International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Fine Needle Aspiration Cytology in Cases of Thyroid Swellings: One Year Study

Dr. Prashant S. Murarkar[1], Dr. Kalpana R. Sulhyan[2], Dr. Alka V. Gosavi[3], Dr. Prashant B. Chege[4]

[1]Assistant professor, [2]Professor and head, [3]Associate professor, [4]Junior Resident,
Department of Pathology, Government Medical College, Miraj.

Corresponding Author: Dr. Prashant S. Murarkar

ABSTRACT

Fine needle aspiration cytology (FNAC) is a simple, rapid, cost-effective technique for pre-operative investigation of thyroid swellings. This study is carried out to highlight the role of fine needle aspiration cytology as a first-line investigation in cases of thyroid swellings and to correlate the cytology findings with histopathological findings wherever possible.

This was a retrospective study of 102 fine needle aspirations (FNA) of thyroid swellings over a period of one year. The results were categorized according to the recent Bethesda classification (2009). Histopathological correlation was done, when surgical specimen was available. The accuracy of cytodiagnosis obtained was 91.67% with a sensitivity of 75%, specificity of 95%, a positive predictive value of 75%, a negative predictive value of 95%, false negative rate of 25% and false positive rate of 5%.

Keywords: Fine needle aspiration; Thyroid swellings; Histopathology.

INTRODUCTION

Fine needle aspiration cytology (FNAC) has been increasingly utilized as pre-operative investigation of thyroid swelling. [1,2] The technique is rapid, minimally invasive & cost-effective procedure. [3] It effectively distinguishes thyroid lesions suitable for surgical resection with those that can be managed conservatively. [4] The aim of this study is to focus the role of FNAC in the diagnosis of thyroid swellings and to correlate cytology findings with histopathology.

MATERIALS AND METHODS

This was a retrospective study done at Department of Pathology, Government Medical College, Miraj, Maharashtra, India over a period of one year (January 2014 to December 2014). FNA was done in 102 cases with thyroid swellings. Patients of all age group and both sexes were included. Out of 102 patients, histopathological specimens of 26 cases were received & the histopathological findings were correlated in these cases.

After the brief explanation of procedure of FNAC and its possible complications to the patient, a written informed consent was taken. The procedure was performed in cytopathology laboratory of pathology department, on an outpatient basis. Fine needle aspiration was performed by using needle of 24 gauge. [5] 2-3 slides were fixed in 95% ethyl alcohol and stained by routine H & E method and Pap method. One slide was kept air-dried and stained with Leishman stain. The smears were reviewed & were interpreted according to recent Bethesda classification (2009) [6] into

6 categories viz. non-diagnostic / unsatisfactory (ND/UNS), benign, atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm/suspicious of a follicular neoplasm (FN/SFN), suspicious for malignancy (SFM), and malignant. The sensitivity, specificity, accuracy, false positive rate (FPR) and false negative rate (FNR) of FNAC for various thyroid lesions were calculated.

RESULTS

FNAC was performed in 102 patients with thyroid swelling, of which 92 cases were females and 10 cases were males with female to male ratio of 9.2:1. Maximum numbers of cases were found in 3rd & 4th decade of age. The distribution of cases is shown in Table 1.

Table 1: Distribution of cases according to cytologic diagnosis based on the Bethesda classification

Category	Cytologic Diagnosis	Cases	Percentage
I	Non-diagnostic / unsatisfactory	7	6.86%
II	Benign	80	78.44%
III	Atypia of undetermined significance/follicular lesion of undetermined significance	2	1.96%
IV	Follicular neoplasm/suspicious of follicular neoplasm	8	7.84%
V	Suspicious for malignancy	1	0.98%
VI	Malignant	4	3.92%
	Total	102	100%

In our study, 80 cases of benign thyroid lesions (Cat.II) were diagnosed. Out of which, 68 cases showed features of colloid goitre or nodular goitre or of colloid cyst. On microscopy, smears showed scattered & clusters of benign follicular epithelial cells against the background of colloid (Fig.1). Many of the cases showed hemosiderophages & foamy macrophages in the background. Histopathology sections showed thyroid follicles of varying sizes containing abundant colloid (Fig.2).

