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IMPRINT SMEAR CYTOLOGY AND HISTOPATHOLOGY OF BREAST LESIONS - A COMPARATIVE EVALUATION WITH REVIEW OF LITERATURE

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ABSTRACT

The objective behind the work was to study the accuracy of imprint cytology, cyto-histological correlation and various patterns of imprint cytology of breast lesions. The study was carried out on 90 patients of breast lumps at a tertiary care hospital over a period of 2 years. A detailed clinical history and routine investigations were noted. Imprint smears were taken from the excised lumps before fixation. Hematoxylin & eosin (H&E) and Papanicolaou (PAP) staining was done. Fibroadenoma and infiltrating duct carcinoma were the commonest lesions found. On imprint cytology, out of 90 cases, 81 (90%) were diagnosed correctly. Imprint cytology when considered along with clinical features and gross appearance of the excised mass, can give an accurate diagnosis.

Key Words: *Imprint Cytology, Breast*

INTRODUCTION

The incidence of breast cancer is rising in the world especially in developing countries such as India. There are various risk factors including late age at first childbirth, fewer children and shorter duration of breast-feeding. According to the National Cancer Registry Programme report on time trends in cancer incidences rates (1982-2005) of Indian Council of Medical Research (ICMR), the estimated breast cancer cases in India in 2010 is 90,659 and of cervical cancer is 103,821. India's National Health Profile 2010 predicted that by 2020, breast cancer will overtake cervical cancer as the most common type of cancer among women in India. Dread of cancer is rampant amongst civilized world. Early detection is the only way to lessen its impact on life especially in case of breast cancers as it is extremely common. The most prevalent cancer in the world today is breast cancer. In India it stands on second position after cervical carcinoma. Preoperative diagnosis has many advantages and can be facilitated by exfoliative and non exfoliative cytology. Imprint cytology allows cytological techniques to be used for the examination of individual cells yet preserves to some extent the histological pattern of the imprinted tissue (Tribe, 1965). It is useful in places where there is lack of trained technicians and equipment needed for frozen section (Tribe, 1965; Solanki *et al.*, 1977). However, imprint cytology cannot replace frozen section in its utility. In this study, an attempt was made to characterise imprint cytology smear pattern of various breast lesions and to establish its accuracy in early detection of malignant lesions. Aims of the present study were-

To establish the accuracy of imprint cytology as a rapid diagnostic method in breast lesions; to correlate imprint cytology diagnosis with histopathology; and to study the various patterns of imprint cytology in breast lesions.

MATERIALS AND METHODS

The study was carried out at a tertiary care hospital over a period of 2 years. It included 90 cases of breast lumps from both sexes. Both outpatient department and surgical ward patients were included. Detailed clinical history included site and duration of lump, rapidity of growth, nipple discharge, menstrual and lactational history, pain etc. Thorough clinical examination of the patients along with local examination of

