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A 3-Year Evaluation Study on Fine Needle Aspiration Cytology and Corresponding Histology

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***Abstract*—**Background and Objectives: Incidence of thyroid carcinoma has been increasing world-wide. In the present study, we evaluated diagnostic accuracy of Fine needle aspiration (FNA) and its efficiency in early detecting neoplastic lesions of thyroid gland over a 3-year period. Methods: Data have been retrieved from pathology files in King Khalid Hospital. For each patient, age, gender, FNA, site & size of nodule and final histopathologic diagnosis were recorded. Results: Study included 490 cases where 419 of them were female and 71 male. Male to female ratio was 1:6. Mean age was 43 years for males and 38 for females. Cases with confirmed histopathology were 131. In 101/131 (77.1%), concordance was found between FNA and histology. In 30/131 (22.9%), there was discrepancy in diagnosis. Total malignant cases were 43, out of which 14 (32.5%) were true positive and 29 (67.44%) were false negative. No false positive cases could be found in our series. Conclusion: FNA could diagnose benign nodules in all cases, however, in malignant cases, ultrasound findings have to be taken into consideration to avoid missing of a microcarcinoma in the contralateral lobe.

***Keywords*—**FNA, hail, histopathology, thyroid.

I. Introduction

THYROID nodules and thyroid carcinomas are increasing worldwide thus leading to adoption of more techniques for early diagnosis. FNA as a simple, cost-effective, non-invasive technique has reduced unnecessary surgeries and allowed detection of thyroid carcinomas at an early stage [1], [2].

Several studies have suggested an overall accuracy rate for FNA to be 95% in detecting thyroid malignancies [3]. However, FNA has its known limitations and diagnostic pitfalls. These limitations include false negative and false positive results as well as lesions that are not clearly benign or malignant. They fall into the indeterminate or suspicious group [3]. Reported pitfalls causing discrepancies are those related to specimen adequacy, sampling technique, the skill of the physician or pathologist as well as the overlapping cytological features between some benign and malignant thyroid lesions [4].

Calcification in thyroid nodules has been noticed in both benign and malignant conditions and is readily detected on ultrasonographic examination. Psammoma bodies were linked to papillary thyroid carcinoma. Some clinicians regard it as of little significance, other studies recommended surgery if calcification is present in a solitary nodule, regardless of FNA results [5].

Thyroid nodules can be classified into solid, mixed, or cystic according to their complexion. Cystic thyroid nodules are estimated to form 15% to 37% of all surgically removed thyroid nodules, most of which are benign [6] However, according to literature, 2% to 18% of cystic and partially cystic nodules are malignant [7]. In addition, many hyperplastic, neoplastic, benign and malignant thyroid nodules may undergo cystic degeneration. It generally develops as a result of hemorrhagic degeneration in preexisting nodules [8]. Therefore, FNA is performed to evaluate the character of such heterogeneous nodules.

Aim of the Work

In the present retrospective study, we evaluated the value of FNA in diagnosing palpable thyroid nodules lesions, both cystic and solid during a 3-year period, and correlated with final histopathology.

II. Material and Methods

Data had been retrieved from histopathology files in King Khalid Hospital, Hail. For each patient, age, gender, site of lesion, size of nodule, FNA diagnosis and final histopathologic diagnosis were recorded. A 10 ml syringe was used and Cameco pistols handle to maintain negative pressure. Slides were air-dried and stained by MG-Giemsa stain. Histological material was formalin-fixed, paraffin embedded and stained by conventional H&E.

Study included consecutive cases diagnosed from January 2014 till December 2016 with their histopathological diagnosis, whenever available. FNAC results were then compared with the histology results to find sensitivity and specificity of FNA results. Calcification on ultrasound examination was also recorded.

In all cytological specimens, comment on adequacy, amount of colloid material, presence of micro/macrofollicles, acini, and papillary fragments have been recorded. Discohesiveness, degree of overlapping, nuclear membrane irregularity, pleomorphism, presence or absence of nucleoli and chromatin pattern were features taken in consideration [3]. The Bethesda System [4] was used for classifying categories into benign, atypical cells of undetermined significance (ASUS), follicular neoplasm, suspicious for malignancy and malignant. Unsatisfactory specimens were excluded from the study.

Statistical Analysis:

SPSS 16 software was used to analyze data, and values were considered significant if p value was < 0.05.

