

Role of imprint cytology in breast lesions.

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Abstract

Background: Rapid cytological diagnosis of various tumors and especially that of breast was first introduced by Dudgeon and Patrick 1927. The accuracy of the imprint method has been increasing over the years both in breast pathology and in other body sites, indeed the average accuracy of (90-94%) in the past has reached (97-98%) in recent years.

Objective: A prospective study was performed to determine the value of this technique in the diagnosis of male and female patients with various breast lesions.

Methods: From June 2005 and February 2006 Imprint cytology was obtained from (110) specimens of (107) patients with various breast lesions in Sulaimania teaching hospital.

Cytological examinations of imprints stained by hematoxiline and eosin stain were examined and compared to histological results to detect its sensitivity, specificity and accuracy rate.

Results: The sensitivity and specificity of imprint cytology for both benign and malignant

breast lesions were 96.3% and 100% respectively; while over all accuracy was 98.9%. False negative diagnosis was seen in a single case of Paget's disease of the nipple (0.9%); however no false positive cases were found.

The cytological diagnosis were malignant in 26 cases (23.7%), including (25) primary malignant tumors and (1) metastatic carcinoma, benign diagnoses were encountered in 71 cases (64.5%), suspicious in 4 cases (3.6%) and unsatisfactory in 9 cases (8.2%).

Conclusion: Imprint cytology is simple, rapid, inexpensive and accurate method for intraoperative diagnosis of breast lesions and can be used as adjunct to frozen section.

Key words: Imprint cytology, breast lesion

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Introduction

Rapid cytological diagnosis of various tumors and especially that of breast was first introduced by Dudgeon and Patrick 1927 through examination of fresh tissue by the wet film method ⁽¹⁾. Since that several series describing imprint cytology of the breast have been published; the acceptance and development of imprint cytology have been hampered because of concerns about its diagnostic accuracy in comparison to frozen section technique. Recent reviewed articles reveal that good correlation exists between imprint

cytology (IC) diagnoses and corresponding final histology, moreover there are several reports on cases of malignancy correctly diagnosed by IC but falsely called negative on frozen section (FS) analysis ⁽²⁾. Intraoperative imprint smears like frozen sections help in on table diagnosis, wherein the fine needle aspiration cytology (FNAC) is inconclusive or suspicious ⁽³⁾. The accuracy of the imprint method has been increasing over the years both in breast pathology and in other body sites, indeed the average accuracy of (90-94%) in the past has reached (97-98%) in recent years ⁽⁴⁾.

The technique of imprint cytology is accurate, simple, rapid, cost-effective and do not require any special instrument, in contrast to frozen section which is more time-consuming, required specialized equipment, need

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well trained histopathologists, expensive and may not be always available⁽⁵⁻¹⁰⁾.

The aim of this study is to assess the role of imprint cytology in the diagnosis of various breast lesions in comparison to the histopathological diagnoses.

Materials and methods

From June 2005 to Feb 2006, all patients who were admitted to the surgical ward of Teaching, Shorish and some private hospitals in Sulaimani city for excisional biopsy of a breast mass or for mastectomy were included in this study.

Imprint cytology was done on freshly removed tissue inside the theater; the suspected area was sliced into several pieces. For small mass, it was bisected, the freshly cut surface of tissue is then imprinted onto a clean glass slide. For large masses, the portion of tissue used for imprinting was trimmed to approximately (1 cm) in diameter, and the same above procedure is repeated⁽¹¹⁾.

The slides were immediately fixed in 95% ethyl alcohol, and then divided into two groups. The first group was withdrawn from the fixative after 10-20 seconds and preceded for rapid H&E stain. The second group remained in fixative (20-30 minutes) for traditional H&E cytological staining. The same piece of tissue used for imprinting was then fixed in 10% formalin for paraffin sectioning and histopathological examination. The first group was stained by the rapid method described by Scopa et al⁽¹²⁾ while the second was stained by the routine H&E procedure described by Gubin⁽¹³⁾.

The lesions were cytologically classified into four groups: 1) Unsatisfactory : contained 4-6 clusters on the entire slide 2) Benign: If they contained cohesive clusters of epithelial cells without atypia 3) Suspicious: presence of atypical cells in a three

dimensional clusters 4) Malignant: when there is sufficient number of malignant cells⁽¹⁴⁻¹⁶⁾.

