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ROLE OF TRIPLE ASSESSMENT TEST TO IMPROVE THE DIAGNOSTIC YIELD OF FINE NEEDLE ASPIRATION REPORTING FOR BREAST CARCINOMA

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Abstract-

Background: Fine needle aspiration cytology (FNAC) is a simple procedure that, when done in the lab under a trained cytologist, the correct diagnosis can be given with ease.

Aims & Objective: The aim of the study is to determine the accuracy of fine needle aspiration cytology (FNAC) in breast cancer diagnosis, the percentage of false negative cytology in our patients, and to confirm the importance of FNAC as part of the triple testing.

Method: The 162 breast cancer patients were reviewed from 2000-2012 in different hospitals in Bahrain. The FNAC results were divided into five groups, according to the report, from C1 to C5. The C1 result was an inadequate sample. C2 & C3 results were benign and likely benign samples. C4&C5 were the malignant results. All of these patients had triple testing (physical examination, radiological imaging and fine needle aspiration cytology) as part of their diagnostic assessment. FNAC results were compared to the provisional clinical assessment and mammography beside histopathology.

Results: 10/162 patients (6.17%) with C2 and C3 results were considered false negative FNAC. These breast cancer patients were diagnosed by the other components of the triple test.148/162 patients were C4 and C5 results. This meant that the accuracy rate in diagnosing breast cancer with FNAC was 91.358% and the false negative rate was 6.17%. All these false negatives were correctly diagnosed in adding two other modalities of triple testing i,e, clinical assessment and radiological imaging (mammography).

Conclusion: In spite of effectiveness, simplicity and validity of fine needle aspiration cytology (FNAC) in the diagnosis of breast cancers, it is still needs the expertise of cytologists, availability of on-site reporting facilities and instant staining techniques to approach the correct diagnosis of breast cancer. The evaluation of breast lumps with the use of triple assessment test to improve the diagnostic yield of FNAC reporting for breast carcinoma by reducing the false negative results.

Keywords- FNAC, mammography, Frozen Section, Histopathology, Lump Breast. Breast Cancer

Introduction

Breast cancer is serious and widespread, that is why a reliable, non -invasive and prompt diagnostic tool such as FNAC as part of triple testing is very helpful to decrease the associated anxiety with diagnosis and leads to early definitive treatment. In time and accurate diagnosis can be achieved by the use of appropriate tissue sampling techniques, optimal tissue processing, and reliable reporting of cytopathologic findings [1].

FNAC of breast lumps is a sensitive, specific and accurate method for grading these lesions into cytological evaluation system (C1 to C5) as practiced in the National Breast Screening Program in the United Kingdom and worldwide [2].

Successful cancer treatment relies on a combination of clinical examinations, imaging studies, and pathologic evaluations. The triple test score (TTS) which includes physical examination, mammography, and fine needle aspiration cytology, is the most popular score to evaluate patients with palpable breast lumps. It is not only increases the reliability of clinicians but also increases the sensitivity and specificity of the diagnostic evaluation and detects patients with breast cancer with an overall greater accuracy [3,4].

The present study was carried out in the department of pathology, King Hamad University Hospital, Bahrain to evaluate the diagnostic accuracy of fine needle aspiration cytology in breast cancer patients in Bahrain. In comparing the results with histological diagnoses of the subsequent open biopsy or mastectomy specimens of these patients. We also studied the percentage of false negative FNAC in the breast cancer patients and what other options were available to reach the diagnosis.

Material and Methods.

This was a retrospective review of 167 patients. All breast cancer patients were operated on by the first author in different hospitals in Bahrain both government run and privately owned. One hundred and sixty two breast cancer patients were reviewed from January 2000 to May 2012.

All of these patients had triple testing (physical examination, radiological imaging and fine needle aspiration cytology) as part of their diagnostic assessment. FNAC results were compared to the provisional clinical assessment, and mammography beside histopathology.

The fine needle aspirations were done according to the standard methods by using a 21 gauge needle and 10 ml disposable syringe. Slides were made from the aspirates and fixed with 95% ethanol. The smears were stained with Giemsa, H&E and papanicolaou stains. The rest of the material was submitted for cellblock preparation. The FNAC results were divided into five groups, according to the report, from C1 to C5. C1 results were inadequate samples. C2 & C3 results were benign and likely benign. C4 & C5 were the malignant results. After thorough examination of the smears the cases were grouped into five major diagnostic classes [5] as, C1: Inadequate; C2: Benign; C3: Atypia likely benign; C4: Possible malignancy; C5: Malignant.

