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Original Research Article

Sonographic evaluation of solitary thyroid nodule with cytopathological correlation

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Abstract

Background: Nodular thyroid disease is a common health problem affecting women affected more frequently than men. Benign conditions like simple thyroid cyst, iodine deficiency disorder, chronic inflammatory disease of thyroid (like Hashimoto‟s thyroiditis) as well as malignancy of different grades (ranging from well differentiated papillary carcinoma to high grade follicular neoplasm) can present with thyroid nodules. Differentiation between two entities based on clinical and biochemical ground alone is hardly possible and here comes the role of high resolution ultrasonography. Because of superficial location USG can identify normal thyroid anatomy and pathologic conditions with remarkable clarity. Based on sonologic features it is possible to predict whether a nodule is malignant or not and hence whether follow-up is sufficient or more invasive procedure is imperative.

Materials & Methods: Fifty sequential adult patients of 15-60years of age presenting with nodular thyroid disease were studied over the period of one and half years (January 2016 to June 2017). Specific USG criteria were used to characterize the nodules so that a probable diagnosis could be made. Sonological diagnoses then compared with cytological results to conclude role of USG to analyse nodular thyroid disease.

Result & Analysis: 50 patients were studied with a mean age of 37.4 years. Benign lesions constitute the majority (total 43 cases) four patients were diagnosed as having papillary carcinoma & three as case of follicular neoplasm. Most of the patients presented with long standing painless palpable thyroid swelling. Majority of malignant thyroid nodules presented as solitary hypoechoic solid nodules with intranodular vascularity. On contrary benign lesions were mainly iso or hyper echoic, multiple or solitary, well margined nodules with perinodular vascularity. Cervical lymphadenopathy & micro calcification were found almost exclusively in papillary carcinoma, whereas peripheral egg shell calcification &comet tail artifacts were seen only in hyperplastic nodules.

Conclusion: Nodular thyroid disease was found to be of female predominance with benign cause's outnumbered malignancy. USG assessment helped assess characteristics of thyroid nodules to reach a provisional diagnosis. We had taken into account parameters and among them taller than wide shape, intranodular vascularity with or with-out perinodular component and marked hypoechogenicity emerged as most useful.

Keywords: Thyroid, Malignancy, USG, FNAC.

1. Introduction

The thyroid gland is unique among endocrine glands, in that it is the first endocrine gland to appear in the foetus. It is the largest of all endocrine glands (weighing about 25 g) and is the only one which is amenable to direct physical examination because of its superficial location. Thyroid nodules are a very common clinical finding, with an estimated prevalence on the basis of palpation that ranges from 3% to 7%.[1]

In a large population study (in Framingham, Massachusetts), clinically apparent thyroid nodules were present in 6.4% of women and 1.5% of men.[2]

During the past 2 decades, the widespread use of ultrasonography (US) for evaluation of thyroid and neck disease has resulted in a dramatic increase in the prevalence of clinically unapparent thyroid nodules, estimated at 20% to 76% in the general population. Moreover, 20% to 48% of patients with a single palpable thyroid nodule are found to have additional nodules when investigated by US.[3,4] Thyroid nodules are more common in elderly person, in women, in those with iodine deficiency, and in those with a history of radiation exposure.

Because of the high prevalence of nodular thyroid disease, it is neither economically feasible nor necessary to submit all or even most thyroid nodules for a complete work-up for the assessment of their structure and function. Therefore, it is essential to develop and follow a reliable, cost-effective strategy for diagnosis and treatment of thyroid nodules. Most patients with thyroid nodules have few or no symptoms, and usually no clear relationship exists between nodule histologic features or size and the reported symptoms.

