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The Accuracy of Fine Needle Aspiration on Superficial Palpable Body Masses in Patients at Tikrit City

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Abstract

Background: Fine needle aspiration (FNA) is accepted as the diagnostic procedure of choice in the management of superficial palpable body masses. The purpose of this study is to evaluate the diagnostic accuracy of fine needle aspiration with histopathological confirmation when it is performed by experienced hands to get more reliable results.

Objective: To evaluate the accuracy and diagnostic performance of fine needle aspiration cytology in the diagnosis of superficial body masses.

Method: A relative study was performed using computer database over a 5 years period. A total of 1162 fine needle aspirations done for patients being evaluated for clinically palpable masses were included in this study from breast, thyroid, lymph nodes, soft tissue, salivary glands, skin and testes. The FNA were interpreted as benign, inconclusive "suspicious", malignant and unsatisfactory "inadequate". Cases were performed and interpreted by experienced cytopathologists. The FNA results were compared with histopathological reports after surgical biopsy.

Results: FNA was diagnostic in 92.2% of patients with diagnostic accuracy of 97.9%. There were 9 false negative and one false positive for malignant diagnosis. The overall sensitivity of FNA was 95.9% and the specificity was 99.6%, using either histopathology or follow up, the positive predictive value was 99.5% and the negative predictive value was 96%.

Conclusion: Highly reliable results can be obtained when patients are referred to specialty-trained cytopathologist for FNA biopsy of superficial palpable mass lesion.

Keywords: Fine needle aspiration cytology; Superficial body masses; Experienced cytopathologists; Sensitivity; Specificity

Introduction

Fine needle aspiration (FNA) is a rapid, accurate, minimally invasive and cost effective method for the diagnosis of different body masses. Primarily the superficial and palpation guided mass lesions and when FNA is performed by trained cytopathologists [1-3], it have become increasingly popular as a valuable tool for initial assessment of various neoplastic and non-neoplastic lesions of many body sites. FNA has an easy approach, being inexpensive and can be performed with little complications without anesthesia with low false negative and false positive rates [4]. Other important primary purpose of FNA is to distinguish benign lesion from malignant lesions and thereby ovoid unnecessary surgical operation and improve surgical selection with considerable resource saving [5].

The reported pitfalls are those related to specimen adequacy, sampling techniques, the skills of the physician performing the aspiration, the experience of the pathologist interpreting the results and overlapping cytologic features between benign and low malignant tumours [6].

Many previous studies concerned with this procedure are done to assess lesions of many specific body site, in this study we perform a systemic study of superficial FNA biopsy with the objective of providing expert FNA services for the clinicians practicing in our community, fine needle aspiration cytology is done from the breast, thyroid gland, lymph nodes, soft tissues, salivary glands, skin and testes from 1162 cases over a five years period.

The aim is to evaluate the accuracy and diagnostic performance of fine needle aspiration cytology in the diagnosis of superficial body masses and to address the cytologic- histopathologic correlation.

Materials and Methods

We establish a retrospective search of the archive of department of pathology in Tikrit teaching hospital for patients who had FNA cytological diagnosis and histopathological evaluation during July 2009-June 2014. An IRB approval was obtained from the office of health and safety in Missouri University of Science and Technology. The accuracy of the FNA findings was assessed by comparing the cytological diagnosis from histopathology reports, obtained with incisional biopsy, excisional biopsy or total organ resection. The FNA were performed by two different specialty trained pathologists utilizing a 22-24 gauge needles attached to a 10 ml syringe mounted on aspiration device [4,5,7]. In most cases two separate passes were inserted into the lesion with the needle. Suction is applied while the needle is moved throughout the lesion multiple times at different angles while aspirating, after the aspirate had been obtained, the section is released, the needle is withdrawn and the specimen is expelled onto glass slides. Smears from the aspirate were fixed in 95% alcohol and stained with hematoxylin and eosin stain. Cytological diagnoses were classified into: inadequate, benign, malignant, inconclusive (when the smear show adequate cellular material but the material was not diagnostic) [5,8,9]. These were "atypical" or "suspicious" results in which the difficulty to achieve the diagnosis is usually related overlapped cellular features between benign and low grade malignant lesions. Results were categorized as "inadequate", when the cellular materials were insufficient for evaluation. Inadequate or unsatisfactory results were reported when

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the cellular clusters were insufficient for assessment, adequate aspirate is controversial and several reports recommend identification of at least six cellular clusters each having more than 10 discernible viable cells also one should depend on noncellular features such as the confidence and experience of the cytopathologist performing the FNA with regard to needle placement, resistance of the mass to the needle, and correlation with history and physical findings to determine whether the material obtained is truly representative and adequate [10,11].