Results

All cases suspicious for malignancy on mammography and clinical evacuations were proceeded to FNAC and tru cut biopsies. Out of 162 study cases, there were 4 cases of C1, 6 cases of C2, 4 cases of C3, 27 cases of C4 and 121 cases of C5 on FNAC [Table-1].

10 cases were misdiagnosed as C2 and C3 but with help of tru cut biopsies two cases were diagnosed as malignant, while 8 cases were assessed with the help of mammography and clinical evaluation (other two modalities of triple test) [Table-2] [Table-3].

The breast carcinoma was diagnosed with help of triple testing; only one case was false negative on clinical assessment while no false negative cases were seen on mammography [Table-1],[Table-2], [Table-3],[Table-4].

Clinical assessment when compared with histopathology had a sensitivity of 99%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 80% [Table-4]. Mammography when compared with histopathology had a sensitivity of 99%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 80% [Table-4].

The false negative cases of C2 (6/6 100%) and C3 (4/4 100%) were added and gave a better yield when used as part of the triple assessment test.

Table 1- Showing Classification of FNAC Performed Pre-op FNAC

Clinical Assessment		Mammography		Classification	Results	Histopathology	
Benign	Malignant	Benign	Suspicious or malignant			Benign	Malignant
Cases with complete record 162							
4	0	4	0	C1	4 (2.4%)	0	4
1	5	1	6	C2	6 (3.6%)	0	6
0	4	0	4	C3	4 (2.4%)	0	4
0	27	0	27	C4	27 (16.2%)	0	27
0	121	0	121	C5	121 (72.5%)	0	121
Cases with incomplete record (were excluded from the study)							
NIL	NIL	NIL	NIL	NIL	5	0	0
5	157	0	162		167	0	162

Sensitivity: 93.67%, Specificity: 100%, Accuracy: 93.82%; PPV:100, NPV:29%

Table 2- Histopathology Results of C2 FNAC

Age	Clinical Assessment	Site	Tumor size	Mammography	Histopathology	Core biopsy	Frozen section	TNM	Operation
47	Suspicious	RUOQ	≤1cm	Suspicious for malignancy	DCIS	Not done	Done Malignant	T1N0M0	MRM+ ALND
51	Suspicious	RUIQ	2-5cm	Suspicious	Invasive Ductal Carcinoma (NOS)	Not done	Done Malignant	T2N0M0	Lumpectomy + ALND
43	Benign	LUOQ	2-5cm	Suspicious for malignancy	Mixed Lobular and Ductal (Atypical Medullary)	Not done	Done Malignant	T2N1M0	Lumpectomy + ALND
72*	Malignant	LUOQ	>5cm	Suspicious for malignancy	Intra-cystic Papillary Carcinoma	Not done	Not done	T3N0M0	MRM+ ALND
32	Malignant	LUIQ	1-2cm	Suspicious for malignancy	DCIS+ Invasive Ductal Carcinoma (NOS)	Not done	Done Malignant	T1N0M0	Lumpectomy + ALND
41	Suspicious	LUOQ	1-2cm	Suspicious for malignancy	DCIS+ Phylloid	Done (Malignant)	Not done	TisN0M0	MRM

RUOQ: Right upper outer quadrant; RUIQ: Right upper and inner quadrant; LUOQ: Left upper outer quadrant; LUIQ: Left upper and inner quadrant; DCIS: Ductal carcinoma In situ; MRM; Modified Radical mastectomy; ALND: Axillary lymph node dissection

Table 3- Results of C3 FNAC

Age	Clinical Assessment	Site	Tumor size	Mammography	Histopathology	Core Biopsy	Frozen section	TNM	Operation
47	Malignant	LUIQ	2-5cm	Malignant	Invasive ductal (NST)	Not done	Not done	T2N1M0	Lumpectomy + ALND
59	Malignant	RUOQ	2-5cm	Malignant	Invasive ductal (NST)	Not done	Malignant	T2N0M0	Lumpectomy +ALND
51	Malignant	RUOQ	1-2cm	Suspicious for malignancy	Invasive lobular	Malignant	Malignant	T2N0M0	Lumpectomy + ALND
54*	Malignant	RT Central	>5cm	Suspicious for malignancy	Malignant phylloid	Not done	Not done	T3N0M0	MRM+ ALND

RUOQ: Right upper outer quadrant; RUIQ: Right upper and inner quadrant; LUOQ: Left upper outer quadrant; LUIQ: Left upper and inner quadrant; DCIS: Ductal carcinoma In situ; MRM; Modified Radical mastectomy; ALND: Axillary lymph node dissection; *Patient No 4 repeated FNAC = C5

