ORIGINAL RESEARCH PAPER

Radiology

KEY WORDS: Color doppler, high resolution ultrasonography, thyroid, ultrasound, ultrasound elastography

Role of Ultrasound and Elastography in the diagnosis of thyroid lesions

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ABSTRACT

Thyroid ultrasonography is a useful tool in the evaluation and management of thyroid disorders. Advanced ultrasound techniques for thyroid imaging has helped the surgeons and endocrinologists to a great extent in their daily clinical and operative practice. This article provides an overview of indications for ultrasound in various thyroid diseases, describes characteristic ultrasound findings in these diseases, and illustrates major diagnostic pitfalls of thyroid ultrasound.

Introduction

Ultrasonography (USG) is the most sensitive imaging modality for the early evaluation of the thyroid lesions. It is non-invasive, easily available and cheap imaging modality without any ionizing radiation. It is the modality of choice for initial characterization of a thyroid nodule. Although thyroid nodules may be detected at computed tomography (CT) and magnetic resonance (MR) imaging, these modalities are not useful for characterization of a nodule. Further, real time ultrasound imaging helps to guide diagnostic and therapeutic interventional procedures in cases of thyroid disease. The major limitation of ultrasound in thyroid imaging is that it cannot determine thyroid function, whether the thyroid gland is underactive, overactive or normal in function; for which a blood test or radioactive isotope uptake test is generally required.[1]

Indications of Thyroid Ultrasonography

1. To confirm presence of a thyroid nodule when physical examination is equivocal.
2. To characterize the internal structure, echogenecity, vascularisation and dimentions of thyroid nodule.
3. To differentiate between benign and malignant thyroid lesions specially with elastography
4. To differentiate between thyroid nodules and other cervical masses like lymphadenopathy and benign cystic neck lesions
5. To evaluate diffuse changes in thyroid parenchyma.
6. To detect post-operative residual or recurrent tumor in thyroid bed or metastases to neck lymph nodes.
7. To screen high risk patients for thyroid malignancy.
8. To guide diagnostic (FNA cytology/biopsy) and therapeutic interventional procedures.

DISEASES OF THYROID

Non-neoplastic lesions

The incidence of thyroid nodules is very high on USG, ranging from 50% to 70%. The most common cause of benign thyroid nodule is nodular hyperplasia. Thyroid adenomas are other common benign neoplasms of thyroid that are mostly solitary but may also develop as a part of multinodular masses. Iso-or hyper-echogenicity of the thyroid nodule in conjunction with a spongiform appearance is the most reliable criterion for benignity of the nodule on gray-scale ultrasound. Other features like nodule size >1 cm, width < length, presence of hypoechoic halo around the nodule (fibrous capsule or compressed thyroid tissue) and coarse/curvilinear calcification are less specific but may be useful ancillary signs. "Ring down" or "comet-tail" artifact or sign is typical of benign cystic colloid nodule. Perinodular flow or spoke-and-wheel-like appearance of vessels on color Doppler examination is characteristic of a benign thyroid nodule. However, this flow pattern may also be seen in thyroid malignancy. A complete avascular nodule is very unlikely to be malignant. The common conditions that present as diffuse enlargement of the thyroid gland include multinodular goitre, Hashimoto's (lymphocytic) thyroiditis, de-Quervain's subacute thyroiditis and Graves' disease. The sonographic features of these processes may be similar but they have different biochemical profile and clinical presentations. Hence, in these conditions, ultrasound findings should be viewed in relation to clinical and biochemical status of the patient.[2]

Multinodular goitre (MNG) is the commonest cause of diffuse asymmetric enlargement of the thyroid gland. Females between 35-50 years of age are most commonly affected. Histologically, colloid or adenomatous form of MNG (Fig1a,b,c,d) is common. The ultrasound diagnosis rests on the finding of multiple nodules within a diffusely enlarged gland. A diffusely enlarged thyroid gland with multiple nodules of similar US appearance and with no normal intervening parenchyma is highly suggestive of benignity, thereby making FNA biopsy unnecessary. Most of the nodules are iso-or hyper-echoic in nature; when enlarged provide heterogeneous echo pattern to the gland. These goitrous nodules often undergo degenerative changes that correspond to their USG appearances: cystic degeneration gives anechoic appearance to the nodule, hemorrhage or infection within the cyst is seen as moving internal echoes/septations, colloidal degeneration produces comet-tail artifact, while dystrophic calcification is often course or curvilinear. Vascular compression due to follicular hyperplasia leads to focal ischemia, necrosis and inflammatory change. The assessment of nodule vascularity is very useful in differentiating MNG from multifocal carcinoma. Nodule with intrinsic vascularity and other features of malignancy can be targeted for biopsy, in preference to other nodules.[3]