Fine needle aspiration cytology (FNAC) is now a well-established, first line, simple and quick screening test as well as the diagnostic tool for surgical and non-surgical goitres. Limitation of FNAC is mainly because of inadequate sampling, in experience of the pathologist and over lapping cytological features. Ultrasonography is an easily accessible, non-invasive way to image thethyroid gland and its pathology. It helps to pin point a possible thyroid abnormality at an early stage and includes the elements of differential diagnosis that result in subsequent thorough examination and timely treatment in appropriate cases. The present study was aimed to determine the role of high resolution ultrasonography in the evaluation of lesions of the thyroid with FNAC correlation.

1.1. Objective
- To evaluate the Grey Scale features including doppler flow pattern of thyroid nodules on Ultrasonography.
- To correlate sono-logical features with the cytological findings after Ultrasound- guided Fine Needle Aspiration Cytology (FNAC)

2.Materials and methodology
Based on the inclusion and exclusion criteria, 50 cases of thyroid nodules, confirmed on ultrasound, were studied over a year in the Department of Radiology, Burdwan medical college and hospital. Each patient was subjected to thorough clinical examination and sonological evaluation by (7-12 MHz) linear array ultrasound transducer to reach a probable diagnosis.

These cases were then subjected to FNA followed by Cytopathological assessment to substantiate ultrasound findings and establish final diagnosis.

2.1. Inclusion Criteria
- Consecutive 100 patients between 15-60 years age presented with palpable thyroid nodule & confirmed on ultrasound were included in the study.
- Both sexes

2.2. Exclusion Criteria
- All patients with diffuse thyroid enlargement.
- Documented or known thyroid malignancy, Congenital thyroid disorders
- Pregnancy

2.3. Methodology
Patients were in supine position with neck extended while conducting USG. After application of water-based acoustic gel in front of thyroid cartilage, transducer was placed over the neck & moved back and forth until the desired images are captured. FNA was performed afterwards. After adequate sample was obtained, the specimen was mounted immediately onto glass slides. Specific USG criteria were used to characterise the nodules so that a probable diagnosis could be made. Cytological analysis from USG guided FNAC was carried away in dept. of pathology. Sonological diagnoses then compared with cytological results to conclude efficiency of thyroid USG to analyse nodular thyroid disease

3. Results
Age distribution of the study population (n=50) Age range of patients in this study was from 15 to 60 years. Mean age was found 37.4 years.

Sex distribution of the study population (n=50) Out of 50 patients studied here majority (40) were female. Only 10 patients were male. Among study population 35 were Muslim and 15 were Hindu. Benign pathologies like hyperplastic goitre and thyroiditis associated thyroid nodules grossly outnumbers malignancy like papillary carcinoma and follicular neoplasm. (Table 1)

Table 1: Occurrence of major pathology

	Papillary thyroid carcinoma	Follicular thyroid neoplasm	Colloid / hyperplastic Nodule	Thyroiditis
Total no of cases	4	3	27	16

Majority of patients under study presented with long standing painless neck swelling, mostly of 1 year to 5 years of duration. (Table: 2)

Table 2: Duration of disease

Duration	Number of cases
< 6 months	7
6 months – 1 year	6
1 year- 5 year	32
>5 year	5

Individual nodules among study population were of various sizes ranging from very small to large enough to occupy a lobe of thyroid as tubulised later (Table: 3)

Table 3: size of nodules

Size	Malignancy	Benignity
< 2 cm	--	10
2 cm – 4 cm	4	27
> 4 cm	3	6

For our study we had taken into account parameters like shape, internal consistency, echogenicity, presence of halo, margin characteristics, vascularity, presence & pattern of calcification, number and presence of cervical lymphadenopathy to characterize thyroid nodules. Sensitivity, specificity, positive & negative predictive value and accuracy were taken into account; among them taller than wide shape, intranodular vascularity with or without per nodular component and marked hypoechogenicity emerged as most useful. Criteria like *irregular margin, micro calcification, and presence of cervical LNs* were highly specific but lack high sensitivity. Absent halo was sensitive enough but lacks specificity. Sensitivity and specificity of various USG criteria in this study are mentioned in table 4.

