Thyroid ultrasonographic characteristics and Bethesda results after FNAB

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Summary

Purpose: Thyroid nodular disease (TND) is a frequent clinical problem and the major concern is the probability of malignancy in a solitary nodule or in one or more nodules of a multinodular goiter. For this purpose, neck ultrasound and fine needle aspiration biopsy (FNAB) under ultrasound guidance have been established as the initial investigation of choice.

Methods: A total of 1113 patients (210 male/903 female) underwent FNABs for the same number of thyroid nodules. Correlated were the demographic profile (age and gender) and sonographic features of these nodules with the FNAB outcome. The Bethesda system (B) for reporting thyroid cytology was used.

Results: Out of total 1113 cases, 255 (22.9%) were characterised as nondiagnostic (B1), 780 (70.1%) were diagnosed as benign (B2), 35 (3.1%) were diagnosed as B3 (atypia/follicular lesion of undetermined significance), 10 (0.9%) were diagnosed as B4 (follicular neoplasm or suspicious for follicular neoplasm), while 13 (1.2%) cases were categorized as B5 (suspicious for malignancy) and 20 (1.8%) as B6 (malignant). When comparing the sonographic features of nodules with benign cytology (category B2) vs those of nodules with cytology category B3-6, irregular shape and ill-defined margins of the nodule, and microcalcifications and the hypoechogenicity increased significantly the possibility for a B3-B6 cytology result (p<0.05). Finally, there was no association of gender and age with the (B) category results.

Conclusion: The aforementioned sonographic findings decrease the possibility for a benign cytology result according to the Bethesda classification system.

Key words: Bethesda classification system, fine needle aspiration biopsy, thyroid nodules, thyroid ultrasound

Introduction

The majority of thyroid nodules are usually incidental findings of asymptomatic, benign lesions discovered by imaging examinations for reasons unrelated to thyroid diseases [1]. 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 [2,3]. 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 presently in up to 15% of nodules. In order to further evaluate the nodules, fine needle aspiration biopsy (FNAB) is generally recommended under certain circumstances [4]. As a diagnostic method, US-FNAB has many advantages, such as
real-time guidance, simple operation, safe, few contraindications and complications, and it is an effective method to identify the benign and malignant thyroid nodules [5,6]. Recent advances in the classification of cytology results and the determination of ultrasound features suspicious for malignancy of nodules has permitted a more accurate management of thyroid nodules.

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 sono-graphic features such as microcalcification, irregular or microlobulated margin, markedly hypoecho-genicity and increased central vascularity [7].

In this study 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 Cancer Hospital). The study was approved by the Scientific Committee of the hospital. Signed informed consent was obtained from the patients.

From April 2014 to January 2018, 1113 patients underwent US-guided FNABs for the same number of thyroid nodules. A total of 210 males (18.9%) and 903 (81.1%) females were enrolled in the study. Their mean age±SD was 56.2±21.6 years (range 16-86). We correlated the demographic profile (age and gender) and sonographic features of these nodules with the FNAB results.

Every patient laid in supine position with a thin pillow under the shoulders, and the neck extended. FNABs were performed 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 were 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.

The ultrasound diagnosis was performed using a 5-12-MHz linear-array transducer and Grayscale and Color Doppler examinations were used. We assessed sono-graphic 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 hypogenericity compared with the normal thyroid) which is considered more suspicious for malignancy. Nodule shape was categorized as round/oval or irregular. 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 a nondiagnostic FNAB outcome, and possibility of malignancy (category B5 and B6) and benignity (category B2).

Statistics

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

Results

Out of total 1113 cases, 255 cases (22.9%) were diagnosed as non-diagnostic (B1), 780 (70.1%) were diagnosed as benign (B2), 55 (5.1%) as B3 (atypia/ follicular lesion of undetermined significance), 10 (0.9%) as B4 (follicular neoplasm or suspicious for follicular neoplasm), while 13 cases (1.2%) were categorized as B5 (suspicious for malignancy) and 20 (1.8%) as B6 (malignant). Remarkably, 11 out of
33 (33%) nodules of B5 and B6 category had a maximum diameter less than 10mm. When comparing the US features of nodules with benign cytology (B2) vs the US features of nodules with cytology category B3-6 (Table 1), we found that irregular shape (6.5% in B2 vs 15.4% in B3-6, p=0.004), ill-defined margins of the nodule (10.6% in B2 nodules vs 20.5% in B3-6 nodules, p=0.033), the presence of calcifications (24.4% in B2 nodules vs 56.4% in B3-6 nodules, p<0.001), and the hypoechoic composition of the nodule (41.9% in B2 nodules vs 65.4% in B3-6 nodules, p<0.001) decreased significantly the possibility for benign (B2) result, whereas features such as the size of nodule, the presence of central vascularity and the composition 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.

**Discussion**

The possibility of malignancy increases significantly with the higher Bethesda rating [11]. Hence, it is useful for the clinicians to be able to predict the possibility of the cytology result.

Numerous studies have shown 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 [12,13]. 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 [14,15]. 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 and 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 [16-18]. Isoechoic or hyperechoic 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 [16-19]. 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 [20-22]. Our study supports that the irregular shape of a nodule, ill-defined margins, and the presence of calcifications and the hypoechoogenicity of the nodule, all these decrease the possibility of a Bethesda benign result and our results are compatible with the literature. 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.

Generally, FNAB is recommended for nodules 10mm or larger in the greatest dimension that have a high- or intermediate-suspicion pattern on sonography, nodules 15mm or larger that have a low-suspicion pattern on sonography, and nodules 20mm or larger that have a very-low-suspicion pattern on sonography [2]. Moreover, it is also recommended 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 10mm in diameter [23]. Opposing this recommendation, 11 out of 33 nodules in our study of B5 and B6 category had a maximum diameter less than 1cm.

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 exclude or confirm malignancy. The US findings that were significantly associated with a less probability of benignity were microcalcifications, irregular shape, irregular margins and hypoechoogenicity of a nodule. Even for smaller nodules of 10mm with high suspicious pattern FNAB is indicated.

Conflict of interests

The authors declare no conflict of interests.

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