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Solitary Thyroid Nodules: A Cyto-Histological Correlation

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Abstract

Objective: Fine needle aspiration cytology is the gold standard diagnostic test for the diagnosis of thyroid nodules. Purpose of the present study was to correlate the fine needle aspiration cytology findings with histopathology of excised specimens.

Material and Methods: In a retrospective study 65 patients with solitary thyroid nodules were assessed. Preoperative FNAC findings and postoperative histopathology findings were analyzed. Patients with multinodular goitre excluded from the study.

Results: A total of 65 patients with solitary thyroid nodule were identified: 21 (32.3%) were male and 44 (67.7%) were females. Age of the patients ranged from 17 to 68 years. Most common benign pathology was colloid goiter (44.6%). Commonest malignancy detected was papillary carcinoma (15.38%).

Statistical analysis of thyroid lesions showed sensitivity, specificity and accuracy to be 70.97%, 100% and 86.15% respectively. Positive predictive value, negative predictive value, false positive rate and false negative rate of FNAC found to be 100%, 79.07%, 0% and 29.03% respectively

Conclusions: Fine needle aspiration cytology is a simple, reliable, accurate and cost effective procedure for the diagnosis of thyroid cancer. It is recommended as the first line investigation for the diagnosis of solitary thyroid nodule.

Keywords: Thyroid; Solitary nodule; Cytology; Biopsy

Introduction

Disorders of thyroid may result from developmental failures, abnormalities of hormone production and structural changes which may or may not be accompanied by changes in function. Nodular thyroid disease describes the presence of a single or multiple nodules within the thyroid gland. Solitary thyroid nodule is a common entity. Majority of these nodules are benign. Nodules are more frequent in women and prevalence increases with age, exposure to ionizing radiation and iodine intake. The causes of thyroid nodules may be benign or malignant. The difficulty facing the clinician is to differentiate between the vast majority of benign lesions and the smaller proportion of malignant neoplasm. The main goal of evaluating these nodules is to identify nodules with malignant potential.

The prevalence of thyroid nodules ranges from 4% to10% in the general adult population and from 0.2% to

1.2% in children[1]. The majority of clinically diagnosed thyroid nodules are nonneoplastic; only 5%–30% are malignant and require surgical intervention[2]. FNAC is, however, not without limitations; accuracy is lower in suspicious cytology and in follicular neoplasm. The main aim of FNAC is to identify nodules that require surgery and those benign nodules that can be observed clinically and decrease the overall thyroidectomy rate in patients with benign diseases.

FNAC is initial screening test and considered the gold standard diagnostic test in the evaluation of a thyroid nodule[3]. FNAC is simple, cost effective, readily repeated, and quick to perform procedure in the outpatient department with excellent patient compliance. Important factor for the satisfactory test includes representative specimen from the nodule and an experienced cytologist to interpret findings.

The purpose of this retrospective study was to review the histopathologic pattern and their relationship with age, sex and to find out correlation of FNAC findings with histopathological finding.

Materials and Methods

A retrospective study was done in 65 patients of solitary thyroid nodule who presented to the Department of ENT, Shri Balaji Institute of Medical Sciences, Raipur, Chhattisgarh.

Diagnoses of the diseases were reached by histopathological examination of thyroid specimens. Information collected included patient's age and sex, preoperative FNAC and the histopathologic diagnosis.

All the patients were analyzed for preoperative FNAC and postoperative histopathological findings. Inclusion criteria included clinically detected solitary thyroid nodule. Statistical analysis was made. True positive, were defined as those samples of malignancy by FNAC and confirmed on histopathology as malignant. True negative were those that were negative for malignancy on FNAC and also on histopathology. False positive were those that were positive for or suspicious of malignancy on FNAC but with no evidence of malignancy on histopathology. False negative were those that were negative for malignancy on FNAC but a diagnosis of malignant disease was made on histopathology.

All FNAC reports were correlated with histopathological diagnosis. Sensitivity, specificity, accuracy, positive predictive value, and negative predictive values were calculated for nonneoplastic and neoplastic lesions.

Observation and Results

Clinical profile and etio-pathology of thyroid swelling

Table 1 showed age and sex distribution among different thyroid pathologies. A total of 65 patients with solitary thyroid nodule were analyzed. 21 (32.3%) were male and 44 (67.7%) were females. Age of the patients ranged from 17 to 68 years. All cases presented with neck swelling. Duration of complaints ranged from 1 month to 10 years.

