identified that these breast cancer subtypes have different histopathological and clinical behaviors and are associated with different age groups and ethnicities,(4,8,9) such as TNBC and HER-2 positive subtypes which are notably common in younger and premenopausal women, more prevalent in African-American and Asian women, exhibiting more metastatic

potential with high relapse rate.(10–15) In developed countries, modified lifestyle, delayed age for marriage, late first child, late-night work schedule, and hormonal replacement therapy are the major risk factors for breast cancer development.(16,17) In incidence and mortality are lack of proper awareness or knowledge of the disease, inappropriate screening programs, delayed diagnosis, and insufficient medical facilities.(18,19) There are multiple therapies available for breast cancer treatment including surgery, radiotherapy, chemotherapy, endotherapy, and immunotherapy.(20,21)Despite the availability of these therapies, breast cancer incidence and mortality remain high.(22,23) In the way of resolving this problem, multiple omics studies identified intra and inter tumor heterogeneity in breast cancer which is the leading cause for relapse or resistance to treatment therapies.(23–26) Further, scientific researchers and clinicians are continuously developing or improving present knowledge and technologies to explore tumor heterogeneity in breast cancer. Improvement or advancement in sequencing tools, such as next-generation sequencing, singlecell sequencing, spatial gene expression profiling, and bioinformatics support, is providing significant support on tumor heterogeneity.(27–29)Also, several authorized agencies are screening the women at high breast cancer risk to reduce the breast cancer incidence. Despite these facilities, a number of new breast cancer cases are still increasing. The main reason is the lack of accurate information and loop in utilizing the availability of these facilities. In addition, currently, the COVID-19 pandemic around the world caused health system or screening programs closures, delay in diagnosis or treatment availability, and increases in advanced-stage diagnoses and mortality.(30–35)