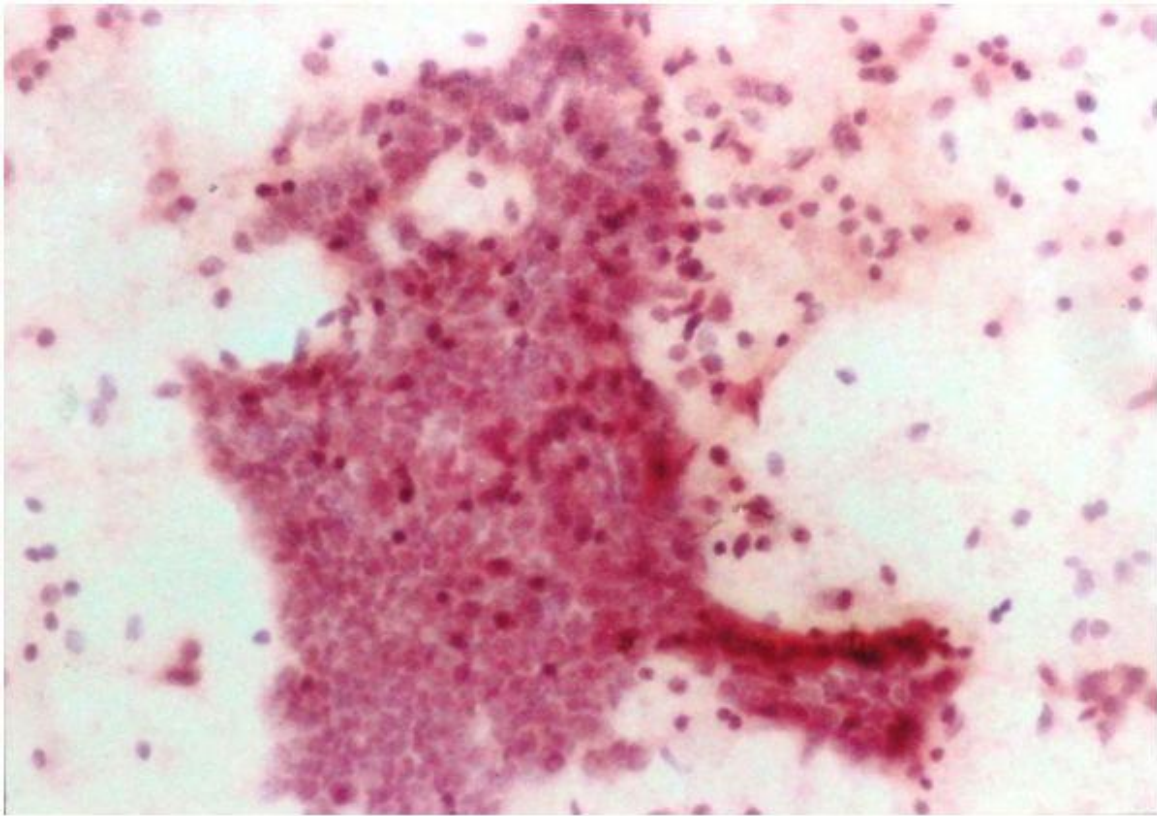


Figure 1: Smear from benign lesion showing uniform cells, normal N: C ratio and fine chromatin. (H.E. X 10)