Table 4: Size of nodules

USG features	% in benign lesions	% in malignant lesions	sensitivity	specificity	Positive predictive value	Negative predictive value
Taller than wide shape	--	86	86	100	100%	98%
Solid in nature	74	57	57	25	11%	79%
Hypoechoic	28	85	86	86	33%	97%
Absent halo	67	85	86	33	6%	82%
Irregular margin	12	57	57	89	44%	93%
Microcalcification	7	43	43	93	50%	91%
Intranodular vascularity	16	100	100	84	50%	100%
Solitary nodule	44	71	71	56	21%	92%
Presence of cervical LNs	19	29	29	81	20%	88%

4. Discussion

In the present study, maximum numbers of cases of thyroid nodules were seen in 25-35 years age group with female predominance. The percentage of benign thyroid nodules (91.43%) was higher than the malignant (8.57%) thyroid nodules. Prevalence pattern and occurrence of major pathologies have correlated with the previous similar studies.

4.1. Shape

Multiple studies have shown that a taller-than-wide shape is specific for malignant nodules (likely because malignant neoplasms grow across normal tissue planes, whereas benign nodules grow parallel to normal tissue planes).[5,6] All but one cases diagnosed as malignant had anteroposterior diameter greater than transverse diameter in our study. On the other hand all cases diagnosed later as benign appeared wider than tall in appearance.

4.2. Internal contents

Thyroid nodules can be completely solid or solid with cystic component. True cysts over 1.5–2 cm are very rare but if present, these are reported to always be benign. A nodule that has a significant cystic component is usually considered as a benign adenomatous (colloid) nodule with degeneration. Comet-tail artifacts are frequently encountered in cystic thyroid nodules and are likely related

to the presence of colloid microcrystals. Chong *et al* [5] described comet-tail patterns as highly sensitive and specific for benignity. When a more densely echogenic fluid is seen layered in dependent portion of a cystic lesion, likelihood of hemorrhagic debris is very high (particularly if associated with sudden pain). Spongiform appearance of thyroid nodules, related to the presence of tiny colloid changes, is usually suggestive of benignity. Papillary carcinomas may rarely exhibit varying amounts of cystic change simulating cystic nodules.[8-10] However, a solid element with vascularity is usually seen too.

74% of malignancy and 57% of benign pathology were found to be solid in our study. Multiple scholar articles including by Solbiati *et al* [10] and Brkljacic *et al* have shown similar pattern of findings. [11] Chong *et al* [5] described comet-tail patterns as highly sensitive and specific for benignity. All cases associated with come-tail artifacts in our study were too found to be hyperplastic nodule.

4.3. Echogenicity

A nodule is generally classified as hypo-, iso-, or hyperechoic in comparison to normal homogeneously hyperechoic thyroid parenchyma. Hypoechogenicity may be associated with thyroid malignancy and is thought to represent densely packed malignant cells with little or no

colloid substance. However, most hypoechoic nodules are benign because of much their higher prevalence. A predominantly hyperechoic nodule, which is uncommon, is more likely to be benign. [12]

Among study population, 18 had one or more hypoechoic nodules and 32 had not. In nodules with cystic changes echogenicity of solid component was considered. All cases of papillary carcinoma, 66% of follicular thyroid neoplasm and 75% of thyroiditis had one or more hypoechoic nodule. None of Colloid nodules were hypoechoic.

4.4. Margin

A thyroid nodule is considered to have poor margin when more than 50% of margin is not clearly defined. Like other parts of body malignant lesions tend to have poorly defined. Ill-defined margin however is not accepted well in many previous studies. Wienke *et al* [5] found this feature as the poorest among all other criteria.

In our study, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of poorly defined margins for diagnosing malignant nodules was found to be 57%, 89%, 44% and 93% respectively.

