

ROLE OF CYTOLOGY, HISTOPATHOLOGY, HORMONAL ASSESSMENT AND IMAGING IN DIAGNOSING THYROID LESIONS-A PROSPECTIVE STUDY

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ABSTRACT

Introduction: Thyroid enlargement is a common problem in the coastal districts of Andhra Pradesh. For accurate diagnosis and early management of these lesions, combination of investigations are necessary. In our institute 20% of cases attending the surgical out patient department are with thyroid enlargement.

Objectives : 1. To evaluate the overall accuracy of FNAC and Imaging in diagnosing non-neoplastic and neoplastic lesions of thyroid taking histopathology as gold standard. 2. To evaluate the role of thyroid function tests (T3,T4 and TSH) in diagnosing various non-neoplastic and neoplastic lesions of thyroid.

Material and Methods : This is a prospective study for a period of 2 years from August 2008 to July 2010 at tertiary care hospital. In 215 patients the data was available for correlation between cytology, ultrasonography and histopathology. Hormonal status was available for analysis in 910 cases with thyroid lesions.

Results: The sensitivity, specificity and overall accuracy in diagnosing non-neoplastic and neoplastic lesions of thyroid on cytology in comparison with histopathology was 71.8%, 94.95% and 84.65% respectively. Overall accuracy in diagnosing non-neoplastic and neoplastic lesions of thyroid on ultrasonography in comparison with histopathology was 100%.

Conclusions: FNAC even though it is simple and cost effective procedure, it has limitations. Ultrasonography was superior to cytology in picking up malignancies associated with multinodular goiter and differentiating follicular adenoma from hyperplastic nodule in a goiter hence ultrasound guided FNAC is more useful. In elderly

females with chronic lymphocytic thyroiditis and high levels of TSH, ultrasonography and histopathological examination aids in ruling out lymphoma.

Key words : Thyroid lesions, Cytology, Hormonal levels, Ultrasonography

INTRODUCTION

Thyroid enlargement is a common problem in the coastal districts of Andhra Pradesh. Thyroid enlargement whether diffuse or in the form of a nodule, needs a battery of investigations, mainly to rule out the possibility of a neoplasm or thyroiditis. FNAC is usually the first line of investigation and other investigations like ultrasound (US) examination, thyroid function tests, thyroid scan, and antibody levels are done subsequently with an aim to select the patients who require surgery and those that can be managed conservatively.

METHODOLOGY

This is prospective study conducted in the department of pathology, at a tertiary care hospital from August 2008 to July 2010. This being a government institute, the patients are first referred to the pathology department for fine needle aspiration. A total of 1214 patients with thyroid swelling had undergone fine needle aspiration first followed by estimation of hormonal levels and ultrasonography.

All the relevant clinical details were recorded. FNAC was done by using non-aspiration technique except for cystic lesions. In case of non-diagnostic aspirates the procedure was repeated. The smears were fixed in 90% Isopropyl alcohol for 30 minutes and were routinely stained with Hematoxylin and Eosin. The air dried smears were stained with May Grunwald stain. The sections were

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routinely processed and stained with Hematoxylin and Eosin. The statistical methods used to analyze the lesions were sensitivity, specificity and overall accuracy.

RESULTS

A total of 1214 cases with thyroid swellings were aspirated during the study period from August 2008 to July 2010. Among the reportable cases, female cases far out numbered males in the ratio of 11:1. Most of the cases reported were in the age group of 21-40 years. 1154/1214 (95.05%) patients were from plain areas and 60/1214 (4.95%) were residents of hilly areas. Commonest clinical presentation was diffuse enlargement of thyroid (n=1096/1214(90.2%). Duration of complaints ranged from 2 months to 10 years.

Total number of cases available for cyto - histopathological correlation and radiological correlation was 215. In the present study 140/215(65.1%) were non neoplastic lesions and 75/215(34.9%) were neoplastic lesions.

Non-neoplastic lesions

Out of 140 cases of non-neoplastic lesions analysed 122/215(87.1%) were diagnosed as nodular goiter on cytology. On comparison with histopathology, 92/122(75.4%) correlated and rest were 15 cases of follicular adenoma, 12 cases of papillary carcinoma and 3 cases of Hashimotos thyroiditis. Nine cases of benign cystic lesions on cytology turned out to be thyroglossal cyst on histopathology. Nine cases of thyroiditis on cytology correlated with histopathology in 7 cases but in 2 cases the diagnosis was nodular goiter (Table -1).