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III. Results

The present study during a 3-year period from January 2014 till December 2017 included a series of 490 palpable thyroid nodules diagnosed by FNA. Females were 419 while 71 were male patients. Male to female ratio was 1:6. Mean age was 36.5 (+/-12.2) and 37.72 (+/-11.8) for benign and malignant cases, respectively. Entities diagnosed on FNA were, in order of frequency, multinodular goiter (MNG)/adenomatoid nodule (33%), cystic lesions including benign cysts and cystic degeneration in MNG (25%), and thyroiditis including Hashimoto thyroiditis (18%). Three cases of acute thyroiditis were diagnosed as well, one case of subacute granulomatous thyroiditis and one case of Riedel thyroiditis. Diagnosis of follicular neoplasm/Hurthle cell lesion was done in total of 16% of cases. Atypical cells consistent with the ASUS entity were diagnosed in 8% of cases, as a separate entity or as atypical cells in MNG, Hashimoto thyroiditis, follicular neoplasm or cystic lesions (Figs. 1, 2). Diagnosis of "malignant" was done in 5% of cases where papillary fragments showing discohesiveness, irregular nuclear outline and/or nuclear grooving and intranuclear inclusions were seen in papillary thyroid carcinoma (Fig. 3).

Histopathologic diagnosis was available for 131 (77.1%) of cases. Confirmed malignant cases were 43/131 (32.82%). Papillary carcinoma/microcarcinoma both conventional and follicular constituted majority of cases followed by follicular carcinoma. Papillary carcinoma showed nuclear clearing and papillary formations (Fig. 4). One case of MALT lymphoma of the thyroid was also diagnosed.

Mean size (+/- SD) for malignant cases was 3.4(+/- 1.3) while for benign 2.4 (+/-1.1), and the difference was statistically significant (p value=0.029). FNA sensitivity in diagnosing both benign and malignant lesions was 14.5% and its specificity was 64.9% out of 131 cases.

Calcification was seen on ultrasound in 16/43 (27.9%) of malignant cases and in 5/86 (11.6%) of benign cases. Six out of 16 PTC were microcarcinomas, two of which were found in the other side lobe. Benign cases were 2 cases of MNG, 2 follicular adenomas and one Hashimoto thyroiditis (Table I). The difference between benign and malignant groups was statistically significant (p value = 0.007).

Out of the 29 false negative cases, 11/29 (37.93%) presented as large cystic lesions, 6/11 there was a missed carcinoma masquerading behind the cyst. In 3/11 cases a carcinoma was found in the contralateral lobe and the remaining 2/11 cases were micropapillary carcinomas incontralateral lobe (Table II).

Four cases (4/29 (13.79%) were diagnosed as Hurthle-cell lesion on FNA, where a tall variant of papillary carcinoma was found in histology. The remaining cases were diagnosed as Hashimoto thyroiditis with ASUS 8/29m(27.59%) and follicular neoplasm (6/29 (20.69%) where 4 cases came out to be follicular carcinoma and 2 cases follicular variant of papillary carcinoma.

Discussion

FNA of thyroid is an accessible, non-invasive and cost-effective method for evaluating thyroid nodules and stratifying risk for malignancy to avoid unnecessary surgical procedures [9].

TABLE I
Characterization of Cases Showing Calcification on Ultrasonography

No.	Age in years	Gender	FNA	Histopathology	Site	Size in cm
1	50	F	Cyst/Suspicious	PTC	Retrosternal	3.5
2	43	F	MNG	PMC	right	4.3
3	52	F	Follicular lesion	PTC	left	2.1
4	43	F	MNG	PMC	right	3.2
5	32	F	Cystic adenomatoid Nodule	PTC	right	4
6	32	F	Hurthle cell neoplasm	PTC	right	2
7	49	F	Suspicious for PTC	PTC	Right	1
8	30	F	HT	PMC	Bilateral	1&0.5
9	69	M	PTC	PTC	left	1
10	30	F	HT	PMC	Bilateral	2.1&0.5
11	50	M	Benign cyst	PMC in contralateral lo small lobe	left	1.5
12	34	F	Benign lesion	PMC in right lobe	left	1.5
13	52	F	Benign lesion	PTC	left	2.3
14	33	M	Cystic lesion with atypia	PTC	left	3
15	51	M	PTC	PTC	right	3.5
16	37	F	Cystic adenomatoid Nodule	PTC	left	2.6
17	19	F	FN	FA	left	2
18	24	F	MNG/ thyroiditis	FA	left	1
19	29	F	MNG	FA	right	2.4
20	37	F	HT	HT	right	3.8
21	24	M	FN	FA	right	1

F= female, M=male, FN=follicular neoplasm, FA=follicular adenoma, PTC = papillary thyroid carcinoma, PMC= papillary micro carcinoma, HT= Hashimoto thyroiditis.

In the present study, an overall accuracy for FNA diagnosis was 77%, however, some malignant lesions have been missed in our experience. Our false negative results were 29%. Although we were able to detect atypical cells in 22/29 of our nodules, still large cystic lesions and carcinomas/micro carcinomas in the contra lateral lobe, constituted a great challenge and source of multiple pitfalls in our practice (Table I).