Twelve cases were diagnosed as lymphocytic thyroiditis. On microscopy, these cases showed scattered & clusters of benign follicular epithelial cells against the background of numerous lymphocytes. At places, lymphocytes were seen impinging on clusters of follicular epithelial cells. Some of the follicular epithelial cells showed hurthle cell change. Histopathology sections of six cases showed thyroid follicles of varying sizes with dense & diffuse infiltration by lymphocytes, at places destructing the follicles. In two out six cases of lymphocytic thyroiditis, follicular epithelial cells showed hurthle cell change.

There were 2 cases classified as atypia of undetermined significance/ follicular lesion of undetermined significance (Cat.III). On microscopy, these cases showed mixed micro & macrofollicular pattern of follicular cells & scant colloid in the background. Some of the clusters showed anisonucleosis, nuclear crowding & overlapping. Occasional cells showed nuclear grooves. On histopathology, one case was reported as follicular adenoma with lymphocytic thyroiditis & other was nodular goitre.

Follicular neoplasm/suspicious of a follicular neoplasm (Cat.IV) included 8 cases. Cytology smears showed sheets of follicular epithelial cells, repetitive microfollicular pattern, occasional macrofollicular pattern and absent or scant colloid on the background (Fig.3). Histopathology sections of one case showed well encapsulated tumor separated from normal thyroid tissue by thick capsule. The tumor was composed of uniform small follicles lined by round to oval cells having mildly pleomorphic nuclei and scant to moderate amount of eosinophilic cytoplasm. The adjacent thyroid was compressed by the tumor. There was no evidence of capsular or vascular invasion (Fig.4). Histopathology of other case showed partially encapsulated nodule composed of varying sized thyroid follicles containing colloid & was reported as adenomatoid goitre.

A single case of suspicious of papillary carcinoma thyroid (Cat.V) was reported. Microscopy showed cellular smears with clusters of follicular epithelial cells, many of which showed crowding and overlapping of nuclei and occasional cells showed nuclear grooves. Histopathology was advised in this case. However patient didn't turned out.

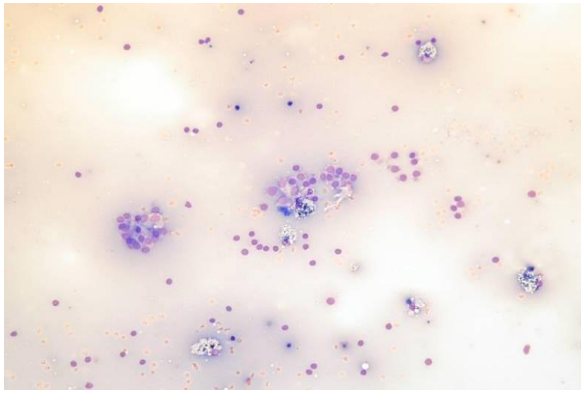

Figure 1: Colloid Goitre: Cytology smear showing scattered & clusters of follicular epithelial cells, foamy macrophages and abundant thin colloid in the background (Pap stain, x 40)

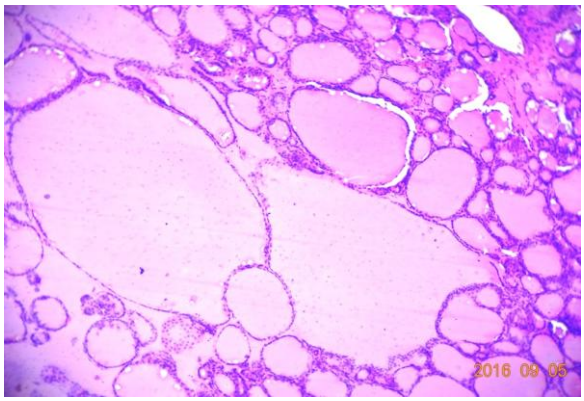

Figure 2: Colloid Goitre: Photomicrograph showing thyroid follicles of varying sizes containing abundant colloid (H & E, x 100)

