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The Diagnostic Value of FNAB for Early Diagnosis of Thyroid Cancer: A Greek Center Experienter [Version 1, 2 Approved, 1 Approved with Reservation]

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Abstract

Purpose: The major concern of thyroid nodular disease is the probability of malignancy. Neck ultrasound and fine needle aspiration biopsy (FNAB) have been established as the initial investigation.

Methods: A total of 563 patients (106 males/457 females) underwent FNABs. We correlated the demographic profile and sonographic features of these nodules with the FNAB outcome and the Bethesda system (B) was used.

Results: Out of total 563 cases, 190 (33.7%) were diagnosed as nondiagnostic (B1), 339 (60.2%) as benign (B2), 17 (3.0%) as atypia/ follicular lesion of undetermined significance (B3), 7 (1.2%) as follicular neoplasm or suspicious for follicular neoplasm (B4) while 5 (0.9%) as suspicious for malignancy (B5) and 5 (0.9%) as malignant (B6). When comparing the sonographic characteristics of nodules with benign cytology (B2) versus the sonographic characteristics of nodules with cytology category B3-6, we found that irregular shape (7.1% in B2 vs 17.6% in B3-6, $p=0.043$), ill-defined margins of the nodule (13.3% in B2 nodules vs 29.4% in B3-6 nodules, $p=0.020$), and the presence of calcifications (34.2% in B2 nodules vs 64.7% in B3-6 nodules, $P=0.001$) reduced significantly the possibility for benign (B2) result. Moreover, two nodules of category B5 and B6 each had a maximum diameter of 9mm and 8mm respectively.

Conclusion: The aforementioned sonographic findings decrease the possibility for a benign cytology result. Even for smaller nodules of 1 cm with high suspicious pattern an FNAB should be considered.

Keywords

Thyroid cancer; FNAB; Bethesda System; Thyroid nodules

Introduction

Thyroid nodules are detected clinically in 5% of females and in 1% of males in non-endemic areas, in autopsy series in 50% and by ultrasound in a wide range of 19 – 68% of the studied populations [1,2]. Thyroid ultrasound is the most sensitive method for the detection of nodular thyroid disease. Although thyroid nodules are mostly benign, malignancy is still a possibility, referred present in up to 15% of nodules. In order to further evaluate the nodules, fine needle aspiration biopsy (FNAB) is generally recommended under certain circumstances [3]. As a diagnostic method, US-FNAB has many advantages, such as real-time guidance, simple operation, safe, few contraindications and complications, and an effective method to identify the benign and malignant thyroid nodules [4,5]. Recent advances in the classification of cytology results and the determination of ultrasound suspicious for malignancy features of nodules has permitted a more accurate management of thyroid nodules [1,6].

There are specific features that imply malignancy or benignity although there is a variability among different researches about these features. Moreover, nondiagnostic biopsies are also common. In our department, patients are referred for ultrasound-guided FNAB when they have a nodule larger than 10mm or suspicious malignant sonographic features such as microcalcification, irregular or microlobulated margin, markedly hypoechoogenicity and increased central vascularity [7]. We determined the frequency and predictors of nondiagnostic FNAB of thyroid nodules and we correlated sonographic features and outcome of biopsy according to malignancy or benignity. Moreover we correlated all these findings with the size of the nodule, as we tried to investigate whether it is necessary to perform FNAB in nodules less than 10mm. Finally, we investigated whether the underlying heterogeneity of the thyroid parenchyma as well as the treatment with L-T4 could affect the FNAB results (benign- malignant).

Methods

This study was conducted in the Department of Endocrinology of a tertiary cancer center (Metaxa Anticancer Hospital). The study was approved by the Scientific Committee of the hospital.

From April 2014 to September 2015, 563 patients underwent US-guided FNABs for the same number of thyroid nodules. A total of 106 males (18.8%) and 457 (81.1%) females were enrolled in the study. Their mean age \pm SD was 56.12 \pm 14.15 years (range = 16 - 86 years). We correlated the demographic profile (age and gender) and sonographic features of these nodules with the FNAB results.

