ORIGINAL ARTICLE

Fine Needle Aspiration Cytology of Follicular-patterned Thyroid Lesions

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ABSTRACT

Introduction: Fine needle aspiration cytology (FNAC) plays a vital role in diagnosing thyroid lesions. However, follicular-patterned lesions need to be evaluated meticulously due to markedly overlapping cytomorphological features.

Aim: To study the role of FNAC in follicular-patterned lesions of thyroid.

Materials and methods: A retrospective and prospective study of 50 cases in which thyroid FNAC showed follicular-patterned lesions along with histopathological correlation wherever available was done over a period of 3 years (January 2013–December 2015).

Results: Out of 50 cases of follicular-patterned lesions, 44 cases were reported as adenomatous goiter (AG), 3 cases each of follicular neoplasm (FN), and follicular variant of papillary thyroid carcinoma (FVPTC) on FNAC. Out of total 24 cases available for histopathological correlation, 5 cases (20.83%) showed discordance and the possible causes for the discordance were analyzed. The diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were 83.3, 42.9, 100, 100, and 81.0% respectively.

Conclusion: Diagnosing follicular-patterned lesions on FNAC is challenging and will remain a "gray zone" for all cytopathologists. Scrupulous and thorough examination of all cytological smears should be done for predominant follicular pattern along with cytomorphological and background details to differentiate follicular-patterned thyroid lesions in order to minimize false-negative diagnosis on FNAC.

Keywords: Fine-needle aspiration cytology, Follicular-patterned lesions, Thyroid.

INTRODUCTION

Thyroid nodular lesions are common clinical problems and need to be evaluated meticulously. Fine needle aspiration cytology of thyroid gland is primarily a "screening test" but is also helpful in diagnosing many thyroid lesions. Follicular-patterned lesions of thyroid fall in the "gray zone" of cytopathology. The differential diagnosis of the follicular-patterned lesions of thyroid comprises of AG/hyperplastic nodule, FN, and FVPTC.[1,2] Various cell patterns are seen on aspirates of thyroid follicular cells by FNAC. These include follicular pattern, which consist of normofollicular/macrofollicular and microfollicular pattern, papillary, syncytial, cystic, and dispersed pattern.[3]

Follicular-patterned lesions are the major cause of false-positive and false-negative results at FNACs. This is because of overlapping cytologic features found in follicular-patterned lesions. This present study was conducted to discuss the cytomorphological features of various follicular lesions and to find out the diagnostic pitfalls while reporting and decreasing the false-negative rates and increasing the sensitivity of FNAC in diagnosing follicular-patterned thyroid lesions.

In this study, the cytological diagnosis was given by observing the predominant follicular cell pattern, cellular details, and the background elements.

MATERIALS AND METHODS

A retrospective and prospective study of 50 cases of FNAC of follicular-patterned thyroid lesions was conducted over a period of 3 years (January 2013–December 2015). Institutional ethical committee approval was obtained prior to the commencement of the study. All the FNA smears of each case were studied thoroughly by correlating with age, sex, clinical details, and cytomorphological features and a definite cytological diagnosis was offered. The inclusion criteria of the present study were patients above the age of 15 years and cytological smears showing predominant follicular pattern on thyroid FNAC. Exclusion criteria were (a) patients less than 15 years and (b) inadequate smears.

The cytological diagnosis was correlated with histopathological diagnosis of those cases whose surgical specimens were received at our laboratory. The aims and objectives were to study the role of FNAC in the diagnosis of follicular-patterned thyroid lesions, to study cytomorphological features of various follicular-patterned lesions of thyroid, and to recognize diagnostic difficulties

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Table 1: Incidence of follicular-patterned thyroid lesions

