Original article

Sonographic assessment of thyroid diseases with histopathological correlation

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ABSTRACT

Introduction : Diffuse enlargement of thyroid gland is a common clinical problem routinely encountered in the outpatient department. The purpose of the study is to assess the various thyroid diseases using ultrasonography and to correlate these findings with histopathological examination.

Materials and methods: This cross sectional study includes50 patients who were referred to Radiology department, SVMCH with complaints of thyroid swelling from June 2015 to February 2016. Patients having a past history of thyroid disease were excluded. Patients were examined using Siemens Accuson X300 ultrasound with high frequency linear probe (5-10Hz). Following parameters like size, site, margins, appearance, echotexture, the vascularity were noted. The diagnosis was confirmed by histopathology correlation.

Results : Majority(80%) of the patients are between 20 to 50 years of age with female predominance (84%).Imaging findings were categorized as multinodular goiter (19 cases), solitary thyroid nodule (12 cases) and diffuse goiter (19 cases). Following histopathological correlation, 100% sensitivity and 94% specificity for multinodular goiter, 100% sensitivity and 92.6% specificity for solitary thyroid nodule and 100% sensitivity and 96.8% specificity for diffuse goiter were detected. Kappa value showed excellent agreement for all these lesions.

Conclusion: The thyroid gland is well suited to ultrasound study because of its superficial location, vascularity, size and echogenicity. Ultrasonography is useful in characterizing thyroid nodules and diffuse thyroid diseases. It provides a good pre-operative diagnosis for the management planning to a surgeon.

Keywords – Thyroid nodules, diffuse thyroid disease, ultrasonography, histopathological examination.

Introduction

Thyroid swelling is a common clinical problem routinely encountered in the outpatient department. Most of the so called thyroid masses are due to diffuse enlargement of thyroid gland (diffuse colloid goiter). Thyroid neoplasms presents in the form of enlarged thyroid mass or thyroid nodule.

Various immunological diseases of thyroid including hypothyroid and hyperthyroid states may present as thyroid enlargement. Clinical evaluation of the thyroid is not always conclusive. In these situations clinicians depends on other diagnostic modalities such as ultrasonography, fine needle aspiration cytology and HPE, to achieve a definite diagnosis. The improvement in technical developments in high resolution B mode ultrasound has improved the ability of ultrasound in the evaluation of superficial region. A 5-8 MHz sector probe is useful in evaluating deep structures. A higher frequency (7–12 MHz) linear probe is useful in visualizing the

superficial structures. Color Doppler ultrasound allows assessment of vascularity within the lesion and helpful in the assessment of vascular lesions and enlarged lymph nodes.

Thyroid glands have rich vascular supply. A pair of superior and inferior thyroid arteries supplies the thyroid parenchyma. Color Doppler ultrasonography (CDUS) is used for the diagnosis of diffuse and nodular thyroid diseases. It allows noninvasive assessment of blood flow, being a sign of intraparenchymal vascularity as well as the evaluation of morphology in thyroid imaging. Thyroid ultrasound is used to guide fine-needle aspiration cytology for nodules with suspicion of being malignant. For initial evaluation of goiter different imaging modalities are available, but for final diagnosis HPE and FNAC were considered as mandatory. Like other techniques FNAC has got its own limitations related to specimen adequacy, sampling techniques etc. Hence histopathological examination of the excised tissue is considered the final diagnostic test.

Clinical evaluation of the thyroid is not always conclusive. In these situations clinicians depends on other diagnostic modalities such as ultrasonography, fine needle aspiration cytology and HPE, to achieve a definite diagnosis.

Advantages of ultrasonography over clinical examination

- Ultrasonography provides a better anatomical representation of the thyroid gland with remarkable clarity based on the account of the superficial location of the gland.
- Ultrasound can clearly reveals the nature of the mass (cystic vs solid).
- To detect the number of nodules i.e. whether the lesion is a solitary nodule or a part of multinodular goiter.
- It is helpful in detecting calcification and the pattern of calcification.
- It also aids in assessing the vascularity of the lesion.
- Invasion of the adjacent structures by the thyroid mass can be elicited by ultrasonography.
- Lymph node status is better evaluated with ultrasound.