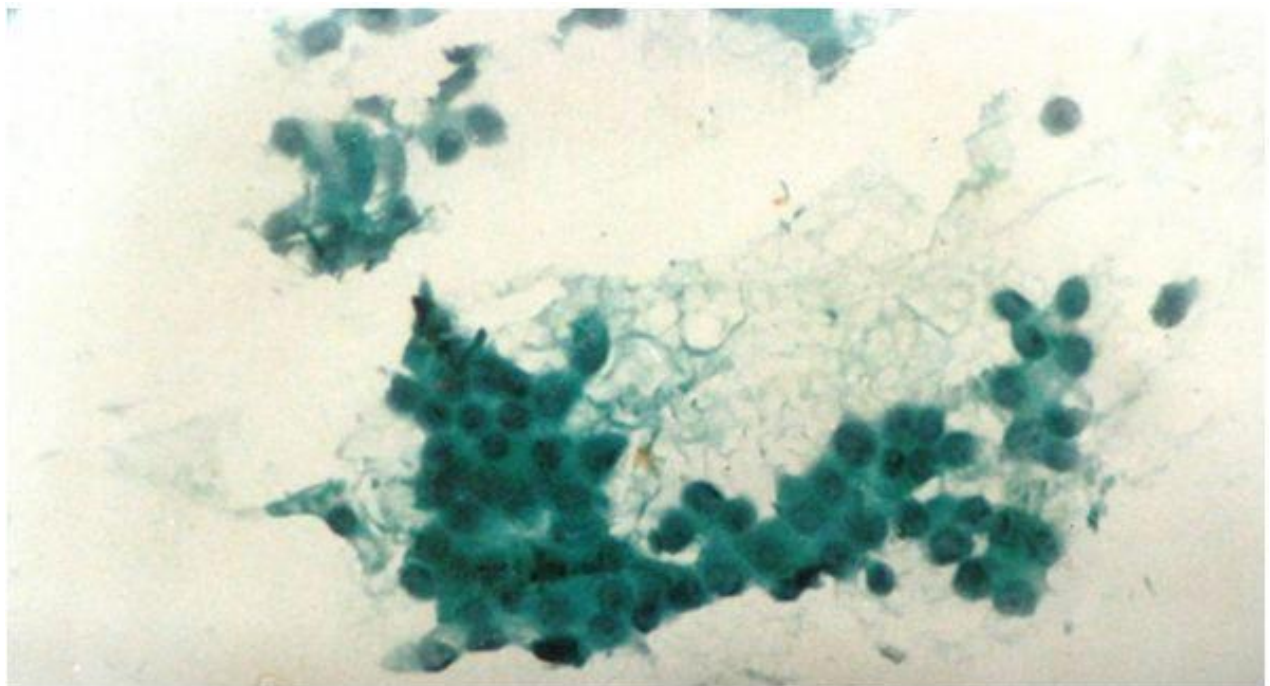


Figure 2: Smear from malignant lesion showing increased cellularity, pleomorphism and hyperchromatic nuclei with prominent nucleoli. (PAP X 20)

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the breast lump was done. Secondaries were looked for in lymph nodes. Relevant routine investigations included FNAC. Imprint smears of the excised lumps (before fixation in formalin) were made by pressing the tissue against glass slides which were fixed in 95% ethyl alcohol for 20 minutes and stained with H&E and PAP stain. Gross and microscopic examination of the imprint smears and the tissue received was done. Imprint smears from breast lesions were studied microscopically and results were noted as either negative for malignancy, positive for malignancy, negative for malignancy with atypia or inadequate. Imprint smears with uniform cells, normal nucleo-cytoplasmic (N: C) ratio, fine chromatin were classified as negative for malignancy (Figure 1).

Smears with increased cellularity, large cells, hyperchromatic, pleomorphic nuclei, high N: C ratio and irregular coarse chromatin were said to be malignant (Figure 2).

Smears showing benign pattern with few atypical cells having high N: C ratio were said to be negative for malignancy with atypia. In these smears, cellularity was moderate to high but nuclear features for diagnosis of malignancy were not clear cut. Smears showing mainly RBCs with occasional or no epithelial cells were regarded as inadequate.

RESULTS AND DISCUSSION

This study was conducted in a tertiary care hospital over a period of 2 years and a total of 90 cases were studied. Imprint smears were made from the unfixed tissue and stained with H&E and PAP stains. Results were compared with histopathology. Age of patients varied from 12 to 70 years. Majority of benign cases and malignant cases were between 21 to 40 years and 41 to 60 years respectively. Out of 90 cases studied, 87 were females and 3 were males. All 90 cases presented with lump in breast. Additional clinical presentations were nipple deformity, ulceration, palpable axillary nodes and peau'd orange. Only one case presented with nipple discharge. Clinically, 45 cases were diagnosed as benign lesions and rest as malignant. On FNA, out of 53 cases, 21 were benign and 23 malignant. Nine cases were inadequate. On gross examination, majority of benign lesions were small, firm, sharply demarcated having gray white cut surface with whorled pattern, slit like spaces and small cysts. On the other hand, malignant lesions were large, poorly circumscribed and firm to hard with a hemorrhagic, necrotic or cystic cut surface. Imprint smears were made and naked eye examination of smears was done using the criteria of Panesar *et al.*, (1972); Solanki *et al.*, (1977) and Singh *et al.*, (1982). Smears from benign lesions were thin and uniform while malignant ones were thick and irregularly spread. Benign smears were mostly hypocellular due to little desquamation of epithelial cells and cells were found in clusters. Imprints from malignant lesions were obtained with more ease than the benign lesions. Most of the smears were hypercellular and cells were arranged in sheets, groups, clusters or were singly scattered. More malignant the tumor, more cellular the imprint; exceptions being carcinoma with dense fibrous stroma which yielded less cells and fibroadenoma inspite of being benign is highly cellular. Out of 90 cases, naked eye diagnosis of slides was benign in 49 cases and malignant in 41. Of the 49 benign cases, 48 were consistent with histopathology and inconsistent in one which was a case of comedocarcinoma showing scant material. In malignancies, 40 correlated with histopathology except one which was a case of phylloides tumor which showed very high cellularity. Out of 90 cases, 49 were benign and 41 were malignant on histopathology. From the 49 benign lesions, imprint cytology was correct in 42 and 7 were inadequate. Out of 41 malignant lesions, imprint cytology was correct in 39 and 2 were inadequate. Overall diagnostic accuracy was 90%. There were no false positives or false negatives. Thus, imprint cytodiagnosis was inconsistent with histopathology in 7 (14.28%) in benign group and 2 (4.87%) in malignant group. Clinical diagnosis was consistent with histopathology in 44 benign lesions and inconsistent in 1 which was sclerosing adenosis (diagnosed as breast carcinoma histopathologically). There was positive correlation in 41 cases of malignancy and inconsistent in 4 which was diagnosed as malignant clinically. Out of 90 cases, 85 (94.44%) cases were correctly diagnosed by clinical examination. Naked eye diagnosis was correct in 88 (97.77%) while imprint cytology was correct in 81(90%) cases.