Type of lesions	No. of cases	Percentage
AG	44	88
FN	3	6
FVPTC	3	6
Total	50	100

Table 2: Distribution of AG cases according to cytomorphological features

Cytological features	Parameters	No. of cases	Percentage
Cellularity	High	25	56.82
	Moderate	19	43.18
Predominant pattern	Macrofollicular	20	45.45
	Microfollicular	24	54.55
Colloid	Scanty	17	38.64
	Moderate	17	38.64
	Abundant	10	22.72
Macrophages	Present	15	34.10
	Absent	29	65.90
Hurthle cells	Present	16	36.36
	Absent	28	63.64

Table 3: Cytological–histological corelation

Cytological diagnosis	No. of cases	Histopathological diagnosis	
		Concordance	Discordance
AG	21	17	4
FN	1	0	1
FVPTC	2	2	0
Total	24	19	5

Table 4: Cytomorphological features of FN on FNAC

Cellularity	Pattern			Colloid	Hurthle cells	Nuclear features
	Macrofollicular	Microfollicular	Other			
H	0	3	SS (1)	+	–	Nuclear overlapping and crowding
H	0	3	SS (1)	–	–	Nuclear overlapping and crowding
H	1	3	SS (1)	–	–	Nuclear overlapping and crowding

(–): Absent; (+): Scanty; (++): Moderate; (+++): Abundant; 0: Absent; 1: Occasional; 2: Frequent; 3: Predominant; SS: Singly scattered; H: High; M: Moderate

Table 5: Cytomorphological features of FVTPC on FNAC

Cellularity	Pattern			Colloid	Hurthle cells	Nuclear features
	Macrofollicular	Microfollicular	Other			
M	0	3	SYN (1) SS (1)	–	–	Anisonucleosis, round, increased N:C ratio, intranuclear cytoplasmic inclusions, nuclear grooves, powdery chromatin, prominent nucleoli
H	0	3	–	–	–	Nucleomegaly, increased N:C ratio, intranuclear cytoplasmic inclusions, nuclear grooves, powdery chromatin, prominent nucleoli
H	1	3	SYN (1)	–	–	Round, increased N:C ratio, intranuclear cytoplasmic inclusions, nuclear grooves, powdery chromatin, prominent nucleoli

(–): Absent; (+): Scanty; (++): Moderate; (+++): Abundant; 0: Absent; 1: Occasional; 2: Frequent; 3: Predominant; SS: Singly scattered; SYN: Syncytial; H: High; M: Moderate

and pitfalls related to FNAC diagnosis. The results were analyzed using Microsoft Excel.

OBSERVATION AND RESULTS

Results are summarized in Tables 1 to 5 and three representative smears are shown in Figures 1 to 3.

There were a total of 24 cases where cytohistological correlation was available. Of these 21 cases had AG, 2 FVPTC, and 1 FN. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 42.9, 100, 100, 81 and 83.3% respectively.