Normal sonographic of thyroid gland

The imaging appearance of thyroid varies depending on the imaging modality used. Normal thyroid on ultrasound appears homogeneously echogenic with a uniform echotexture[1]. The thyroid lobes are normally 4–6 cm in craniocaudal length and 1.3–1.8 cm in their horizontal and transverse dimensions; the isthmus normally has an anteroposterior thickness of up to 3 mm[2]. High resolution ultrasound is useful for examination of the normal thyroid gland and associated abnormalities. Ultrasound has no adverse effects like radiation and is non-invasive, feasible, low price. Applications like real time ultrasound are useful to guide interventional procedures. Color and spectral Doppler can be used to assess the vascularity of the thyroid gland and to measure the vessel parameters. Thyroid gland has rich arterial blood supply which is supplied by superior and inferior thyroid arteries respectively. The vessels in thyroid gland show low resistance flow and high peak systolic velocity (PSV). The normal PSV in intra thyroid arteries ranges from 15-30 cm/second, but in Graves, it is more than 100cm/sec[3].

Aims and objectives

1. To assess the sonographic features of various thyroid diseases using duplex sonography.

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2. To correlate the ultrasound findings with histopathological examination.

Materials and methods

This cross sectional study includes 50 patients who referred to Radiology department, Sri Venkateshwaraa Medical College with complaints of thyroid swelling. Approval from ethical and scientific committee was obtained. The study protocol was explained to the patient. After taking informed consent, the subjects were examined using Siemens Accuson X300 ultrasound with high frequency linear probe and in cases where lesion is of greater size or for better delineation of adjacent structures curvilinear probe is used. The patient was asked to lie down in supine position with hyperextended neck with the help of pillow.

There was no sex discrimination for selection of the cases and patients with a known malignancy or lesions adjacent to the thyroid are excluded from the study. Both grayscale imaging and color patterns were documented. After the excision of the nodule/gland, it was correlated with histopathological examination. Statistical analysis is done using SPSS 22, sensitivity and specificity, kappa analysis.

Following ultrasound parameters were evaluated [4]

1. Echo texture
   Homogeneous / Heterogeneous
2. Diffuse or Focal involvement of the gland
3. Lesion
   Present/Absent
4. Shape
   Wider than tall / Taller than wide /Irregular
5. Margin
   Well-defined smooth / Well-defined spiculated / Ill-defined
6. Echogenicity
   Marked hypoechogenicity /Hypoechogenicity /Isoechogenicity/Hyperechogenicity
7. Halo
   Thin/ thick/ absent
8. Degenerative changes
   Colloid/Cystic
9. Calcification
   Micro calcification /Macro calcification /Rim calcifications.
10. Vascularity
    Present / Absent

Depending upon B mode and color Doppler ultrasonographic findings, provisional diagnosis was made on clinical history and physical examination and these were compared with Histopathologic findings.

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Observations

The present study includes 50 patients referred to the department of Radiology, for sonographic evaluation of thyroid swellings.

Table 1- Age wise distribution

Age in years	Frequency (%)
20-29	12 (24%)
30-39	15 (30%)
40-49	14 (28%)
50-59	7 (14%)
<60	2 (4%)

Total-50 (100%)

This table shows the distribution of patients among various age groups.

Table 2- Gender wise distribution

Gender	Frequency (%)
Males	08 (16%)
Females	42 (84%)

Total-50 (100%)

This table shows the number of male and female patients referred for sonographic examination of thyroid lesions.

TABLE 3- Distribution of thyroid lesions based on ultrasonography findings

S. No	Ultrasonography findings	Frequency (%)
1	Diffuse goiter	19 (38%)
2	Solitary thyroid nodule	12 (24%)
3	Multinodular goiter	19 (38%)

This table shows the distribution of thyroid lesions according to the appearance of the thyroid lesions detected on sonographic examination.