Table 4- Results of Triple assessment

Diagnostic Modalities		Histopathology		Sensitivity	Specificity	PPV	NPV
		Benign	Malignant				
Clinical Assessment	Benign	4	5	99%	100%	100%	80%
	Malignant	157	157				
	Total	161	162				
Mammography	Benign	4	5	99%	100%	100%	80%
	Malignant	157	157				
	Total	161	162				
FNAC	Benign	14	4	93.67%,	100%	100%	29%
	Malignant	148	158				

PPV: Positive Predictive Value, NPV: Negative Predictive values (P=0.000 for all modulates)

The FNAC alone showed 6.17% false negative results while no false positivity was seen. While the sensitivity was 93.67%, Specificity was 100%, Accuracy was 93.82%, PPV was 100 and NPV was 28.57%. The sensitivity and specificity came up to 100% with the triple assessment test. The sensitivity and specificity of all the modalities used in triple assessment when combined together was 99% and 93.67%, respectively. The concordance for the triple assessment was 99%, positive predictive value was 93.3%, negative predictive value was 100%, sensitivity was 100% and specificity was 80% [Table-2]. P value was significant (0.000).

Discussion

FNAC is a pre-operative test to evaluate any breast lump. It can prevent unnecessary surgery particularly in adolescents [6]. It is also reliable in breast cancer diagnosis, thus it lead to the reduction of frozen section histopathology by about 80%. FNAC showed 97.22% sensitivity, 99.46% specificity, 97.22% PPV, 99.46% NPV and 99.095% accuracy [7,8]. The diagnostic accuracy of FNAC in general depends on site, type of the lesion, the experience of the aspirator, the quality of the preparation and the skills of the cytopathologist [9,10].

In our study, breast cancer was diagnosed accurately in 93.82%; sensitively: 93.67%, specifically: 100%, and falsely negative in 6.17%.

One of the studies showed that when comparing FNAC to core biopsy, both had the same predictive value with FNAC being more cost effective [11,12].

In our study, tru cut biopsies showed better results and two false negative cases of class C2 and C3 on FNAC were diagnosed as malignant.

Diagnosis of breast lumps and in particular breast cancer has improved dramatically when combining FNAC with clinical and radiological assessments. In our group of patients, even frozen section was done rarely to help in diagnosing breast cancer.

In a study the triple test assessment was found useful in diagnosis with an accuracy rate of 99.3% [3]. The modified triple test, which includes ultrasound (US) and core biopsy to the original triple test, has improved the results and overcome the false negative results [13].

Clinical examination was in favor of malignant disease in 157 patients. However histopathology confirmed malignancy in 157 patients and none was proved to be benign. Similarly, benign diagnosis was made on physical examination in 5 patients. However histopathology confirmed benign diagnosis in 4 patients only with the remaining 1 patient being diagnosed as malignant. Thus histopathology confirmed malignant breast disease in 158 patients in total. Our findings are consistent with other studies, where in one study it was found that the sensitivity, specificity, positive and negative predictive values were: 98%, 100%, 100% and 96.4% respectively [14].

Radiological examination by mammography was in favor of malignant disease in 157 patients. However histopathology confirmed malignancy in 157 patients and none was proved to be benign. Similarly benign diagnosis was made on physical examination in 5 patients. However histopathology confirmed benign diagnosis in 4 patients only with the remaining 1 patients being diagnosed as malignant. Thus histopathology confirmed malignant breast disease in 158 patients in total. Our results of mammography are much better as compared to mentioned in the literature [9,15]. When triple assessment was compared with the results of histopathology we found that concordance for triple test was 99%, specificity was 100% and sensitivity was 99%. Positive predictive value was 100%, negative predictive value was 80% and 'p' value was significant (0.000). When our results were compared with the available literature, it was found much consistency with our data [9,13,15,16].

Abnormal cytology report (C2 - C5) is routinely used as part of the triple assessment in diagnosis of malignant breast lesions. The value of it has been questioned in recent years in view of an equivocal (C2, C3) results when compared with core biopsy. Our study results are not consistent with many studies mentioned in the literature and one in Arab country [16]. Our results of triple test evaluations are higher as compared to this study by Arora, et al [16].

Conclusion

In spite of effectiveness, simplicity and validity of fine needle aspiration cytology (FNAC) in the diagnosis of breast cancers, it is still needs the expertise of cytologists, availability of on-site reporting facilities and instant staining techniques to approach the correct diagnosis of breast cancer. The evaluation of breast lumps with the use of triple assessment test to improve the diagnostic yield of FNAC reporting for breast carcinoma by reducing the false negative results.

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Conflict of Interest: The authors declare that there is no conflict of interests.

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