Research Article

Cytodiagnosis of thyroid lesions with histopathological correlation and evaluation of discrepant cases

Shaista Mushtaq Hamdani, Ruby Reshi

Department of Pathology, Government Medical College, Srinagar, Jammu and Kashmir, India.
Correspondence to: Shaista Hamdani, E-mail: shaistahamdani@gmail.com

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Abstract

Background: Fine-needle aspiration cytology (FNAC) of the thyroid gland is practiced worldwide as a very economical and reliable diagnostic procedure.

Objectives: To show the effectiveness of this inexpensive and simple procedure for the diagnosis of different thyroid lesions, particularly differentiation of malignant and benign lesions. We also sought to highlight the probable causes of error and possible remedies in the cases showing cytomorphological discrepancy.

Materials and Methods: A total of 180 cases of thyroid swellings were aspirated during our study period of 1 year (from November 2009 to October 2010). Cases were divided into six groups: (1) a nondiagnostic group where aspirate was inadequate and diagnosis was not offered; (2) a benign group that included different goiters and thyroiditis; (3) a group of lesions showing atypia of undetermined significance or follicular lesions of undetermined significance; (4) follicular neoplasm or suspicious of follicular neoplasm; (5) suspicious of malignancy; and (6) a malignant group that included nonfollicular malignant tumors of thyroid. Cases showing cytomorphological disparity were reevaluated.

Results: The overall accuracy of the technique was 88% with a sensitivity of 90.62%, a specificity of 85.71%, a positive predictive value of 89.65%, and a negative predictive value of 85.71%. Approximately 6% of cases could not be diagnosed because of inadequate aspiration. On histopathology, seven cases failed to show any cytohistological correlation.

Conclusions: FNAC is a minimally invasive, highly accurate, and cost-effective procedure for the assessment of patients with thyroid lesions and helps in differentiating lesions that require surgery from those that can be managed conservatively.

KEY WORDS: Fine-needle aspiration cytology, thyroid lesion, cytodiagnosis, histopathology discrepancy

Introduction

The diseases of thyroid gland are of great importance because most are amenable to medical and surgical management, and one of the most challenging tasks a modern physician faces is judging the nature of the thyroid lesion and thereby advocating precise and adequate management of thyroid lesions. The differential diagnosis of thyroid lesions is crucial as malignancy necessitates surgery whereas strict patient follow-up is necessary in case of benign lesions.[1]

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The diagnosis of thyroid lesions using aspiration cytology was first reported by Martin and Ellis in 1930.[2] Fine-needle aspiration of thyroid is now practiced worldwide and proven to be most economical and reliable diagnostic procedure to identify thyroid nodules that need surgical excision and thyroid nodules that can be managed conservatively.[3] Fine-needle aspiration biopsy (FNAB) is considered to be the "gold standard" in the selection of patients for surgery.[1] When FNAB was added to the diagnostic workup, the rate of thyroid

surgery was cut in half, which resulted in substantial savings in healthcare expenditures.[4]

The aim of this study was to evaluate the results of thyroid fine-needle aspiration cytology (FNAC) and correlate them with histology, wherever available. We also scrutinized the cases showing any discrepancy in cytohistological findings with the aim of establishing possible causes of errors.

Materials and Methods

This study was carried out in our department over a period of 1 year from November 2009 to October 2010. Thyroid swellings were aspirated using 23/24 gauge disposable needles fitted with 20 ml disposable syringes using standard procedures.[5] All the slides were stained with Geimsa stain, hematoxylin and eosin, and Papanicolaou stain following recommended steps.[6]

Diagnosis of cytological smears was carried out according to The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).[7] All the available resected samples were routinely processed, stained with hematoxylin and eosin, and correlation of cytological findings with histopathological diagnosis was carried out by descriptive statistical evaluation.

Cases with cytohistological disparity were selected, and case history and cytological smears of these cases were reevaluated for the detection of possible causes of failure.

Results

A total of 180 cases of thyroid swellings were aspirated during the study period and the diagnosis was made in 169 cases. Even after repeated aspirations at different sittings, 11 cases (6.11%) could not be diagnosed because of inadequate samples.