Patients clinical information were obtained including clinician type, patient age, sex, FNA site (breast, thyroid, lymph nodes, lymph nodes, soft tissue, salivary glands, skin and testis), history and clinical findings, FNA results and final histopathological report and whether the FNA diagnosis represent new or recurrent disease (Figure 1).

Suspicious diagnosis was assigned if the cytological features were suggestive but not completely fulfills the criteria for being malignant (i.e., high nuclear cytoplasmic ratio, prominent nucleoli, hyperchromasia, thick irregular nuclear membrane). A diagnosis of suspicious for malignancy was occasionally given if the cytologic material was not fixed well, the smear were too thick or hypocellular, or for other technical factors that would preclude a diagnosis of malignancy.

In addition to the above three categories cases were deemed as unsatisfactory if the specimens were inadequate. An inadequate specimen is defined in our laboratory as one which was composed predominantly of blood elements or hypocellular. These unsatisfactory specimens naturally warranted a repeat FNA if clinically indicated.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated for all groups of body masses. For statistical purposes the suspicious and malignant cases were grouped together. That was done to assure a greater sensitivity, as a suspicious cases, like malignant cases would most likely require subsequent histopathological confirmation in the form of excisional biopsy or lumpectomy.

To identify the mass as being malignant or benign and to provide the correct diagnostic subtype, all the FNA biopsies results from patient underwent subsequent surgical biopsies were compared for diagnostic concordance using the histopathological results as standard. Sensitivity [12] is the ability to identify malignancy correctly by FNA when cancer is present, while specificity is the ability to render benign diagnosis when malignancy is absent. The PPV [12] is an indication of the degree of confidence with which the clinician can regard a positive FNA result and it is calculated as the number of true malignancies divided by all lesions diagnosed as malignant by FNA. The NPV is