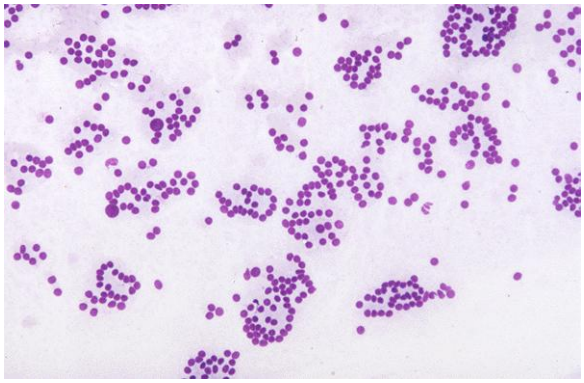

Figure 3: Follicular neoplasm (Category IV): Cytology smear showing follicular epithelial cells with repetitive microfollicular pattern. Absent or scant colloid in the background (Pap stain, x 40)

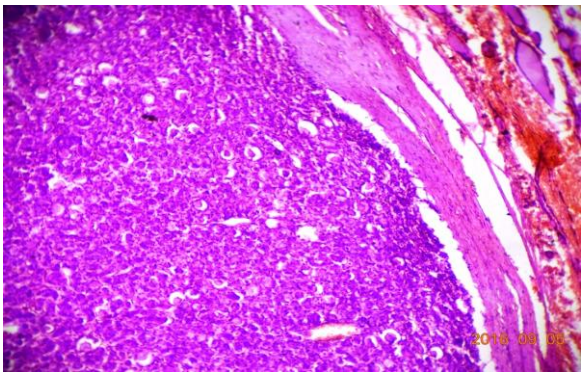

Figure 4: Follicular adenoma: Photomicrograph showing well encapsulated tumor separated from normal thyroid tissue by thick capsule (H & E, x 40)

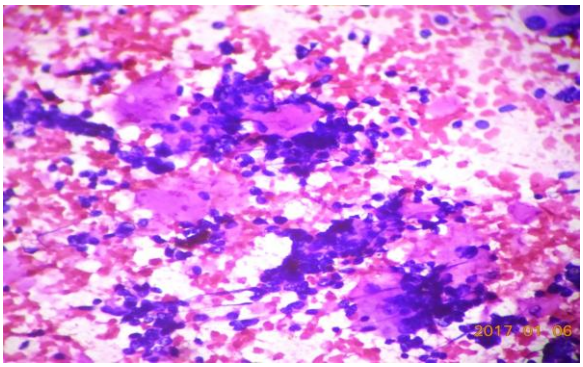

Figure 5: Medullary carcinoma thyroid: Cytology smear showing scattered and dyscohesive clusters of round to oval to polygonal cells having pleomorphic vesicular nuclei with fine and stippled or coarsely granular chromatin & scant eosinophilic cytoplasm. The background shows dense amorphous eosinophilic material (Amyloid). (H & E, x 40)

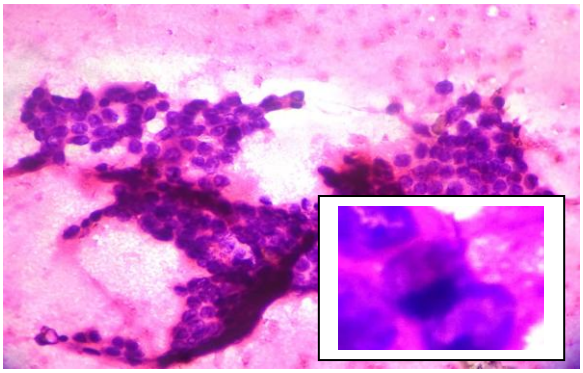

Figure 6: Papillary carcinoma thyroid: Cytology smear showing clusters of follicular epithelial cells, many of which showed ground glass appearance, crowding and overlapping of nuclei. (H & E, x 100). Inset shows intranuclear inclusions.

