
Original Research Article

Follicular Lesions of Thyroid Cytopathology-Diagnostic Pitfalls

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Abstract

Context: Fine-needle aspiration (FNA) is well known non invasive tool for diagnosis of thyroid nodules thereby drastically reducing the number of surgeries. However the most common limitation of FNA is in follicular lesions termed 'follicular neoplasms'. This is due to the inability in differentiating benign follicular lesions from malignant. The aim of the study was to study the cytomorphology of follicular lesions of thyroid and to study the sensitivity and specificity of FNA in follicular lesions.

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Settings and Design: Retrospective study of 5 years duration from January 2011 to June 2016. All cases which have undergone both FNA and biopsy in our institute and diagnosed as follicular/hurthle cell adenoma, follicular/hurthle cell carcinoma and follicular variant of papillary carcinoma on histopathology are included.

Statistical analysis used: The data collected was tabulated and analysed by proportions and percentages. Statistical Package for the social sciences (SPSS) version 20.0 software was used to analyse the data.

Results: Out of the 39 cases studied, 14 were given a diagnosis of "follicular neoplasms" on FNA. 16 were given as benign lesions (nodular goitre, adenomatoid goitre, colloid nodule). One each reported as hurthle cell neoplasm and suspicious for malignancy. Seven cases reported as suspicious for papillary carcinoma. 10 out of 14 reported as follicular neoplasms on FNAC were benign and 4 were malignant on histopathology. The rate of malignancy was 35.8%. The most common malignancy was follicular carcinoma.

Conclusions: There was overlap between benign and malignant follicular patterned lesions on cytology. Follicular lesions prove to be a major challenge in the application of FNA in thyroid lesions.

Keywords: Fine-Needle Aspiration; Follicular Cell Carcinoma; Histopathology.

Introduction

Fine-needle aspiration (FNA) is a most important and widely accepted non invasive tool in the evaluation of thyroid nodules [1]. When

FNA was used in the diagnosis of thyroid lesions, the rate of thyroid surgery was reduced to half thereby significantly reducing the morbidity and health expenditures [2]. Follicular thyroid lesions account for 29% of all cytologic diagnoses. They

have generally been considered a “gray zone” in diagnostic thyroid cytology [1]. Because of overlapping cytologic features, differentiating benign and malignant follicular lesions becomes a challenge. The risk of carcinoma in a case of follicular neoplasm rendered on cytology is estimated at 20% to 30% [2]. Therefore many patients diagnosed with a follicular lesion by FNA undergo surgical excision for a definitive diagnosis. Follicular carcinoma traditionally has been considered the second most common malignant neoplasm of the thyroid (after papillary carcinoma) [3]. The use of FNA to distinguish benign from malignancy is difficult because the criteria for distinguishing between them are based upon histologic evidence of transcapsular or vascular invasion [3].

The aim of this study was to study the cytomorphology of follicular lesions of thyroid and correlate the cytological diagnosis with histopathologic diagnosis.

Subjects and Methods

It is a retrospective study of 5 years duration from January 2011 to June 2016. All the cases which have undergone both FNA and biopsy in SDM College of medical Sciences & Hospital and diagnosed as follicular lesions on histopathology are included. Information was collected regarding patient demographics (age, gender) and initial FNA diagnosis. A total of 39 cases who had undergone both FNA and surgery for histopathology were studied. FNA was performed using a 23 gauge disposable needle attached to a 5 ml syringe and suction applied. Minimum of 2 passes were done from different areas. Additional passes were carried out if the material did not meet the adequacy criteria after on site examination. The adequacy criteria included at least six clusters of thyroid follicular cells containing at least 10 cells/group in 2 slides after 2 passes. For histopathology routinely received surgical specimens in 10 % formalin were processed in automated tissue processor Leica 1020 used. Air dried Leishman and alcohol fixed pap, H & E stained FNA slides and H & E stained histopathological slides were retrieved. For purpose of this discussion, follicular lesions of the thyroid are defined as 1. Follicular adenoma and carcinoma, 2. Hurthle cell adenoma and carcinoma and 3. Follicular variant of papillary carcinoma of thyroid.