TABLE 4- Distribution of thyroid lesions based on HPE findings

S. No	HPE	Frequency (%)
1	Multinodular nodular goiter	18 (36%)
2	Benign follicular adenoma	9 (18%)
3	Thyroiditis	19 (38%)
4	Others *	4 (8%)

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This table shows the distribution of thyroid lesions based on HPE findings.

TABLE 5- Comparison of USG findings with HPE based of diagnostic validity of the test

Multinodular goiter	Ultrasound	HPE
Sensitivity	100%	100%
Specificity	94%	100%
Positive predictive value	89.4%	100%
Negative predictive value	100%	100%
Solitary thyroid nodule		
Sensitivity	100%	100%
Specificity	92.6%	100%
Positive predictive value	75%	100%
Negative predictive value	100%	100%
Diffuse goiter		
Sensitivity	100%	100%
Specificity	96.8%	100%
Positive predictive value	94.7%	100%
Negative predictive value	100%	100%

This table shows the correlation between USG and HPE for detecting thyroid diseases.

TABLE 8- Kappa analysis correlation for ultrasonography and HPE findings for thyroid lesions

S.no		Percentage agreement	Kappa value
1	Multinodular goiter	96%	0.8
2	Solitary thyroid nodule	94%	0.8
3	Diffuse goiter	98%	0.9

This table shows kappa value and percentage agreement for USG and HPE for diagnosing thyroid lesions.

Results

In our study, out of 50 patients, majority of the affected population (82%) age group is between 20 to 49 years (**Table 1**). 42 patients (84%)were females (**Table 2**). Different lesions based on the ultrasonographic appearance were categorised as diffuse goiter 19 (38%) cases, solitary thyroid nodule 12 (24%) cases and multinodular goiter 19 (38%) cases accordingly (**Table 3**). In our study there is an equal proportion of diffuse goiter (38%) and multinodular goiter (38%). Lesions based on HPE are multinodular goiter 18 (36%) cases, benign follicular

adenoma 9 (18%) cases, thyroiditis 19 (38%) cases and remaining *4 (8%) cases, majority were follicular carcinoma (**Table 4**). Correlation between USG and HPE based of diagnostic validity of the test for thyroid lesions (**Table 5**) showed good sensitivity and positive predictive value of ultrasound for diagnosing thyroid lesions when compared with HPE (highly specific test).Multinodular goiter had a sensitivity of 100% with positive predictive value of 89.4%, solitary thyroid nodule of sensitivity 100% with positive predictive value of 75%, diffuse goiter of sensitivity 100% with positive predictive value of 94.7%respectively.Kappa value and percentage agreement of ultrasound when compared with HPE in diagnosing thyroid lesions, there was an excellent agreement beyond chance (**Table 6**). For multinodular goiter showed a percentage agreement of 96% with Kappa value of 0.8, solitary thyroid nodule 94% and 0.8 and diffuse goiter 98% and 0.9 respectively.

Discussion

Thyroid disorders presenting as swellings constitute a significant number of cases encountered among the patients in our country and attending various OPD's in our hospital. Although thyroid is a superficial gland easily accessible to physical examination, it needs various biochemical and radiological investigations to confirm the diagnosis. The present study has been done in the Department of Radiodiagnosis, Sri Venkateshwaraa Medical College and Research center, Ariyur, Pondicherry. The study included a total of 50 patients presenting with thyroid swelling, referred to department of Radiodiagnosis from the departments of Surgery, Medicine and ENT. Thyroid function test analysis was done and was compared with the Doppler parameters. Histopathological correlation has been obtained for each case. On account of the superficial location of the thyroid gland, high resolution real time grey scale and color Doppler sonography can demonstrate normal gland anatomy and pathological conditions with remarkable clarity. This technique being non-invasive, economical and without radiation hazards, has come to the fore as an appropriate study in the diagnostic evaluation of thyroid diseases.