DISCUSSION

A palpable thyroid nodule whether benign or malignant has always been a matter of concern and requires
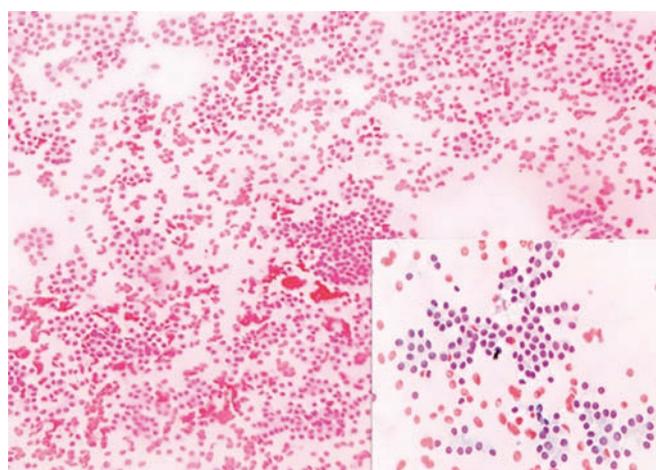
Fig. 1: Adenomatous goiter showing high cellularity. Inset showing macrofollicular and microfollicular pattern on a background of thin colloid. Papanicolaou stain, ×10
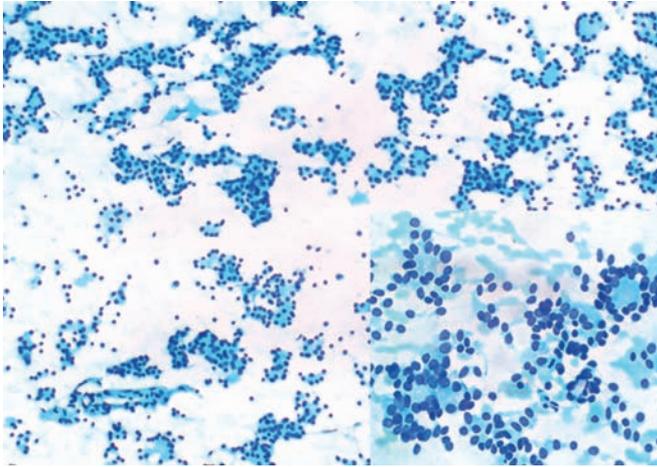
Fig. 2: Follicular neoplasm with high cellularity and cells arranged in predominantly microfollicular pattern, Papanicolaou (PAP) stain, ×10. Inset showing cellular overcrowding and overlapping, PAP stain, ×40
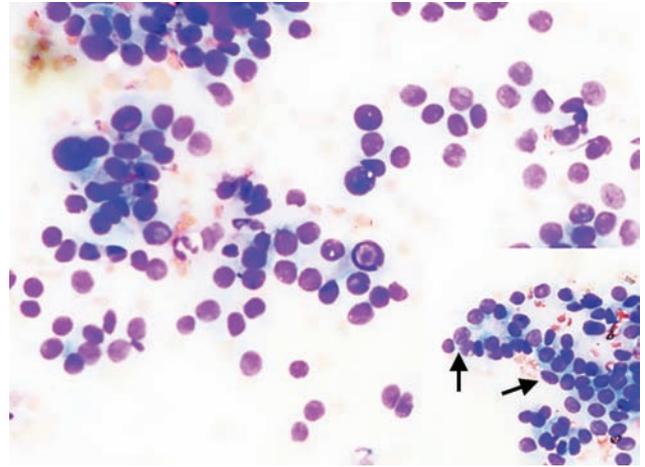
Fig. 3: Follicular variant of papillary thyroid carcinoma showing classical intranuclear cytoplasmic inclusions, ×40. Inset: Nuclear grooves (arrows), ×40. May–Grünwald Giemsa stain

thorough evaluation and management. Fine needle aspiration cytology being a simple, outpatient diagnostic procedure helps in providing a definitive diagnosis in all thyroid lesions so that further management can be appropriately carried out. On cytology, a thyroid lesion is designated as follicular when growth pattern of the lesion is either follicle forming or follicular patterning. The follicles are classified further based on their size as microfollicles or macrofollicles.[4]

This retrospective and prospective study was carried out over a period of 3 years (January 2013–December 2015). Out of a total of 348 cases of thyroid FNACs, 50 showed follicular-patterned thyroid lesions which included AG, FN (follicular adenoma and follicular carcinoma), and FVPTC.[1,2,5]

The incidence of follicular-patterned thyroid lesions was 14.36%, falling within the reported incidence of 5 to 29%.[6] Among the follicular-patterned thyroid lesions, the incidence of AG was 88% followed by FN (6%) and FVPTC (6%) (Table 1).