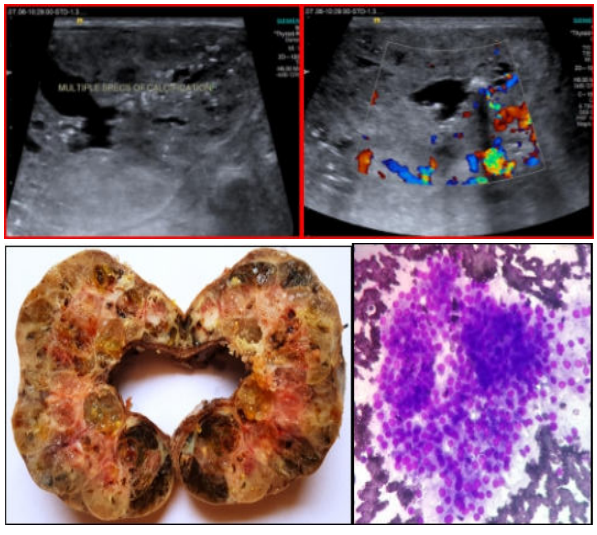


Figure 1a Multiple specs of calcification Figure 1b Colour Doppler of multinodular goiter Figure 1c Gross photograph showing multiple nodules of variable sizes filled with colloid Figure 1d Giemsa stain showing benign thyroid follicular epithelial cells

Graves' disease (Thyrotoxicosis) is an autoimmune disease characterized by thyrotoxicosis (Figure2a,b). Females between 20 and 50 years are most commonly affected. On gray-scale USG, thyroid is diffusely enlarged (2-3 times its normal size), hypoechoic and heterogeneous. Color flow imaging reveals a spectacular "thyroid inferno" with marked hyper vascularity. This pattern demonstrates extensive intra-thyroid flow both in systole and diastole. In contrast to Hashimoto's thyroiditis, return of normal thyroid appearance is possible at the time of remission. The ultrasound picture of Graves' disease may be indistinguishable from Hashimoto's thyroiditis and de Quervain's thyroiditis; however, clinical picture varies significantly between these three conditions.[4]

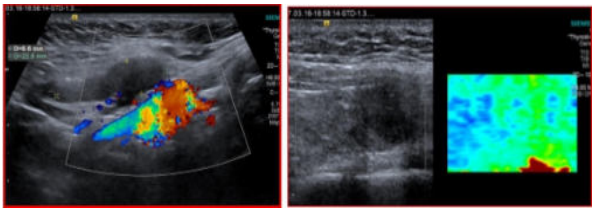


Figure2 a,b Diffuse bilateral heterogenous echotexure of thyroid with normal stiffness on elastography

Thyroiditis Thyroiditis is inflammation of the thyroid. It can be categorized as chronic lymphocytic thyroiditis (including autoimmune and Hashimoto thyroiditis), de Quervain (subacute or granulomatous) thyroiditis, acute (infectious) thyroiditis, Riedel (fibrous) thyroiditis, or, rarely, some other form of thyroiditis. Of these subtypes, chronic lymphocytic thyroiditis is the most common. Hashimoto's thyroiditis is an autoimmune disorder common in females over 40 years of age. Its diagnosis is confirmed by demonstration of serum thyroid antibodies and antithyroglobulin antibodies. The characteristic US appearance is focal or diffuse glandular enlargement with coarse, heterogeneous and hypoechoic parenchymal echo pattern. Presence of multiple discrete hypoechoic micronodules (1-6 mm size) is strongly suggestive of chronic thyroiditis. Color Doppler may demonstrate slight to markedly increased vascularity of the thyroid parenchyma. Small atrophic gland represents end stage Hashimoto's thyroiditis. Both benign and malignant nodules are known to co-exist within a background of diffuse Hashimoto's thyroiditis; on ultrasound, hyperechoic nodules are more likely to be benign, whereas hypoechoic nodules are more likely to be malignant. However, a PET scan or FNAC may be required to differentiate them. Hashimoto's thyroiditis is associated with an increased risk of thyroid malignancies like follicular or papillary carcinoma and lymphoma. Moreover, in patients of Hashimoto's thyroiditis, USG examination may reveal presence of perithyroidal satellite lymph nodes, especially the "Delphian" node just cephalad to the isthmus Figure 3. These perithyroidal lymph nodes are extremely useful in diagnosis of the thyroiditis when correlated with USG, clinical and laboratory findings. origin) and malignant lymph nodes.[5,6]