Ultrasound was performed with a SIEMENS ACCUSON X 300 machine using a multi frequency transducer (5 and 10MHz) which provides images details of thyroid anatomy and various pathological conditions of thyroid gland.

Diffuse enlargement of thyroid gland can occur during puberty, lactation etc. Other pathological lesions such as thyroid neoplasm also present in the form of thyroid mass or thyroid nodules. Various immunological diseases of the thyroid including hypothyroid and hyperthyroid states may present as thyroid enlargement.

In the case of thyroid, ultrasound offers an extension to the physical examination for the confirmation of the mass lesion, characterization of the gland and response to therapy.

This is a cross sectional study of a group of fifty patients, referred to us with brief clinical history, physical examination and provisional clinical diagnosis. All the patients were examined sonographically and the results were analyzed using various sonographic parameters and the thyroid function test analysis were correlated with that of Doppler parameters findings and subsequently correlated with HPE.

The study comprised 50 patients between age group from 20 to 80 years. The youngest patient in our study was 20 year old female and the eldest was 69

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year old female. Majority of cases 82% affected were in the age group of 20 to 49 years.

Waters DA et al[5] reported their experience with 120 patients whose age group was between 13 to 84 years. Yokozawa T et al[6] reported their experience with 678 patients in which case the mean age was 52.2±11.9 years. Kim EK et al[7] reported their study including 132 patients with age group of 20 to 77 years. Wunderbaldinger P et al[8] conducted a study which included 74 years with age group of 23 to 84 years. Screaton NJ et al[9] reported their study comprising 198 patients whose age group range was 14 to 80 years. Rosario PWS et al[10] reported their experience with 84 patients of whose age group range was 19 to 65 years.

Of the 50 patients in our study group, females constituted 84% and males 16%.

Won- Jin Moon et al[11] studied 831 patients (731 women, 115 men; mean age, 49.5 years ± 13.8). Kim EK et al[7] reported their experience with 132 patients in which 91% were females and 10% were males.

Wunderbaldinger P et al[8] conducted a study among 74 patients of which 63.5% were females 36.5% were males. Wienke JR et al[12] reported their experience with 70 patients in which 90% were females and 10% were males. Su DH et al[13] conducted a study of 24 patients which consisted of 96% females and 4% males. Rosario PWS et al[10] reported their study including 84 patients among which 71.4% were females 28.6% males.

All the above studies indicate that females are much more commonly affected than males and our study is in agreement with this finding.

Differentiation of a mass lesion into multinodular, solitary thyroid nodule and diffuse goiter is probably one of the most important application of ultrasound in evaluation of thyroid lesions. Out of 50 patients, we categorized 19 cases multinodular, 12 cases solitary thyroid nodule and 19 diffuse goiter which were later correlated by HPE.

Out of 19 cases of Multinodular goiter on sonography, 17 (89.4%) cases were proved to multinodular goiter on HPE, with an exception of 2 (10.6%) cases, which were proved to be Hashimoto's thyroiditis and Follicular carcinoma respectively.

Out of 12 cases of Solitary thyroid nodule on sonography, 9 (75%) cases were proved to solitary thyroid nodule (benign follicular adenoma) on HPE, with an exception of 3 (25%) cases, which were proved to be Parathyroid adenoma, foci of Follicular variant of papillary carcinoma and follicular carcinoma.

Out of 19 cases of diffuse goiter on sonography, 18 (94.7%) cases were proved to be diffuse goiter on HPE, with an exception of 1 (5.3%) case which was proved to be multinodular goiter.

In 2009, Rehman AU et al conducted a study on 310 cases of MNG, 12 (3.87%) were malignant and M:F ratio was 2.53:1 and 122 cases of Solitary thyroid nodule, 14 (11.47%) cases were found malignant with M:F ratio of 1:1.76[14].

