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Imprint smear- A valid intraoperative diagnostic tool in breast lesions

Authors
Dr Ronald J. Bosco, Dr Sarada V., Pramila R
Trichy SRM Medical College
Email: *ronaldaswathy@gmail.com*, Mobile: 9489214244

Introduction

Intraoperative cytology is a common technique used in the diagnosis of CNS neoplasms. Similarly, Imprint cytology technique in breast lesions is a simple and cost effective on table diagnostic tool where facilities for the commonly used frozen section studies are not available.[1-6] Imprint is comparable to frozen section as a tool for intra operative and post-mortem diagnosis[7-10] In this study we evaluate the accuracy of imprint cytology in rapid on table diagnosis of breast lesions in comparison with histopathology.

Subjects and Methods

The present study is a cross sectional study performed on all specimens of breast lesions received over a period of 17 months from September 2012 to January 2014. All breast specimens including mastectomy, lumpectomy, excision are included in the study with the exclusion of trucut biopsy. A total number of 71 cases were obtained.

Clinical and gross details of the patients were recorded. Imprint cytology of freshly excised tissue is prepared and stained with toluidene blue and Giemsa stains. The smears were studied and specific cytological diagnosis were made independently. The imprint smear findings are categorized into benign and malignant groups. Routine hematoxylin and eosin staining were done on tissue sections after fixation and histopathological diagnosis were made for the lesions. Taking histopathology as a gold standard, sensitivity, specificity, positive predictive value and negative predictive value for diagnosing malignant lesions by imprint cytology are calculated.

Results

In the present study, out of 71 cases obtained from mastectomy, lumpectomy and excision, 59 cases were benign and 12 cases were malignant cases. The benign lesions were found to be more common with a 83% of distribution. Distribution of lesions in the present study are summarised in the table 1. Among all the lesions, fibroadenoma was found to be the commonest lesions (56%) followed by invasive ductal carcinoma (17%). Fibrocystic disease was found as an individual disease in 10% cases and also in association with fibroadenoma in 17% of cases. Overall, breast lesions were common in the third and fourth decade of life (58%). Relative number of benign and malignant lesions in different age groups are summarised in figure 1.

In Imprint smear, most of the malignant lesions showed high cellularity except one case ,which was subjected to mastectomy after lumpectomy. Fibroadenoma showed predominantly high to moderate cellularity, except for two cases, which showed small cohesive clusters of cells with presence of myoepithelial cells and based on that, those lesions were interpreted as benign proliferative lesion on imprint smear. Histopathology showed increased stromal cellularity in the above cases, reflected by the presence of fibroblasts in imprint smear. Sixty percent of the hypocellular lesions included gynacomastia and fibrocystic disease. Cases of fibrocystic disease with hypercellularity on imprint smear showed associated ductal hyperplasia in histopathological examination. One case of epidermal cyst showed only anucleated squamous cells on imprint cytology. Cellularity of various lesions in imprint smear is summarised in the table 2. Necrosis was identified by imprint smear in all malignant cases and two cases of granulomatous mastitis. Other secondary features appreciated in imprint smear evaluation of were cystic change, hyperplasia and apocrine metaplasia.

Presence of myoepithelial cells was found to be specific for diagnosis of benign lesions by imprint smear study. Significance of myoepithelial cells in the diagnosis of benign lesions are summarised in the table 3, table 4. Six benign lesions were found to have no myoepithelial cells, including two cases of granulomatous mastitis dominated by inflammatory cells. Others include fibrocystic disease with scanty cellularity, gynacomastia with stroma predominant pattern, epidermal cyst and benign stroma predominant phylloides tumor which yielded hypercellular spindle cells in imprint smears.

Current study showed that in comparison with histopathology, imprint smear has 100% sensitivity and specificity in diagnosing a malignant lesion. The significance of imprint smear in the diagnosis of malignancy are summarised in the table 5, table 6.

Table 1 Distribution of various lesions in the present study

Lesions	No of cases
Fibroadenoma	28
Fibroadenoma with fibrocystic disease	12
Fibrocystic disease	7
Gynacomastia	6
Benign phylloidestumor	1
Intra ductal papilloma	1
Epidermal cyst	1
Granulomatous mastitis	3
Ductal carcinoma	12
Total	71

Table 2 Cellularity of various lesions in imprint smears

Cellularity	FA	FCD	GYN	PAP	PHYL	GM	EC	CA	TOTAL
High	30	3	1	1	1	3	0	11	50
Moderate	8	1	2	0	0	0	0	0	11
Low	2	3	3	0	0	0	1	1	10
Total	40	7	6	1	1	3	1	12	71

Table 3 Presence of myoepithelial cells in imprint smears of benign and malignant lesions

	Nature of lesion by histopathology	
	Benign	Malignant
Myoepithelial cells present in imprint smear	53	0
Myoepithelial cells absent in imprint smear	6	12

Table 4 Significance of myoepithelial cells in the diagnosis of benign lesions by imprint smear

Presence of myoepithelial cells in a benign lesion by imprint smear	Sensitivity	Specificity	Positive predictive vale	Negative predictive vaue
	89.83%	100%	100%	66.67%

Table 5 Number of benign and malignant lesions by imprint smear and histopathology

	Nature of lesion by histopathology	
	Benign	Malignant
Benign lesion by imprint smear	59	0
Malignant lesion by imprint smear	0	12