Statistical Analysis: The data collected was tabulated and analysed by proportions and

percentages. Statistical Package for the social sciences (SPSS) version 20.0 software was used to analyse the data. Statistical test like sensitivity, specificity, positive and negative predictive value were calculated.

Results

Among the 39 cases studied 28 (72%) were females and remaining 11 (28 %) were males. The youngest patient was 19 year old and the oldest patient was 73 year old. Mean age was 38.5 year. Majority were in the age group of 21-30 years. Right lobe was involved in 64% of cases followed by left lobe in 28%. In 8% of cases both the lobes were involved. The 39 cases studied were 19 follicular adenoma, 4 hurthle cell adenoma, 9 follicular carcinoma, 6 follicular variant of papillary carcinoma, 1 hurthle cell carcinoma.

14 out of 39 cases were reported as follicular neoplasms on FNAC. 16 cases were given as benign lesions (Nodular goitre-10, Colloid nodule-5, Adenomatoid goitre-1) on FNAC. Seven cases reported as suspicious for papillary carcinoma. One each reported as hurthle cell neoplasm and suspicious for malignancy (Table 1).

Among 14 cases reported as Follicular neoplasms on FNAC Majority of them 10 (71.4%) turned out to be benign conditions and only 4 (28.6%) were malignant on histopathology. Among these 10 cases 8 were follicular adenoma, 2 hurthle cell adenoma and 4 were follicular carcinoma. FNA smears of these cases showed high cellularity with repetitive follicles with scant colloid. Cells were uniform with

Table 1: FNA and Histopathologic diagnosis.

FNA Diagnosis	Histopathological Diagnosis				
	Benign		Malignant		
	FA	HA	FC	HC	FVPC
Follicular Neoplasms(14)	8	2	4	-	-
Suspicious for Papillary carcinoma/ Papillary carcinoma/ (7)	1	-	2	-	4
Hurthle cell neoplasm(1)	-	-	-	1	-
Suspicious for malignancy(1)	-	-	1	-	-
Benign lesions(Nodular goitre-10, Colloid nodule-5, Adenomatoid goitre-1)	10	2	2	-	2
Total(39)	19	4	9	1	6

* FA-Follicular adenoma, HA-Hurthle cell adenoma, FC-Follicular carcinoma, HC-Hurthle cell carcinoma, FVPC-Follicular variant of papillary carcinoma

minimal anisonucleosis. One case that was given as Hurthle cell neoplasm was Hurthle cell adenoma on histopathology.

Out of 7 cases of suspicious papillary carcinoma on FNA, four were follicular variant of papillary carcinoma. Three cases differed on histopathology among which one was follicular adenoma and 2 were follicular carcinoma. FNA smears of follicular variant of papillary carcinoma showed enlarged nuclei with nuclear crowding, grooves with overlapping. Papillae were not seen.

Out of 16 cases which were rendered other benign diagnosis on FNA viz nodular goiter, colloid nodule and adenomatoid goitre, ten cases were follicular adenoma, 2 were Hurthle cell adenoma, 2 were follicular carcinoma and 2 were follicular variant of papillary carcinoma. These cases were missed on FNA due to plenty of colloid and lack of repetitive follicles. One case reported as suspicious of malignancy on FNAC was follicular carcinoma on histopathology.

The rate of malignancy in the follicular neoplasms was 28.6%. Overall malignant follicular lesions in our study were 16 cases accounting for 41%. Thus the sensitivity of FNA for follicular lesions was 68.75% (80%-95% for thyroid nodules in general), specificity-52%, Positive predictive value -50% and negative predictive value of 70.5%.

Discussion

The rate of malignancy in the follicular neoplasms was 28.6%. Overall malignant follicular lesions in our study were 16 cases accounting for 41% of all cases. This was slightly higher than Deveci et al and Baloch et al [4,5]. Majority of the patients of follicular lesions were less than 40 years which was similar to Deveci et al [4]. There was a female preponderance in our study which was contrary to that of Deveci and Baloch [4,5]. Majority (58%) were less than 3 cms and the commonest malignancy encountered was follicular carcinoma (50%) (Table 2).