Meko and Norton suggested that thyroid lobectomy should be considered in large, cystic/solid thyroid nodules even if their cytological diagnosis is benign. They reported false-negative rates up to 30%, in large cystic nodules more than 3 cm, compared to small and solid nodules 3 cm or larger [10]-[12].

Increased numbers of Hurthle cells and distinction between non-neoplastic populations and neoplastic cells was another diagnostic challenge. Auger [13], in his review article about Hürthle cells, named after the German histologist Karl Hürthle in 1894, pointed that it was a misnomer and that they are

actually C cells [14].

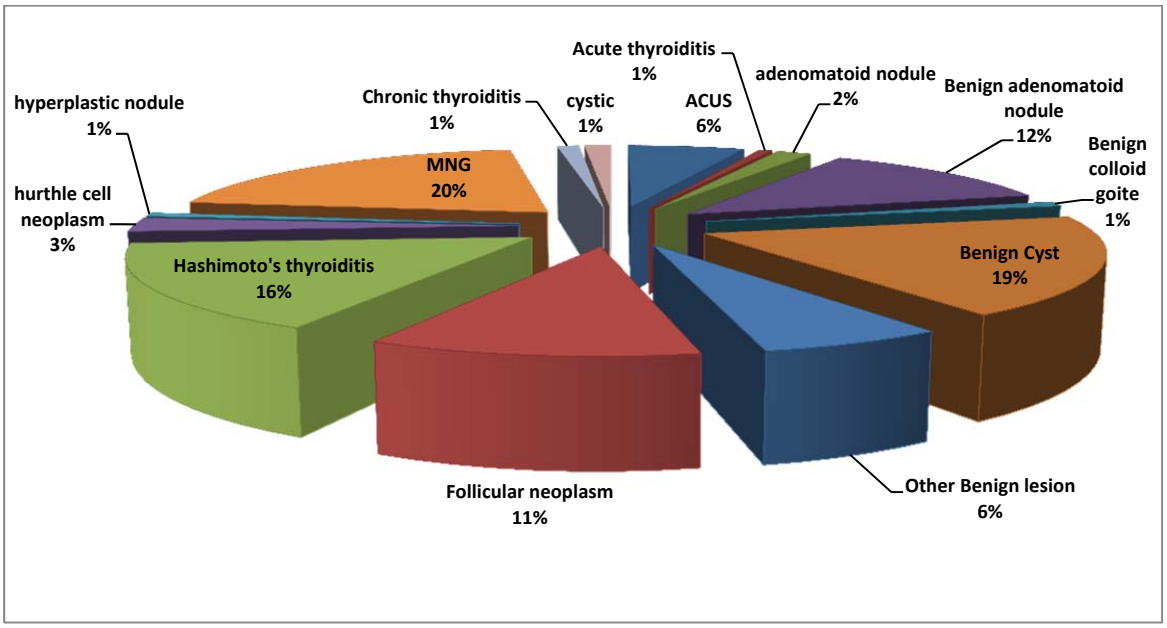

Fig. 1 Types of Benign Lesions in 490 cases diagnosed by FNA

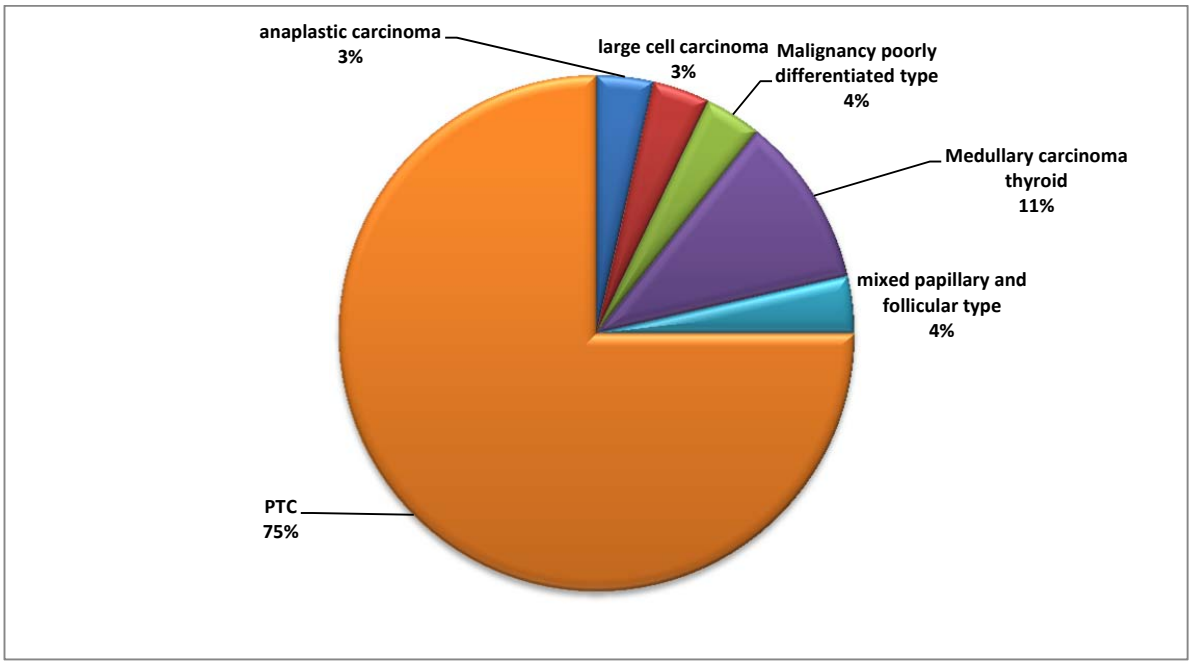

Fig. 2 Types of Malignant Thyroid Cancer in 490 Lesions diagnosed by FNA

TABLE II
FNA VERSUS HISTOLOGY IN 29 FALSE NEGATIVE CASES

	No.	%	FNA Diagnosis (no.)	Histological Diagnosis
Large Unilateral cystic lesion	11	37.93%	-Cyst fluid only (2) -Benign cyst (1) -Cyst fluid with atypical cells (AUS)(8)	-PTC -PTC contralateral side - Microcarcinoma
Hurthle Cell Lesion	4	13.79	-Hurthle Cell Neoplasm	-PTC background Hashimoto -PTC Tall cell variant
Hashimoto Thyroiditis	8	27.59%	Chronic Thyroiditis with AUS(8)	PTC background Hashimoto
Follicular Neoplasm	6	20.60	Follicular lesion/neoplasm With atypical cells(6)	Follicular Carcinoma Follicular variant of Papillary

PTC=Papillary Thyroid Carcinoma

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By light microscopy, Hürthle cells refer to modified follicular cells exhibiting abundant finely granular cytoplasm, a round nucleus, and a variably conspicuous nucleolus .They are sometimes called "oxyphils and oncocytes" [15], [16]. Oncocytic change is usually seen in a variety of lesions in the thyroid, both non neoplastic like MNG/nodular hyperplasia and Hashimoto thyroiditis, and neoplastic like follicular adenoma, follicular carcinoma, papillary thyroid carcinoma, and medullary thyroid carcinoma [17]. Authors then suggested to combine cytological criteria, along with other clinical parameters such as size, distribution, and radiographic characteristics of the lesions, in order to get a better diagnosis [18].