Neoplastic lesions

In follicular adenomas correlation between cytology and histopathology was 48/54 (88.8%) and rest of the six cases were nodular goiter. 100% correlation was seen between cytology and histopathology in papillary carcinomas and in 10 cases with suspicious of malignancy on cytology, 9 cases of papillary carcinoma and one case of Non Hodgkins lymphoma which was confirmed by immunohistochemistry was observed. (Table-2)

Cases available for comparing ultrasonographic features

with histopathology was in 215 cases. Both in non-neoplastic lesions and neoplastic lesions of thyroid there was 100% correlation between ultrasography and histopathology, (Table-3)

In 910 cases biochemical levels were available for analysis. In majority of thyroid lesions both neoplastic and non neoplastic lesions were euthyroid 644/910 (70.8%). 219/234 (93.5%) of Hashimoto's thyroiditis were hypothyroid and 15/234 (6.5%) were euthyroid. 3/11 (27.3%) of papillary carcinoma were hypothyroid and 8/11 (72.7%) were euthyroid. A case of lymphoma was hypothyroid with very high levels of TSH not responding to thyroxine therapy (Table-4).

The sensitivity, specificity and overall accuracy in diagnosing non-neoplastic and neoplastic lesions of thyroid on cytology in comparison with histopathology was 71.8%, 94.95% and 84.65% respectively. The sensitivity, specificity and accuracy in diagnosing non-neoplastic and neoplastic lesions of thyroid on cytology in comparison with ultrasonography was 71.8%, 94.95% and 84.65% respectively. Overall accuracy in diagnosing non-neoplastic and neoplastic lesions of thyroid on ultrasonography in comparison with histopathology was 100%. The positive predictive value of cytology as a screening test was 92% and negative predictive value was 80.7%.

DISCUSSION

Fine needle aspiration cytology (FNAC) of the thyroid gland is now a well-established, first-line diagnostic test for the evaluation of diffuse thyroid lesions as well as of thyroid nodules with the main purpose of confirming benign lesions and thereby, reducing unnecessary surgery.^[1] Although there is a large body of world literature claiming the accuracy and usefulness of thyroid cytology, there is also evidence showing possible limitations and pitfalls of this procedure.^{[2],[3]} Different imaging techniques are now used for preoperative diagnosis of thyroid nodules like radionuclide scanning, high-resolution ultrasonography etc. However, FNAC is still regarded as the single most accurate and cost-effective procedure, particularly if ultrasound is used as a guide for better sample collection^[4]

Fig 1A:Clinical photograph of Multinodular goiter with prominent cystic change and of long duration assuming large size



Fig 1B: Cytology showing abundant colloid with few thyroid follicular epithelial cells H & E 100X

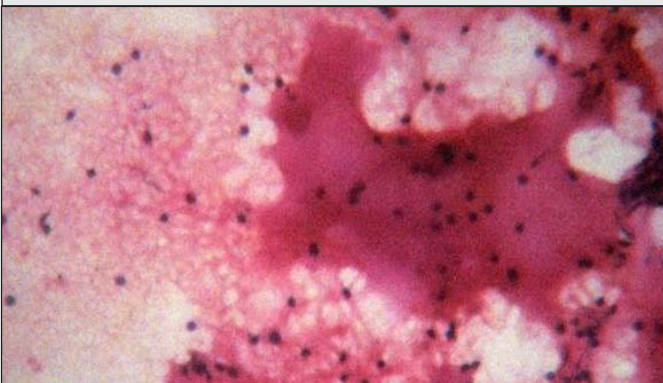


Fig 1C:Imaging showing papillary carcinoma with multinodular goiter and prominent cystic change

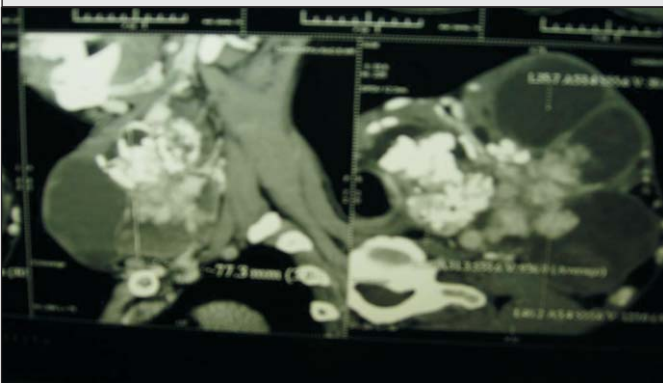


Fig 1D: Gross examination showing multinodular goiter with prominent cystic change with small grey white granular areas.



