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ORIGINAL ARTICLE

Significance of Cell Pattern Approach in Fine Needle Aspiration Cytology of Thyroid Lesions.

Naresh Pahuja, Manisha Tambekar, Reeta Dhar, D.B.Borkar

Department of Pathology, MGM Medical College, Kamothe, Navi Mumbai.

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*Corresponding Author

Naresh Pahuja

Abstract

AIMS: To study the application of cell pattern analysis in the interpretation of thyroid lesions and to evaluate diagnostic accuracy of thyroid FNAC. **MATERIALS & METHODS:** A prospective study of 175 cases of thyroid FNAC were studied over a period of 2 years (May 2012- April 2014) in department of pathology of tertiary care hospital, Navi Mumbai. Two cases with inadequate aspirate were excluded from this study. The predominant cell pattern such as normofollicular/macrofollicular, microfollicular, cystic, syncytial, papillary and dispersed were noted in each case. The final diagnosis was given by viewing the cell pattern, cellular features and the background elements. The FNAC results were correlated with histological diagnosis in 50 cases. The sensitivity and specificity were evaluated. **RESULTS:** The normo/macrofollicular pattern was seen in 61.06% of nodular goitre and 7.69% of follicular neoplasm. Microfollicular pattern was predominantly seen in 76.92% of follicular neoplasm and 40% of papillary carcinoma. Syncytial pattern was seen in 40% of papillary carcinoma and 38.88% of Hashimoto's thyroiditis. Papillary pattern was seen in 20% cases of papillary carcinoma and cystic pattern was seen in 27.48% of nodular goitre. The diagnostic accuracy, sensitivity and specificity was 92%, 66.66%, 100% respectively. **CONCLUSION:** FNAC is a simple, sensitive, cost effective and diagnostic technique for evaluation of thyroid lesions. The combined approach of cell morphology, background details along with predominant cell pattern will be helpful in diagnosing thyroid lesions on FNAC and hence increasing diagnostic accuracy.

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Introduction

Fine needle aspiration cytology (FNAC) of thyroid gland is a first line diagnostic test for evaluation of goiter and most effective test for preoperative diagnosis of solitary thyroid nodule, thereby reducing unnecessary surgeries. Limitations of FNAC are because of inadequate sampling, overlapping cytological features and inexperience of cytologist¹. Depending upon the type of thyroid lesions the follicular cells might be arranged in different patterns like normofollicular/macrofollicular, microfollicular, cystic, syncytial, papillary, dispersed and these patterns were noted in each case^{1,2}. Therefore, in our study, the cytological diagnosis was arrived by identifying the predominant cell pattern along with cellular morphology and background elements. The final cytological diagnosis was correlated with histopathological diagnosis.

Material and Methods

A prospective study of 175 cases of thyroid FNAC were studied over a period of 2 years (May 2012 – April 2014) in department of pathology of tertiary care hospital, Navi Mumbai.

Before aspiration, physical examination of thyroid gland was carried out to assess its size, mobility during deglutition, its nodularity and clinical signs of thyrotoxicosis.

FNAC was performed using aspirate and non- aspirate technique. 10 ml syringe with 23-gauge needle were used. The aspirated material was smeared on slides, immediately fixed in 95% ethyl alcohol solution and staining was performed using Papanicolaou, Haematoxylin and Eosin and May-Grunwald Giemsa stains.

Cases in which sample was inadequate were excluded from this study. The predominant cell pattern (macrofollicular, normofollicular, papillary, syncytial, dispersed and cystic), cellular details and background elements were noted in each case. FNAC results were classified into: 1) Inadequate 2) Non-neoplastic 3) Neoplastic 4) Suspicious³. Preoperative FNAC diagnoses were correlated with the final histopathological diagnosis.

Among these 173 cases, histopathology of 50 cases was available for comparison. The specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of FNAC were calculated by using the formulae given below^{4,5}.

Sensitivity = True Positivity x 100 / True Positivity + False Negative.

Specificity = True Negative x 100 / True Negative + False Positive.

Negative predictive value = True Negative x 100 / False Negative + True Negative.

