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ORIGINAL ARTICLE

Thyroid ultrasonographic charasteristics 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 cytopathology 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

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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 sonographic features such as microcalcification, irregular or microlobulated margin, markedly hypoechogenicity 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 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. 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 heterogenicity 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), 35 (3.1%) 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

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

Demographic and sonographic features	*Bethesda category II (n=780) (90.9%)*	*Bethesda category III-VI (n=78) (9.1%)*	*p value*
Age, mean (SD), years	57.3 ± 24.2	53.1± 13.3	NS
Males/females	124/656	19/59	NS
Shape			
Irregular shape	6.5%	15.4%	0.004
Margins			
Ill-defined	10.6%	20.5%	0.033
Calcifications			
Calcifications present	24.4%	56.4%	<0.001
Size of nodule			
Mean diameter ± SD (cm)	1.58 ± 0.81	1.49 ± 0.84	NS
Solitary nodule	39.3%	42.6%	NS
Composition			
Solid nodule only	97.2%	98.7%	NS
Underlying echogenicity of the parenchyma			
Heterogenicity	75.9%	82.1%	NS
Echogenicity of nodule			
Hypoechoic	41.9%	65.4%	<0.001
Central vascularity			
Central vascularity present	17.2%	19.2%	NS
Patients on LT4 treatment	48.6%	56.4%	NS

NS: non significant

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 hypoechogenicity 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 hypoechogenicity 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.

References

1. Russ G, Leboulleux S, Leenhardt L, Hegedus L. Thyroid incidentalomas: epidemiology, risk stratification with ultrasound and workup. Eur Thyroid J 2014;3:154-63.
2. Haugen BR, Alexander EK, Bible KC et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2016;26: 1-133.
3. Dean DS, Gharib H. Epidemiology of thyroid nodules. Best Pract Res Clin Endocrinol Metab 2008;22:901-11.
4. Frates MC, Benson CB, Charboneau JW et al. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. Radiology 2005;237:794-800.
5. Moon HJ, Son E, Kim EK, Yoon JH, Kwak JY. The diagnostic values of ultrasound and ultrasound-guided fine needle aspiration in subcentimeter-sized thyroid nodules. Ann Surg Oncol 2012;19:52-9.
6. Kim DW, Lee EJ, Kim SH et al. Ultrasound-guided fine-needle aspiration biopsy of thyroid nodules: comparison in efficacy according to nodule size. Thyroid 2009;19:27-31.
7. Frates MC, Benson CB, Charboneau JW et al. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. Ultrasound Quarterly 2006;22:231-8; discussion 239-40.
8. Gharib H, Papini E, Paschke R et al. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations. Endocr Pract 2010;16:468-75.
9. Cibas ES, Ali SZ. The Bethesda System For Reporting Thyroid Cytopathology. Am J Clin Pathol 2009;132:658-65.
10. Cibas ES, Ali SZ. The Bethesda System for Reporting Thyroid Cytopathology. Thyroid 2009;19:1159-65.
11. Bongiovanni M, Spitale A, Faquin WC, Mazzucchelli L, Baloch ZW. The Bethesda System for Reporting Thyroid Cytopathology: a meta-analysis. Acta Cytol 2012;56:333-9.
12. Bhatki AM, Brewer B, Robinson-Smith T, Nikiforov Y, Steward DL. Adequacy of surgeon-performed ultrasound-guided thyroid fine-needle aspiration biopsy. Otolaryngol Head Neck Surg 2008;139: 27-31.
13. Greenblatt DY, Woltman T, Harter J, Starling J, Mack E, Chen H. Fine-needle aspiration optimizes surgical management in patients with thyroid cancer. Ann Surg Oncol 2006;13:859-63.
14. Hegedus L. Clinical practice. The thyroid nodule. N Engl J Med 2004;351:1764-71.
15. Mandel SJ. A 64-year-old woman with a thyroid nodule. JAMA 2004;292:2632-42.
16. Horvath E, Majlis S, Rossi R et al. An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management. J Clin Endocrinol Metabol 2009;94:1748-51.
17. Tae HJ, Lim DJ, Baek KH et al. Diagnostic value of ultrasonography to distinguish between benign and malignant lesions in the management of thyroid nodules. Thyroid 2007;17:461-6.

18. Ito Y, Amino N, Yokozawa T et al. Ultrasonographic evaluation of thyroid nodules in 900 patients: comparison among ultrasonographic, cytological, and histological findings. Thyroid 2007;17:1269-76.
19. Brito JP, Gionfriddo MR, Al Nofal A et al. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. J Clin Endocrinol Metabol 2014;99:1253-63.
20. Henrichsen TL, Reading CC, Charboneau JW, Donovan DJ, Sebo TJ, Hay ID. Cystic change in thyroid carcinoma: Prevalence and estimated volume in 360 carcinomas. J Clin Ultrasound 2010;38:361-6.
21. Lee MJ, Kim EK, Kwak JY, Kim MJ. Partially cystic thyroid nodules on ultrasound: probability of malignancy and sonographic differentiation. Thyroid 2009;19:341-6.
22. Kim DW, Lee EJ, In HS, Kim SJ. Sonographic differentiation of partially cystic thyroid nodules: a prospective study. Am J Neuroradiol 2010;31:1961-6.
23. Gharib H, Papini E, Paschke R et al. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations. J Endocrinol Investig 2010;33(5 Suppl):51-6.