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In our study, clinically, patients with small, freely mobile lump without axillary nodes were considered as benign while those with large, firm to hard lump, fixed to skin and other structures with palpable nodes were considered malignant. Similar criteria were utilized by Singh *et al.*, (1982) and Singh *et al.*, (1984) in their study. Tribe (1965) found that gross examination of breast lump was able to distinguish between benign and malignant tumors in 95.1% cases. Suen *et al.*, (1978) studied 473 breast lesions and suggested that in grossly malignant lesions, imprint cytology was enough for intraoperative diagnosis. Singh *et al.*, (1982) found that imprint cytodiagnosis gives 100% results when considered along with clinical examination and gross appearance. On histopathology, 49 (54.44%) cases were benign and 41 (45.55%) were malignant in our study. Fibroadenoma and fibrocystic disease were found to be the most common benign lesions while infiltrating duct carcinoma was commonest malignancy. In study of Tribe (1965) out of 510 breast lesions, 226 (44.31%) were malignant and 284 (54.68%) were benign. Fibrocystic disease was the commonest benign lesion. Solanki *et al.*, (1977) studied 27 benign and 23 malignant lesions. Fibroadenomas and infiltrating duct carcinomas were commonest lesions. Singh *et al.*, (1982) evaluated 40 benign and 30 malignant lesions of which fibroadenomas and carcinomas were most common. Singh *et al.*, (1984) correlated aspiration cytology and imprint cytology in 100 lesions with histopathology and found 65 were benign and 35 malignant. Cox *et al.*, (1991) evaluated 114 lumpectomy margins by imprint cytology which included 82 infiltrating duct carcinomas. Naked eye examination of the stained smears revealed 49 benign and 41 malignant cases. Criteria used by Panesar *et al.*, (1962); Solanki *et al.*, (1977) and Singh *et al.*, (1982) were utilised in our study. Criteria for diagnosis on imprint cytology were similar to those utilised by Tribe (1965); Pilar and Rubenstone (1968); Solanki *et al.*, (1977) and Singh *et al.*, (1984). In our study, from 49 benign lesions, 41 imprint smears were negative for malignancy, 7 were inadequate, 1 showed atypia but it correlated with histopathology and included under negative for malignancy group. From the malignant lesions, 39 smears were positive for malignancy and 2 were inadequate. Thus out of total 90 cases, 81 were correctly diagnosed and 9 were inadequate by imprint cytology. Accuracy of imprint cytology was 85.71% in benign group and 95.12% in malignant lesions. Thus malignant lesions were more correctly diagnosed with no false positive results. Lee (1982) studied 115 breast lesions by imprint cytology of which 36 benign and 66 malignant lesions were diagnosed correctly. There were 2 false positives, 7 false negatives and 4 suspicious for malignancy. Total diagnostic accuracy was 92.9%. Ballo and Snegie (1996) studied 124 cases showing specificity of histopathology to be 100%. In a study of Carmichael *et al.*, (2004) overall concordance between imprint cytology and histology was 90%. For imprint cytology, overall sensitivity was 91% and specificity was 89%. Positive predictive value was 97% and negative predictive value was 73%. Singh *et al.*, (1984) in a study of 100 cases obtained 86% diagnostic accuracy by imprint method, with 2 false positives and 1 false negative. In benign group, 56(86.1%) and 30 (85.7%) from malignant group were diagnosed correctly. Khanna *et al.*, (1991) studied 86 cases (17 benign, 69 malignant) of which 15 and 64 benign and malignant cases were diagnosed correctly. Diagnostic accuracy was 91.8% with 1 false negative and 6 unsatisfactory smears. Similarly Akhtar *et al.*, (2010) and Dutta *et al.*, (2001) reported 100% sensitivity, specificity, positive and negative predictive value when atypia was considered as negative on imprint cytology. High sensitivity, specificity and accuracy results of 97.1%, 99.4% and 98.3% were observed by Veneti *et al.*, (1996). Hiregoudar *et al.*, (2006) studied 40 cases of which 21 were malignant and 19 were benign. Accuracy of 100% and 97.5% was observed in for diagnosing benign and malignant lesions respectively. Very small or very large sized cancer and a high degree of differentiation were major causes of false negative aspirates. Such a result was obtained in a case of carcinoma with dense fibrous stroma which probably prevented exfoliation of neoplastic cells. Other causes of false negative results were due to interpretative errors or insufficient cells (Suen, 1978). A negative imprint does not necessarily exclude malignancy. Imprints should always be interpreted in the light of gross findings (Suen, 1978). A negative diagnosis should be disregarded if the gross appearance of the lesion suggests malignancy (Suen, 1978). In present study, accuracy rate was 90%. Imprints from benign lesions were hypocellular as supported by Dudgeon and Barrett (1934); Tribe (1965); Pilar and Rubenstone (1968) and Singh *et al.*, (1982). However no false