Malignant lesions (Cat.VI) included 2 cases of papillary carcinoma thyroid, one case of medullary carcinoma and poorly differentiated carcinoma each. Case of medullary carcinoma thyroid showed cellular smears with scattered and dyscohesive clusters of round to oval to polygonal cells having pleomorphic vesicular nuclei with fine and stippled

(neuroendocrine-like) or coarsely granular chromatin & scant eosinophilic cytoplasm. The background showed dense amorphous eosinophilic material (Amyloid) (Fig.5). Histopathology smears showed nests of tumor cells surrounded by dense pink stroma containing amyloid. Tumor cells were round to oval cells with punctate chromatin with mild nuclear pleomorphism.

Cytology smears of cases of papillary carcinoma showed cellular smears with clusters of follicular epithelial cells, many of which showed crowding and overlapping of nuclei and nuclear grooves. Intranuclear inclusions were also noted (Fig.6). Histopathology sections showed well-formed papillae lined by tumor cells. The nuclei showed ground glass chromatin, overcrowding & overlapping. Psammoma body was also noted (Fig.7).

A single case of poorly differentiated carcinoma was reported. Cytology showed cellular smears with clusters of round to oval cells with highly pleomorphic vesicular nuclei with scant cytoplasm. Numerous mitotic figures were also noted. Histopathology was advised in this case also. However, in this case also patient didn't turned out.

This study also included 7 cases which were non-diagnostic / unsatisfactory. These cases on microscopy didn't fulfill the adequacy criteria of thyroid FNA.

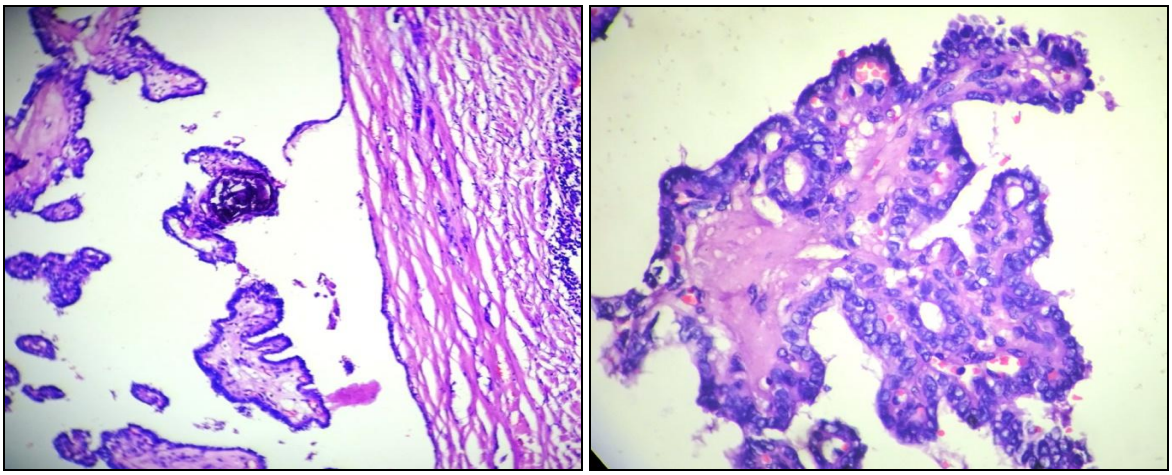

Figure 7: Papillary carcinoma thyroid: Photomicrograph showing well-formed papillae lined by tumor cells. Psammoma body is also noted. (left) (H & E, x 40). The nuclei show ground glass chromatin, overcrowding & overlapping (right) (H & E, x 100).

Out of 102 cases, histopathological investigation was done in 26 (25.49%) cases. (Table.2).