Histopathological examination of excised specimens included 29 (44.6%) cases of colloid nodular goitre, 12 (18.5%) follicular adenoma, 10 (15.4%) papillary carcinoma, 6 (9.2%) follicular carcinoma, 2 (3%) hurthle cell carcinoma, 3 (4.6%) hashimoto's thyroiditis and 3 (4.6%) cases of benign cystic lesion. Female (47.7%) predominance was noted in colloid goitre.

The majority of the cases (90.76%) were seen in the age group 21-60 years. Maximum number of cases (30.78%) presented in fourth decade. The young age group 0-20 years and the elderly group above 60 years constituted 6.15% and 3.08% respectively.

Correlation of FNAC with HPE finding

For the correlation purposes thyroid lesions have been divided in two major groups, nonneoplastic and neoplastic on the basis of cytology finding.

Table 2 showed correlation of FNA and biopsy among non-neoplastic thyroid lesion. Cytology finding of the non-neoplastic group (n=43 cases) included simple and nodular colloid goitre (35 cases), benign cystic lesion (6 cases) and hashimoto's thyroiditis (2 cases). Neoplastic lesions (n=22 cases) included follicular neoplasm (13 cases), papillary carcinoma (8 cases) and one case of hurthle cell carcinoma.

Comparison of cytology with histopathological findings was performed. 36 cases were diagnosed as colloid goitre by FNAC. On HPE finding it confirmed as colloid nodular goitre (29 cases, true negative), follicular adenoma (5 cases, False negative) and papillary carcinoma (2 cases, False negative). Among 6 cases of benign cystic lesion, three cases confirmed as benign cyst (true negative) and one case as hashimoto's thyroiditis (False negative) on histopathological finding. Three cases of hashimoto's thyroiditis confirmed on HPE finding as hashimoto's thyroiditis (2 cases, true negative) and one case of hurthle cell carcinoma (False negative).

Table 3 showed correlation of FNA and biopsy among neoplastic thyroid lesion. 22 cases were diagnosed as neoplastic lesions by FNAC and also confirmed as neoplastic lesions on HPE (True positive). Among these 13 cases of follicular neoplasia were confirmed on HPE finding as follicular adenoma (8 cases) and follicular carcinoma (5 cases). All cases of papillary carcinoma (8 cases) and hurthle cell carcinoma (1 case) have same diagnosis confirmed on histopathological examination.

In 34 (79.07%) cases of non-neoplastic lesions, histological findings were consistent with the cytology results. In neoplastic lesions all 22 (100%) histological findings were consistent with the cytology results. Overall, cyto-histological correlation was found to be 86.15%.

Table 4 showed statistical Analysis of Thyroid gland biopsy result. Statistical analysis and cytohistologic correlation of thyroid lesions showed sensitivity, specificity and accuracy to be 70.97%, 100% and 86.15% respectively. Positive predictive value, negative predictive value, false positive rate and false negative rate of FNAC found to be 100%, 79.07%, 0% and 29.03% respectively.

Discussion

The prevalence of thyroid nodules ranges from 4% to 10% in general population and from 0.2% to 1.2% in children[1]. The majority of clinically diagnosed thyroid nodules are nonneoplastic; only 5% -30% are malignant[2]. In India thyroid cancer is 1% of all head and neck cancers.

Although the mechanism underlying thyroid nodule formation and growth is poorly understood, nodules are more common in women, in older persons, in persons exposed to ionizing radiation, and in persons living in areas endemic for iodine deficiency.

The age of patients ranged from 17 to 68 years. Among total of 65 patients, 21 (32.3%) were male and 44 (67.7%) were females with F: M ratio of 2:1. The majority of patients (30.78%) were in their fourth decade of life. Solitary thyroid nodules are 4-9 times more common in females as compared to males[4].

The majority of the cases (90.76%) were seen in the age group 21-60 years. The young age group 0-20 years and the elderly group above 60 years constituted 6.15% and 3.08% respectively.

The thyroid disease in particular NCG was seen in almost all age groups and its high prevalence in the age group 21-60 years (86.21%) was similar to other observations.

The incidence of malignancy in this study was 27.69%. The incidence of malignancy can be as high as 43.6%. The incidence of papillary carcinoma in the present study

was 55.56%. In the literature, incidence of papillary carcinoma varies from 50% to 80%[4]. Papillary carcinoma is the most common type of thyroid cancer, comprising approximately 80% of all primary thyroid malignancies[5].

All FNAC reports were correlated with histopathological diagnosis. Sensitivity, specificity, accuracy, positive predictive value, and negative predictive values were calculated for nonneoplastic and neoplastic lesions.

