Fine needle aspiration cytology - A reliable diagnostic tool in the diagnosis of Thyroid gland enlargements

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ABSTRACT

To evaluate the accuracy and efficacy of fine needle aspiration cytology (FNAC) in the diagnosis of Thyroid gland enlargements. A retrospective analysis was done at Department of Pathology, Government Medical College and General Hospital, Anantapur, Andhra Pradesh, India. One hundred and fifty cases were included in this study. However in 10 cases aspirate was unsatisfactory and in 20 cases surgery was not performed and these cases were excluded from study. A total of 120 cases included in the final study. Detailed history, physical examination, routine investigations and other details of 120 patients were collected. FNAC with minimum two passes were performed in each case. Staining done with Haematoxylin and Eosin stain and Papanicolaou stains. FNAC smears and histopathology slides were reviewed. Among 120 cases 100 (83.66%) were reported cytologically as benign and 20 (16.66%) were malignant. But histologically 98 (81.66%) were benign and 22(18.33%) were malignant. Commonest benign lesion of thyroid in both cytology and histology was nodular colloid goiter. Follicular adenoma was the second commonest one. Among malignant conditions papillary carcinoma was the commonest one in our FNAC samples, follicular carcinoma was the commonest in our histopathology samples. Four cases of false positive and 6 cases of false negative were observed. Sampling errors were mainly responsible for these false negative diagnoses. FNAC showed an accuracy of 96.6%, sensitivity 75%, specificity 95.83%, positive predicative value (PPV) 81.81% and negative predicative value (NPV) of 93.81%. Our results were similar to other international studies and suggest that FNAC is more specific and sensitive in detecting thyroid malignancy. Therefore its useas a reliable diagnostic test cannot be over emphasized. FNAC is an accurate and reliable diagnostic tool to evaluate the cause of Thyroid gland enlargements provided strict adherence to adequacy criteria are maintained.

Keywords: Thyroid, fine needle aspiration cytology, nodular colloid goiter, papillary carcinoma.

INTRODUCTION

Enlargement of thyroid gland is a common occurrence in most parts of the world especially in the iodine deficient goiter belt areas, where the prevalence may be as high as 40%.[1] The development of goiter is a concern to both the patient and the clinician because of the fear that the swelling may be malignant. Most goiters, however; are benign, and even in solitary nodules selected for surgery on clinical grounds malignancy is found in only around 10%.[2] The value of isotope scanning is limited by its poor differentiation of benign from malignant disease.[3] Similarly, no sonographic criteria can reliably distinguish benign from malignant disorders.

In contrast to these scanning techniques, which give an indirect indication of the nature of the lesion. Fine needle aspiration provides a means of obtaining thyroid tissue for direct cytological examination without the need for surgery. The procedure, which is well tolerated and easily performed in an outpatient department, has been used extensively. A skilled cytologist can achieve excellent diagnostic accuracy.[4-9]

Good number of studies proved that FNAC is a highly effective method of selecting patients for surgery in the cases of solitary thyroid nodule. But regarding role of FNAC in the diagnosis of goiter has very few studies only.[10-14] This study is aimed at evaluating our experience of FNAC in the diagnosis of Thyroid gland enlargements.

MATERIALS AND METHODS

Over a period of Three years (June 2004 to June 2007), 150 cases of Thyroid gland enlargements were retrieved from files of the cytopathology in the Department of Pathology, Government Medical College and General Hospital, Anantapur, AndhraPradesh India. The details of the cases like age, sex, provisional clinical diagnosis, FNAC and histopathological reports were noted. A total of 150 cases of cytopathology and 130 cases of histopathological diagnosis of thyroid enlargement cases were independently made within study period. However in 20 patients aspirate was unsatisfactory and 10 cases surgery was not performed and these cases were excluded from the study. The total number of cases included in the final analysis were 120.