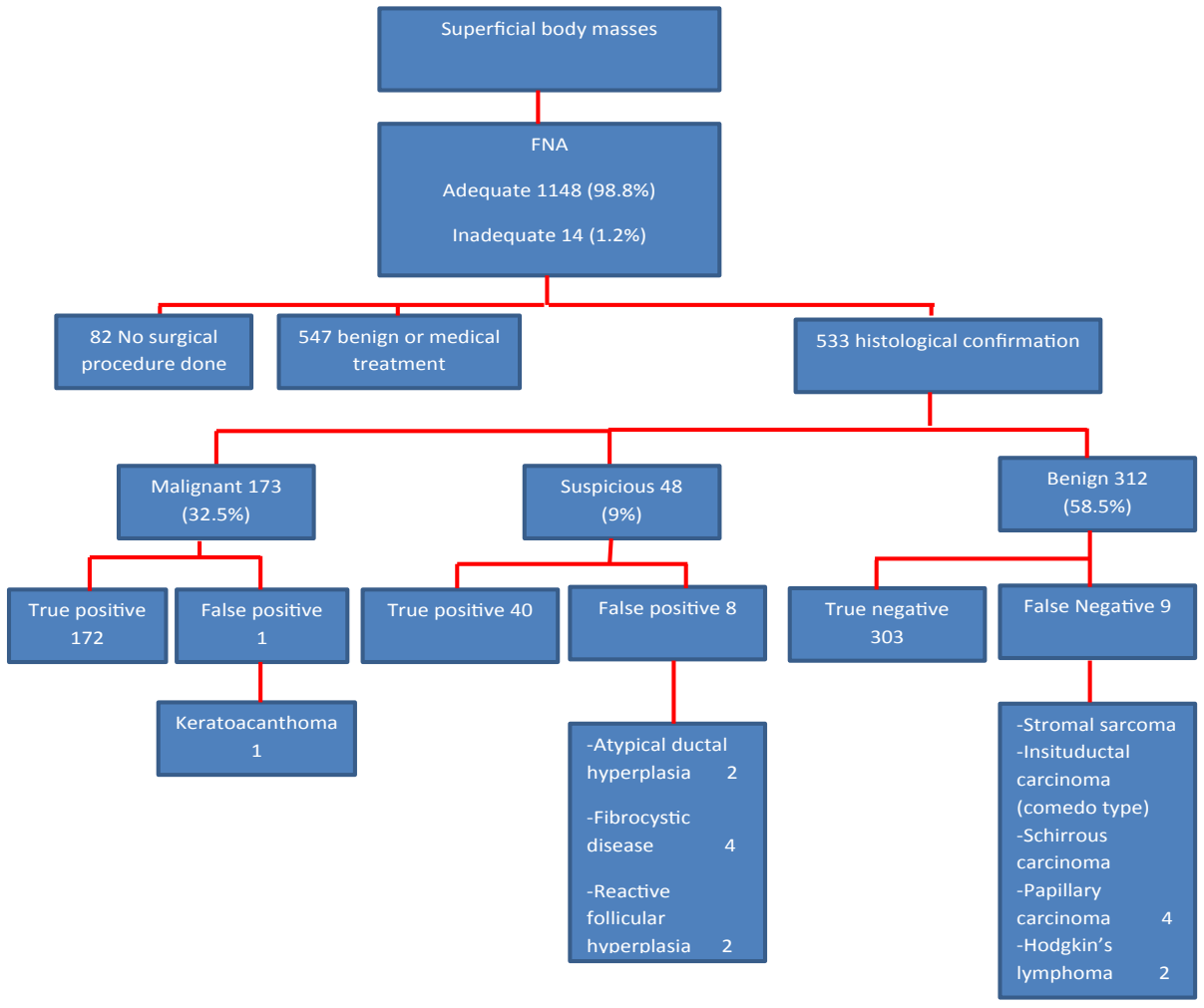

Figure 1: Summary of results Of FNA of entire series.

the number of true negative results expressed as a proportion of all negative FNA results.

The true positive (a), true negative (d), false positive (b) false negative (c), the sensitivity, specificity and PPV for detecting malignancy were calculated by using the results from patients who had both diagnostic FNA and a histopathological diagnosis. The NPV was calculated by using all benign FNA results whether or not further histologic tissue biopsy was taken. Sensitivity=a/(a+c) × 100, specificity=d/(d+b) × 100, PPV=a/(a+b), NPV=d/(d+c) × 100 and the diagnostic accuracy=(a+d/a+b+c+d) × 100(10). A p-value of <0.05 was considered statistically significant using data analysis tool bar Microsoft Excel.

Breast	N0.	Thyroid	No.	Lymph nodes	No.	Soft tissue	No.	**Salivary glands**	**No.**	**Skin**	**No.**	**Testis**	**No.**
Benign: (n=801)								Benign:					
FCD	99	Colloid goiter	242	RFH	58	Lipoma	30	Sialadinitis (acute and chronic)	15	Benign nevus	3	Abscess	3
Inflammatory (acute and chronic)	40	Hashimoto's thyroiditis	10	Acute supporative lymphadenitis	26	Abscess	27	Pleomorphic adenoma	16	Keratinous cyst	5	Epidid moorch tis	2
Fibroadenoma	45	DeQuervain thyroiditis	1	Chronic nonspecific lymphadenitis	33	Branchial cyst	17	Warthin's tumor	12	Epidermal Inclusion cyst	3		
Gynecomastia	12	Thyroglossal duct cyst	2	Tuberculous lymphadenitis	22	Hemangioma	18	Autoimmune sialadinitis	1	BFH	1		
Ductectasia	14	Hydatid cyst	1	Toxoplasma lymphadenitis	7	Lymphangioma and lymphatocele	5	Benign lymphoepithelial lesion	1				
Intraductal papilloma	4					Dermoid cyst	5	Malignant:					
ADH	2					Angiolipoma	2	Malignant mixed salivary gland tumor	1	SCC	10	Seminoma	8
Benign phyllodes	3					Fat necrosis	2			DFP	3		
Lipoma	5					Simple cyst	2	Inconclusive:					
						Fibroma	2	Low grade neoplasm	1		0		0
						Proliferative myositis	1	Unsatisfactory:	0		0		0
						Congenital torticollis	1	Total	47		25		13
						HE	1						
Malignant: (n=272)													
Ductal carcinoma	124	Papillary carcinoma	11	HL	34	Small round blue tumor	5						
		Anaplastic carcinoma	5	NHL	15	Low grade sarcoma	4						
				Metastatic carcinoma	45	High grade sarcoma	7						
Inconclusive: (n=75)													
Atypical FCD	6	Follicular neoplasms	17	Atypical lymphoid proliferation	2	Spindle cell lesion	1						
Suspicious of malignancy	8	Hurthle cell neoplasms	4	Suspicious of lymphoma	14								
Suspicious of lymphoma	1												
Suspicious of lobular carcinoma	6												
Proliferative breast lesions	16												
Unsatisfactory: (n=14)	2		7		4		1						
Total	387		296		260		134						