In this study, the patients ranged in age from 15 to 62 years with a mean age of 37.18 years. The commonest age group was 31 to 40 years (21 cases, 42%) followed by 21 to 30 years (10 cases, 20%), 41 to 50 years (8 cases, 16%), 51 to 60 years (5 cases, 10%), 11 to 20 years (4 cases, 8%), and 61 to 70 years (2 cases, 4%). Out of these 50 cases, 46 (92%) were females and 4 (8%) males, with male to female ratio of 1:11.5 showing female preponderance. The study conducted by Deveci et al[7] showed patients ranging in age from 16 to 87 years with an average age of 52 years and female preponderance where 372 cases were females and 87 were males. The study conducted by Mateša et al[8] also showed female preponderance with a male to female ratio of 1:4.8.

Out of these 50 cases, histopathological correlation was available in 24 (48%) cases. On histopathological examination, concordance was seen in 19 cases and discordance in 5 cases. Out of five discordant cases, three cases diagnosed as AG on FNAC were reported as follicular adenoma, one case diagnosed as AG on FNAC was FVPTC, and one case diagnosed as FN was FVPTC on histopathology.

Adenomatous Goiter

Adenomatous goiter in our study comprised the largest population of cases of follicular-patterned lesions with an incidence of 88% (44 cases) on FNAC, while other authors showed an incidence of 40 and 58.9%.[1,5] Of these, 41 patients were females and 3 males. Majority belonged to the age group of 31 to 40 years (18 cases, 36%) followed by 41 to 50 years (8 cases, 16%), 21 to 30 years (7 cases, 14%), 51 to 60 years (5 cases, 10%), 11 to 20 years (4 cases, 8%), and 61 to 70 years (2 cases, 4%).

Cytological smears of the 44 cases of AG in the present study showed 25 cases (56.82%) with high cellularity and 19 cases (43.18%) had moderate cellularity. About 24 cases (54.55%) showed predominantly microfollicular pattern and 20 (45.45%) macrofollicular pattern (Fig. 1); 17 cases (38.64%) showed moderate amount of colloid, 17 (38.64%) showed scanty colloid, and 10 (22.72%) abundant colloid. Macrophages, including cyst macrophages and hemosiderin-laden macrophages, were seen in 15 cases (34.10%) and were absent in 29 (65.90%) cases. Hurthle cells were present in 16 cases (36.36%) and were not seen in 28 cases (63.64%) (Table 2).

Among the 25 cases of AG with high cellularity, background and accompanying components, such as abundant colloid, cystic changes, stromal fragments, and follicular cells in honeycomb arrangement were observed. These were labeled as benign lesions.

Histopathological reports were available for 24 patients out of the total 50. Of these 24 cases, 17 were consistent

with AG and 4 showed discordance. Of the four discordant cases, three were diagnosed as FA and one as FVPTC (Table 3). Greaves et al[2] also observed similar discordance wherein three out of five lesions were diagnosed as AG on FNAC but turned out to be FA by histology. Guhamallick et al[9] observed similar discordance. Discordance in our cases might have occurred due to aspiration from colloid-rich macrofollicular areas of the neoplasm. This may be resolved by giving multiple passes through various sites of the lesion under ultrasound guidance.

Follicular Neoplasm

Incidence of FN was 6% (3 cases) of the total 50 cases of follicular-patterned lesions. Out of these, two cases (4%) were in the age group of 31 to 40 years and one case (2%) was in the age group of 21 to 30 years. Shobha et al,[1] in their study of 30 cases of follicular-patterned lesions, encountered 17 cases (56.66%) of FN. Of the three cases of FN, two were females and one was male.

All three cases of FN showed high cellularity, predominant microfollicular and dispersed pattern, nuclear overlapping, and crowding with no colloid (Fig. 2). However, one case showed macrofollicular pattern and scant colloid (Table 4). All these were diagnosed as FN on FNAC. Out of these three cases, histopathology was available only in one case and was diagnosed as FVPTC on histopathology. In Bommanahalli et al[10] study, out of the 12 cases of cytologically diagnosed FNs, three cases were confirmed to be as FVPTC on histopathology. This could be avoided by repeat aspirations from different parts of thyroid nodule.[9]

Follicular Variant of Papillary Thyroid Carcinoma

The incidence of FVPTC was 6% (3 cases) out of total 50 cases of follicular-patterned lesions. The studies done by other authors showed a higher incidence of FVPTC among the follicular-patterned lesions of thyroid. Shobha et al[1] found only one case of FVPTC out of 30 cases accounting to 3.34% of all the follicular-patterned lesions. In our study, all the three cases of FVPTC were females, two in the age group of 21 to 30 years and one in the age group of 31 to 40 years with a mean age of 29 years.