Table-1: Thyroid Swellings diagnosed by FNAC, and their comparison with histopathological diagnosis (Figures in the parenthesis represent the number of cases)

Thyroid Lesion	FNAC	Histopathology
Benign	100 (83.66%)	98 (81.66%)
Nodular colloid goiter	60 (50.00%)	58 (48.33%)
Follicular adenoma	18 (15.00%)	18 (15.00%)
Sub acute thyroiditis	16 (13.33%)	14 (11.66%)
Hashimoto's thyroiditis	6 (5.00%)	8 (6.66%)
Malignant	20 (16.66%)	22 (18.33%)
Follicular carcinoma	4 (3.33%)	10 (8.33%)
Papillary carcinoma	10 (8.33%)	8 (6.66%)
Undifferentiated Carcinoma	2 (1.66%)	2 (1.66%)
Lymphoma	4 (3.33%)	2 (1.66%)

FNAC had been performed for Thyroid gland enlargements using a 23 gauge needle fitted to a 10ml of disposable syringe, with minimum of two passes in each case. The procedure took a fraction of a minute. The aspirated contents of the needle were expelled on to glass slides. Usually four slides smear were made, two were immediately fixed in 95% ethyl alcohol for about 45 minutes and the remaining two were air dried and then fixed. The slides were stained with Haematoxylin and Eosin (H&E) and Papanicolaous stains respectively and examined with light microscope. A definitive diagnosis of goiter made, when the smears showed follicular cells, which are arranged in mololayered sheets, clumps, groups or as dissociated bare nuclei with abundant colloid with or without foamy and hemosiderin laden macrophages. A diagnosis suggestive of goiter was given in cases, where the smears were diluted with blood and the scanty colloid, although an adequate number of benign follicular cells were seen. Other diagnosis were given depends on the related cytological features.

Table-2: Summary of False Positive and False Negative results of FNAC

FNAC Diagnosis	Histopathological Diagnosis
False Positive (4)	
Papillary Carcinoma - 2	Nodular goiter - 2
Lymphoma - 2	Hashimoto's thyroiditis - 2
False Negative (6)	
Sub acute Thyroiditis - 2	
Nodular colloid goiter - 4	Follicular carcinoma - 6

Histopathology reports were available in 120 cases. In rest of 30 cases with a cytological diagnosis of goiter either no surgery was performed as the cytological diagnosis corroborated with the clinical diagnosis and surgery was not advised or the patient did not return to the hospital or unsatisfiedsmears. The correlation between cytological and histological diagnoses was determined in 120 cases. The FNAC smears (H&E stained and Papanicolaou stained) and histopathological sections of all cases were reviewed.

RESULTS

Table-1 shows, FNAC diagnosis with its histopathological correlation. Among 120 cases of Thyroid gland enlargements cytologically 100 (83.66%) cases were diagnosed as benign and 98 (81.66%) cases were malignant. The benign diseases include 60 (50.00%) Nodular colloid goiter (Fig.1 and 2), 18 (15%) were follicular adenoma (Fig.3), 16 (13.33%) cases as Sub acute hyroiditis, 6 (5.00%) were Hashimoto's thyroiditis. The malignant cases were 20 (16.66%). Among them 4 (3.33%) were follicular carcinoma (Fig.4), 10(8.33%) were papillary carcinoma, 2 (1.66%) anaplastic carcinomas and 4 (3.33 %) were lymphomas. Histopathologically 98 (81.66 %) cases were diagnosed as benign lesions and 22 (18.33%) were malignant lesions.