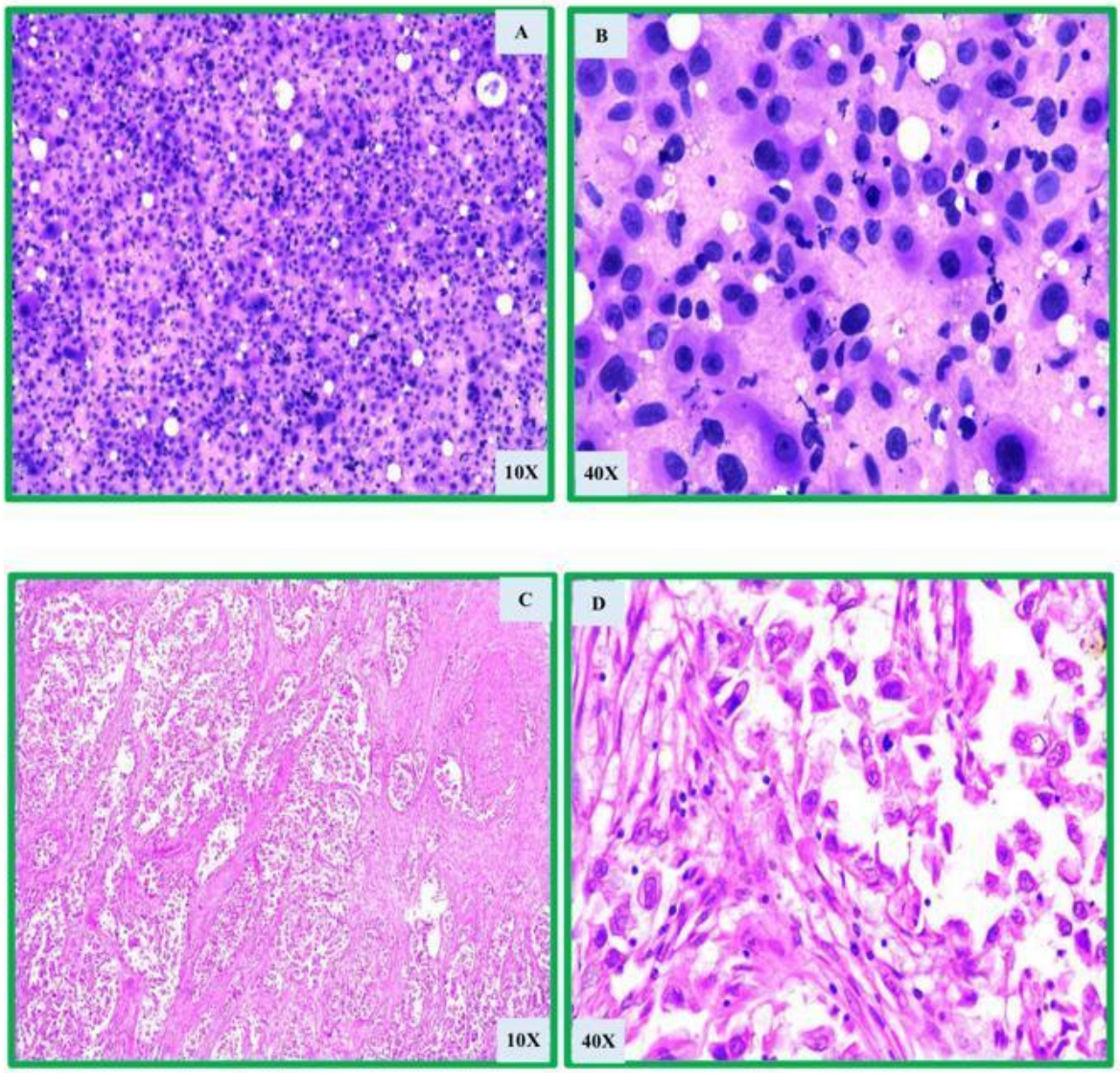

Figure 1- A & B: Highly cellular smears showing single cells. The cells are pleomorphic with presence of increased N:C ratio, hyperchromatic nuclei, prominent nucleoli, irregular nuclear membrane and moderate amount of eosinophilic cytoplasm. Abnormal mitosis seen. **C & D:** Low and high power views showing sheets of pleomorphic cells with minimal trabeculae formation. The cells are atypical with increased N:C ratio, hyperchromatic nuclei, prominent nucleoli, irregular nuclear membrane and moderate amount of eosinophilic cytoplasm. Abnormal mitosis seen.