Table 2: Correlation between cytological & histopathological diagnoses

Category	Cytopathological Diagnosis	Number of cases where surgical specimens were received	Histopathological Diagnosis	No. of cases
I*	ND/UNS (n=7)	-	-	-
II	Benign (n=80)	20	Nodular goitre	13
			Lymphocytic thyroiditis	6
			Papillary carcinoma thyroid with chronic lymphocytic thyroiditis	1
III*	AUS/FLUS (n=2)	2	Follicular adenoma with lymphocytic thyroiditis	1
			Nodular goitre	1
IV	FN/SFN (n=8)	2	Follicular adenoma	1
			Adenomatoid goitre	1
V	SFM (n=1)	0		
VI	Malignant (n=4)	2	Medullary carcinoma thyroid	1
			Papillary carcinoma thyroid	1

(ND/UNS-Non-diagnostic/unsatisfactory, AUS/FLUS-Atypia of undetermined significance/follicular lesion of undetermined significance, FN/SFN- Follicular neoplasm/suspicious of a follicular neoplasm, SFM- suspicious for malignancy, TN-true negative, FN-false negative, TP-true positive, FP-false positive)

*In the present study, we have not considered cases in non-diagnostic / unsatisfactory category (Cat.I) and atypia of undetermined significance/follicular lesion of undetermined significance category (Cat.III) for calculations because these cases could not be classified either as benign or malignant on cytology.

Table No.3: Relation between cytological and histopathological diagnosis

Cytological Diagnosis	Histopathological Diagnosis		Total
	Benign	Neoplastic	
Benign	19 (TN)	1 (FN)	20
Follicular neoplasm	1 (FP)	1 (TP)	02
Suspicious & malignant	0	02 (TP)	02
Total	20	04	24

In our study, the accuracy of cytodiagnosis was 91.67% with a sensitivity of 75%, specificity of 95%, a positive predictive value of 75%, a negative predictive value of 95%, false negative rate of 25% and false positive rate of 5%.

DISCUSSION

Thyroid nodules are a common clinical problem. These include developmental, inflammatory, hyperplastic and neoplastic disorders. Thyroid problems are mainly seen in 3rd & 4th decade of life with female predominance. FNAC of the thyroid is the key preoperative investigation of thyroid lesions. Majority of nodules are benign, but when they are discovered, probability of malignancy must be excluded using FNA. It helps to determine whether surgical removal of a detected nodule is recommended or not. However, FNAC has some limitations such as inadequate sampling, inability to distinguish between benign and malignant follicular lesions in the absence of nuclear features of papillary carcinoma, indeterminate diagnosis of follicular neoplasm which includes cellular adenomatoid nodule, follicular adenoma and follicular carcinoma.

The present study showed female predominance with female to male ratio of 9.2:1. Maximum cases were found in 3rd & 4th decade of age. Handa et al [7] & Pandey et al [8] also reported female predominance with most of the cases in 3rd & 4th decade in their studies.

In our study, maximum number of cases i.e. 80 cases (78.44%) were seen in Category II i.e. benign, 2 cases (1.96%) was of atypia of undetermined significance, 8 cases (7.84%) of follicular neoplasm/suspicious of a follicular neoplasm, 01 case (0.98%) was suspicious for malignancy, 04 cases (3.92%) were malignant, and 7 cases (6.86%) were Non diagnostic/unsatisfactory. Mehra and Verma [9] & Kaler et al [10] also reported similar findings in their studies.