4.5. Halo

Classically described thin peripheral hypoechoic halo completely or incompletely encircling a thyroid nodule associates with benign nodules. It is considered as compressed normal thyroid parenchyma around a slow growing colloid nodule. Apart from this classical pattern, with today's high-resolution ultrasound, a second type of halo has been described. Cerbone *et al* [13] found a thick irregular a vascular (with occasional interruption) halo in the setting of malignancy that may signify the fibrous capsule surrounding a neoplastic growth, mostly follicular or Hürthle cell type, and is therefore, more concerning.

In our study perinodular halo was present in 33% and 15% of benign and malignant nodules respectively.

4.6. Calcifications

Calcifications may be identified in up to one fourth of thyroid nodules and it is the types (rather than the mere presence per se) that help characterize the lesions 12. Micro calcifications appear as small (<1 mm) acrogenic foci without acoustic shadowing and are highly specific for thyroid cancer [14].

It is hypothesized that these micro calcifications are imaging counterpart of aggregates of psammoma bodies, the laminated spherical concretions characteristic of papillary cancers, (but occasionally found in benign nodules and Hashimoto's thyroiditis). Coarse or dense calcifications causing posterior acoustic shadowing represent dystrophic calcifications present in areas of fibrosis and signify benignity. However, coarse calcifications, either associated with microcalcifications or appearing in the center of a

hypoechoic nodule, may be ominous for malignancy [15,16]. Peripheral or "egg-shell" calcification, once thought to indicate a benign nodule can be found in malignant nodules also (rarely), particularly if there is interruption of this rim calcification, indicating probable invasion. Medullary thyroid carcinomas often exhibit bright echogenic foci either within the primary tumor or within metastatically involved cervical lymph nodes. Pathologically, these densities are caused by reactive fibrosis and calcification around amyloid deposits, characteristic of medullary carcinoma. In our study considering malignancy on basis of microcalcification had shown 43% and 93% of sensitivity and specificity respectively.

4.7. Vascularity

Using color flow Doppler (CFD) and power Doppler, nodule vascularity is traditionally categorized as absent, only perinodular and intranodular with or without perinodular type. Most hyperplastic nodules are hypovascular compared to normal thyroid parenchyma. By contrast most well differentiated thyroid carcinomas are generally hypervascular, with irregular tortuous chaotic vessels. Poorly differentiated and anaplastic carcinomas often appear hypovascular because of extensive necrosis associated with their rapid growth. Intranodular vascularity [16] with or without perinodular component is considered of malignancy specially if there is high blood flow with anarchical structure of concerning vessels.

With the advent of newer generation of highly sensitive Doppler instruments, overlapping of the two populations of nodules significantly has increased, reducing the diagnostic value of Doppler fndings. Our study also featured similar result.

4.8. Number of nodules

It is generally believed that malignancy is more common in a solitary nodule, and that multinodularity is usually associated with benign disease. However malignant & benign nodules often coexist.10-20% of papillary carcinomas may be multicentric. Lymphoma arising on the background of thyroiditis associated nodules is a well-known entity. Though rare, medullary thyroid carcinomas & metastases to thyroid can be multiple. Thus mere presence of multiple nodules with in thyroid does not indicate benignity. In our study solitary nodule was seen associated with 44% of benign and 71% of malignant nodules.

4.9. Cervical lymphadenopathy

About 15-30% of thyroid malignancy present with palpable cervical lymph nodes. Nodal metastases commonly occur in 1papillary carcinoma (30-40%) while Follicular carcinomas usually spread haematogeneously with cervical lymphadenopathy in 10-15% cases. First pre

&para-tracheal, then upper jugular lymph nodes are affected. Because of presence of thyroid gland itself, however, central neck or paratracheal lymph nodes are difficult to evaluate. Metastases from papillary carcinoma may show cystic necrosis as well as microcalcification similar to that seen in primaries. Larger the size of a lymph node more is the chance of being that malignant. Shape of the enlarged node is also crucial. When Short/Long axis ratio is seen to be 0.5 or more FNA of course should be done to rule out malignancy. Preservation of hilar echogenicity (postulated due to presence of lymphatic channels embedded in fatty tissue) is a feature of benignity. In malignancy this echogenicity is replaced by malignant cells. Evans *et al*, however, cited that malignancy can cause only mild disruption of central architecture (and hence can be unrecognised by USG), and complete loss of hilum is usually a late feature. Vassallo *et al* [17] also stressed that besides determining the presence and width of hilum, cortical thickening should also be taken into account.