Case 1: Intraductal Carcinoma Breast

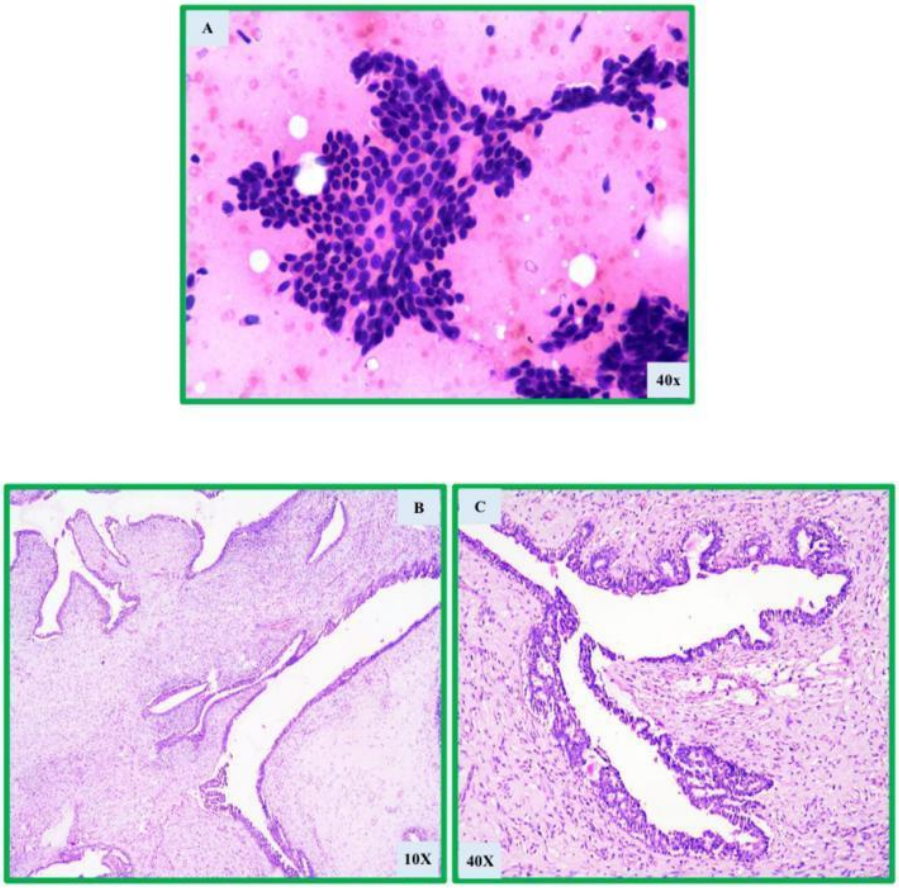

Figure 6- A: Fibromyxoid stromal fragments with spindle Cells seen in a hemorrhagic background. **B & C:** Sections show leaf like epithelial formation. subepithelial condensation with increased stromal cellularity seen adjacent to the epithelium.

Case 6: Phyllodes Breast

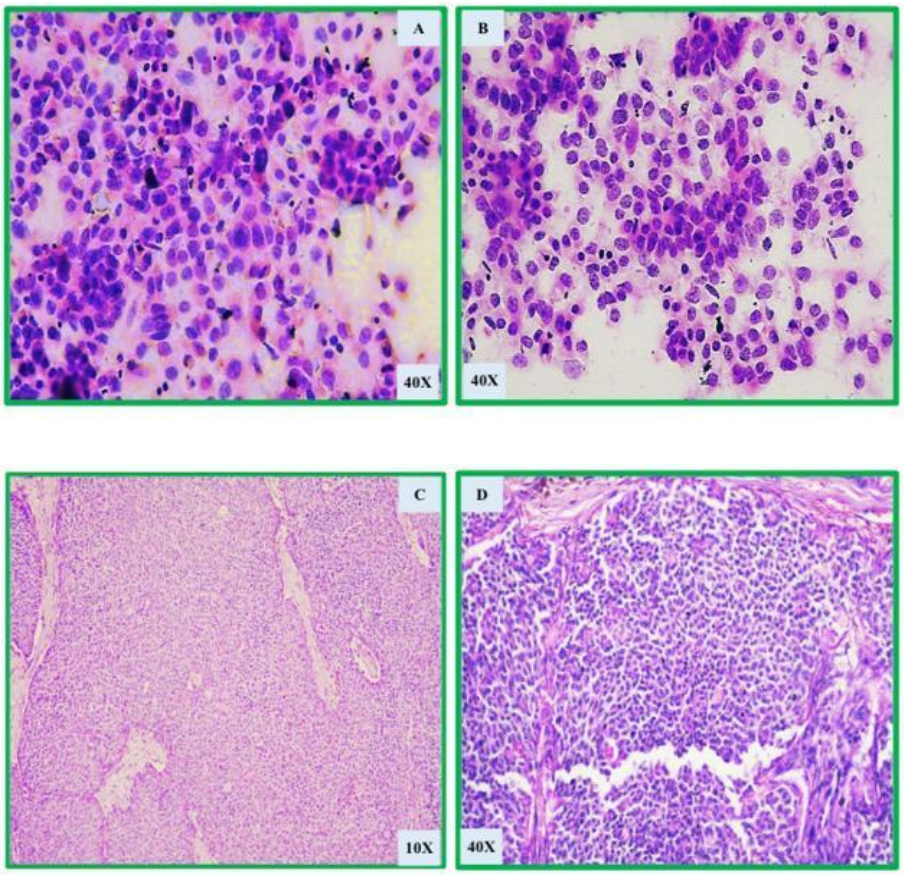

Figure 5- A & B: Cellular smears with presence of small round blue cells having salt and pepper nuclear chromatin. **C & D)** small blue monomorphic cells seen in sheets. High power view shows stippled nuclear chromatin