Table-2 shows summary of false positive and false negative results of FNAC , which revealed four false positive results

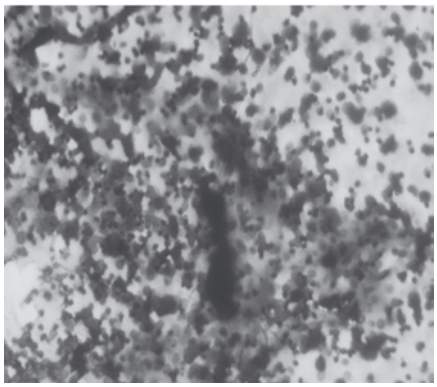

Fig. 1. Photomicrograph showing colloid goiter on FNAC (H&Ex400)

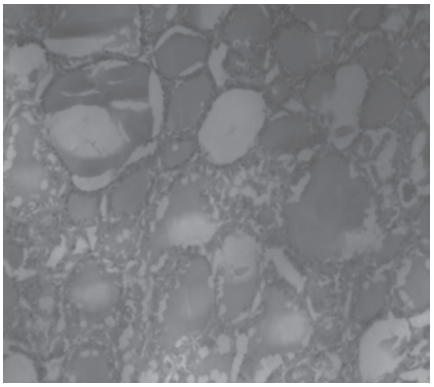

Fig. 2. Photomicrograph of colloid goiter on histopathology shows follicles filled with abundant colloid (H&E x 400)

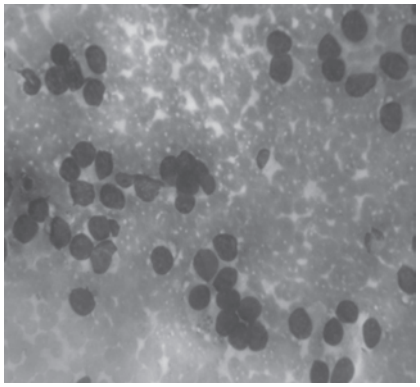

Fig. 3. Photomicrograph of follicular neoplasm on FNAC (H&Ex400)

Table-3: Sensitivity, specificity, PPV, and NPV in malignancies of Thyroid

Thyroid Malignancy	Sensitivity	Specificity	PPV	NPV
Follicular Carcinoma	62.50%	100%	100%	94.82%
Papillary Carcinoma	100%	98.24%	80%	100%
Undifferentiated Carcinoma	100%	100%	100%	100%
Lymphoma	100%	98.33%	50%	100%

and six false negative results. Table-3 shows the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in malignancies of Thyroid.

DISCUSSION

Enlargement of Thyroid gland is a common occurrence in most regions of the world. Less than 5% of solitary nodules of Thyroid are malignant.[2] In iodine deficient areas the incidence of goiters among thyroid swellings is much higher. India has the world's biggest goiter belt in the sub Himalayan region. Besides the sub Himalayan region many other states in India are endemic for goiter. Many investigators have shown that FNAC is the single most sensitive, specific and cost effective method in the evaluation of thyroid swellings.

The clinical challenge has been to identify the malignance pre operatively and thus minimize the indication for surgery for benign lesions.[15,16] FNAC is usually the first line of investigation along with other investigations like thyroid scan, ultrasound examinations, hormonal assay and antibody levels with an aim to triage patients into those who would require surgery and those who can be managed conservatively.[17,18] During our study period fluid was aspirated from thyroid cysts in few patients, all of whom had solitary nodules clinically. In most of them the nodules disappeared after aspiration. Cytological examination of the cyst fluid showed no malignant cells in any case. (These cases not included in the study because no surgery had done). Similar experience reported by Franklyn *et al*.[19]

Reported performance characteristics of FNAC and histopathology show wide range of concordance. Schnurer

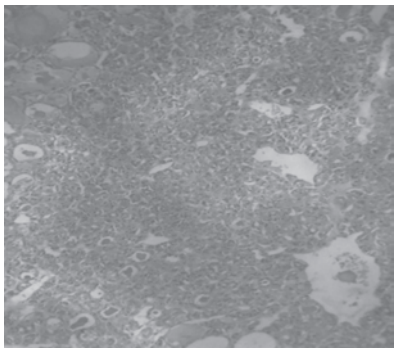

Fig. 4. Photomicrograph of follicular carcinoma on histopathology (H&Ex400)