Figure 3 A case of thyroiditis showing Delphian nodes

De Quervain's thyroiditis (subacute granulomatous thyroiditis) characteristically presents with painful swelling in lower neck, fever and constitutional symptoms, typically following a viral illness. USG examination shows characteristic focal hypoechoic areas (map like) and enlargement of one or both thyroid lobes. Level VI chain lymph nodes (pre-tracheal, the preferential site of thyroid drainage) are found to be enlarged in majority of patients. FNAC shows granulomas with lymphocytic destruction of the follicular epithelial cells. It should be differentiated with primary tuberculosis of thyroid which is a very uncommon entity. Figure4a,b,c,d

Riedel's thyroiditis (chronic fibrous thyroiditis/invasive fibrous thyroiditis) is the rarest type of inflammatory thyroid disease. On ultrasound, Riedel's thyroiditis may present as a diffuse hypoechoic process with ill-defined margins and marked fibrosis

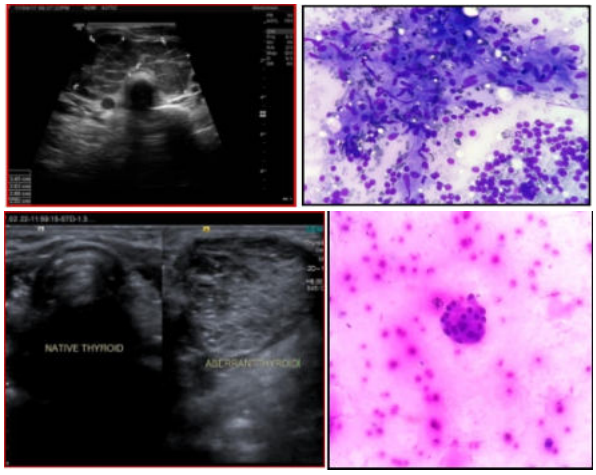


Figure 4 a Bilateral heterogenous echotexture with multiple heteroechoeic nodular lesions Figure4b Epithelioid cell granulomas with caseation necrosis on Geimsa stain (Tuberculosis) Figure4c Agenesis of normal thyroid with aberrant thyroid Figure4d FNAC show benign thyroid follicular epithelial cells in the background of colloid

Neoplastic Lesions

Ultrasound features Suggesting Malignancy [7,8,9]

1) **Calcification :** It can be seen in both benign and malignant processes, more closely associated with malignancy

Microcalcifications

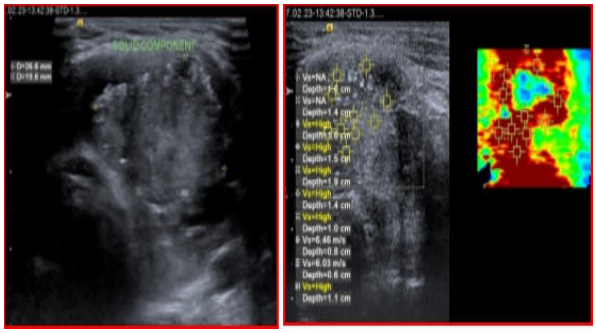
- punctate echogenic foci without posterior shadowing
- most specific finding associated with malignancy (~95%)
- associated with papillary thyroid carcinoma (Figure5a,b,c,d)
- colloid nodules shows ring-down (comet tail) artefact

Coarse calcifications

- can be seen in both benign and malignant nodules
- associated with both papillary thyroid carcinoma and medullary thyroid carcinoma

Peripheral rim calcification

- can be seen in both benign and malignant nodules



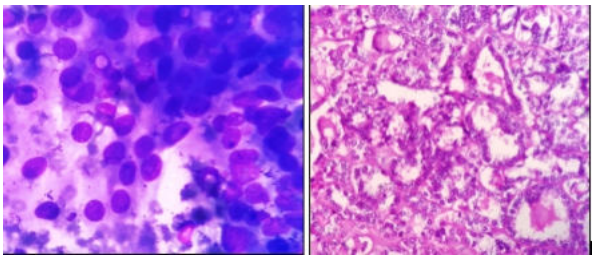


Figure 5a Calcification in the solid component of the nodule Figure5b Elastography showing redness in the stiff area indicated for FNA sampling Figure5c Geimsa stain showing intranuclear inclusion of papillary carcinoma thyroid Figure 5d Microscopic examination on H&E shows papillary pattern with nuclear clearing