Positive predictive value = True Positive x 100 / False Positive + True Positive.

Accuracy = True Positive + True Negative x 100 / True Positive + False Positive + True Negative + False Negative.

Results

Predominant cell pattern in 173 cases were as follows [Table 1]

Table 1: Distribution of predominant cell pattern in different thyroid lesions.

Cytological Diagnosis	Normo / Macro follicular	Microfollicular	Papillary	Syncytial	Cystic	Dispersed	Total
Thyroglossal Cyst					2(100%)		02
Colloid Cyst					2(100%)		02
Nodular Colloid Goiter	80(61.06%)	13(9.92%)			36(27.48%)	2(1.52%)	131
Hashimotos Thyroiditis	1(5.55%)			7(38.88%)		10(55.55%)	18
Follicular Neoplasm	1(7.69%)	10(76.92%)		1(7.69%)	1(7.69%)		13
Hurthle Cell Neoplasm		1(100%)					01
Papillary Carcinoma		2(40%)	1(20%)	2(40%)			05
Anaplastic Carcinoma				1(100%)			01
Total	82	26	1	11	41	12	173

1. The Normo/Macrofollicular pattern

The normo/macrofollicular pattern is characterized by sheets, clusters, or intact follicles^{1,2}. This pattern was seen in 61.06% of nodular goiter and 7.69% of follicular neoplasms [Figure 1].

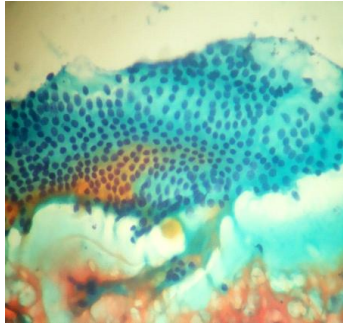


Figure 1: Follicular cells in normo/macrofollicular pattern (Pap, X40)

2. Microfollicular pattern

A microacinar arrangement of follicular cells without well-defined lumen is referred to as rosette. When lumen is well defined, it is called as micro follicle^{1,2} [Figure 2]. This pattern was seen in (76.92%) of follicular neoplasms, (40%) of papillary carcinoma, (9.92%) of nodular goiter and one case of hurthle cell neoplasm [Figure 2].

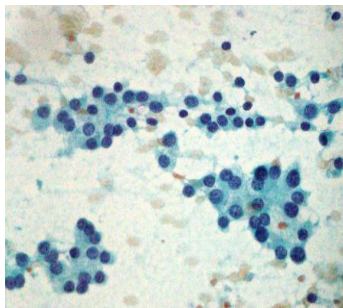


Figure 2: Follicular cells in microfollicular pattern (Pap, X40)

3. Papillary pattern

It is characterized by single or multilayered epithelial cells showing peripheral palisading of nuclei with fibrovascular core is called as papilla [Figure 3]. Papillae may show branching. Some of them are abortive without fibrovascular core^{1,2}. The papillary pattern was seen in 20% of papillary carcinoma [Figure 3].

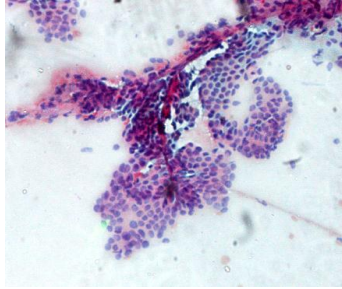


Figure 3: Follicular cells in papillary pattern (MGG, X10)

4. Syncytial pattern

Sheets of follicular cells with loss of polarity and lack of distinct cell borders is called syncytial pattern^{1,2}. This pattern was noted in 40% of papillary carcinoma, 38.88% of Hashimoto's thyroiditis and one case (100%) of anaplastic carcinoma [Figure 4].

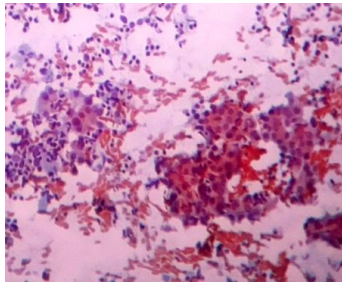


Figure 4: Follicular cells, Hurthle cells and lymphocytes arranged in syncytial pattern (Pap, X10)

5. Dispersed cell pattern

Loosely cohesive clusters and scattered follicular cells are referred to as the dispersed cell pattern^{1,2}. It was predominantly observed in 55.5% of Hashimoto's thyroiditis [Figure 5].