Follicular carcinomas were another pitfall as a follicular lesion could be seen on cytology with some atypical cells where follicular carcinoma could only be confirmed by finding capsular and/or vascular invasion. In other cases, a sampling error with low cellularity could have been the reason of false negative diagnosis.

Some previous studies suggested that nodules more than 4 cm could carry a higher risk of malignancy [19]. In our experience, the mean size of malignant nodules was higher than benign nodules but less than 4 cm in size. Taking into consideration the presence of calcification, 16/43 of our malignant cases showed calcified foci on ultrasound (U/S) examination with variable degrees of hypervascularity. However, 5/8 benign lesions also harbored calcified foci. The difference between both lesions was statistically significant (p value =0.007). Several other studies have also highlighted the importance of calcification and recommended surgical removal of the nodule containing calcification regardless of the FNA finding [20].

To conclude, FNA is a valuable, non-invasive tool for early diagnosis of thyroid carcinoma. However, triple assessment similar to that done in breast carcinoma, is preferred, combining U/S findings, clinical and cytological findings. An increased size, calcified foci, and atypical cells on FNA should alert the surgeon to the possibility of carcinoma in palpable nodules.

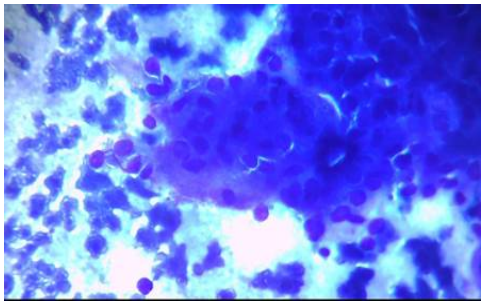

Fig. 3 FNA showing papillary fragment with discohesive cells; Giemsa X 400

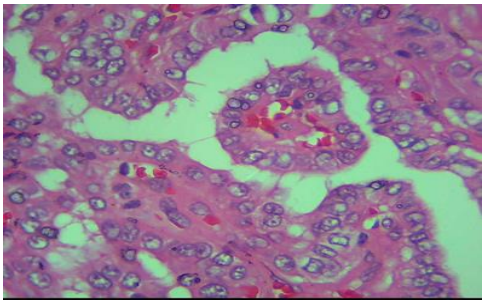

Fig. 4 Papillary Carcinoma with nuclear clearing; H&E X 400

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