Absent or narrowed hilum along with cortical thickening particularly if it is eccentric should be regarded as an sign of malignancy. Papillary carcinoma is often associated with cystic appearing metastatic LNs. Blurred or spiculated margin of a lymph node may signify extra-capsular spread. Doppler flow pattern should also be taken into account. As afferent major vessels enter into LNs through hilum central vascularity should always be present and flow must be much more compared to peripheral cortical flow.[18] Tschammler *et al* found displacement of vessels (curved course of vessels), focal absence of perfusion, presence of only peripheral vessels without central vascularity etc were useful criteria.

Undoubtedly it is the constellation of findings instead of a single criterion that helps to predict nature of thyroid nodule and that too in the pretext of appropriate clinical scenario.[5,6] Unfortunately in some cases even combination of features may not be able enough to judge a nodule whether benign or not and we have to rely on pathologic assessment.[6,7] Reverse is also true. Only pathological assessment may be inconclusive in many cases. Cases where pathological assessment fail to rule out malignancy (like in case of poor sampling) concurrent USG features may help decide whether repeat FNA or surgery is imperative or not, and if yes then what will be the extent of surgery. USG can also help stratify risk factors. For example if a nodule is borderline in size for FNA, it may be reasonable to conduct FNA if the nodule has a suspicious USG appearance, but to continue medical surveillance for benign looking ones. Ultrasound also can identify additional small non-palpable thyroid nodules. USG can determine of accuracy of FNA by palpation and can help to place needle efficiently where blindly needle application is

impossible or risky.[10] This is particularly true for complex nodules or deep seated ones reducing non-diagnostic cytology or sampling error. In the setting of multiple nodules USG helps identify the most significant nodule. In a nutshell, combinations of USG features are of value to predict whether a nodule is highly likely to be malignant or not and that ultrasound does not replace FNA cytology; rather, the two modalities are complementary two each other. Clinical evaluation including assessment of personal risk factors and ultrasound appearance combined with FNA cytology provide the most optimum way to characterise thyroid nodules.

We had tried to accomplish the study yet its outcome may differ from various standard studies in some aspects and it is needless to mention about various limitations encountered which in one or other way may adversely influence our study result.

These limitations are as follows:
1) Earlier vs. today machines may account for discrepancy of result from other study
2) Small study population may adversely affect
3) Correlation with cytopathology (instead of histopathology) which of course is inferior
4) Precise inclusion criteria cut off may differ from other study
5) We were able to presume about follicular neoplasia but not distinguish between follicular adenoma & carcinoma

5. Conclusion

A cross-sectional observational type of analytical study was carried out in Department of Radio-Diagnosis in Burdwan Medical College & Hospital from January 2016 to June 2017 over 50 cases, between 15-60 years age, referred with palpable thyroid swelling. All cases were clinically as well as sonographically studied to confirm the presence and conclude about nature of underlying thyroid nodule. Sonography also aided in accurate needle placement particularly in cases of nodule with large cystic component or those situated in posterior (deep) aspect of thyroid gland.

Majority of patients presented with long standing (mostly of 1 year to 5 years of duration) painless thyroid nodule of 2-4 cm in size without remarkable lymphadenopathy or systemic issues. Benign lesions (43) outnumbered malignant ones (7).

We had considered parameters like shape, internal consistency, and echogenicity, presence of halo, margin characteristics, vascularity, presence & pattern of calcification, number and presence of cervical lymphadenopathy to characterize thyroid nodules. Sensitivity, specificity, positive & negative predictive value and accuracy were taken into account. Among them taller

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