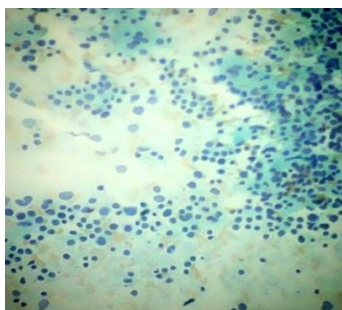


Figure 5: Follicular cells and lymphocytes are in dispersed cell pattern (Pap, X10)

6. Cystic pattern

This pattern shows presence of hemosiderin laden macrophages in a granular background^{1,2}. In our study, the cystic pattern was seen in 27.48% of nodular colloid goiter, 7.69% of follicular neoplasm, all cases of colloid cyst and thyroglossal cyst [Figure 6].

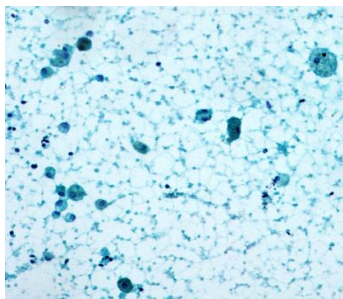


Figure 6: Hemosiderin macrophages & granular background in cystic pattern (Pap, X40)

Among the 173 cases, surgical specimens of 50 cases were received. The cyto-histopathological correlation [Table 2] was done. Concordance of diagnosis was seen in 34 cases of nodular goiter. Discordance was seen in 5 cases; among them, 1 case was diagnosed as papillary carcinoma, 3 as follicular adenoma and 1 case as Hashimoto's thyroiditis. Out of 3 cases of follicular neoplasm discordance was seen in one case which was confirmed as papillary carcinoma. One case of colloid cyst given on cytology was confirmed as colloid goiter with cystic change. All the cases of thyroglossal cyst, thyroiditis, hurthle cell neoplasm, papillary and anaplastic carcinoma were cyto - histopathologically concordant.

Table 2: Cyto-histomorphological correlation.

Cytology Diagnosis	Total Cases	Histopathology	
		Concordance	Discordance
Nodular Goiter	39	34	Papillary carcinoma. (01) Follicular Adenoma. (03) Hashimoto's thyroiditis with colloid goiter. (01)
Thyroglossal Cyst	01	01	
Colloid Cyst	01		Colloid Goiter .(01)
Thyroiditis	01	01	
Follicular Neoplasm	03	02	Follicular variant of Papillary carcinoma.(01)
Hurthle cell	01	01	

Neoplasm			
Papillary Carcinoma	03	03	
Anaplastic Carcinoma	01	01	
Total	50	43	07

Table 3: Accuracy of diagnostic test of FNAC in thyroid lesions.

Test(FNAC)	Benign on histopathology	Malignant on histopathology
Positive Test	False Positive [FP]	True Positive [TP]
Negative Test	True Negative [TN]	False Negative [FN]

Table 4: Correlation of FNAC and final histopathological diagnosis.

Histopathology	Benign Final Pathology Diagnosis	Malignant Final Pathology Diagnosis	Total
Cytopathology			
Neoplastic	FP = 00	TP= 08	08
Non- Neoplastic	TN = 38	FN = 04	42
Total	38	12	50

Over all sensitivity, specificity and diagnostic accuracy of FNAC in diagnosing thyroid lesions of thyroid were 66.66%, 100%, and 92% respectively. The positive predictive value and negative predictive value in diagnosing neoplasms were 100% and 90.47%, respectively [Table 5].

Table 5: Comparison of specificity, sensitivity and accuracy of FNAC with other studies.