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positives were found in our study. Imprints from malignant lesions were hypercellular. Similar findings were made by Pilar and Rubenstone (1968); Singh *et al.*, (1982); Khanna *et al.*, (1991) and Solanki *et al.*, (1977). These features are attributed to loss of cohesiveness of tumor cells. Errors in diagnosis of malignant tumors were due to paucity of cellular material or lack of clarity of cellular structures or indefinite malignant characteristics (Lee, 1982). Errors in diagnosis of benign tumors was due to large number of clumped cells (Lee, 1982). In our study, 9 smears were found to be inadequate, 7 of which were benign and 2 were malignant. Smears could be inadequate due to faulty technique or small or fibrotic lesions. There was a single inadequate smear of comedocarcinoma, which showed amorphous material as there is possibility of smear being taken from necrotic area. Hiregoudar *et al.*, (2006) observed a false negative rate of 2.5% which was a case of intraductal carcinoma reported as benign on imprint smear. Therefore, it was concluded that a negative imprint does not necessarily exclude malignancy. Imprints should always be interpreted in the light of gross findings. Negative diagnosis should be disregarded if gross appearance of lesion suggests malignancy. It was observed that adhering to certain criteria gave better results (Singh *et al.*, 1982). Tissue surface to be imprinted should be flat, there should be no fat protruding from the edges, as these smudge the smear. First imprints contain excess tissue fluid and blood, subsequent imprints gave better cytological results. Quality of smears can be improved by blotting the cut surface of the specimen by an absorbent material to remove excess of fluid and blood. Benign lesions require more pressure during imprinting. Malignant tissue imprints were more cellular than those of benign. Qureshi *et al.*, (2007) also inferred from his study on 199 patients that imprint cytology is a reliable way of quick and accurate diagnosis and helps in appropriate management of the patients.

Therefore, to conclude, imprint cytology is a simple, reliable and quick method. In places where frozen section facilities are not available, intraoperative imprint cytology when considered along with clinical features and gross appearance of the excised mass, can give an accurate diagnosis. It can be used for rapid diagnosis in postmortem examination.

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