Ultrasonic Features of Thyroid Cancers and Benign Thyroid Nodules for Determining the Necessity of Fine Needle Aspiration Cytology

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The convenience and non-invasiveness of thyroid ultrasonography have made it the first choice for initial assessment of thyroid nodules. Fine-needle aspiration cytology (FNAC) is usually performed immediately after observation by ultrasonography or under its guidance. Quick staining methods have enabled a diagnosis of the nature of thyroid nodules within minutes. However, in cases where many nodules are present at the same time, it can be unclear as to which one to pick for FNAC. When a nodule is suspected to be malignant, FNAC is also needed. If clinicians can accurately identify with ultrasonography the characteristics of thyroid nodules with high risks of malignancy or benignity, there would be a faster and more accurate determination of whether FNAC is required, thereby leading to a faster and more accurate diagnosis or rule-out of thyroid cancers and a potential decrease in the burden of healthcare and other costs. The present review identifies these characteristics so that results of thyroid ultrasonography can be maximized and FNAC only used when necessary.

KEY WORDS — benign thyroid nodule, fine-needle aspiration cytology, thyroid cancer, thyroid ultrasonography

Introduction

The convenience and non-invasiveness of thyroid ultrasonography [1] have made it the first choice for initial assessment of thyroid nodules [2]. Fine-needle aspiration cytology (FNAC) is usually performed immediately after observation by thyroid ultrasonography, or under ultrasonographic guidance. Currently, methods exist for the rapid staining of specimens, e.g. Riu’s method [3]. The smear is first covered with solution A (0.17% eosin Y and 0.05% methylene blue in methanol) for 30 seconds, and then in solution B (0.14% methylene blue, 0.12% azure I, 2.52% Na2HPO4·12H2O and 1.25% KH2PO4 in distilled water) for 1.5 minutes. Finally, the staining mixture is washed off the slide with distilled
water. As a result of the swiftness of this staining method, an experienced cytopathologist can diagnose the nature of a thyroid nodule within minutes from aspiration and staining of specimens to reading of results.

However, in cases where there are multiple nodules present in the thyroid gland at the same time, it is important to know which one is appropriate for aspiration. Conversely, if the nodule looks suspicious for thyroid malignancy, we will ask the patient to wait for the results. If the specimen looks inadequate after staining and reading, FNAC can immediately be re-performed for highly suspicious cases. Hence, knowledge of the characteristic patterns of thyroid nodules is critical for determining the possibility of thyroid cancers when there is presence of multiple nodules.

With the advent of high-resolution ultrasonography, the possibility of detecting small thyroid nodules has become much higher. From the perspective of the burden on our healthcare system and cost-effectiveness, it is impossible to perform FNAC for all thyroid nodules [4]. Therefore, it is also critical to identify which patterns strongly favor benign lesions.

The present review identifies the ultrasonographic characteristics of thyroid cancers and benign thyroid lesions in hope of enabling clinicians to perform thyroid ultrasonography and FNAC efficiently in the diagnostic process.

**Ultrasonographic Characteristics and Patterns of Thyroid Cancers**

**Papillary thyroid cancers**

Papillary thyroid cancer is the most common thyroid cancer [5]. The ultrasonographic features of papillary thyroid cancer are usually hypoechoic (Fig. 1) and sometimes isoechoic [6]. The ultrasonographic texture is heterogeneous (Fig. 1) [5,6]. The margin can be unclear or clear, depending on the presence of tumor invasion [6]. Partial cystic degeneration cannot exclude malignancy. Discrete particles representative of microcalcifications are important signs of papillary thyroid cancer [6] (Fig. 2). However, medullary thyroid cancer can also present this sign [1,5], whereas benign lesions rarely do [5].

**Medullary thyroid cancers**

Medullary thyroid cancer can be sporadic or familial. Cacitonin and carcinoembryonic antigen are the markers of this type of cancer [7]. In familial medullary thyroid cancer, ret oncogene screening is a very important screening method for the family members of a patient with medullary thyroid cancer [8]. However, ultrasonography is also a useful and...
convenient tool for screening. The sonographic patterns of medullary thyroid cancer are isoechoic or hypoechoic nodules with an irregular margin without halo signs (Fig. 3) [5]. Some tumors can present microcalcifications, and even mix with coarse calcification that has acoustic signs (Fig. 4) [1,5].

