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Feasibility of Fine Needle Aspiration Cytology in the Diagnosis of Breast Lumps

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Abstract

Objective*: The study aimed principally to evaluate the feasibility and accuracy of Fine Needle Aspiration Cytology (FNAC) in the diagnosis of breast lumps by comparing the results with the histopathological diagnosis.*
Methodology: *Data were pros-precatively collected from 103 female patients. All patients had palpable breast lumps for whom initially aspiration cytology of the lump has been done followed by partial or total surgical lump excision for final histopathological diagnosis and to compare the results.*
Results: *Of all FNAC specimens, 98 (95%) were adequate for cytological interpretation. Of those evaluated cytologically, 62 (62.8%) were benign, 9 (9%) were suspicious for malignancy and 27 (27.5%) were malignant. Of the surgical histopathological specimens, 40 (40.8%) were malignant.*
Conclusion: *The FNAC procedure is a rapid method, easy to perform, of little cost and easily accepted by the patients and it provides a high specificity and quite reasonable sensitivity rates that can be used for rapid diagnosis and screening.*
Recommendation: *FNAC results are better interpreted in correlation with the clinical and imaging findings to allow better management for the patient and is better to be used with ultrasound guidance for better and adequate aspirates*

Keywords: *Breast Lumps (Masses), Tumour, Fine Needle Aspiration Cytology (FNAC), Biopsy, Histopathology*

Introduction

Breast cancer is the most common malignancy in women around the world. Information on the incidence and mortality of breast cancer is essential for planning health measures[1]. Significant progress has been achieved over the past 30 years in improving survival rates following an invasive breast cancer diagnosis. This improvement is likely the result of advances in the efficacy of breast cancer diagnosis and treatments[2]. When cancer is suspected, microscopic analysis of breast tissue is necessary for a definitive diagnosis and to determine the extent of spread (in situ or invasive) and characterize the type of the disease[3].

Cytology is the science which can differentiate between normal cells, neoplastic cells and inflamed cells. Johannes Müller (1801-1858), a pathologist in Berlin, was the first, in 1838, to show cancer cells as they appeared in the microscope on scrapings from the cut surface of surgically excised tumors[4] .

Fine needle aspiration cytology is the best and most commonly used method for sampling proliferative lesions and masses and it can be easily performed in a practice setting. Sampling of tumors by means of narrow gauge needle was first described in 1930 in USA and become popular in late 1950s[5].

A FNAC is a semi-invasive method to extract a small sample of the questionable breast tissue that allows the pathologist to describe the type of the cancer in detail[6]. It is simple, safe, cost effective and accurate method for the initial diagnosis and for guiding treatment and used routinely in the initial evaluation of breast masses[7]. The technique is countered by the difficulty of interpretation where in some cases normal cytology never excludes the possibility of cancer [8] . In cytological examination a uniform population of cells often suggests the mass is benign, whereas variation in cells suggests malignancy[9] .

Objective

To assess the feasibility of FNAC as a method of diagnosing breast lumps by comparing the cytological results with the surgical histopathological (i.e,biopsy) diagnosis and to assess the sensitivity , specificity and other statistical values of FNAC procedure in the diagnosis of breast lumps (independent of clinical and imaging modalities).

Methodology

The study revealed one hundred and three (103) patients presented with breast lumps to the outpatient

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department in Al-Hakeem general hospital and/or private clinic within a period of 5 years (Feb.2009 to Jan.2014). The history taking includes: Age of patient, chief complain and its duration, marital state, reproductive history, lactation, previous history of breast disease, history of trauma to the breast, smoking, family history and history of contraceptive pills taking.

Complete physical examination of the patients was done in addition to the local examination of the breast lump or mass regarding its size, shape, consistency, its relationship to the skin and underlying tissue, and overlying skin changes, nipple discharge and retraction. Axillary and other lymph nodes were also examined.

FNAC, radiography, ultrasongraphy and other investigations whenever needed were applied. Partial or total surgical excision (biopsy) was subsequently performed for all these lesions , and biopsies were all histopathlgically examined and confirmed. The cytological and histopathological procedures and readings are done within the histopathology lab of Al-Sadr medical city.