Fig 1E:Sections show area of nodular goiter with lymphoid aggregates and micropapillary carcinoma H&E 100 X

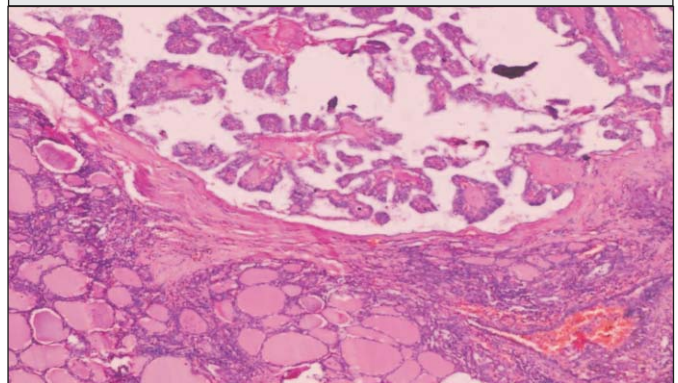
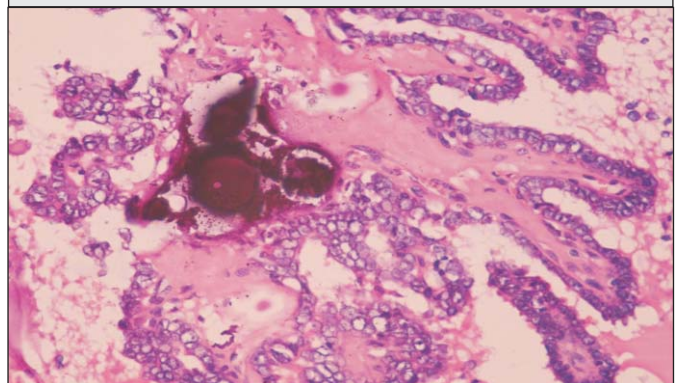


Fig 1F:Sections showing papillary carcinoma with psammoma body H & E 400X



The age of the patients with thyroid lesions ranged from 8 yrs to 72 yrs. 53.08% were in the age group of 21-40 years with mean age of 30.5 ± 9.5 years. Study by Uma Handa et al^[5] showed the mean age of patients as 37.69 ± 14.93 years. Mean age was 47 years in studies by Kumar H and J. Daykin et al^[6] and it was 47.8 years in studies by Boelaert K, Horacek J et al.^[7]

Female cases outnumbered male cases with a female to male ratio of 11.64:1. The ratios were 5.65:1 in studies by Fariba Binesh, Ali Akbar Salariin et al^[8], and 6.65:1 in studies by H. Kumar. J. Daykin et al^[6] and 6.6:1 in study by Boelaert K, Horacek J et al^[7].

In the present study 78.63% of cases had the duration of complaints between 6 months to 1 year. According to

Fig 2 A: Clinical photograph of Non Hodgkins lymphoma with prominent nodule on left side



Fig 2 B: Imaging showing diffuse hypoechoic area with irregular margins.



Fig 2 C: Cytology showing monomorphic population of lymphocytes with tingible body macrophage and nuclear debris in the background

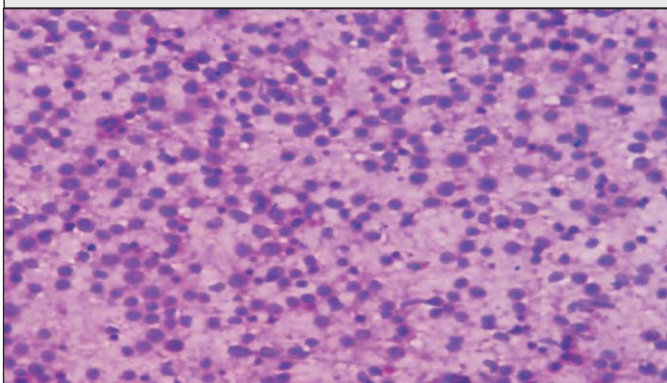


Fig 2 D: Non Hodgkins lymphoma: Sections showing diffuse sheets of monotonous population of lymphocytes destroying the thyroid follicles, H&E, 100X