Table 4: Correlation between cytological & histopathological diagnoses

Category	Cytopathological Diagnosis	Number of cases where surgical specimens were received	Histopathological Diagnosis	No. of cases
I*	ND/UNS (n=7)	-	-	-
II	Benign (n=80)	20	Nodular goitre	13 (TN)
			Lymphocytic thyroiditis	6 (TN)
			Papillary carcinoma thyroid with chronic lymphocytic thyroiditis	1 (FN)
III*	AUS/FLUS (n=2)	2	Follicular adenoma with lymphocytic thyroiditis	1
			Nodular goitre	1
IV	FN/SFN (n=8)	2	Follicular adenoma	1 (TP)
			Adenomatoid goitre	1 (FP)
V	SFM (n=1)	0		
VI	Malignant (n=4)	2	Medullary carcinoma thyroid	1(TP)
			Papillary carcinoma thyroid	1(TP)

In our study the sensitivity was 75%, specificity 95%, positive predictive value of 75%, and a negative predictive value of 95%. Our results were comparable with Cap J et al [11] study where FNAC of thyroid is reported to have sensitivity ranges from 65% to 98%, a specificity of 72% to 100%, a positive predictive value of 34% to 100%, and a negative predictive value of 83% to 100%.The diagnostic accuracy for cytologic diagnosis was 91.67% in the present study which is comparable with Bista et al [12] study which showed diagnostic accuracy of 92.1%.

A False positive case means case which is cytologically diagnosed as neoplastic but later confirmed as benign on histopathology. The false positive rate

(FPR) in our study was 5%. Caruso & Muzzaferri et al [13] in their study reported false positive rate of <6% and Bartolazzi et al [14] study reported 2.2%. In our study, a false positive case of follicular neoplasm on cytology was reported as adenomatoid goitre on histological examination. The slides were reviewed. The cytology showed cellular smears showing repetitive microfollicular pattern & occasional macrofollicular pattern and absent colloid. At places, few clusters showed moderate anisonucleosis. Similar features can be seen in adenomatoid goitre. Hall TL et al [15] showed that distinction between adenomatoid goitre & a follicular neoplasm may be very difficult.

False negative case means case which is cytologically diagnosed as benign but later confirmed as neoplastic on histopathology. The false negative rate (FNR) in our study was 25% which is slightly higher when compared with Suen KC et al [16] study, in which the incidence of false negative FNA cytology results ranged from 1.5 to 11.5%. It may be because of small sample size of histopathology specimens for correlation. In our study, a case was diagnosed as benign-lymphocytic thyroiditis which on histological examination showed papillary carcinoma with chronic lymphocytic thyroiditis. On reviewing cytology slides of this case, smears showed clusters of follicular cells admixed with lymphocytes. At places, aggregates of follicular cells showed Hurthle cell change. Occasional clusters showed moderate anisonucleosis. It is possible that the needle did not enter the area of papillary carcinoma but might have hit only the areas of lymphocytic thyroiditis.

There were two cases (1.96%) diagnosed as follicular lesion of undetermined significance on cytology. Incidence is comparable with Cibas E et al study. [17] They reported an incidence ranging from 3-6%. The cases in our study turned out as follicular adenoma with lymphocytic thyroiditis and nodular goitre on histopathology. These cases could not be categorised into specific cytologic diagnosis. Cytology slides in one case showed mixed pattern of follicular cells and scant colloid in the background. At places, few clusters showed moderate anisonucleosis, nuclear crowding and occasional nuclear grooving. Differential diagnoses considered were hyperplastic nodule, follicular adenoma and follicular variant of papillary carcinoma. On histopathology, it was diagnosed as follicular adenoma with lymphocytic thyroiditis. Cytology slides of another case showed sheets and few clusters of follicular cells with scant colloid in the background. Occasional cluster showed anisonucleosis. On histopathology, confirmed as a case of nodular goitre. In hyperplastic stage of nodular goitre, follicular cells may show anisonucleosis and scant colloid.

CONCLUSION

FNAC is a rapid, simple, minimally invasive and cost-effective procedure in the investigation of thyroid swelling with good sensitivity, specificity and accuracy. It has high positive and negative predictive value. So, it effectively distinguishes thyroid lesions suitable for surgical resection with those that can be managed conservatively.

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How to cite this article: Murarkar PS, Sulhyan KR, Gosavi AV et al. Fine needle aspiration cytology in cases of thyroid swellings: one year study. Int J Health Sci Res. 2017; 7(4):77-83.

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