The results of FNAC fall into the following categories:

1) Inadequate (acellular) specimen
2) Benign (Negative): normal epithelial pattern and cytologic features
3) Suspicious for malignancy: the cells are not interpretable with certainity as carcinoma.
4) Malignant (Positive): the cells are indicative of malignancy.

The FNAC and the histopathological results were compared by entering the data into a comparison table (table no.7) which will give the number of true-positive(TP), true-negative(TN), false-positive(FP) and false-negative(FN) FNAC results. These values were then used to calculate the following statistics (by using standard formulas).

1) Sensitivity = TP / TP + FN × 100%
2) Specificity = TN / TN + FP × 100%
3) Positive Predictive Value(PPV) = TP / TP + FP × 100%
4) Negative Predicyive Value (NPV) = TN / TN + FN × 100%
5) Accuracy = correct cases / total number of cases studied × 100%

Results

Table 1 Distribution of patients according to age

Age group in years	Benign		Malignant	
	No. of patients	%	No. of patients	%
< 20	8	12.9	-	-
20 - 29	31	50	-	-
30 - 39	19	30	1	2.4
40 – 49	3	4.8	4	9.7
50 - 60	-	-	24	58.5
>60	1	1.6	12	29.2
Total no.of patients	62	60.1	41	39.9

The age of female patients was ranged from 18 to 66 years (the mean age =36.3).The peak incidence of benign breast lesions occurred in the 3rd decade of life (50%), while the peak incidence of malignant cases occurred in the 6th decade of life (58.5 %)

Table 2 Clinical presentations of patients

Clinical Presentations	Benign		malignant	
	No. of patients	%	No. of patients	%
Lump	62	100	41	100
Pain & discomfort	33	53	11	26.8
Nipple discharge	4	6.4	5	12.1
Nipple retraction	-	-	8	19.5
Skin changes	-	-	5	12.1
Axillary lymph nodes	-	-	6	14.6

All patients were presented because of their breast lump. The second most common presenting feature was breast pain and discomfort. Among the patients with the malignant breast lesions, the breast pain and nipple retraction were the next two common presenting features which occurred in 11 (26.8%) and 7(19.5%) patients respectively.

Table 3 Size of the breast lumps

Size of lump	Benign		Malignant	
	No.of patients	%	No. of patients	%
< 2 cm	53	85.5	7	17
2 – 5 cm	7	11.3	28	68
>5 cm	2	3,2	6	14.6
Total no.of patients	62	60.1	41	39.9

Most patients (92.2%) were presented with breast masses less than 5 centimeters in diameter

Table 4 The cytological diagnosis of FNAC

Cytological	Diagnosis	No. of patients (%)	Total no.
Inadequate (Unsatisfactory)	Aspirates	5 (4.8)	5
Benign Looking Cells (Negative Cytology)	Fibrocystic disease	33 (32)	62
	Fibroadenoma	13 (12.6)	
	Duct ectasia	3 (2.9)	
	Inflammatory	2 (1.9)	
	Not specified	11 (10.6)	
Suspicious for Malignancy	(Positive Cytology)	9 (8.7)	36
Malignant Looking Cells	(Positive Cytology)	27 (26.2)	
Total	No. (%)	103 (100)	103

5 aspirates (4.8%) were considered inadequate for cytological diagnosis because they did not contain sufficient cellular material. Therefore, among the remaining 98 adequate aspirates, 62 aspirates(63%)

were benign on cytological examination. 9 cases (9%) were suspicious for malignancy. 27 aspirates (27.5%) were clearly identified by the cytological examination to be malignant. For the purpose of statistical measurement, the suspicious cytological cases were considered as (positive) cytologically.

Table 5 Classification of cases according to the final histopathological diagnosis

Histopathological	Diagnosis	No.of patients(%)	Total no.
Consistent with Benign lesions	Fibrocystic disease	38 (61.3)	62
	Fibroadenoma	15 (24.1)	
	Duct ectasia	2 (3.2)	
	Inflammatory / Chronic abscess / antibioma	7 (11.3)	
Consistent with Malignant lesion	Invasive ductal cancer	37 (90.2)	41
	Invasive lobular cancer	3 (7.3)	
	Ductal carcinoma insitu	1 (2.5)	
Total	No.	103	103

62 patients (60%) had confirmed to have benign pathology, and 41 cases (40%) had proven to be malignant. All of the clearly identified malignant (positive) aspirates had proved to be malignant on the subsequent histopathological examination