Microscopically benign thyroid follicular lesions were most commonly characterized predominantly by amacrofollicular pattern consisting of large clusters and sheets of follicular cells with small dark round nuclei in a background of moderate colloid (Fig. 1). This was similar to the study by Faquin et al. [6]. The flat sheets of cells result from fragmentation of macrofollicles with expulsion of colloid during the smear preparation [3]. The malignant lesions were predominantly composed of microfollicles (small follicular groups of 6-12 follicular cells in a ring with or without a small amount of central colloid) [3]. The follicular variant of papillary thyroid carcinoma on FNA can pose difficulty in the diagnosis on FNA especially when the nuclear

Table 2: Comparison of clinical and Histopathological parameters

Parameters	Present study	Deveci Sahil A et al	Baloch Zubair W et al
Rate of malignancy	35.8%	22%	30%
Age	57%	53%	20%
<40 years	43%	47%	80%
>40 years			
Sex	42.8%	41%	75.5%
Male	57.2%	33%	24.5%
Female			
Size	>3cm-42% <3cm-58%	-	>3cm-55% <3cm-23%
Commonest malignancy	FC-50%	FVPC-87.83%	FVPC-67.56%

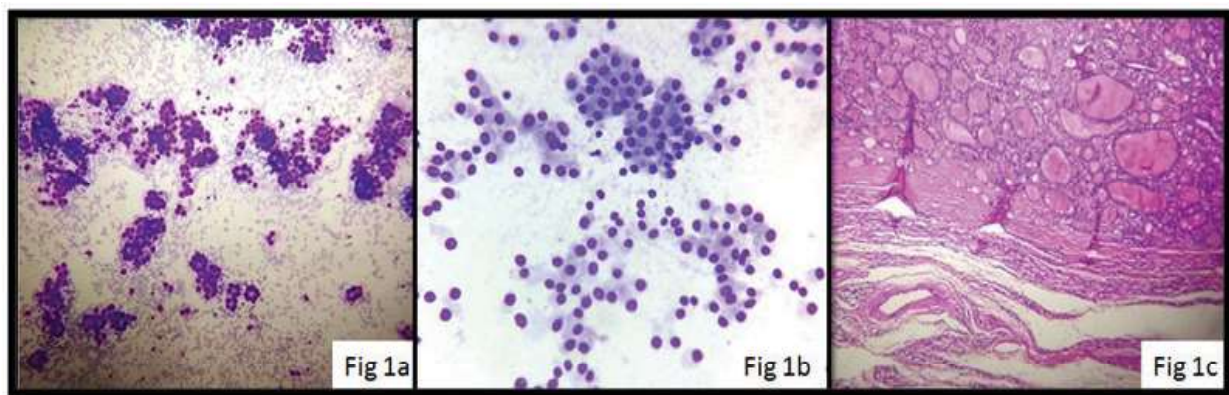


Fig 1: Follicular adenoma. Fig 1a: FNA (Leishman 10X)-Thyroid follicular cells arranged predominantly in repetitive follicular pattern. Fig 1b: FNA (Leishman 40X)-High power view of follicles. Fig 1c: Biopsy (H & E 10x) Follicles of varying sizes filled with colloid. Capsule is free from invasion.