Anaplastic thyroid cancers
Clinically, a rapidly-growing mass indicates anaplastic thyroid cancer or lymphoma [9,10]. The ultrasonographic characteristics of anaplastic thyroid cancer are heterogeneous and hypoechoic nodules (Fig. 5). There are no halo signs and the margin may be ill-defined (Fig. 6) [9].

Lymphoma
Four ultrasonographic patterns can be noted in lymphoma [10]: (1) single nodular goiter with extreme hypoechogenicity, while the remainder of the thyroid is normal (Fig. 7); (2) bilateral single nodular goiter pattern with low echogenicity and posterior enhancement; (3) bilateral multiple nodular...
goiter pattern with extremely hypoechoic nodules and posterior enhancement (Fig. 8); (4) diffuse goiter pattern with diffuse low echogenicity. The fourth pattern is difficult to distinguish from Hashimoto’s thyroiditis by ultrasonography. However, due to its rapid growth, it is not difficult to make a differential diagnosis.

**Follicular thyroid cancers**

Conventional echographic patterns have been found to be of minor relevance in differentiating follicular adenoma from follicular carcinoma [11]. However, Seo et al [12] reported that isoechoic or hypoechoic echogenicity, a predominantly solid or mixed echotexture, and the presence of microcalcifications or rim calcifications are associated with follicular carcinoma. The predominantly solid or mixed echotexture has an odds ratio of 8.1, and the presence of microcalcifications or rim calcifications has an odds ratio of 13.5 [12]. Thyroid ultrasound elastography is a new diagnostic tool for the differential diagnosis of malignant from benign lesions. Scores 4–5 are highly suggestive of malignancy, while scores 1–3 are suggestive of benign lesions [11]. A recent report on thyroid ultrasound elastography [13] found that the frequency of malignancy is 88% with a score of 4–6, and the frequency of benign nodules is 90% with a score of 1–3; however, only one case of follicular carcinoma was included in this study. More studies are needed to prove the value of thyroid ultrasound elastography as a diagnostic tool. If a solid thyroid nodule has halo signs (Fig. 9) and FNAC shows a cluster of follicular cells (Fig. 10), subtotal thyroidectomy should be considered for removal of the nodule, and subsequent pathological evaluation should be carried out to determine the presence of capsular invasion or vascular invasion so as to determine the next step in the management of patients.

**Ultrasonographic Findings of Metastatic Cancers to the Thyroid**

Ultrasonographic findings of metastatic cancer to the thyroid gland may show diffusely heterogeneous...
and hypoechoic change, or nodular but also heterogeneous and hypoechoic change (Fig. 11) [14]. With the exception that diffuse change can mimic changes observed in Hashimoto’s thyroiditis, the changes in nodular lesions as a result of metastatic cancer are similar to other malignancies but with absence of microcalcifications.

Ultrasonographic Characteristics of Benign Thyroid Nodules

Nodule size is usually inadequate for ruling out risk of malignancy [15]. If observation by detailed ultrasonography shows a pure cyst, it can be considered benign. Benign nodular lesions can also be determined by exclusion if none of the malignant sonographic characteristics such as marked hypoechogenicity, microlobulated or irregular margins, microcalcifications, and a taller-than-wide shape are present on ultrasonography [15].

Recently, Bonavita et al [16] reported that grouping of thyroid nodules into reproducible patterns of morphology (i.e. pattern recognition) rather than analysis of individual sonographic features, is extremely accurate in the identification of benign nodules. They found that spongiform configuration, cysts with colloid clots, giraffe pattern and diffuse hyperechogenicity have 100% specificity for benignity. They estimated that identification of benign nodules could obviate more than 60% of FNAC.