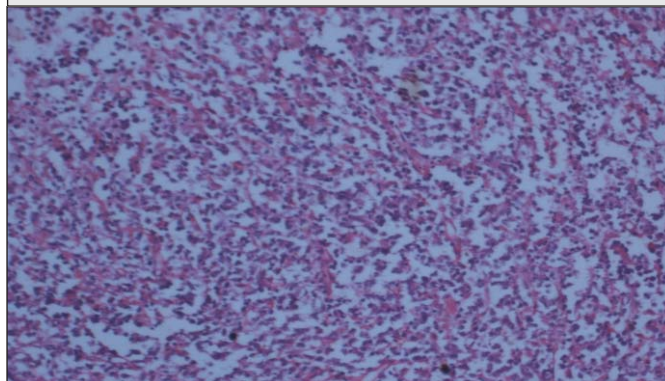


Fig 2 E: IHC of Non Hodgkins lymphoma: Tumor cells positive for CD 20, IHC 100X

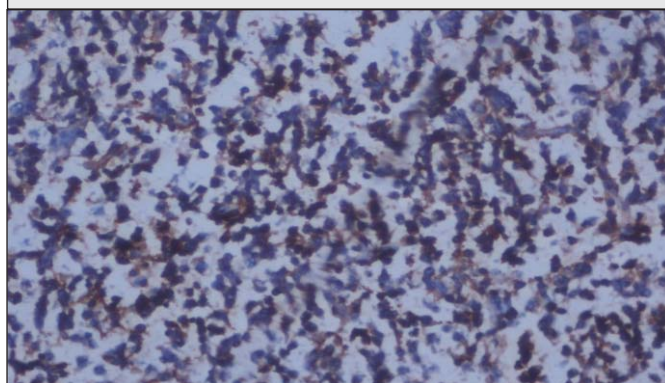
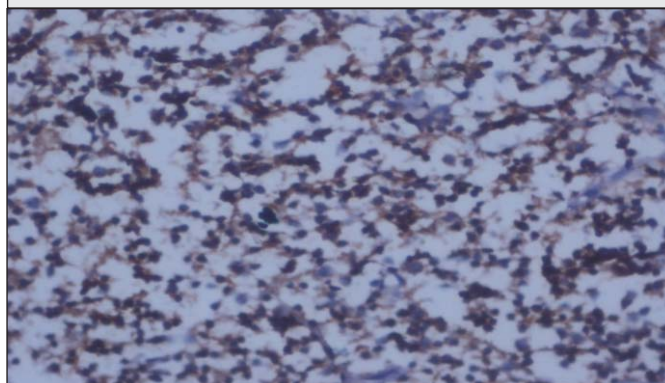


Fig 2 F: IHC of Non Hodgkins lymphoma: Tumor cells positive for LCA, IHC 100X



studies by Uma Handa and Susant Garg et al^[5] 62.21% were having presence of thyroid enlargement for more than one year.

Most of the patients had a diffuse enlargement of thyroid in 1096 cases as compared to solitary nodule in 118. Study by Boelart K, Horacek Jet et al^[7] revealed diffuse

swelling in 639 cases and 861 solitary nodules. 1154/1214 (95.05%) patients were from plain areas and 60/1214 (4.95%) were residents of hilly areas.

Traditionally, patients with multinodular goiter have been considered at lower risk of malignancy than those with solitary nodule. In the present study 12/122 (9.83%)

cases of papillary carcinoma was associated with nodular goiter and the diagnosis was missed on cytology. The small focus of papillary carcinoma could be detected on histopathology and ultrasonography (Fig 1 A to F). Hence, in nodular goiter ultrasonographic guided aspiration is preferable when compared to blinded aspiration. All the nodules should be aspirated especially in long standing goiters with prominent cystic change. In the study by Waseem Memon et al^[9], out of 105 patients operated for multinodular goiter, eight (7.6%) had different thyroid cancers among these, papillary carcinoma was found to be the most common cancer. In the study by Raghuvver Pedamallu MS et al^[10] among the 98 patients operated on for multinodular goiter, 7 cases of papillary carcinoma, and 2 cases of the follicular variant of papillary carcinoma was noticed.

Chronic lymphocytic (autoimmune) thyroiditis is one of the most common causes of non-toxic goiter in children and accounts for most of the acquired juvenile hypothyroidism. Asymptomatic goiter is the most common presentation though subclinical hypothyroidism and growth failure are frequently seen. Thyroid function is variable depending on the degree of thyroid destruction. In children, the process may arrest before complete loss of thyroid function and spontaneous recovery occurs. Those who become hypothyroid must take thyroxine supplement. Development of thyroid dysfunction is insidious and may not be accompanied by symptoms and clinical signs. In pediatric and adolescent age groups it is imperative to correct thyroid dysfunction to achieve optimal growth and development.^[11]

In the study by Gopalakrishnan et al^[12] ninety-eight subjects (aged 8-18 years) with a diagnosis of juvenile autoimmune thyroiditis and diffuse goiter were studied. Their observations were in 24 subjects (24.5%) thyroid function was normal (euthyroidism), 32 (32.6%) had subclinical hypothyroidism, and the remaining 42 subjects (42.9%) had hypothyroidism. Doeker et al^[13] observed that frequency of autoimmune thyroiditis diagnosis has three fold increased since 1995 in their department

In the present study 15.6% of cases were diagnosed as Juvenile thyroiditis. On cytology besides lymphocytes and hurthle cells, epithelioid granulomas was frequently observed. All these cases were hypothyroid indicating delay in the diagnosis. Clinically these cases presented with nodular swelling of thyroid and were asymptomatic. On ultrasonographic examination of these cases they showed either diffuse hypoechoic areas or micronodules which is a definitive feature of thyroiditis. Hence, ultrasonography is a useful diagnostic tool in diagnosing thyroiditis.