Study	No. of FNA C	No.of Histology samples	Sensitivity	Specificity	PPV	NPV	Accuracy
GPS Yeoh, KW chan ⁵ . (1999)	1236	149	56%	90%	74%	80%	79%
Uma Handa et al ⁶ . (2008)	434	-	97%	100%	96%	100%	98.4%
Jyothi B. Lingegowda ⁷ . (2010)	219	219	67.7%	98.9%	88.9%	96%	95.4%
S.Gulia, M Chaudhary et al ⁸ . (2011)	140	52	100%	90%	100%	90.5%	92.3%
Arup Sengupta et al ⁹ .	178	20	90%	100%	100%	98.7%	98.88%

Pinki Pandey et al ¹⁰ .(2012)	447	112	57.14%	90%	80.28 %	70.58 %	83.33%
Komal Singh Likhar et al ¹¹ . (2013)	234	27	66.67%	100%	–	–	88.89%
Our study(2014)	173	50	66.66%	100%	100%	90.47 %	92%

Discussion

Thyroid enlargement is a common occurrence in most regions of the world and it has to be investigated to rule out the possibility of a neoplasm. FNAC is a safe, inexpensive and reliable technique in the initial evaluation of thyroid lesions along with other investigations like ultrasonography, thyroid function test, thyroid scan and antibody levels^{8,12}. The results obtained there by, can reduce the number of unnecessary surgeries. FNAC has an overall accuracy rate around 75% in the detection of thyroid malignancy³.

Specimen adequacy is the presence of five to six groups of well preserved follicular cells, with each group containing 10 or more cells^{1,8,13,14}. In our study, two cases could not be reported because of inadequate sample and were excluded from the study. This can be avoided from a combination of good aspiration technique and immediate examination of specimen adequacy by the cytopathologist. Interpretation of thyroid FNAC depends on recognition of various cellular patterns and morphology along with background elements like colloid and cystic macrophages etc.

The differential diagnosis of smears with predominantly normo/macro follicular pattern includes nodular goiter and follicular neoplasm^{1,2}. The presence of monolayered sheets of epithelial cells representing macrofollicles and degenerative changes with abundant colloid would suggest possibility of non-neoplastic lesions¹⁴. In our study, this pattern was predominant in nodular goiter (80/131) cases [Table 1]. One of five discordant cases was histopathologically diagnosed as papillary carcinoma. The cause of detection failure was the presence of minute foci of a papillary carcinoma that was missed during aspiration and this can be resolved by ultrasound guided aspiration^{7,15}. Three of five discordant cases of nodular goiter in our study were follicular adenomas [Table 2]. This was due to aspiration from colloid- rich macro follicular areas of neoplasm. Similar diagnostic pitfall was encountered by Guhamallick et al¹⁵ and Bommanahalli et al¹. One of the five cases in our study were diagnosed as Hashimotos thyroiditis with colloid goiter on histopathology [Table 2]. This finding was concordance with a study of Uma Handa et al in 2014⁶. In their study out of 45 cases of colloid goiter, 2 cases were diagnosed as thyroiditis with colloid goiter on histopathology. This might be due to overlapping of cytomorphological features or a geographical miss on aspiration.

The microfollicular pattern is predominantly seen in hyperplastic nodule, follicular adenoma, follicular carcinoma, follicular variant of papillary carcinoma (FVPTC) and thyroiditis^{1,2}. These are known as follicular-patterned lesions¹⁶. In our study, this pattern was predominantly seen in follicular neoplasm (10/13) cases [Table 1]. M S Deveci et al¹³ reviewed 339 FNAC cases of "follicular lesion" and reported a 22% of malignancy rate whereas our study showed 4% malignancy rate. One of three discordant cases of follicular neoplasm which was diagnosed as follicular variant of papillary carcinoma on histopathology [Table 2] was due to increased cellularity, presence of follicular structures and paucity of nuclear features of papillary carcinoma^{1,10,13,14,15,17}. Cellularity, nuclear size, pleomorphism of cell and amount of colloid are helpful to distinguish neoplastic from non-neoplastic lesions^{1,16}. Absence of colloid strongly favors diagnosis of neoplasm¹.