FCD: Fibrocystic Disease; RFH: Reactive Follicular Hyperplasia; ADH: Atypical Ductal Hyperplasia; HE: Hemangioendothelioma; HL: Hodgkin's Lymphoma; NHL: Non-Hodgkin's Lymphoma; BFH: Benign Fibrous Histiocytoma; SCC: Squamous Cell Carcinoma; DFP: Dermatofibrosarcoma Protuberans.

Table 1: FNA biopsy results for lesions according to different body sites.

Results

A total of 1162 patients underwent FNA during the study period, patient age ranged from 9 months-90 years, with median age was 45 years. Out of these 89 cases (7.8%) are nondiagnostic; 1.4% (14 cases) were inadequate and 6.4% (75 cases) were inconclusive. The majority of FNA procedures were performed on female patients (817 females; 70% of the study group).

The FNA results according to the site of origin are illustrated (Table 1), when the most common site aspirated is the breast (387 cases) followed by thyroid gland (296 cases), followed by lymph nodes (260 cases), soft tissue (134 cases), salivary glands (47 cases), skin (25 cases) and testes (13 cases) (Table 1).

The majority of aspirates were benign for each individual body sites (225 out of 387 breast aspirates), 257 out of 296 for thyroid, 148 out of 260 for lymph nodes, 116 out of 134 for soft tissues, 45 out of 47 for salivary glands, 5 out of 13 for testes and 13 out of 25 for skin aspirates. The most common benign lesion was colloid goiter nodules they were 234 cases (20%), followed by fibrocystic disease of the breast 99 cases (8.5%), reactive follicular hyperplasia 58 cases (5%), soft tissue lipomas 30 cases (2.6%) and pleomorphic adenoma of salivary glands 16 cases (1.4%). Malignancy is represented most commonly by carcinoma which represent 100% of breast, thyroid, salivary glands and skin malignancies while in lymph nodes it represent 48%, sarcoma represents 100% of soft tissue malignancies and seminoma represent 100% of testicular malignancies. Indeterminate or nondiagnostic results were divided into inconclusive and inadequate cases. Inconclusive when the cellular material is adequate but nondiagnostic, rendering the diagnosis of (atypical or suspicious). Suspicious cases were included with the malignant cases to achieve greater sensitivity, when the suspicious cases also need histopathological confirmation.

In total 533 patients underwent surgical diagnostic procedures for histopathological confirmation of their FNA results are summarized (Table 2).