Ultrasound is the most sensitive method for diagnosing intrathyroid lesions, and is valuable for identifying many malignant and potentially malignant thyroid nodules. Ultrasound features that are helpful in differentiating the two includes microcalcifications, irregular or microlobulated margins, marked hypoechoic, a lesion that is taller than wide, and intranodular vascularity within a solid thyroid nodule. Despite clear identification, no single ultrasound criterion is reliable in differentiating benign from malignant thyroid solid nodules, but many combined US features may aid in predicting the benign or malignant nature of a given nodule^[14]. In the present study all the non neoplastic lesions and neoplastic lesions on ultrasonography correlated with histopathology.

The hormonal patterns in the present study was that majority of the patients presented with nodular goiter 583/910 (64%) out of which 547/583 (93.8%) were euthyroid, 30/583(5.14%) were hyperthyroid and 6/583 (1.02%) were hypothyroid. In a study by C.K.Sang et al^[15] majority of the patients had nodular goiter 83.3% of which 47.6% had euthyroidism, 11.9% had hyperthyroidism and 2.4% had hypothyroidism. 219/234 (93.5%) cases with diagnosis of Hashimoto's thyroiditis were hypothyroid and 15/234 (6.5%) were euthyroid.

There is mounting evidence that serum concentration of TSH is an independent predictor for the diagnosis of thyroid malignancy in patients with nodular thyroid disease. Patients with higher serum TSH concentration and borderline cytological results may require more aggressive investigation and treatment when compared

with those with lower baseline TSH levels. In a study by Haymart et al^[16], the likelihood of malignancy was 16% when TSH was < 0.06 ml U/ml, 25% for TSH between 0.40 and 1.39 mlU/ml, 35% for TSH between 1.40 and 4.99 mlU/ml and 52% in those with TSH of 5.0 ml U/ml or greater. In the present study out of 11 cases with diagnosis of papillary carcinoma on cytology 4/11 (36.36%) had high TSH levels more than 5mlU/ml.

In one case a female aged 50 years had very high levels of TSH (TSH=64.6mlU/ml) with normal hematological investigations. She came with diffuse swelling of thyroid since six months, on aspiration the smears showed reactive population of lymphocytes with germinal center cells, tingible body macrophages, mitotic figures and the diagnosis offered on cytology was florid lymphocytic thyroiditis. She was on oral thyroxine therapy. After a period of two months she came with the complaints of increased thyroid swelling and pain. On examination the swelling increased in size with a single prominent nodule on the left side. The patient was advised to have a scan. On ultrasonography the diagnosis offered was suspicious of malignancy. Repeat aspiration was advised by the clinician and features on cytology was florid lymphocytic thyroiditis /lymphoma. Excision biopsy was advised and showed the features of Non Hodgkins lymphoma which was confirmed by immunohistochemistry (positive for LCA and CD 20). (Fig 2 A to F)

In malignant lesions there was hundred percent correlation between cytology and USG findings. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy in diagnosing non neoplastic and neoplastic lesions of thyroid on cytology in comparison with histopathology was 71.8%, 94.95%, 92%, 80.7% and 84.65% respectively [Table 5]. In the present study overall accuracy in diagnosing nonneoplastic and neoplastic lesions of thyroid on ultrasonography in comparison with histopathology was 100%. In the study by Mahira Yunus et al^[17] the accuracy based on ultrasonography was 74.8%.

CONCLUSION

1. In long standing multinodular goiter with

prominent cystic change, duration of swelling more than 5 years and of huge size has to be subjected to imaging and ultrasonography guided FNAC, in order to rule out association of small focus of papillary carcinoma.

2. Juvenile thyroiditis constituted 15.6% of the cases in the present study and can present as nodular swelling with euthyroid state, hence periodic follow up is necessary to ensure early therapy.
3. In cases with diagnosis of suspicious of malignancy on cytology, imaging and histopathological examination is mandatory to arrive at the accurate diagnosis.

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