Table 6 Breast diseases with FNAC diagnostic errors

Diagnosis	Type of the error		
	Inadequate aspirate	False negative	False positive
Fibrocystic diseasr	3	-	2
Fibroadenoma	1	-	1
Duct ectasia	-	1	-
Non specified	-	6	-
Malignant	1	-	-

Only 7 of the benign cytological (negative) aspirates had proven histopathologically to be malignant. The false-negative results of the cytological diagnosis had occured in the duct ectasia(1 case) and in the non specified benign results(6 cases). The histopathological examination of the suspicious aspirates had confirmed 6 of them to be malignant and 3 to be benign (fibrocystic disease 2, and fibroadenoma 1).

Table 7 Comparison between FNAC & histopathological results of the 98 adequate cytological aspirate cases

FNAC diagnosis	Surgical (histo pathological) diagnosis		Total no.
	Benign	Malignant	
Benign	55 (TN)	7 (FN)	62
Suspicious	3 (FP)	6 (TP)	9
Malignant	0 (FP)	27 (TP)	27
Total no.	58	40	98

58 patients (59.2%) had confirmed to have benign pathology, and 36 cases (40.8%) had proven to be malignant

Table 8 Statistical values

Statistical name	%
Sensitivity	82.5
Specificity	95
Positive Predictive Value(PPV)	91.6
Negative Predictive Value(NPV)	88.7
Accuracy	89.7

Discussion

Accurate diagnosis of breast lesions depends on a triple assessment approach comprising clinical, imaging and pathologic examinations[10]. Fine Needle Aspiration is an extremely useful method , it has the purpose of obtaining diagnostic material for cytological study which can obviate the need for standard excisional biopsy[5]. It has the advantage of a microscopic preparation consistent with the tissue of origin, without the changes that occur in histological sections by fixation and processing[8].FNAC has great acceptance than any other diagnostic methods due to its simplicity,quickness, inexpensiveness and that it can be performed with little complications . However, rates of correct diagnosis with the FNAC vary, where the diagnostic accuracy of FNAC can range from 72% - 95%[11] .

In this study, 5 (4.8%) aspirates contained insufficient material for cytological study , which were incorrectly judged to contain sufficient material at the time of procedure. The histopathological examination had confirmed 4 (80%) of them to be benign and one (20%) to be malignant .In a study done by Chaiwunn and Thorner ,they found frequency of inadequate specimens varied tremendously from 0.7 – 47%[12] ,while Nguansangiam S. and his collegues found that only 4.2% of cases had inadequate mammary epithelial cells that the cytological diagnosis could not be made[13].One of the important problem associated with FNAC was the variable but sometimes unacceptably high rate of inadequacy[14].The exact definition of what constitutes an inadequate aspirate remains an enigma[10]. Inadequate specimens are labeled “nondiagnostic” or “unsatisfactory”[15].The adequacy of FNAC is dependent on multiple factors including the nature of the lesion,the available technology,vascularity of the mass,the experience of the operator and the criteria used to judge adequacy of the specimen[10,15].However, some authors suggested some measures to reduce the rate of inadequacy including proper training of the physicians who perform the aspirate, the use of ultrasound guided FNA and immediate evaluation by pathologist using rapid stainig of the specimen[11].

62 (63%) cases were cytologically of benign results (negative aspirates) in which 7 of them had histopathologically proven to be malignant (i.e,false

negative). Therefore, the overall false negative rate in this study was 11% (7 of 62) which is in the range as had been reported in other studies, 2.5 – 17.9%(reviewed in Chaiwun and Thorner,2007)[12].A significant false negative rate for FNAC also has been found by Ishikawa in the range of 1.2–10.6% [16]. The false negative rate is defined as the percentage of patients with benign cytology in whom malignant lesions are later confirmed on excisional biopsy[15] which could lead to missed or delayed diagnosis of malignancy. The underlying causes for false negativity can be grouped into diagnostic errors and true false negative factors. Diagnostic errors can be attributed to lack of training, overload of cases, and miscorrelation with the patient's clinical and radiologic findings. In the true false negative factors, the denominators are poor sampling technique, small tumour size or mislocalization of the tumor , hypocellularity and the presence of a particular histologic tumour types or a well-defined tumor demonstrating minimal atypia[10,13].