FNA results	**Histopathological diagnosis**
Breast (n=228)	
Benign (115):	
FCD (37)	FCD (37)
FCD (1)	Phyllodes tumor (1)
FCD with epithelial hyperplasia (1)	FCD with focal florid epitheliosis (1)
Breast abscess (17)	Breast abscess (17)
Breast abscess (1)	Ductectasia (1)
Tuberculous mastitis (1)	Granulomatous mastitis (1)
Fibroadenomas (35)	Fibroadenomas (35)
Fibroadenoma (1)	Blunt duct adenosis (1)
Juvenile cellular fibroadenoma (1)	Stromal sarcoma (1)
Juvenile atypical fibroadenoma (1)	Insitu ductal (comedo carcinoma) (1)
Ductectasia (4)	Ductectasia (4)
Gynecomastia (4)	Gynecomastia (4)
Lipoma (3)	Lipoma (3)
Lipoma (1)	Fat necrosis (1)
Intraductal papilloma (2)	Intraductal papilloma (2)
Benign phyllodes (4)	Benign phyllodes (4)
Lipoma (1)	Poorly differentiated invasive ductal carcinoma (1)
Malignant (n=97):	
Invasive ductal carcinoma (97)	Invasive ductal carcinoma (97)
Inconclusive (n= 16):	
Suspicious for malignancy (7)	Ductal carcinoma (7)
Suspicious of malignancy (3)	Lobular carcinoma (3)
Suspicious of proliferative breast disease with malignancy (2)	Atypical ductal hyperplasia (2)
Suspicious of malignancy (4)	FCD with florid epitheliosis (4)
Thyroid (n=102)	
Benign (n=75)	
Colloid goiter (60)	Colloid goiter (60)
Nodular hyperplasia with papillary changes(1)	Papillary carcinoma (1)
Colloid goiter changes (3)	Papillary microcarcinoma (3)
Chronic thyroiditis (9)	Chronic thyroiditis (9)
Thyroglossal duct cyst (2)	Thyroglossal duct cyst (2)
Inconclusive (16):	
Follicular neoplasms (13)	Follicular adenomas (10), hyperplastic nodule in colloid goiter(2), papillary carcinoma(1), follicular variant.
Hurthle cell neoplasm (3)	Hashimoto's thyroiditis (1), Hurthle cell adenoma (2)
Malignant (n=11):	
Papillary carcinoma (8)	Papillary carcinoma (8)
Anaplastic carcinoma (3)	Anaplastic carcinoma (3)
Lymph nodes (n=84):	
Benign (n=29):	
Reactive follicular hyperplasia (7)	Reactive follicular hyperplasia (7)
Acute suppurative lymphadenitis (4)	Acute suppurative lymphadenitis (4)
Chronic nonspecific lymphadenitis (11)	Chronic nonspecific lymphadenitis (11)
Chronic nonspecific lymphadenitis (1)	Hodgkin lymphoma(nodular sclerosis) (1)
Tuberculous lymphadenitis (3)	Tuberculous lymphadenitis (3)
Tuberculous lymphadenitis (1)	Tuberculous lymphadenitis with concomitant Hodgkin's lymphoma
Toxoplasma lymphadenitis (2)	Toxoplasma lymphadenitis (2)
Inconclusive (n=15)	
Atypical lymphoid proliferation (2).	Angioimmunoblastic lymphadenopathy (1), infectious mononucleosis (1)
Suspicious of HL (10)	HL (8), reactive follicular hyperplasia (2)
Suspicious of NHL (3)	NHL (3)
Malignant (n= 39)	
HL (14)	HL (14)
NHL (7)	NHL (7)
Metastatic carcinoma (18)	Metastatic carcinoma (18)
Soft tissue (n=67):	
Benign (n=58)	
Lipoma (17)	Lipoma (17)
Atypical lipoma (1)	Lipoma (1)
Abscess (12)	Abscess (14)
Branchial cyst (7)	Branchial cyst (7)
Hemangioma (10)	Hemangioma (10)
Lymphangioma&lymphangiocele (3)	Lymphangioma and lymphangiocele (3)
Dermoid cyst (1)	Dermoid cyst (1)
Angiolipoma (2)	Angiolipoma (2)
Fat necrosis (1)	Fat necrosis (1)
Fibroma (1)	Collagenous Fibroma (1)
Schwannoma (1)	fibroma (1)
Proliferative myositis (1)	Proliferative myositis (1)
Benign hemangioendothelioma (1)	Benign hemangioendothelioma (1)
Malignant (n=9)	
Small round blue tumor (2)	Extraskeletal Ewing's sarcoma (2)