In Follicular neoplasm, nuclear enlargement if present is generally a uniform change involving most or all of the cells from the lesion whereas in Hyperplastic nodular goiter and Hashimotos thyroiditis nuclear enlargement and

pleomorphism (if present) is focal phenomena¹. Features highly suggestive of carcinoma include prominent nucleoli and necrotic debris in the background¹.

Follicular cells in syncytial pattern could be seen in papillary carcinoma, follicular/hurthle neoplasm and medullary carcinoma, along with thyroiditis^{1,2}. In our study, this pattern was mainly seen in thyroiditis (7/18) cases [Table 1], followed by papillary carcinoma, follicular neoplasm and anaplastic carcinoma. Observation of “lymphoid cells impinging on thyroid follicular cells” along with cellular details are useful to differentiate between various differential diagnosis^{1,18}.

The presence of papillae and pseudo papillae in an aspirate hints a differential diagnosis of Grave's disease, hyperplastic nodule and papillary carcinoma^{1,2}. Out of 5 cases of papillary carcinoma diagnosed on FNAC only one case (20%) showed predominantly papillary pattern followed by microfollicular (40%) and syncytial (40%). High cellularity, papillary tissue fragments with or without fibrovascular core and nuclear features (pale nuclei, finely granular powdery chromatin, intranuclear cytoplasmic inclusion and nuclear groove) are diagnostic of papillary thyroid carcinoma^{1,18,19}. Transpolar nuclear grooves in more than or equal to 20% of follicular cells is virtually diagnostic of neoplasm, most likely Papillary carcinoma^{1,2,22}. Presence of more than three intranuclear inclusions in the enlarged nuclei on single aspirate is almost pathognomonic of Papillary carcinoma of thyroid^{1,22}.

Dispersed pattern is commonly seen in thyroiditis and neoplastic lesions like hyalinising trabecular adenoma, hurthle cell neoplasm, medullary carcinoma and lymphomas^{1,2}. In our study this pattern was seen mainly in thyroiditis.

Cystic pattern/change is seen in developmental/congenital, hyperplastic and neoplastic entities like cystic papillary thyroid carcinoma and rarely in follicular neoplasm¹. In our study cystic pattern was seen in nodular goiter (36/131) cases [Table 1], followed by colloid cyst, thyroglossal cyst and follicular neoplasm. In cystic lesions, after aspiration fluid, attempt should be made to aspirated from solid area^{1,18}. Thus USG guided FNAC can become useful to aspirate from solid lesion. One case of colloid cyst was diagnosed as colloid goiter on histopathology. This was probably due to geographical miss when FNAC was done.

According to this study Normo/macrofollicular and cystic pattern was commonly seen in nodular goiter. Whereas syncytial, microfollicular and papillary were commonly seen in neoplasms and thyroiditis.

Out of total 50 cases of cyto-histomorphological correlation, 42 cases (%) were non- neoplastic and 8 cases (%) were neoplastic. Diagnostic accuracy, PPV and NPV were 92%, 100% and 90.47% respectively. These findings were comparable with S.Gulia et al⁸. study who reported diagnostic accuracy, PPV and NPV were 92.3%, 100% and 90.5% respectively.

The specificity of 100% in our study was similar with studies done by Uma Handa et al⁶, Komal singh likhar et al¹¹ and Arup sengupta et al⁹. [Table 5]. The sensitivity of 66.66% was correlating with studies done by Jyothi B. Lingegowda et al⁷ and Komal Singh Likhar et al¹¹. [Table 5] and they noted sensitivity of 67.7% and 66.67% respectively.

CONCLUSION:

FNAC of thyroid lesion is a simple, sensitive, cost effective and diagnostic technique for evaluation of thyroid lesions. The cell pattern approach in diagnosing thyroid lesions on FNAC raises differential diagnosis. By observing cell morphology, background details along with predominant cell pattern, final diagnosis can be clinched easily and accurately. Papillary, microfollicular, syncytial pattern are commonly seen in neoplasm. In our study, diagnostic accuracy, sensitivity and specificity was 92%, 66.66% and 100% respectively. Meticulous examination of all the smears for predominant cell pattern, cellular morphology & background details will be of great importance in minimizing false negative diagnosis in thyroid FNAC.

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