Heydar Ali Esmaili et al studied 1639 patients from October 2007 to September 2011 with solitary or multiple nodules and FNAC was done. Results were classified as Benign [1054-64.3%], Malignant [128-7.8%] Suspicious [306-18.66%], and inadequate for diagnosis [151-9.2%]. 192 patients underwent surgery and HPE was done. As compared with FNAC results sensitivity of 91.6 %, specificity of 100%, and accuracy of 97%was found and strongly supported the fact that FNAC has high diagnostic accuracy in evaluation of thyroid disorders[15].

In 2012, Sreeramulu PN et al conducted a prospective study of clinical, sonological, and pathological

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evaluation of thyroid nodule. Based on their results the sensitivity of and specificity of FNAC was 74% and 100% respectively. All lesions suspicious on FNAC proved malignant on HPE[16].

Hence, results of our sonographic evaluation of thyroid lesions were encouraging, giving 100% sensitivity and 94% specificity for multinodular goiter, 100% sensitivity and 92.6% specificity for solitary thyroid nodule and 100% sensitivity and 96.8% specificity for diffuse goiter after HPE correlation.

DIAGNOSTIC PITFALLS

Major diagnostic pitfalls of thyroid ultrasound include

1. In thyroid malignancies, cystic components can be mistaken for benign cyst or cystic degeneration in a benign nodule. Solid component with vascularity or any solid outgrowth with microcalcifications can be useful in differentiating these lesions.
2. Sometimes, cystic or calcified lymph node metastasis adjacent to the thyroid gland can be mistaken for benign nodule in multinodular thyroid disease. Differentiating features like incomplete rim of thyroid parenchyma around the mass and no movement of the mass with the thyroid gland during swallowing favors extrathyroid lymph nodal metastasis. Cystic metastases are more common in papillary carcinoma thyroid and calcified metastases can be seen in both papillary and medullary carcinoma thyroid.
3. Papillary and follicular carcinoma of diffuse infiltrative, hypervascular nature can be mistaken for other types of thyroiditis (such as Graves' disease or Hashimoto's thyroiditis); likewise multifocal carcinoma may be mistaken for benign multinodular goiter. Features suggestive of benignity are diffuse thyroid enlargement with multiple nodules of similar ultrasound appearance and with no normal intervening parenchyma. Features that suggest malignancy include irregular or nodular enlargement of thyroid gland, local invasion and nodal metastases.

Conclusion

The thyroid is well suited for ultrasound study because of its superficial location, vascularity, size and echogenicity. Utility of thyroid ultrasound has gone far beyond just the initial diagnostic approach. Highly sensitive probes allow accurate characterization of the nature of the thyroid nodules and lymph nodes. The greater sensitivity of ultrasonography technique helps in facilitating the detection of small occult nodules, which can be missed on clinical examination. It also aids in postoperative follow up.

Ultrasonography is also useful in characterization of thyroid nodules/diffuse thyroid diseases. The characteristics of nodules on ultrasound like hypoechogenicity, microcalcification, hypoechoic halo and irregular margins helps in differentiating benign and malignant lesions.