Low grade sarcoma (4)	Low grade sarcoma (4)
High grade sarcoma (3)	high grade sarcoma (3)
Salivary glands (n=25)	
Benign (=23)	
Sialadenitis (2)	Chronic nonspecific sialadenitis (2)
Pleomorphic adenoma (13)	Pleomorphic adenoma (13)
Warthin's tumor (6)	Warthin's tumor (6)
Autoimmune sialadenitis (1)	Autoimmune sialadenitis (1)
Benign lymphepithelial lesion (1)	Benign lymphoepithelial lesion (1)
Inconclusive (1):	
Low grade neoplasm (1)	Monomorphic adenoma (1)
Malignant: (n=1)	
Malignant mixed salivary gland tumor (1)	Malignant mixed salivary gland tumor (1)
Skin (n= 19) :	
Benign (n=9)	
Benign nevus (3)	Benign nevus (3)
Keratinous cyst (3)	Keratinous cyst (3)
Simple cyst (2)	Epidermal inclusion cyst (2)
BFH (1)	BFH (1)
Malignant (n=10)	
SCC (7)	SCC (7)
SCC (1)	Keratoacanthoma (1)
DFP (2)	DFP (2)
Testis (n=8):	
Benign (n=3)	
Epididymoorchitis (2)	Epididymoorchitis (2)
Abscess (1)	Abscess (1)
Malignant (n=5)	
Seminoma (5)	Seminoma (5)

Table 2: The concordance of 533 FNA cases results with histopathological diagnoses.

49 patients of these 533 had inconclusive FNA with subsequent surgical biopsies. In 82 cases, either no surgery is done despite an indication by FNA or no available information. 547 cases (47%) were spared surgery as these patients had benign lesions and receive conservative treatment or on occasions, they diagnosed as medically treated malignancy.

Of 533 cases those underwent FNA and also had available histopathological results, 439 (82%) had diagnostic results either benign or malignant, and concordant FNA-histopathological results, there were nine cases that have discrepant FNA-histopathological results representing cases of missed malignancy and one false positive. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy are show (Table 3).

An overall sensitivity for FNA of 97% has been obtained (range, 87-100%), specificity of 97%, PPV of 95.9%, NPV of 97% and accuracy of 96.6%. The sensitivity of thyroid was the lowest this is because of sampling error in huge multinodular goiter.

To study the correlation between FNA and histopathology the p-values for benign (Table 4) and malignant cases (Table 5) were calculated with high statistical significance (<0.05).

The suspicious cases were included one time with the benign cases (Table 6) and in the other with the malignant cases (Table 7).

p-values:

benign=7×10^{-9}; malignant=5×10^{-11}; Benign+suspicious=1×10^{-9}; Malignant+suspicious=2×10^{-11}

7-1/7=6/7%, 5-2/5=3/5%, (the percentage of change is higher with adding suspicious cases to the benign ones).

Discussion

In this study, we perform a systematic study of superficial palpable masses FNA cytology by an experienced cytopathologists performing the sampling and interpretation. The results from this series of patients confirm that FNA from different superficial body masses is an accurate and highly sensitive method of diagnosis and to distinguish benign from malignant lesion. Ljung et al. [13] conclude that FNA when performed by physician who is well trained is highly accurate, diagnostic method that carried minimal morbidity and with 2% cancer missing whereas, the physician without formal training missed 25%. This is agreed with [3,7,14,15,] In this study 9 cases are recorded as false negative of missed malignancy. False negative is not a limitation of FNA only but also seen in histopathology. Ballo and Sneige [14] study 124 case of palpable breast masses, they conclude that the sensitivity in detecting

FNA	Histopathology Benign	Malignant	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
Breast: Benign Suspicious Malignant	112 (TN) 6 (FP) 0 (FP)	3 (FN) 10 (TP) 97 (TP)	97	95	95	97	96
Thyroid Benign suspicious malignant	71 (TN) 0 (FP) 0 (FP)	4 (FN) 16 (TP) 11 (TP)	87	100	100	94.7	96
Lymph nodes Benign Suspicious Malignant	27 (TN) 2 (FP) 0 (FP)	2 (FN) 14 (TP) 39 (TP)	96	93	94.6	93	95
Soft tissue Benign Malignant	58 (TN) 0 (FP)	0 (FN) 9 (TP)	100	100	100	100	100
Salivary glands Benign Malignant	24 (TN) 0 (FP)	0 (FN) 1 (TP)	100	100	100	100	100
Skin: Benign Malignant	8 (TN) 1 (FP)	0 (FN) 10 (TP)	100	89	90	100	94
Testis: Benign Malignant	3 (TN) 0 (TP)	0 (FN) 5 (TP)	100	100	100	100	100

Abbreviations: TN: True Negative; TP: True Positive; FP: False Positive; FN: False Negative

Table 3: Correlation between cytologic and histologic diagnoses with corresponding statistical results (sensitivity, specificity, positive predictive value, negative predictive value, and accuracy

Histopathology	FNA
112	115
71	75
27	29
58	58
24	24
8	8
3	3
P value=7×10^{-9}	

Table 4: The study of correlation between histopathology and fine needle aspiration results for benign cases.