Of the 180 cases, 126 (70%) were from urban areas and 54 (30%) were from rural areas. The age of the patients ranged from 7 to 80 years with a mean age of 43.5 years and the female/male ratio was 6.5:1. The major presenting symptom in most of the patients (170) was diffuse swelling and/or nodular swelling of the thyroid. Other symptoms were less frequent pain in the thyroid region in eight patients, discomfort in the neck in two patients, and cervical lymphadenopathy in three patients. Patients mentioned a history of swelling being present for more than 1 year in 75 (41.66%) cases, 1–12 months in 77 (42.77%) cases, and within 1 month in 28 (15.55%) cases.

The thyroid swelling was diffuse in 88 (48.88%) cases and nodular in 92 (51.11%) cases. The swelling was tender in 6 (3.33%) cases and nontender in 174 (96.66%) cases. Majority of the swellings 172 (95.55%) were mobile whereas mobility was restricted in eight (4.44%) cases. The consistency varied from soft in 157 (87.22%), firm in 14 (7.77%), hard in 5 (2.77%), to cystic in 4 (2.22%) cases. Maximum number of patients presented with swellings ranging in size from 2.5 × 3 cm to 3 × 5 cm. Some patients presented with nodular swellings as small as 1 cm in diameter. The largest swelling measured 10 × 15 cm.

Thyroid function tests were performed in all the patients. Of them, 153 (85%) patients were found to be euthyroid, 15 (8.33%) hyperthyroid, and 12 (6.66%) hypothyroid. Hyperthyroidism was found in eight patients with solitary or multiple nodules, four patients with diffuse swelling, and three patients with thyroiditis. Of the 17 patients diagnosed with Hashimoto's thyroiditis, 7 (41.17%) patients showed a positive thyroid peroxidase antibody test. FNAC of 180 patients resulted in the diagnoses shown in Table 1.

Majority of the cases reported cytologically were benign (125), followed by malignant (26), and follicular or suspicious of follicular neoplasm (12). Follicular neoplasms and Hurthle

Table 1: FNAC results of 180 patients based on TBSRTC[7]

FNAC diagnosis	Number of patients (%)
I. Nondiagnostic/ Unsatisfactory	11 (6.11)
II. Benign	
Adenomatoid nodule, colloid nodule	106 (58.88)
Hashimoto's thyroiditis	17 (9.44)
Subacute thyroiditis	2 (1.11)
III. Atypia of undetermined significance (AUS)/Follicular lesion of undetermined significance	2 (1.11)
IV. Follicular neoplasm/suspicious of follicular neoplasm	
Follicular neoplasm	10 (5.55)
Hurthle cell neoplasm	2 (1.11)
V. Suspicious of malignancy	4 (2.22)
VI. Malignant lesions	
Papillary carcinoma	24 (13.33)
Medullary carcinoma	1 (0.55)
Anaplastic carcinoma	1 (0.55)

FNAC, fine-needle aspiration cytology; TBSRTC, the Bethesda system for reporting thyroid cytopathology; AUS, atypia of undetermined significance

Table 2: Histopathology results of 50 patients

HPE results	No. of patients	% Age (n = 50)
Colloid and adenomatoid Goiter	20	40
Follicular and other adenomas	9	18
Hashimoto's thyroiditis	1	2
Papillary carcinoma	19	38
Medullary carcinoma	1	2

HPE, histopathological examination

Table 3: Correlation of cytological and histopathological diagnosis (n = 50 patients)

Cytological diagnosis	Histopathological diagnosis								
	Colloid goiter	Hashimoto's thyroiditis	Adenomatous goitre	Follicular adenoma	Hyalinising trabecular adenoma	Hurthle cell neoplasm	Papillary carcinoma	Medullary carcinoma	Total
Colloid goiter/ colloid nodule	17	–	–	–	–	–	3	–	20
Hashimoto's thyroiditis	–	1	–	–	–	–	–	–	1
Follicular neoplasm	–	–	1	7	1	–	1	–	10
Hurthle cell neoplasm	–	–	–	–	–	1	–	–	1
Papillary carcinoma	1	–	–	–	–	–	14	–	15
Medullary carcinoma	–	–	–	–	–	–	–	1	1
Suspicious of malignancy	1	–	–	–	–	–	1	–	2
Total	19	1	1	7	1	1	19	1	50