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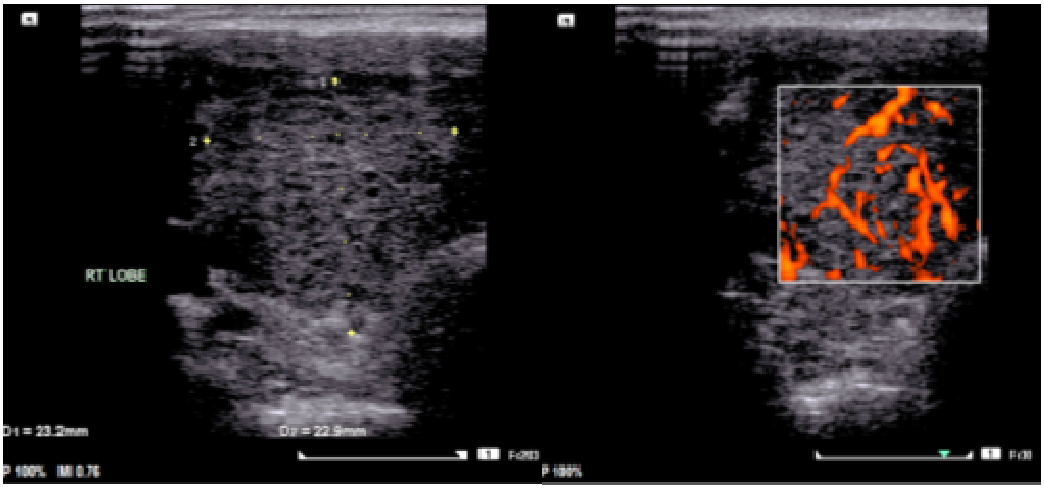
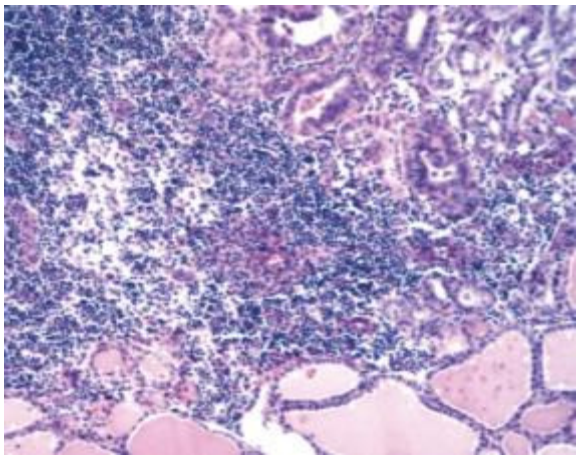
Case 1



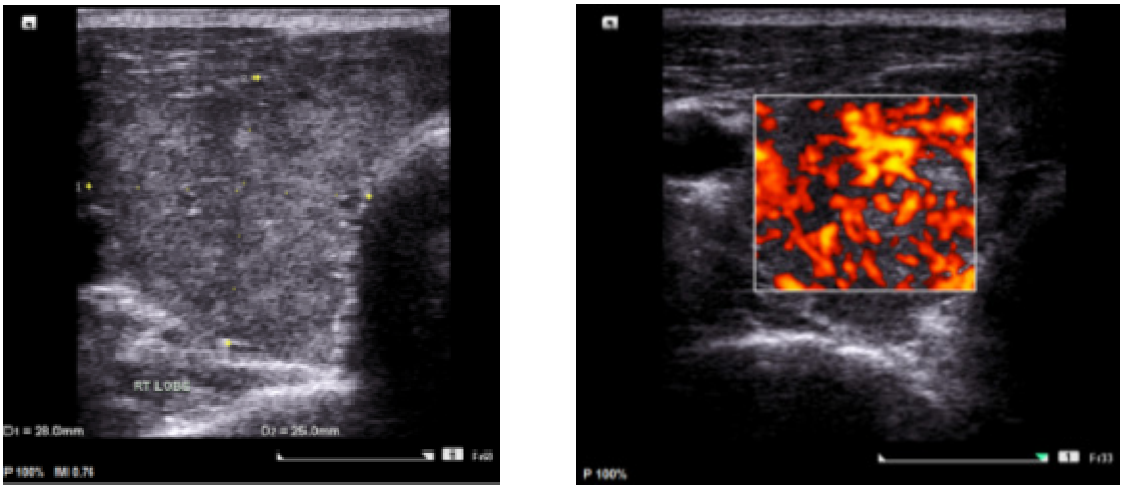
Hashimoto's thyroiditis. Transverse ultrasound showing A- enlarged gland with diffuse and heterogenous parenchyma with multiple hypoechoic nodules and linear striations. B- Power Doppler showing increased vascularity (thyroid inferno).