Histopathology	FNA
97	97
11	11
39	39
9	9
1	1
10	11
5	5
P value=5×10^{-11}	

Table 5: The study of correlation between histopathology and fine needle aspiration results for malignant cases.

Histopathology	FNA
128	131
87	91
43	45
58	58
24	24
8	8
3	3
P value=1×10^{-9}	

Table 6: The study of correlation between histopathology and fine needle aspiration results for Benign+ suspicious.

Histopathology	FNA
113	113
27	27
55	55
9	9
1	1
10	11
5	5
P value=2×10^{-11}	

Table 7: The study of correlation between histopathology and fine needle aspiration results for Malignant+ suspicious.

a malignant neoplasm was higher for FNA than for core biopsy (97% vs. 90%) i.e., the false negative is higher in core biopsy than FNA and the addition of core biopsy fail to increase the sensitivity in carcinoma detection. This is owing to the ability of FNA to sample a larger area by numerous multidirectional passes of the needle this is increase the probability of successful sampling especially in small lesions and the maintenance of a tactile sensitivity [16]. Sun et al. [17] conclude that if FNA is performed by pathologists were more sensitive than core biopsy, this related to the immediate examination for cellularity and quality and additional aspiration of the tumor if inadequate initial specimen.

To analyze our false negative cases, two cases were diagnosed as juvenile atypical (cellular) fibroadenomas. In histopathology one was stromal sarcoma, a rare condition which can be easily confused with fibroadenoma on cytological analysis, one study of 28 cases found that FNA was reported as benign in all cases of nonepithelial breast malignancy in which it was used, while core biopsy produced a significant improvement in the diagnosis rates [18,19]. The other case of *in situ* ductal carcinoma (comedocarcinoma) misdiagnosed as juvenile atypical fibroadenoma in 23 years old female & because of the patient age is an important consideration in diagnosing breast tumors as stated by Rogers [20], and to be more conservative in the diagnosis of breast cancer in young female without delay in histopathological confirmation, with caution against definitive benign diagnosis if the cells are hyperchromatic and many of them lack small regular nucleoli with paucity of single bipolar nuclei in the background. The third false negative breast mass which diagnosed as lipoma and histologically proved to be poorly differentiated invasive ductal carcinoma (schirrous type), factors contributing to false negative results may include: small tumor size, hypocellularity and inadequate sampling of a particular histologic type as low grade carcinoma or schirrous carcinoma (fibrotic lesion) [15,21,22] with special recommendation of core biopsy here to yield more diagnostic material than FNA when dealing with fibrotic lesions [13]. The best way to minimize these missed malignancies is the use of team work for a "triple diagnosis" which is a combination of physical examination, mammography and FNA that has been shown to be highly sensitive and specific in the diagnosis of breast cancer [9,23-25].

Four cases of thyroid aspirates were false negative, they were two papillary carcinoma and two papillary microcarcinomas, this is related to sampling error when sampled cells captured by the needle are not from the tumor nodule or may be related to heterogeneity within the nodule, false negative FNA of thyroid occurred in 4 (3.9%) of our patients, this is consistent with reports in the literature that suggest a false negative rate of 2%-7% [26,27]. The more routine use of ultrasound-guided FNA biopsy to direct sampling toward the solid nodule will minimize but not prevent the occasional false negative results. These results are not uncommon in this situation because clinically papillary carcinoma are present in at least 10% of huge multinodular goiter, this is because of multiplicity of nodules and impartiality to aspirate all of the nodules [28-30]. It has been demonstrated that ultrasound guidance is useful, that is it allows to direct sampling toward the solid impalpable nodules that may represent carcinoma [31].