False negative diagnosis

The false-negative rate is defined as the percentage of patients with "benign" cytologic findings who are confirmed to have malignant lesions of the thyroid.

In present study false negative rate was found 29.03%. False-negative errors are worrisome because they imply missed malignant lesions. False-negative diagnoses may occur because of sampling error or interpretive mistakes[6,7]. Regardless of the cause, for fine-needle aspiration biopsy to be considered a useful and reliable diagnostic technique, false-negative results must be acceptably low.

In a study by Gharib and Goelner reported false-negative rates in the seven series ranged from 1.3% to 11.5%, with an average rate of 5.2%[8]. Caruso and Mazzaferri found an identical false-negative rate of 5% (range, 1% to 6%) based on pooled data from 10 series[9]. Ashcraft and Van Herle (1981) noted that false-negative results varied in reported series from 2% to 50%[10]. In another study by Agrawal (1995) false negative rate was noted 4%[11].

Gupta M et al observed the false negative rate of 20% in cases of neoplastic lesions and mentioned that It constitutes a serious limitation of this technique since these malignant lesions would go untreated. The incidence of false negative results is as low as 1% to as high as 30%[12].

False-Positive Diagnosis

False-positive reports do not constitute a major problem with fine-needle aspiration. The false-positive rate is the percentage of patients with "malignant" fine-needle aspirates who are found to have benign lesions on histopathology.

In present study false positive rate was observed 0%. The false-positive rate varied from 0% to 7.7% (average, 2.9%) in the seven series study[8]. 0.5% rate was reported by Ashcraft and Van Herle[10]. In another study it was observed 2%[11].

Campbell and Pillsbury reported 1.2% rate on the basis of a literature survey. He also concluded that, overall 1 in 40 patients with a "benign" fine-needle aspiration biopsy specimen may have a malignant lesion, and 1 in 100 patients with a "malignant" fine-needle aspiration biopsy specimen may actually have benign disease[13].

Sensitivity, Specificity and accuracy

Two values used to estimate the accuracy of fine-needle aspiration biopsy for malignancy are sensitivity and specificity. The estimation of sensitivity and specificity depends on how the suspicious category is handled[6]. If suspicious cytologic results are considered as positive, then sensitivity will increase and specificity will decrease. On the other hand, if the suspicious results are considered as negative, specificity will increase and sensitivity will decrease.

In present study sensitivity, specificity and accuracy were observed 70.97%, 100% and 86.15% respectively which were comparable to other study. Suresh Kumar et al (2008) observed overall sensitivity 77%, specificity 100% and accuracy 97.7%[14]. Sensitivity of 65% to 98% and a specificity of 72% to 100% were observed in a study by Gharib and Goelner[8].

Gupta M et al (2010) observed sensitivity, specificity, and accuracy of FNAC for solitary thyroid nodules 80%,

86.6%, and 84%, respectively[12], whereas sensitivity, specificity, and accuracy of FNAC were 93.5%, 75%, and 79.6%, respectively, in a study by Bouvet et al. FNAC as a diagnostic test for thyroid nodules demonstrated an accuracy of 90.9%, a sensitivity of 76.5%, a specificity of 95.9% in another study[11].

All these data suggest that fine-needle aspiration is slightly more specific than sensitive in detecting thyroid cancer and confirm it as a reliable diagnostic test.

Positive and negative predictive value

Positive predictive value is defined as the proportion of those with a positive test result who actually have disease. Negative predictive value is defined as the proportion of those with a negative test result who do not have disease.

In present study Positive predictive value and negative predictive value of FNAC was found 100% and 79.07% respectively. It was 86.7% and 92.2%, respectively in study by Agrawal S[8]. Negative predictive value of 64% to 96% and positive predictive value of 72% to 99% was observed by Gharib and Goelner in a study of seven series[8].

All cases of papillary carcinoma diagnosed by FNAC were papillary carcinoma on histopathological examination also. This is in accordance with previous studies[4,12].

Guhamallick et al. (2008) in their study of 288 cases mentioned that most of the earlier studies reported higher numbers of false negative cases in their series and concluded that high rate of failure to diagnose cancer could be attributed to the failure of aspiration from precise locations. They found 13 cases (5.22%) with cytohistological discrepancy and divided it into eight groups to discuss the possible sources of error and methods to rectify these problems[15].

