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A Study of Accuracy of Intra Operative Imprint Cytology in Malignant Breast Tumors

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ABSTRACT

Breast cancer is the most common cancer in the western world. For diagnosis of breast cancer, many a times FNAC leads to a diagnosis that is "suspicious, but not confirmatory". The need for intra-operative confirmation of the nature of the tumor as benign or malignant led to frozen section and imprint cytology. Unlike Frozen section, Imprint cytology does not require any specialized equipment, less time consuming, the disadvantages of freezing the tissue and serial sectioning are absent in it. 30 cases who were all women, for this study were sourced from cases admitted. A proforma was used to collect relevant information from all the selected patients. Patients were treated accordingly, imprint cytology was taken and regular follow up was done. In the present study, the overall diagnostic accuracy was 70%. The sensitivity was 70.4%. The specificity was 66.7%. Positive predictive value was 95% with a negative predictive value of 20%. The false negative rate was 29.6%. The false positive rate was 33.3%.

INTRODUCTION

Due to changes in lifestyle and food habits, malignancies in various parts of the body like oral cavity, breast, lungs, GI tract, etc. have become common. Particularly in women most common reason for visiting a surgeon is breast tumors^[1]. For most of the malignancies, Fine Needle Aspiration Cytology has been widely studied and accepted as a diagnostic tool, but FNAC has its own limitations in terms of both sensitivity and specificity. However, the accuracy of the diagnosis is entirely dependent on the experience and dedication of the cytopathologist. FNAC diagnosis depends only on the aspirated material. The tissue immediately adjacent to or contained within another part of tissue may harbor malignant cells. The chance of getting false negative results is more in FNAC as it is a blind procedure using needle poked into the lesion. Many a times FNAC leads to a diagnosis that is "suspicious, but not confirmatory"^[2,3]. The need for intra-operative confirmation of the nature of the tumor as benign or malignant led to the adoption of Frozen-Section technique. The frozen-section biopsy requires specialized equipment, which may not be always available. Therefore as an alternative to frozen-section technique, imprint smears from these tumors were stained with Hematoxylin and Eosin. The method does not require any specialized equipment, less time consuming, the disadvantages of freezing the tissue and serial sectioning are absent in it. Rapid hematoxylin and eosin staining of imprint smears were tried in cases of malignant tumors and has given promising results. Hence, the present study is undertaken to note the accuracy of intra-operative imprint smears in malignant breast tumors in comparison with histopathological examination, which is the gold standard test for detection of malignant lesions^[4].

MATERIALS and METHODS

Sample Size: 30 cases.

Inclusion Criteria:

- All female patients undergoing resection of breast tumors.
- Only elective cases.

Exclusion Criteria:

- Patients with recurrence of malignancy after previous mastectomy surgery.
- All emergency cases.

Method of Collection of Data (Including Sampling Procedure if Any): In this prospective study, 30 female patients with breast tumors were selected based on inclusion and exclusion. Institutional ethical clearance was obtained. Detailed clinical history was taken and

thorough physical examination was done in each patient. Complete pre-operative work up-investigations and medical fitness for surgery were obtained. The patient was informed about the procedure and informed consent was obtained before the patient was subjected to surgery. Based on clinical examination and FNAC findings, Patients underwent modified radical mastectomy or lumpectomy or simple mastectomy with or without axillary sampling. After clinical examination, in cases where FNAC showed malignancy, patient was taken up for modified radical mastectomy., in cases where FNAC showed suspicious of malignancy, patient was taken up for lumpectomy., in cases where FNAC showed benign, Core needle biopsy was done and based on that report, appropriate surgery was done. N2 nodal status patients were taken for surgery, after three cycles of neo adjuvant chemotherapy. During surgery, after removal of the tumor it was bisected to note the macroscopic features. Then, the cut surfaces were pressed onto a clean glass slide and fixed in 95% methanol. Special emphasis was given to tumor bearing area. Rapid hematoxylin and eosin staining were done. The smears were interpreted by the cytopathologist. The results of the imprint smears were compared with final histopathological examination (paraffin section).

RESULTS and DISCUSSIONS

Table 1: Distribution of Study Participants Based on Imprint Cytology Finding

Imprint cytology finding	Number (N)	Percentage (%)
Malignant	20	66.67
Benign	10	33.33
Total	30	100

Table 2: Distribution of Study Participants Based on Type of Tumor Histology

Tumor histology	Number (N)	Percentage (%)
Fibro adenosis	3	10.0
IDC	25	83.3
ILC	2	6.7
Total	30	100

Out of 30 cases, 20 were malignant 10 were benign (Table 1). Out of 30 cases, 25 were Intra ductal carcinomas. 2 were intra lobular carcinoma, 3 were Fibroadenosis (Table 2). Of the 30 cases, intra-operative imprint smear could detect 19 malignant cases accurately. A total of 10 cases were reported to be benign. 8 false negative reports and 1 false positive reports were noted (Table 3). Imprint smears have proved superior to frozen-sectioning due to the inherent disadvantages in the latter. Proponents of touch preparation claim that in the hands of an experienced cytopathologist, it may even be more accurate than permanent sections because it samples the entire surface area of the resected specimen. FNAC though has been a powerful tool pre-operatively., it has its own limitations with regard to sensitivity and specificity. Most often it leads to a diagnosis that is

Table 3: Association Between Intra-Operative Imprint Cytology Result and Post-Operative Histopathology Report (HPR) of Study Participants. N=30

Malignant status		Post-Operative HPR	Benign n (%)	Total n (%)	Chi-square value, df	p value#
Imprint cytology	Malignant	19 (70.4)	1 (33.3)	20 (66.7)	1.667,1	0.25
	Benign	8 (29.6)	2 (66.7)	10 (33.3)		
Total		27 (100)	3 (100)	30 (100)		

Note: # p value based on Chi-square test, df-degrees of freedom.