Case 5: Neuroendocrine Breast Cancer

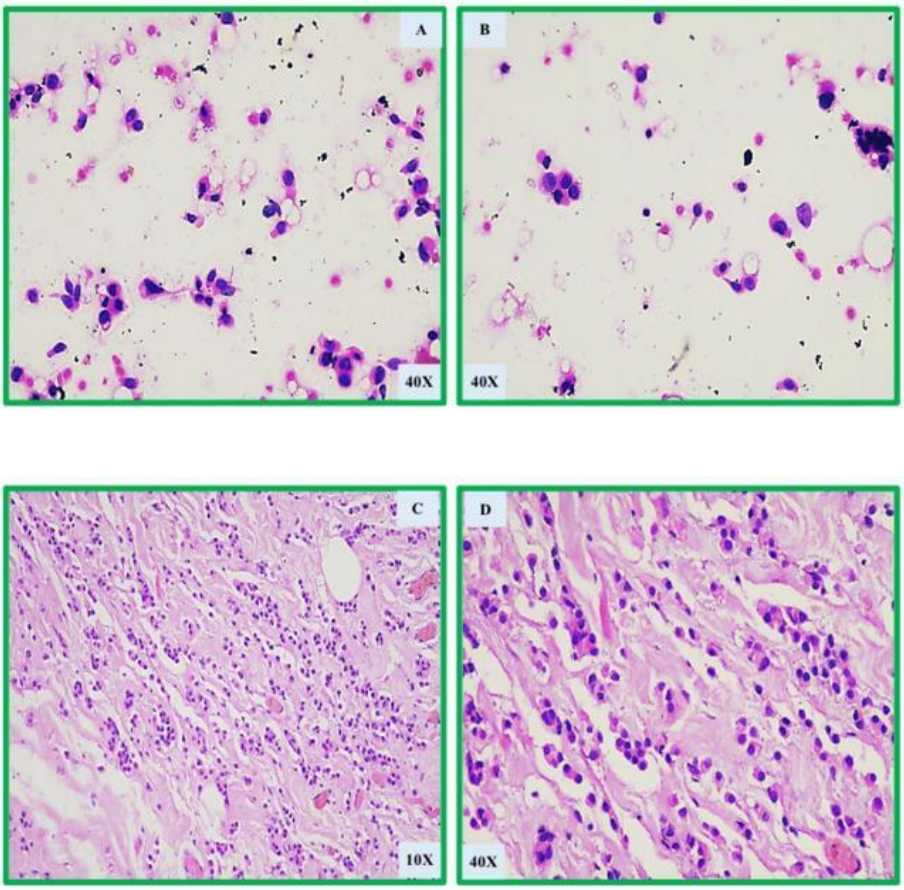

Figure 4- A& B: Sparsely cellular smears with presence of small single cells lying cells showing round to oval hyperchromatic nuclei and intracytoplasmic vacuolations. **C&D)** Tumor cells arranged in Indian file pattern. The individual cells are monomorphic, small and lacking nucler atypia