In our study follicular adenoma was misdiagnosed as colloid nodular goitre in cytology. Cytological differentiation between follicular neoplasm and nodular goiters is often very difficult. Aspirations in these cases were probably done over colloid rich macrofollicular areas of the neoplasm[15].

Two cases of papillary carcinoma misdiagnosed as colloid goiter on cytology. According to Guhamallick et al. the cause of detection/ diagnosis failure was possibly the presence of small minute foci of a papillary thyroid carcinoma that were missed during aspiration.

Hurthle cell carcinoma was misdiagnosed as hashimoto's thyroiditis on cytology. Similar mistakes were also reported earlier by some authors[15]. According to Guhamallick et al. importance was probably not given to the absence of follicular cells, dyscohesiveness of Hurthle cell clumps, prominent anaplasia, nucleoli of Hurthle cells, and only the focal presence of lymphocytes. They found clumps of Hurthle cells with a focal presence of lymphocytes suggesting a diagnosis of hashimoto's thyroiditis.

Papillary thyroid carcinoma is readily identified using FNAC because of its unique cytologic features. Diagnosis is correct for papillary thyroid carcinoma in approximately 90-100% of FNAC specimens when correlated with the histology of the final surgical specimen.

The main limitation of cytology is the differentiation of benign from malignant follicular neoplasms. FNAC specimens of follicular neoplasms and Hurthle cells are commonly interpreted as indeterminate or suspicious. This results in low FNAC accuracy rates for follicular carcinomas.

Conclusion

We conclude that FNAC diagnosis of malignancy is highly significant and such patients should be subjected

to surgery. A benign FNAC diagnosis should be viewed with caution as false negative results do occur and these patients should be followed up and any clinical suspicion of malignancy even in the presence of benign FNAC requires surgery. Fine-needle aspiration biopsy is safe, accurate, and cost-effective. The procedure has a central role in the management of thyroid nodules and should be used as the initial diagnostic test.

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Legend Tables

Table 1: Age and Sex distribution of different Thyroid pathologies

HPE	Sex	Age Group						Total	
		10-20	21-30	31-40	41-50	51-60	61-70		
Adenoma	M	1	-	1	-	1	-	3	12 (18.5%)
	F	-	4	1	1	3	-	9	
Colloid goiter	M	-	1	3	-	3	1	8	29 (44.6%)
	F	2	3	7	5	3	1	21	
Papillary Carcinoma	M	1	-	-	4	1	-	6	10 (15.4%)
	F	-	1	-	2	1	-	4	
Follicular Carcinoma	M	-	-	-	-	-	-	-	6 (9.2%)
	F	-	-	5	1	-	-	6	
Hashimoto Thyroiditis	M	-	-	2	1	-	-	3	3 (4.6%)
	F	-	-	-	-	-	-	-	
Benign Cyst	M	-	-	-	-	1	-	1	3 (4.6%)
	F	-	1	1	-	-	-	2	
Hurthle cell Ca	M	-	-	-	-	-	-	-	2 (3%)
	F	-	1	-	1	-	-	2	
Total		4 (6.15%)	11 (16.92%)	20 (30.78%)	15 (23.07%)	13 (20%)	2 (3.08%)	65	

Table 2: Nonneoplastic lesions diagnosed by FNAC and their comparison with HPE findings

FNAC Report	n=43	HPE report	n=43	Remark
Colloid nodular goiter	36	Colloid nodular goitre	29	True negative
		Follicular Adenoma	5	False negative
		Papillary carcinoma	2	False negative
Benign cystic lesion	4	Benign cyst	3	True negative

		Hashimoto thyroiditis	1	False negative
Hashimoto's Thyroiditis	3	Hashimoto's thyroiditis Hurthle cell Carcinoma	2 1	True negative False negative

Table 3: Neoplastic lesions diagnosed by FNAC and their comparison with HPE findings

FNAC Report	n=22	HPE report	n=22	Remark
Follicular Neoplasia	13	Follicular Adenoma Follicular Carcinoma	8 5	True positive True positive
Papillary carcinoma	8	Papillary carcinoma	8	True positive
Hurthle cell Carcinoma	1	Hurthle cell Carcinoma	1	True positive

Table 4: Statistical Analysis of Thyroid gland biopsy result

Test (FNAC)	Standard test (HPE) Positive	Negative
Positive	22 (True positive)	0 (False positive)
Negative	9 (False negative)	34 (True negative)

Sensitivity = 70.97%, specificity = 100%, accuracy = 86.15%, False positive rate = 0%, False negative rate = 29.03%, Positive predictive value = 100%, Negative predictive value = 79.07%,