Every patient lay in a supine position with a thin pillow under the shoulders, and the neck extended. FNABs were conducted using a 23-gauge needle attached to a 10-ml disposable plastic syringe under US guidance with a free-hand technique. Each lesion was aspirated at least twice and all cystic fluid was aspirated as much as possible in the cystic portion of the nodules, and afterwards, FNAB was performed on the solid portion of the nodules. Materials obtained from FNAB were smeared on glass slides, cytology samples were sent to the Pathology Department, and the results were reported by cytopathologists in an official report form. A specimen was considered as "adequate" and diagnostic if there was a minimum of six groupings of well-preserved thyroid cells, at least 10 cells per group [8]. The possible categories of diagnostic cytological results were: benign (including colloid nodules, hyperplastic nodules, and thyroiditis), malignant, suspicious for malignancy, and indeterminate (including follicular or Hürthle cell neoplasm, atypia, or follicular lesion of undetermined significance). The Bethesda system (B) [9,10] for reporting thyroid cytopathology was used and FNAB results are divided into six categories: 1. Nondiagnostic, 2. Benign, 3. Atypia/ follicular lesion of undetermined significance (AUS/FLUS), 4. Follicular neoplasm/ suspicious of follicular neoplasm, 5. Suspicious of malignancy, and 6. Malignant.

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The ultrasound diagnosis were performed using a 5–12-MHz linear-array transducer and Grayscale and color Doppler examinations were used. We assessed sonographic features such as number of nodules, size of prominent nodule, echotexture (solid, cystic or mixed), echogenicity (hyperechoic/ isoechoic or hypoechoic), shape, multiplicity, margins, vascularity and the presence of calcifications. Echogenicity of the solid portion was categorized as either hyperechoic (for nodules showing hyperechogenicity compared with the normal thyroid) and isoechoic (for nodules showing isoechogenicity compared with the normal thyroid) which are considered less possible for malignancy, or hypoechoic (for nodules showing hypogenicity compared with the normal thyroid) which is considered more suspicious for malignancy. Nodule shape was categorized as round/ oval or irregular shape. Internal components were defined as solid, cystic or mixed. Margins were classified as well-defined regular or ill-defined and irregular. Vascularity patterns were: central or absent / peripheral. Each patient was asked whether he/she was on L-T4 treatment. Moreover, we assessed if there was mild or diffuse underlying heterogeneity of the parenchyma which is usually encountered in Hashimoto thyroiditis.

Each demographic and sonographic data was analyzed for its association with possibility of benignity (category B2 vs categories B3-6).

Data were analyzed using SPSS analytical software 22 (SPSS Inc – IBM Corporation, New York, United States). Chi-square tests (for differences of proportions) and t-tests (for differences in means) were used. Variables with p-values of less than 0.05 were considered significant upon analysis.

Results

Out of total 563 cases, 190 (33.7%) cases were diagnosed as non diagnostic (B1), 339 (60.2%) were diagnosed as benign (B2), 17 (3.0%) as B3 (atypia/follicular lesion of undetermined significance), 7 (1.2%) as B4 (follicular neoplasm or suspicious for follicular neoplasm), while 5 (0.9%) cases were categorized as B5 (suspicious for malignancy) and 5 (0.9%) as B6 (malignant). Remarkably, two nodules of category B5 and B6 each had a maximum diameter of 9mm and 8mm respectively. When comparing the u/s features of nodules with benign cytology (B2) vs the u/s features of nodules with cytology category B3-6 (Table I), we found that irregular shape (7.1% in B2 vs 17.6% in B3-6, $\chi^2=4.66$, $p=0.043$), ill-defined margins of the nodule (13.3% in B2 nodules vs 29,4% in B3-6 nodules, $\chi^2=6.4$, $p=0.020$), and the presence of calcifications (34.2% in B2 nodules vs 64.7% in B3-6 nodules, $\chi^2=12.3$, $P=0.001$) decreased significantly the possibility for benign (B2) result, whereas features such as the size of nodule, the presence of central vascularity, the composition and the hypoechoicity of the nodule did not affect the possibility for B2 vs B3-6 result. Finally, there was no association of gender, age or LT-4 treatment with the Bethesda category result.