cell neoplasms cannot be classified as benign or malignant lesions by cytology alone.[5] The benign group included benign follicular nodules such as adenomatoid nodule and colloid nodule and different cases of thyroiditis whereas all malignant lesions without any overt follicular architecture were included in the malignant group. Two cases showed focal features suggestive of papillary carcinoma, including nuclear grooves, enlarged nuclei with pale chromatin, and alterations in nuclear contour and shape in an otherwise predominantly benign-appearing sample. These were categorized as lesions with atypia of undetermined significance (AUS). Two of the cases showed only one or two features of papillary thyroid carcinoma (PTC) that were focal and not widespread through the follicular cell population. These were diagnosed as suspicious of malignancy.

Of the total 180 patients whose FNAC was carried out in our department, 50 underwent surgery in this hospital. The resected specimens of these patients were subjected to histopathology and the results obtained are shown in Table 2.

FNAC and histopathological findings in operated cases were compared [Tables 1 and 2] and the accuracy of FNAC for detection of benign and malignant lesions was evaluated taking histopathology as the reference standard test. Table 3 shows correlation of cytological diagnosis and histopathological diagnosis in these cases.

Discussion

Thyroid enlargement, whether diffuse or in the form of a nodule, leads to a battery of investigations, mainly to rule out the possibility of a neoplasm or thyroiditis. FNAC is usually the first line of investigation and other investigations such as ultrasound examination, thyroid function tests, thyroid scan, and antibody levels are carried out subsequently with an aim to select the patients who require surgery and those that can be managed conservatively.[8,9]

FNAC of the thyroid is widely used as it is safe, rapid, inexpensive, and reliable in the diagnosis of thyroid nodules.[10] The overall accuracy of FNAC exceeds 90%.[11] The sensitivity and accuracy of FNAC is as high as 95% in experienced hands. Positive predictive value of 90%–98% and a negative predictive value of 94%–99% have established FNAC as an individual diagnostic modality.[12] However, in some cases, the cytological findings are equivocal and histological diagnosis is essential. Distinction between follicular adenoma and well-differentiated follicular carcinoma, and diagnosis of malignancy in the presence of chronic thyroiditis and diagnosis of cystic papillary carcinoma by FNAC are still controversial.[13]

There is a variation between different rates calculated by various authors. The overall sensitivity and specificity in our study was 90.62% and 85.71%, respectively. The accuracy of the FNAC in comparison to histopathological examination was 88%. Bakhos et al.[19] observed that sensitivity, specificity, and accuracy of FNAC were 93%, 96%, and 88%, respectively, which is almost similar to those reported in the present study. They, however, reported that in various studies conducted on the said subject, as reported in the literature, sensitivity of the thyroid FNAC ranges from 65% to 99% and specificity from 72% to 100%, depending on the proficiency of both the aspirator and the interpreter.

Of the total 50 cases that turned up for cytohistological correlation, there were 7 cases with cytohistological discrepancy. These cases were evaluated for possible sources of error and methods to rectify these problems.

Case 1: Cytological smears showed abundant colloid with moderate number of follicular cells arranged in sheets and

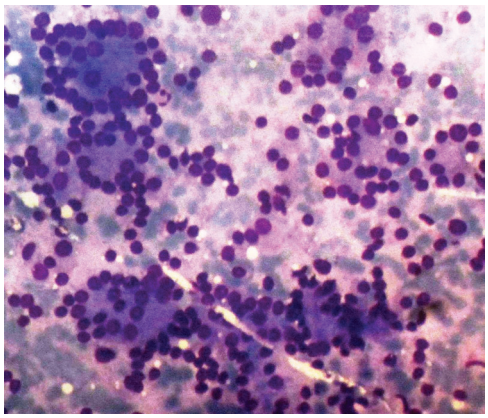

Figure 1: Photomicrograph showing thyroid follicular cells in syncytial clusters forming microfollicles in a repetitive manner diagnosed as follicular neoplasm on cytology (Geimsa, 40 ×).