Table-4: Comparison of results of present study with previous studies

Study	Concordance Between FNAC & Histopathology
Schnurer et al	93.00%
Harach et al	58.30%
Das et al	90.00%
Kunori et al	98.00%
Hag et al	91.40%
Sandeep R Mathur et al	97.01%
Present study	96.60%

et al evaluated 284 cases operated for goiter where a prior FNAC was performed and found a concordance between cytology and histology in approximately 260 cases.[13] In a series of 48 cases of nodular goiters with histological correlation Harach et al found a concordance in only 28/48 cases, while in 18 cases they could not exclude follicular neoplasm (16), thyroiditis (2) and there was cystic change in 2 cases.[12] Das *et al* reviewed the cytomorphologic features of 441 cases of solitary nodular goiters with thyroidectomies performed in only 27 cases. They reported an accurate cytological diagnosis in 18/21 cases of goiters.[10] Kunori *et al* are of the view that diagnostic accuracy for goiters has considerably improved with the advent of FNAC and ultrasound. In their institutional experience the accuracy rate for goiters improved from 88% to more than 98% after the induction of FNAC and ultrasound.[11] In a another publication about role of FNAC in management of thyroid lesions in a district hospital Hag *et al* have reported a concordance in 32/35 cases of goiter.[14] From All India Institute of Medical Sciences, New Delhi, India Sandeep *et al*[22] reported concordance between cytological and histopathological was 77.38 %. In our study FNAC showed an accuracy of 96.6%, Sensitivity 75%, Specificity 95.83%, Positive Predicative Value 81.81% and Negative Predicative Value of 93.81%.

In our study the incidence of malignancy was 18.33%, which is in accordance with many studies. Four false positive results came in our study on cytologically. Among them two cases of papillary carcinoma which were diagnosed histologically as nodular colloid goiter and two cases of lymphomas were confirmed by histologically as hashimoto's Thyroiditis. Six false negative results also came in our study on cytologically. Among them two cases were sub acute thyroiditis and four cases were nodular colloid goiter. All these cases were diagnosed in histologically as follicular carcinoma.

The limitations of Fine needle aspiration cytology include its inability to distinguish benign from malignant follicular neoplasm which needs surgical excision to provide a

histological diagnosis and false negative ratio, owing largely to sampling error.[19] An adequately cellular aspirate is indispensable for an accurate diagnosis. An accurate diagnosis may not be possible even in the hands of experts on a sparsely cellular aspirate. Presence of six groups of follicular cells on at least two slides from different passes recommended by Hamburger et al seems to be a fairly reasonable criterion for adequacy.[20] Sampling errors were responsible for the under diagnosis of neoplasm in six of our cases. Aspiration from multiple sites may be useful preventing sampling error. Most authors recommend preparation of 4-6 smears from different areas of the nodule.[20,21] Papillary hyperplasia and hyperplastic nodules are well known to occur in adenomatous goiters and could have been responsible for an erroneous diagnosis of follicular neoplasms.[22] It may be appropriate to inform the clinician about the limitations of FNAC in such situations.

Our results were similar to other international studies (Table-4) and suggest that FNAC is more specific than sensitive in detecting thyroid malignancy and therefore its use, as a reliable diagnostic test cannot be over emphasized.

However, the interpretation errors from this study can be reduced if aspirate were obtained from different portions of the nodules, expert cytopathologists to review and interpret the slides, the use of ultrasound guided FNA procedures, and the use of immunohistochemical and genetic markers.

We concluded that the Fine needle aspiration cytology (FNAC) is a well-established technique for pre operative investigation of Thyroid gland enlargements. This technique is almost noninvasive, cost effective, and free of complications in expert hands and efficient method of differentiating benign and malignant lesion, there by reducing unnecessary surgeries. Strict adherence to adequacy criterion and meticulous examination of all the smears are paramount importance in achieving a high rate of diagnostic accuracy. A benign FNAC diagnosis should be viewed with caution as false negative results do occur and these patients should be followed up. Thus we encourage our clinicians to embrace this investigative procedure in the management of our patients.

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