2) Echogenicity

- Hypoechoic solid nodule
- most papillary thyroid carcinomas
- nearly all medullary thyroid carcinomas
- benign nodules can be hypoechoic
- if no other malignant features (e.g. calcifications) then hypoechoic nodules are typically biopsied after reaching size criteria
- isoechoic solid nodule: 25% (follicular and medullary)
- hyperechoic solid nodule: 5% chance of being malignant
- large cystic component favours a benign entity although a significant proportion of papillary carcinomas will have a cystic component
- while a halo around a well-marginated hypoechoic or isoechoic nodule is typical of a follicular adenoma

Lymph nodes

- enlarged regional lymph nodes are suspicious for thyroid malignancy, esp. papillary thyroid carcinoma
- microcalcifications in regional lymph nodes are highly suspicious
- lymph nodes with cystic change are highly suspicious
- loss of normal fatty hilum, irregular node appearance
- increased colour Doppler flow is suspicious
- no threshold criteria for lymph node biopsy
- biopsy if suspicious features
- consider biopsy if >8 mm

Sonographic features favouring a malignant nodule (Figure 6a,b)

- hypoechoic solid
- presence of microcalcifications: almost always warrants a FNA
- local invasion of surrounding structures
- taller than it is wide
- large size: the cut off is often taken as 10 mm to warrant a FNA
- suspicious neck lymph nodes suggesting metastatic disease
- intranodular blood flow

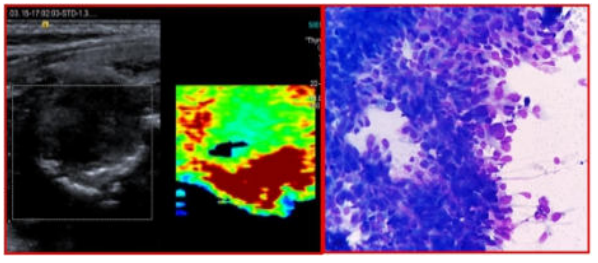


Figure 6a Strian elastography shows red area which represents malignant with green benign areas. Figure6b Giemsa stain showing marked anisonucleosis with hyperchromasia and coarse chromatin anaplastic carcinoma thyroid

Elastography

Ultrasound elastography is a dynamic technique that estimates stiffness of tissues by measuring the degree of distortion under external pressure. Thyroid gland elastography is used to study hardness/elasticity of the thyroid nodule to differentiate malignant from benign lesions. A benign nodule is softer and deforms more easily, whereas the malignant nodule is harder and deforms less when compressed by ultrasound probe. The pressure is performed either by the hand held US transducer or by physiological movements (e.g., carotid pulsation). This results in the elastographic image, also known as elastogram, which is represented as a color coded image superimposed on the B-mode image and displayed next to it on the screen. Strain elastograms of nodules are qualitatively evaluated with a stepwise scoring system, according to the prevalent color in the nodule. The two principal scoring systems are those classified by Asteria et al.[10] and Rago et al.[11]The first one, based on the breast strain USE scale of Itoh et al.[12,] includes four different patterns . The thyroid nodules with scores 1 and 2 are considered benign and those with scores 3 and 4 are classified as suspicious for malignancy. However, some authors have found that assigning benignity to score 3 further increases the specificity of the method for cancer detection [13].The limitations of elastography are a result of technical issues associated with the application and physics of the technique as well as the histological features of the nodules, leading to misinterpretations and pitfalls.

Conclusion

The radiologists play a critical role in the management of thyroid disease and to decide whether to biopsy a nodule on the basis of USG criteria, or to use proper FNAB technique for thyroid biopsy. Elastography may be used to guide the followup of lesions negative for malignancy at FNA. Given the high prevalence of thyroid nodules and the substantial costs related to their workup and management, the use of elastography could be a valuable tool for a better selection of nodules that need FNAB. The radiologist should be aware of these lesions and be familiar with specimen processing, and recognize the cytologic appearances of thyroid lesions, all of which will facilitate in understanding of the management of thyroid nodules.

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