Table 4: Diagnostic Indices of Intra-Operative Imprint Cytology to Diagnose Malignant Tumor of Breast

Sl.No.	Indices of screening test	Imprint cytology (95% Confidence interval)
1.	Sensitivity	70.4 (60.0-78.7)
2.	Specificity	66.7 (55.8-75.1)
3.	Positive predictive vale	95 (88.7-98.3)
4.	Negative predictive value	20 (12.6-29.1)
5.	False negative rate	29.6 (20.3-38.9)
6.	False positive rate	33.3 (23.9-43.1)
7.	Accuracy	70 (60.0-78.7)

Table 5: Comparison of Values of Various Studies and Our Study

Study	Year	N	FP	FN	Sensitivity	Specificity	PPV	NPV
Cox	1991	114	3	0	100	97	100	88
Saarela	1997	53	11	63	38 85	38	89	
Klimberg	1998	83	0	0	100	100	100	100
Creager	2002	137	15	20	80 85	40	97	
Tribe CR	1973	311	0.7%	5.2%	--	--	--	--
Our study	2014	30	1	8	70.4	66.7	95	20

Table 6: Comparison of Sensitivity, Specificity, Accuracy of Our Study with Other Studies

Study	Sensitivity	Specificity	Accuracy
Khanna AK	98.4	100	94.3
Ku NN	100	97.1	97.7
Veneti S	97.1	99.4	98.3
Our study	70.4	66.7	70

“suspicious, but not confirmatory”. In a clinical scenario, the consultant surgeon will be in a dilemma to counsel and propose the appropriate surgical modality of treatment. In our series we have evaluated the accuracy of intra-operative imprint smears in malignant breast tumors. The proposed ideology is that the tumor cells will adhere to a slide to a greater degree than fat. The sensitivity, specificity, PPV and NPV in our study is compared to other studies here. Cox and colleagues were the first to report the use of touch preparations for intra-operative evaluation of margin status in 1991. In a study of 114 patients undergoing partial mastectomy for breast malignancies, touch preparation was 97% accurate. Saarela^[5] in 1997 reported a sensitivity of 38% and a specificity of 85% which was in contrast to other workers who claimed it to be high. Klimberg^[6] in 1998 reported 100% sensitivity, specificity, PPV and NPV each^[7]. Creager *et al.* in 2002 reported a sensitivity of 80% and a specificity of 85%. Several studies have compared the diagnostic accuracy of imprint smears with that of frozen-section. Tribe CR^[8] suggested that the two techniques are roughly equivalent, with imprint smears having a slightly higher propensity for false positive results. Khanna^[9] reported a sensitivity of 98.4% and specificity of 100%, Scopa reported an accuracy rate of 94.3%. Kim K in 1990 reported the efficacy of intra-operative imprint cytology to be superior to frozen section. Vinod Shidham^[10] reported a strong favour for routine practice of imprint cytology during intra-operative consultation. In our series, we

reported a sensitivity of 70.4%, specificity of 66.7%, PPV of 95% and NPV of 20%. We had 8 false negative cases which were reported benign on imprint smear and final histopathology was intra-ductal carcinoma. 3 cases were benign and all were fibroadenosis. One false positive case which reported malignant in Imprint cytology but proven to be benign in histopathology. 25 cases were intra-ductal carcinomas, 2 cases were intra lobular carcinoma (Table 4,5).

Proper pre-operative counselling with the patient and relatives in the ideology of triple assessment, with incorporation of intra-operative imprint smears, will avoid a repeat surgery. The recent consensus of breast conservation surgery for carcinoma of breast is assuming more importance. Intra-operative imprint smears are the key tools to assess the margin status during these surgeries. Re-excision of the margins can be performed during same surgery if imprint smears are positive., thus avoiding a second surgery. The data suggest that the factors that reduce the risk of local recurrence include excising the tumor to an adequate margin, the use of post-excision radiation and the use of tamoxifen in patients with estrogen-receptor positive disease.

CONCLUSION

In the present study, the overall diagnostic accuracy was 70%. The sensitivity was 70.4%. The specificity was 66.7%. Positive predictive value was 95% with a negative predictive value of 20%. The false negative rate was 29.6%. The false positive rate was 33.3%. The

entire margin can be evaluated in case of breast conserving surgeries. The status of sentinel lymph node can be assessed in minutes. Finally we conclude that imprint smears are simple, accurate, rapid and cost-effective diagnostic tool for intra-operative evaluation of breast tumors. The sensitivity and specificity support their utility intra-operatively wherein facilities for frozen-sections are not available.

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