Case 4: Lobular Carcinima Breast

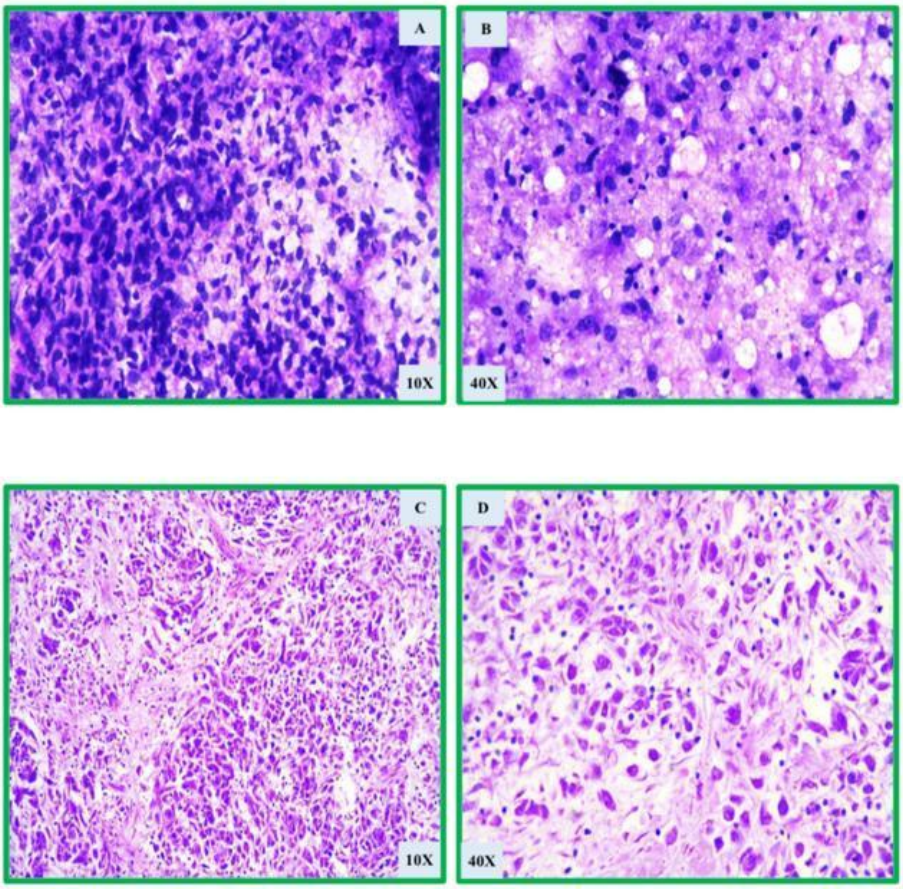

Figure 3- A & B: Cellular smears showing large pleomorphic spindle shaped cells. **C & D:** Sections show neoplastic cells arranged in sheets and dispersed individually. Individual cells showing severe pleomorphisim high and N:C ration, hperchromatic nuclei and scanty cytoplasms.

Case 3: Metaplastic Carcinima Breast

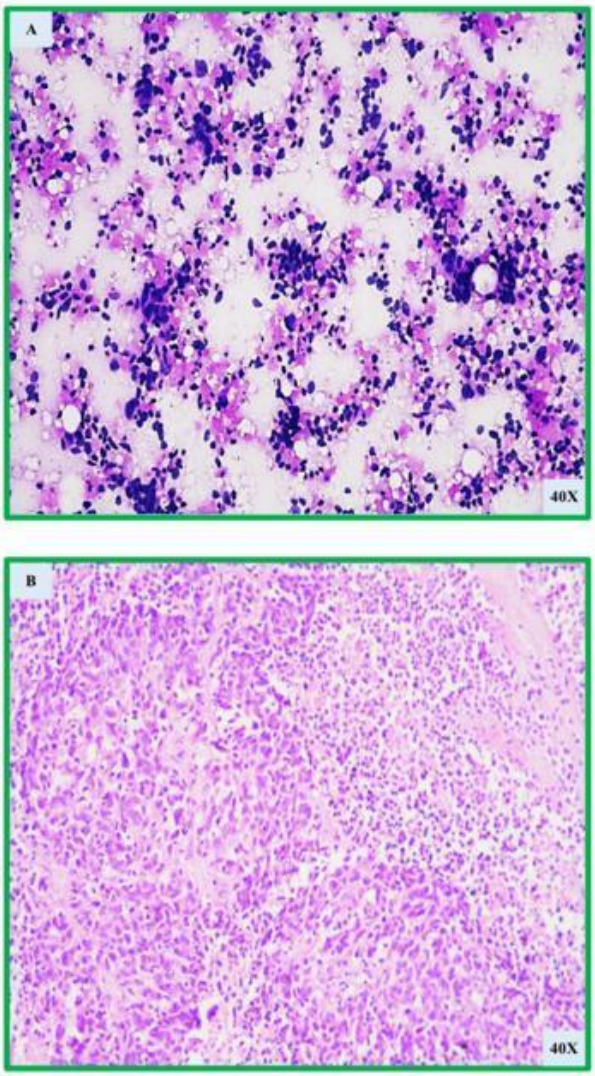

Figure 2- A: Moderately cellular smears showing pleomorphic cells; some forming clusters and some lying singly with hyperchromatic nuclei, vesicular nuclear chromatin, irregular nuclear membrane and moderate amount of eosinophilic cytoplasm in a lymphoplasmacytic cell backgrond. **B)** Tumor is seen having a well circumscibed pushing border. The cells are arranged in a syncytial growth pattern. Individual cells show pleomorphism with surrounding lymphoplasmacytic infiltrate

Case 2: Medullary Carcinma Breast

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