Statistical analysis: The clinical efficacy and diagnostic accuracy of imprint cytology was done by using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPP), and accuracy rate were measured. For statistical analysis all unsatisfactory and suspicious cases were excluded.

Results

One hundred and ten specimens, surgically removed from (107) patients including (96) specimens from females and (14) from males. The specimens were (93) excisional biopsies and (17) mastectomy specimens (15 from females, and 2 from male patients). We have (6) masses from (3) female patients with bilateral lumpectomy. There were 14 males (12.7%), and 96 (87.3%) females, with female to male ratio of 6.9:1.

Table (1) shows age distribution for patients with histologically benign and malignant breast lesions. The age ranged from 15 to 75 years with a mean of 36 years. Most benign lesions were in the second decade while most of the malignant tumors were in the fourth decade of life.

Table (2) shows the histological and cytological results. Histological results were 81(73.6%) benign and 29 (26.4%) were malignant however cytological diagnosis was benign in 71(64.5%), malignant in 26 (23.6%), suspicious in 4 (3.6%), and 9 (8.2%) cases were unsatisfactory.

In comparison with histological diagnosis the sensitivity and specificity of imprint cytology were (96.3%) and (100%) respectively, PPV was 100% and NPV was 98.6% and accuracy was 98.9% as represented in Table (3). There was no difference found between the results of the rapid and the routine

haematoxylin and eosin staining methods.

previously reported studies are shown in table (4).

The comparison of the current study imprint cytology results with that of

Table 1: Age distribution of patients according to histological diagnoses.

Age groups	Lesion		Total
	Benign	Malignant	
10--19	11	0	11(10%)
20--29	28	1	29(26.4%)
30--39	16	7	23(21%)
40--49	19	8	27(24.5%)
50--59	6	5	11(10%)
60--69	1	6	7(6.7%)
70--79	0	2	2(1.8%)
Total	81	29	110(100%)

Table 2: Correlation between cytology and histological diagnoses of breast lesions

Histological diagnosis	Cytological diagnosis				Total
	Negative cases	Suspicious cases	Positive cases	Un satisfactory	
Benign	70 (86.4%)	2 (2.5%)	0 (0%)	9 (11.1%)	81 (100%)
Malignant	1 (3.4%)	2 (7%)	26 (89.6%)	0 (0%)	29 (100%)
Total	71 (64.50%)	4 (3.60%)	26 (23.70%)	9 (8.20%)	110 (100%)

Table 3: Statistical analysis of all breast lesions

Statistical tests	No. of cases
Histological diagnoses	110
Imprint cytological diagnoses	97
Unsatisfactory cases	9
True positive (TP)	26
True negative (TN)	70
False positive (FP)	0
False negative (FN)	1
Deferrals (suspicious)	4
Predictive Values:	
Sensitivity	96.3%
Specificity	100%
Positive predicted value (PPV)	100%
Negative predicted value (NPV)	98.6%
Accuracy	98.9%

Table 4: Imprint cytology in literature compared to the present study

Authors	Patients No.	No. FP	No. FN	Sens (%)	Spec (%)	Accu (%)	Deferrals
Scopa <i>et al.</i> ,1990	82	0(0%)	0(0%)	100%	100%	100%	4(4.9%)
Khanna <i>et al.</i> ,1991	86	0(0%)	1(1.25%)	98.4 %	100%	98.8 %	6(6.9%)
Rosa <i>et al.</i> ,1993	407	0(0%)	7(1.72%)	97.6 %	100%	98.3 %	12(2.9%)
Veneti <i>et al.</i> ,1996	351	1(0.28%)	5(1.4%)	97.1%	99.4 %	98.3 %	7(1.99%)
Scucchi <i>etal.</i> ,1997	1197	0(0%)	9(0.75%)	97.5%	100%	99.2 %	9(0.75%)
Albert <i>et al.</i> ,2000	173	3(1.7%)	4(2.3%)	96. 5%	90 %	95.4 %	12(6.9%)
Current study, 2006	107	0(0%)	1(0.99)	96.3%	100%	98.9%	4(3.9%)

Discussion

Unsatisfactory imprint cytology was found in (9) cases (8.2%), four of them were gynecomastia, two cases of lipoma, and the remaining three cases found in fibrocystic disease of the breast (two cases) and one case of fat necrosis. Since the (4) cases of gynecomastia composed entirely of fibroadipose tissue and the (3) cases of lipoma and fat necrosis composed of fat cells only they were considered as unsatisfactory, similar results were found in other studies⁽¹⁷⁻²⁰⁾.