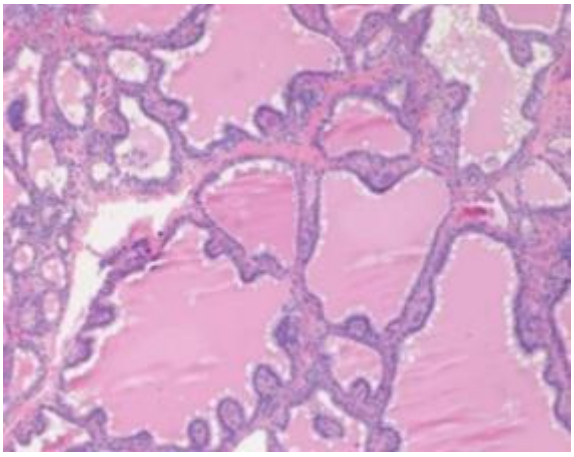
C

C- H&E stain shows lymphoid follicle formation with areas of follicular destruction, features of Hashimoto's thyroiditis.

Case 2



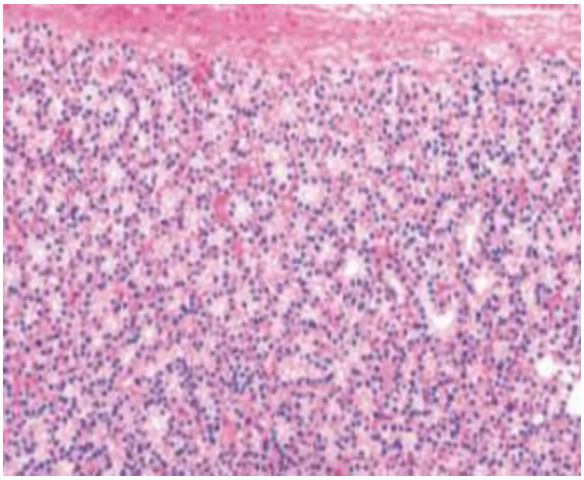
Graves' thyroiditis. Transverse ultrasound of right lobe showing a- enlarged gland with diffuse and heterogenous parenchyma with multiple ill-defined nodules. B- Power Doppler showing increased vascularity (thyroid inferno).



C

C- H&E stain shows back to back arrangement of the glands with epithelial hyperplasia, features consistent with thyroid gland hyperplasia.

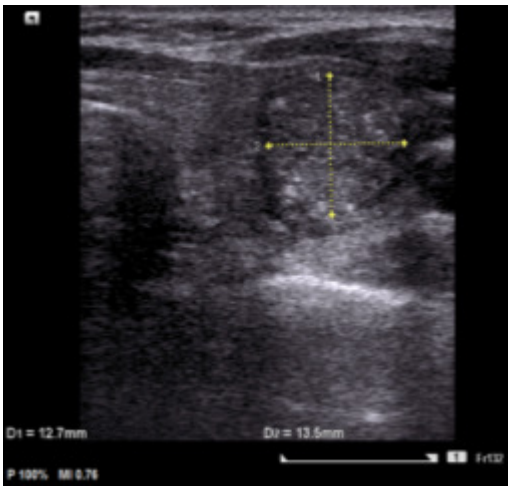
Case 3

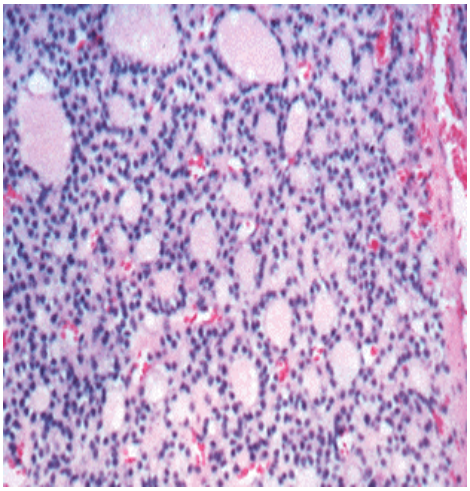


A B

Adenomatous nodule. Transverse ultrasound showing A- homogenous nodule with peripheral thin hypoechoic halo. B- H&E stain shows close arrangement of uniform sized follicles features suggestive of adenomatous nodule.

Case 4





B

Follicular adenoma. Transverse ultrasound showing A- heterogenous nodule with peripheral thin hypoechoic halo. B- H&E stain showing follicular adenoma.

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