Depicted in Figs. 12–15 are some typical images of benign thyroid nodules. Fig. 12 shows a pure cyst. Fig. 13 shows ultrasonography of benign multinodular goiter with hypoechoic colloid goiter at the left lobe (A), and adenomatous goiter with isoechogenicity and without a well-defined margin at the right lobe (B). Fig. 14 depicts ultrasonography of benign multinodular goiter, where one of the nodules presented with multiple septa, similar to the giraffe pattern reported by Bonavita et al [16]. Fig. 15 shows ultrasonography of benign multinodular goiter with colloid goiter at the left lobe, similar to spongiform configuration reported by Bonavita et al [16].
Determination of Appropriate Nodule for FNAC With or Without Ultrasonographic-guidance

Within an iodine-deficient area, the prevalence of thyroid nodules is usually high, and multinodules can also be present. In such cases, it is not necessary to carry out aspiration for every thyroid nodule. Cavaliere et al [17] developed a useful ultrasound score for selecting thyroid nodules requiring FNAC within an iodine-deficient area. Although it is not practical to calculate the score for every nodule before each aspiration, they stressed the relative...
importance of characteristics for malignancy presented in ultrasonography. An absent or incomplete halo has the highest score (2.3), followed by solitary nodule (2.0), microcalcification (1.8), anteroposterior diameter/transversal diameter ≥1 (1.4), hypoechogenicity (1.4), and solid echostructure (1.1). When the total score is lower than 2.5, FNAC is not recommended as the risk of malignancy is only 0.4%. When the total score is more than 5.4, FNAC is recommended as the risk of malignancy is now 5.6%.

Popowicz et al [18] reported that in small nodules (≤15 mm), microcalcifications [odds ratio (OR): 19.12], height-to-width ratio ≥1 (OR: 8.57), solitary occurrence (OR: 3.29), and hypoechogenicity (OR: 3.18) were independent risk factors for malignancy. In large nodules, microcalcifications (OR: 13.10), height-to-width ratio ≥1 (OR: 8.55), and hypoechogenicity (OR: 4.02) were independent risk factors for malignancy. Jabiev et al [19] reported that the combination of hypoechogenicity, irregular borders and microcalcifications had a strong association with differentiated thyroid cancer with an OR of 30.1 (95% confidence interval 7.76–119.2). Recently, a large series in which 3,404 nodules in 2,082 cases were analyzed showed that the risk factors in thyroid ultrasonography for predicting malignancy are as follows: margin irregularity, hypoechogenic pattern and microcalcification (OR: 63.2, 13.3, 7.03, respectively) [15].

All the reports presented [15,17–19] microcalcifications as important indicators of malignancy. Although only cytological results were presented without histopathological confirmation, Chammas et al [20] found that the risk of malignancy is 41.18% with an ultrasonogram showing microcalcification, 33.33% with both micro- and coarse calcification, and 0% with only coarse calcification. The definition of coarse calcification is a diameter more than 2 mm with an acoustic shadow, clustered or isolated. The definition of microcalcification is punctuate, hyperechoic foci that measure ≤2 mm in diameter with or without a posterior acoustic shadow and without comet tail signs. Therefore, microcalcification, but not coarse calcification, is an important sign of malignancy. However, the findings of Bonavita et al [16] may be the most convenient and useful for excluding nodules for FNAC.

Presented in Figs. 16A and 16B is a case with two thyroid nodules in the same lobe. One nodule was a colloid nodule and the other was a cancerous nodule of the papillary thyroid. Although the benign nodule can be identified before aspiration, the hypoechoic nodule can only be suspected as malignant. Accumulating the relevant experience is thus essential for determining which nodule is benign, thereby making FNAC unnecessary, and which nodule is undetermined or highly suspected nodule, making FNAC necessary.

**Fig. 16.** Ultrasonography (transverse section) of case with two thyroid nodules in the right lobe. (A) One of the nodules was a colloid nodule, and (B) the other was nodule with papillary thyroid cancer.
Conclusion

It is important to be familiar with the characteristics and patterns of thyroid nodules with a high risk of malignancy, and those that indicate benignity. This could lead to more accurate and faster results for diagnosing thyroid cancer, and decrease the burden of healthcare and costs.

References