While in two cases of fibrocystic disease there were no cells apart from inflammatory cells, similar findings described by Albert *et al*⁽¹⁴⁾.

There were no false positive cases in all imprints taking; similar finding was seen by other investigators^(3,12,20). This is probably because of the clear morphological features, adequate samples or results enhanced by using intraoperative cytology coupled with gross examination of surgical specimens^(2,10). There was only one false negative case later appeared to be Paget's disease of the nipple, similar results found by Veneti *et al*⁽⁹⁾ which explained by lack of clear cytological

evidence of malignancy with either few cells that could be easily missed or small cells which difficult to distinguish from normal cells that need to be evaluated with other histological parameters.

The rate of false negative in present study was (0.99%) which is higher than Scopa *et al.*⁽¹²⁾, and Scucchi *et al.*⁽²⁾ (0% and 0.75% respectively), but lower than that reported by Khanna *et al.*⁽²⁰⁾, Veneti *et al.*⁽⁹⁾ Rosa *et al.*⁽¹⁰⁾, and Hiregoudar *et al.*⁽³⁾ (1.25%, 1.4%, 1.72%, and 2.5%) respectively.

There were (4) deferral (suspicious) cases (3.9 %) in current study, which was high in comparison to Succhi *et al.*⁽²⁾ (0.75 %), Veneti *et al.*⁽⁹⁾ (1.99%) and Rosa *et al.*⁽¹⁰⁾ (2.9%) but lower than Scopa *et al.*⁽¹²⁾, Albert *et al.*⁽¹⁴⁾ and Khanna *et al.*⁽²⁰⁾ (4.9%, 6.9% and 6.9%) respectively.

This difference may be due to higher number of cases in the previous studies compared to the current study, this allows the pathologist to gain good experience and confidence in the technique, another reason is the use of scraping method with imprinting, this

allows high number of cells to detached from the tumour hence more material to be studied, and lastly if the pathologist had any doubt in mind he always inclined to call the lesion suspicious rather than malignant⁽¹⁵⁾.

Two cases of fibroadenoma, were considered as suspicious because of florid cell population and considerable atypia, It has been found throughout this study that on imprinting fibroadenoma a surprisingly large amount of cellular materials is transferred to the slide, this hypercellularity that usually associated with malignant imprints was a confusing element in the cytological diagnosis of these tumors, similar finding was mentioned by other authors^(10, 12, 21). The other two cases (invasive ductal carcinoma and Paget's disease) were considered as suspicious due to paucity of cellular material, and the lack of definite malignant characteristics⁽²⁾.

The sensitivity of the method was (96.3%) which is lower than that reported by other studies^(12, 20, 22), this may be due to sample size as the malignant cases in current study was smaller than other studies. The high specificity(100%) which is similar to other comparative study^(3, 22) might be due to the preservation of cellular details, avoiding problems and artifacts of freezing in FS⁽²³⁾. Creager concluded that the sensitivity&specificity of IC are similar to that of FS⁽²⁴⁾. The accuracy of the method was (98.9%) which is slightly higher than Veneti *et al.*⁽⁹⁾ (98.3%), Rosa *et al.*⁽¹⁰⁾ (98.3) and Khanna *et al.*⁽²⁰⁾ (98.8%), but lower than that of Scopa *et al.*⁽¹²⁾ (100%) and Scucchi *et al.*⁽²⁾ (99.2%). IC smears are being increasingly used to evaluate sentinel lymph node which is the first lymph node to receive lymphatic drainage from the site of the primary tumour with high sensitivity(93%)⁽²⁵⁾ and specificity

(99.2,100%)^(26, 27). Worldwide research is in progress even with regard to immunohistochemisry and DNA markers in IC.⁽²⁶⁻²⁸⁾.

In conclusion Imprint cytology is simple, rapid, inexpensive and accurate method for intraoperative diagnoses of breast lesions and can be used as adjunct to frozen section. Further studies, on larger samples in comparion with FS are needed to establish the method in the common clinical practice.

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