The malignant (positive) aspirates in this study involve both the clearly identified malignant FNAC results and the suspicious one's (where suspicious cytology assumed to be positive for malignancy). 9 cases were cytologically suspicious for malignancy and 27 cases were clearly identified by the cytological examination to be malignant. Accordingly, 36 cases(36.7%) were considered to have positive FNAC results. A primary cytologic diagnosis of suspicious lesion had been given when there were some atypical cellular features without definite evidence of malignancy. This study had a suspicious FNAC diagnosis of 8.7% which is slightly higher than Josip Mišković et al. study[17].However, a study done by Day C. et al.had found that the suspicious FNAC diagnosis lie in the range of 4 – 17%[11]. The percentage of true positivity (proportion of histologically proven cancers detected cytologically) has ranged from 69 to 96% in some studies[18]. Out of the 36 positive FNAC results , 3 of them only had given false positive results with a chance of positive results being incorrect to be 8% (3 out of 36). A false-positive diagnosis indicates that a patient with a "malignant" FNAC result was found on histopathological examination to have benign lesions[15]. Hypo-cellularity, cell necrosis, and epithelial hyperplasia are some of the factors that may be encountered in evaluating a difficult smear, mimicking atypical or malignant lesions giving a false positive diagnosis[10]. Some studies reported a false positive rate of 5.5%[11] while others found the rate to be uncommon occurring in 0 – 2,5%[12].These differences might lie on the grouping of the suspicious cases together with or separated from malignant cases. It has been reported that most benign lesions misinterpreted cytologically as possibly malignant belong to the fibrocystic disease category(fibroadenoma) in which there are instances wherein the diagnosis of fibroadenoma on cytology is not straight forward[19].

This study had found that the FNAC has the ability to correctly classify patients as having breast cancer(i.e,SENSITIVITY "SN") in 82.5% of the time, and the probability of patients with negative FNAC that truly not having cancer (i.e, SPECIFICITY "SP") were found to be 95% . Actually, these values are very close to the results found by both Ramesh SW et al.[20](SN=88.2%, SP=100%) and Hashemzadeh SH et al[21](SN=89.7%, SP=97.6%). However, Chaiwun and Thorner study[12] was found that the diagnostic performance of FNAC regarding the sensitivity is lying in the range of 75% - 98% and the specificity of 60% - 100% .

The most clinically useful indices of the technique's validity are the positive predictive value(PPV) and the negative predictive value(NPV). PPV is the percentage of patients with positive FNAC who truly have breast cancer.In this study,patients with palpable breast lumps and positive FNAC aspirates were found to have 91% chance of having malignant disease, which is very close to the lowest limit range (93% - 100%) found by Chaiwun and Thorner[12].The NPV is the percentage of patients with negative FNAC aspirates who actually not having breast cancer.The study found that a negative FNAC can correctly rule out breast cancer in 89% of the time,and this rate is close to the highest limit range (67% - 95%)revealed by Chaiwun and Thorner.

Bulgari and his collegues were concluded that FNAC is still a useful test in breast diagnosis, and it may assist clinical decision-making as far as whether patients should progress to surgical management or should have further core/excisional biopsy before planning surgery[22]. A recent meta-analytical review including 25 studies of FNAC has shown that for the palpable breast masses, it is highly accurate to differentiate benign from malignant tumours[23] .

Conclusions

The FNAC procedure is a rapid method, easy to perform, of little cost and easily accepted by the patients.It can be applied for palpable masses as well as impalpable or diffuse swellings or enlargement of the breast . The technique provides a high specificity and quite reasonable sensitivity rates that can be used for rapid diagnosis and screening. As the accuracy rate of FNAC is increased, surgeon can go straight-forward to one stage definitive treatment of breast cancer instead of two-stage surgery.

Recommendations

1) Fine needle aspiration is better to be used with ultrasound guidance to guarantee obtaining adequate aspirates for more accurate cytological diagnosis.
2) The surgeon should be acquainted with additional techniques such as core-needle or excisional biopsy in cases with high index of cytological suspicion for malignancy.
3) FNAC results are better interpreted in correlation with the clinical and imaging findings to improve its statistical values and to allow better management for the patient.

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