Table 1: Demographic and sonographic features according to benign (B2) or not (B3-6) cytology.

Demographic and sonographic features	Bethesda Category 2 (n= 339) (90.8%)	Bethesda Category 3-6 (n= 34) (9.2%)	p-value
Age, mean (SD), years	55.88 ± 14.43	50.54 ± 15.45	NS*
Male/female	68/271	7/27	NS
Shape			
Irregular shape	7.1%	17.6%	0.043
Margins			
Ill-defined	13.3%	29.4%	0.020
Calcifications			
Calcifications present	34.2%	64.7%	0.001
Size of nodule			
Mean± S.D (mm)	15.81±6.9	16.40±7.3	NS
< 10mm	10.0%	8.8%	NS
> 10mm	90.8%	91.2%	NS
Solitary nodule	46.0%	41.2%	NS
Composition			
Solid nodule only	48,5%	44,1%	NS
Underlying echogenicity of the parenchyma			
Heterogeneity	79.1%	79.4%	NS
Echogenicity of nodule			
Hypoechoic	50.1%	61.8%	NS
Central Vascularity			
Central vascularity present	19.5%	20.6%	NS
Patients on LT4 treatment	52.5%	50.0%	NS
*NS = Not significant			

Discussion

The possibility of malignancy increases significantly with the higher Bethesda rating [6]. Hence, it is useful for the clinicians to be able to predict the possibility of the cytology result.

Numerous studies have showed that FNAB is a sensitive and specific procedure for the diagnosis of thyroid cancer and is a useful method that provides guidance to primary surgery and prevents unnecessary procedures [11,12]. The clinical significance of thyroid nodules is to exclude the possibility of thyroid cancer. Depending on sex, age, radiation exposure, family history and other factors it occurs in 7-15% of thyroid nodules [13,14]. Nodules with high suspicion of malignancy are those who are solid and hypoechoic or a solid hypoechoic component in a partially cystic nodule with one or more of the following features: irregular margins, microcalcifications, taller than wide shape. Intermediate suspicious of malignancy are those nodules who are hypoechoic solid nodule with a smooth regular margin, but without microcalcifications, extrathyroidal extension, or taller than wide shape [15-17]. Isoechoic or hypere-

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choic solid nodules without microcalcifications, extrathyroidal extension, or taller than wide shape have a low risk for malignancy, whereas spongiform or partially cystic nodules without any of the suspicious sonographic features have a very low risk of malignancy as well [15-18]. Finally, pure cystic nodules are most likely benign and FNAB is not indicated.

An irregular margin implies the demarcation between nodule and parenchyma is obviously evident but shows an irregular, infiltrative or spiculated course. The presence of microcalcifications regularly confer a higher risk of malignancy [19-21]. Our study supports that the irregular shape of a nodule, ill defined margins, and the presence of calcifications decrease the possibility of a Bethesda benign result and our results are compatible with the literature. Moreover, we estimated those specific characteristics that are more likely to be related to malignancy and we found that irregular shape of a nodule, ill defined margins, and the presence of calcifications decreased significantly the possibility for benignity more than other suspicious features that were examined separately. It is highly suggested that every clinician takes into account all the specific features of a nodule and decides whether to perform FNAB or surgical excision.

The 2015 ATA guidelines [1] recommend fine-needle aspiration for nodules 10 mm or larger in the greatest dimension that have a high- or intermediate-suspicion pattern on sonography, nodules 15 mm or larger that have a low-suspicion pattern on sonography, and nodules 20 mm or larger that have a very-low-suspicion pattern on sonography. These guidelines also recommend that on first evaluation, nodules considered to be suspicious by medical history or sonographic characteristics should be considered for aspiration if they are less than 10 mm in diameter [22]. Opposing to this recommendation, two nodules in our study of category B5 and B6 each had a maximum diameter of 9mm and 8mm, respectively.

In conclusion our study suggests that decisions about whether to perform FNAB should be based on the presence of suspicious US findings in order to refute or confirm malignancy. The US findings that were significantly associated with a less probability of benignity were microcalcifications, irregular shape and irregular margins. Even for smaller nodules of 10mm with high suspicious pattern an FNAB is indicated.

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