Smear examination of FVPTC cases in this study showed moderate to high cellularity with predominantly follicular pattern, characteristic nuclear features of PTC, and absence of colloid (Table 5). These findings correspond to published literature, in which cytological examination in FVPTC is characterized by hypercellularity with a prominent microfollicular pattern with a few syncytial follicular cells, but no obvious papillae and typical nuclear features in a proportion of cells, viz.,

pale powdery chromatin, intranuclear inclusions, nuclear grooves, and chewing gum colloid.[11,12]

Out of three cases of FVPTC, histopathology was available in two cases with 100% concordance. We gave a definitive diagnosis of FVPTC on FNAC based on moderate to high cellularity, typical nuclear features of papillary carcinoma with a predominant follicular pattern, and syncytial and dispersed pattern in one (Fig. 3). Third case of FVPTC which was wrongly diagnosed as AG on FNAC, discordance was due to absence of classic nuclear features of PTC, probably due to geographical miss on FNAC. Geographical miss can be resolved by performing ultrasound-guided aspiration. Wu et al[13] reported that the cytological diagnosis of FVPTC could be difficult because of the paucity of nuclear changes of PTC which can be mistaken as hyperplastic nodule. Baloch and Livolsi[4] diagnosed such lesions as suggestive of PTC and recommended intraoperative frozen sections or touch preparations for definitive diagnosis. Similar admixture of patterns was observed by Manimaran et al[14] in their study of 22 cases of FVPTC.

In this study, all the cases showed nuclear grooves and inclusions, nucleomegaly, powdery chromatin, and prominent nucleoli. Similar observations were made by Manimaran et al[14] and Aron et al.[15] Hurthle cells and psammoma bodies were not seen in any of our cases. Manimaran et al[14] reported similar results.

The sensitivity of a particular test is the statistical index of the diagnostic efficacy of the particular test. In the context of FNAC, it implies that if FNAC is positive, it definitely means the presence of disease, but if it is negative, it does not rule out the disease. In the present study, the sensitivity and specificity were 42.9 and 100% respectively. The study done by Shobha et al[1] showed a higher sensitivity of 70.6% and a specificity of 100%. Sharma[16] showed a sensitivity and specificity of 63.6 and 82.4% respectively. Overall diagnostic accuracy on FNAC for follicular-patterned lesions was 83.3%, whereas other authors showed a diagnostic accuracy of 80, 77, and 79%.[1,5,16] The positive and negative predictive values in our study were 100 and 81% respectively, whereas Sharma[16] showed a value of 43.75 and 91.3% respectively.

CONCLUSION

Fine needle aspiration cytology is a simple and inexpensive method of diagnosing non-neoplastic and neoplastic lesions of thyroid gland. The FNAC has low sensitivity for differentiating follicular adenoma from follicular carcinoma and hence, histopathological examination remains the gold standard for differentiating these two lesions. Due to overlapping cytomorphological features of benign and malignant follicular-patterned lesions, one should carefully look for nuclear features specific for

papillary thyroid carcinoma. Diagnosing follicular-patterned lesions on FNAC is challenging and will remain a "gray zone" for all cytopathologists. To decrease the rate of false-negative cases, FNAs should be performed under ultrasound guidance from different parts of the lesion. Scrupulous and thorough examination of all cytological smears should be done for predominant follicular pattern along with cytomorphological and background details to differentiate follicular-patterned thyroid lesions in order to minimize false-negative diagnosis on FNAC.

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