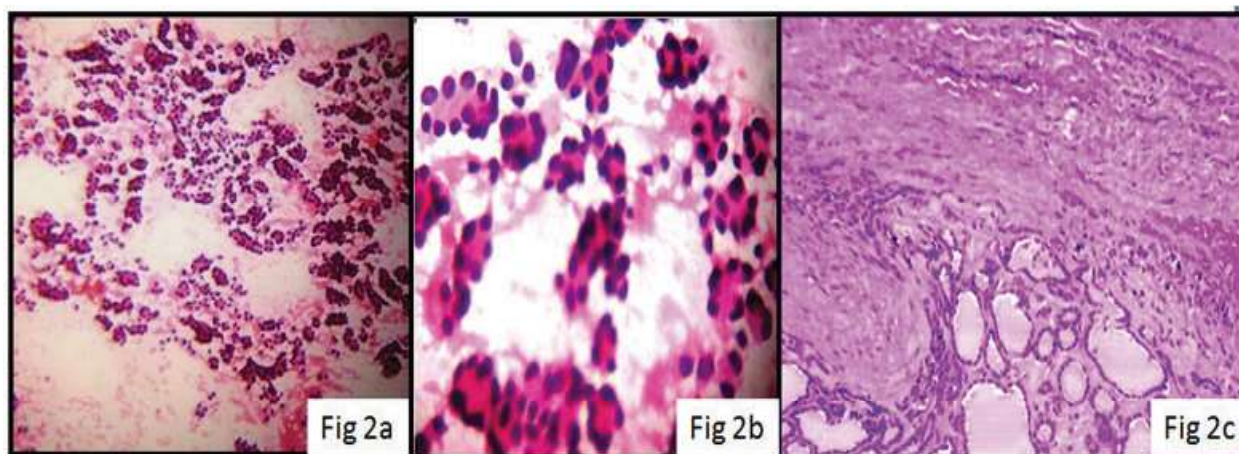


Fig. 2: Follicular carcinoma. Fig 2a:FNA (H & E 10X)-Thyroid follicular cells arranged predominantly in repetitive microfollicular pattern. Fig 2b:FNA (H & E 40X)-High power view of follicles. Fig 2c:Biopsy (H & E 10x) Follicles of varying sizes filled with colloid. Capsule is invaded by the follicular cells.

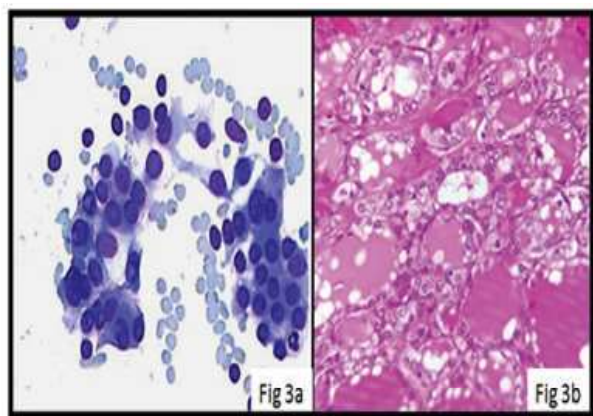


Fig 3: Follicular variant of papillary thyroid carcinoma. Fig 3a: FNA (Leishman 40X) Follicular sheets arranged in follicles and sheets. Most of the follicular cells show intranuclear inclusions. Fig 3b: Biopsy (H & E 40X) Follicles are lined by cells having optically clear nuclei and show intranuclear inclusions.

features are very subtle. The follicular variant of papillary carcinoma can present with microfollicles and can mimic a follicular neoplasm especially when the nuclear features like nuclear grooves and occasional intranuclear pseudoinclusions are lacking or are very subtle. But in a subset of cases, the nuclear features can be quite subtle resulting in misclassification of these lesions.

Hurthle cells are wide-polygonal eosinophilic cells which have a hyperchromatic nucleus and granular cytoplasm rich in mitochondria. These cells can also be seen in Hashimoto thyroiditis, nodular goiter and well-differentiated thyroid cancers [7].

Conclusion

In our study no distinguishing cytologic features between the benign and malignant follicular lesions were seen. There was an overlap between benign and malignant follicular patterned lesions on cytology. Thus follicular lesions prove to be a major challenge in the use of FNA in thyroid follicular lesions and remain a gray area in cytologic diagnosis of thyroid lesions. Further study with a larger study cohort is required to evaluate the combination of cytologic findings with specific clinical parameters (such as gender, age, and nodule size), which together may enhance preoperative risk stratification of patients with follicular thyroid lesions [1].

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