Two cases of lymph node aspirates were false negative, one of them is proved histologically to be Hodgkin's lymphoma (nodular sclerosis type) that is not yield sufficient cellular materials for diagnosis and misdiagnosed as chronic lymphadenitis. This misdiagnosis can be avoided by repeated FNA or core biopsy if the lymphadenopathy persists. The use of immunohistochemistry and flow cytometry with proper interpretation of cytologic features can help in reducing the margin of error in cytodiagnosis of Hodgkin's lymphoma [32]. A false negative rate of 2.4% is obtained from the current study regarding lymph nodes cases.

The false negative rate is related to failure to obtain a representative samples and difficulty in interpretation of a well differentiated neoplasms, a rate of 3.4% is obtained by Steel et al. [33]. Dong et al. [34] reviewed 139 cases of primary and recurrent lymphomas demonstrate a rate of 5% false negative, based on both cytomorphology and flow cytometry with diagnostic accuracy of 67% with improvement with the addition of flow cytometry (77%). A study done by Chhieng et al. [35] 14.6% of the cases were false negative concluding that the cytological diagnosis of Hodgkin's lymphoma can be challenging when the classical

Reed-Sternberg cells are absent as in our study concerning nodular sclerosis type with associated scant cellularity due to associated fibrosis of the involved lymph nodes this is agreed with Das et al. [36]. The other false negative case was diagnosed as tuberculosis lymphadenitis where it confirmed histologically to be Hodgkin's lymphoma obscured by the reactive inflammatory process of tuberculosis when there was a conspicuous aggregate of numerous lymphocytes, histiocytes and caseous necrosis in the background. Concomitant Hodgkin's lymphoma with tuberculosis is a rare entity and difficult clinical situation to identify because of similar clinical presentations [37]. It is related to suppressed T-cell immunity which predispose to tuberculous infection [38]. Acid fast smear of the lymph node aspirate was positive for Mycobacterial bacilli with histological confirmation of multiple necrotizing caseating granulomatous lesions surrounded by epithelioid cells with diffused nodal architectural effacement by large atypical lymphoid cells and numerous Reed-Sternberg cells (mixed cellularity type). 21% of the cases of lymph node aspirates were nonhematological metastatic malignancies originate from unknown primary site with excellent overall detection by FNA biopsy.

Two cases of atypical lymphoid proliferation reported as suspicious, one diagnosed clinically and histologically as angioimmunoblastic lymphadenopathy. The other suspicious case is diagnosed histologically and clinically as infectious mononucleosis with presence of numerous immunoblasts and atypical lymphocytes.

Soft tissue, salivary glands and testicular fine needle aspiration in this series demonstrate a sensitivity and specificity of 100%, that is excellent rate for detection of benign and malignant entities. Regarding fine needle aspiration of skin lesions, there was one case of false positive, in which the cytological diagnosis of squemous cell carcinoma, which proved histological to be keratoacanthoma which is pathologically regarded as avariant of highly differentiated squamous cell carcinoma, that can be overlapped with it, but still it can be regarded as benign nonprogressing squemous proliferation [39-41] with sensitivity rate of 100% and specificity of 89%.

Our overall false negative rate is 4% was clearly influenced by selection bias, as the vast majority of patients who had a benign biopsy results did not undergo surgery & consequently were not included in this study. Therefore if FNA biopsy is done with the use of "triple test" for breast masses and ultrasound guidance by experienced radiologist and experienced cytopathologist with the aid of clinical, flow cytometry and immunohistochemical analysis, one should expect a false negative rate of less than 4%.

As demonstrated in the results, the percentage of change in the accuracy that came from p-value was higher (6/7% >3/5%) when the suspicious cases added to the benign ones, which gives an indication that most of the suspicious cases tend to be malignant [42,43].

In summary, our current report provides valuable information for clinician on the utility of FNA clinical services. In many cases, this technique replaces surgical procedure and can be used to direct the patient for conservative treatment or surgery. If the aspirate was obtained and interpreted by an experienced cytopathologist, false negative and false positive FNA biopsy results are uncommon. Therefore patients with positive biopsy results for malignancy can undergo definitive surgery and patient with biopsy results negative for malignancy can be monitored unless surgery is indicated with serial follow up with or without repeated FNA biopsy which should be considered safe.

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