Table 6 Significance of imprint smear in the diagnosis of malignancy

Diagnosis of a malignant lesion by imprint smear study	Sensitivity	Specificity	Positive predictive vale	Negative predictive vaue
	100%	100%	100%	100%

Table 7 Comparison of distribution of benign and malignant cases with previous

Study	Sample size	Benign	Malignant
Khanna et al[11]	1315	61.3%	38.7%
Hassanian et al[4]	110	73.6%	26.4%
Malik et al[12]	1824	89%	11%
Present study	71	83.09%	16.91%

Table 8 Comparison of sensitivity, specificity, positive predictive value, negative predictive value and accuracy of imprint cytology in literature

Study	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
Ammar et al[1]	-	-	-	-	94%
Hiregouder et al[2]	-	-	-	-	97.5%
Hassanian et al[4]	96.3%	100%	100%	98.6%	98.9%
Maria F et al[5]	100%	100%	-	-	-
Sushma et al[9]	-	-	-	-	90%
Khanna et al[11]	98.4%	100%	-	-	98.8%
Akhtar et al[21]	100%	100%	100%	100%	100%
Lee et al[22]	-	-	-	-	92.9%
Dutta et al[23]	-	-	-	-	94%
Scopa et al[24]	100%	100%	-	-	100%
Present study	100%	100%	100%	100%	100%

Discussion

Carcinoma of the breast is one of the leading cause of death almost exclusively in women, but can also occur in men. There is a requirement for rapid diagnostic tool for on table diagnosis to decide on the mode and extent of surgery. Presently frozen section is the widely used technique, which is expensive. In this context, review of literature and present study validates the role of imprint smear in this regard.

Comparison of distribution of benign and malignant cases with previous literature are summarised in the table 7. Observations in our study varied slightly due to variable sample size and duration of study. Peak age group for malignancy was 40-49 in present study, comparable with previous literature[4,13] Malik et al reported ductal carcinoma as the most common malignant lesion which is compatible with the present study[12].

Tissue surface to be imprinted should be flat, there should be no fat protruding from the edges, as these smudge the smear. First smears usually contain excess tissue fluid and blood, subsequent imprints usually give 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.[9] These techniques were adopted in the present study.

According to literature, imprint smears with cytological features like uniform sized cells, normal nucleo-cytoplasmic (N: C) ratio, fine chromatin are classified as 'negative for malignancy'. Smears with increased cellularity, large, hyperchromatic, pleomorphic nuclei, high N: C ratio and irregular coarse chromatin are features of malignancy. Exceptions can be observed where carcinoma with dense fibrous stroma yields less cellularity[6]. Fibroadenoma inspite of being benign, are usually highly cellular.[9] Smears showing predominantly benign pattern with few atypical cells having high N: C ratio can be reported as' negative for malignancy with atypia'. Smears showing predominantly hemorrhage with occasional or no epithelial cells can be regarded as inadequate[9,14-19]. Haeri et al described a criteria for imprint cytology including cellularity, loss of cohesion, atypia, myoepithelial cells and nucleoli which were also followed in this study for evaluation[20]

In this study, smears from benign lesions are thin and uniform while malignant are thick and irregularly spread. Most of the smears were hypercellular with sheets, clusters or singly scattered pattern. More malignant the tumor, more cellular are the smears with more loss of cohesiveness. These findings were comparable with the literature.

Present study had 100% sensitivity, specificity, accuracy in diagnosing benign and malignant lesions, also taking into account the gross and clinical findings. All these results was comparable with the previous literature. Comparison of sensitivity, specificity, positive predictive value, negative predictive value and accuracy of imprint cytology in literature is summarised in the table 8. Suen et al analysed 473 breast cases and found out that in all cases where gross and clinical findings suggested malignancy, imprint smear was able to diagnose lesions accurately[25].

Errors in diagnosis of malignant tumors are due to paucity of cellular material, lack of clarity of cellular structures or indefinite malignant characteristics. Smears can be inadequate due to faulty technique, small size of the lesion and in cases of fibrotic lesions. Comedocarcinoma may yeild amorphous material because of the possibility of smear being taken from the necrotic area. Misdiagnosed lesions by imprint cytology are reported in literature which includes papillary lesions, lesions showing low-grade atypia, lesions showing low cellularity, lesions with ductal hyperplasia or ductal carcinoma in situ, lobular carcinoma, low-grade carcinomas (e.g., tubular carcinoma), small foci of carcinoma or a complex proliferative/atypical hyperplastic foci in fibrocystic diseases and radiotherapy induced changes.[3,25-28] Literature shows that a positive diagnosis of malignancy is more reliable than negative diagnosis and they imply the importance of latter cases subjected to lumpectomy to rule out underlying malignancy.[9,29]

Imprint cytology should always be interpreted in the light of clinical and gross findings[2,28,30]. Negative diagnosis should be disregarded if gross appearance of lesion suggests malignancy.[25]This technique doesn't provide information on the depth of infiltration of tumor although it might provide information on the original site of tumor.[30]Imprint cytology has the advantage of providing better cellular morphology and fewer artifacts. On the other hand Frozen Sections provides more tissue architectural details but frequently hampered by freezing artefact.[2,10,20,29]

Cases like Fibroadenomas can present a very worrying appearance particularly in pregnancy, lactation or when they occur in an elderly woman. Necrotic debris can be seen in inflammatory conditions. Inflammatory conditions can be associated with marked reactive atypia of epithelial cells.[29]

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