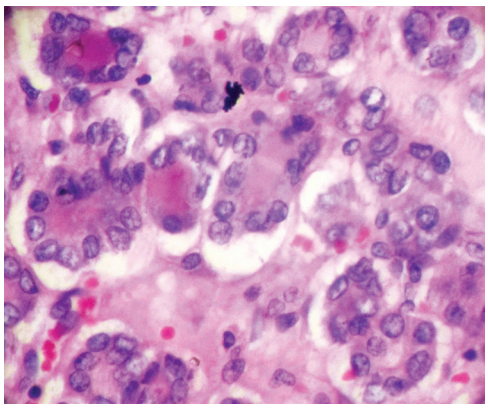

Figure 2: Photomicrograph of the same case as above diagnosed as follicular variant of papillary thyroid carcinoma with typical nuclear features of papillary carcinoma on histopathological examination (H&E, 40 ×).

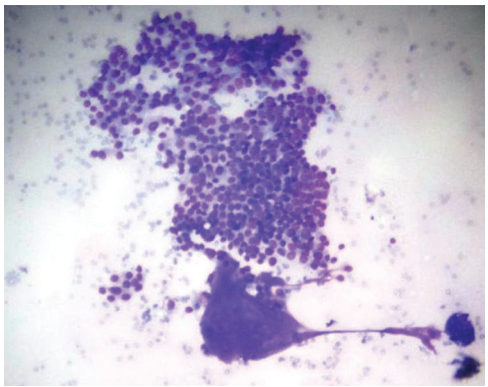

Figure 3: Photomicrograph showing thyroid follicular cells forming papillary structures with distinct anatomical border and "chewing gum" colloid in a case of papillary carcinoma of the thyroid (Geimsa, 10 ×).

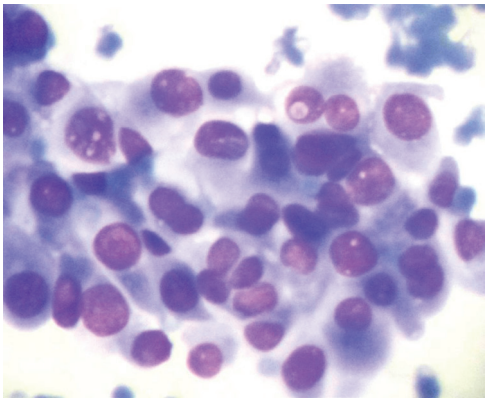

Figure 4: Photomicrograph showing dense metaplastic cytoplasm of the cells and intranuclear cytoplasmic inclusion in a case of papillary carcinoma of the thyroid (Geimsa, 40 ×).

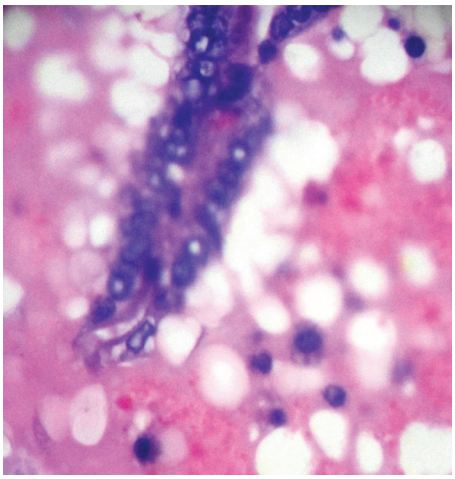

Figure 5: Photomicrograph showing papillary carcinoma with cystic degeneration which is a common pitfall in the diagnosis of such lesions on cytology (H&E, 40 ×).

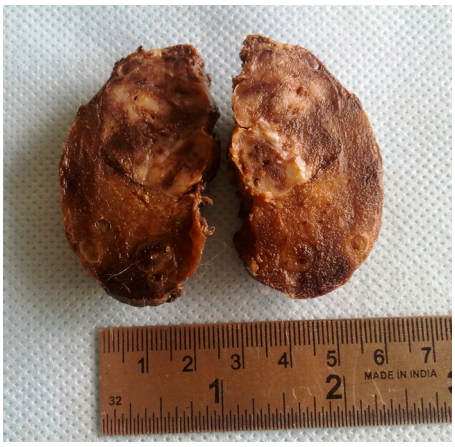

Figure 6: Gross photograph of a thyroid lobe showing papillary carcinoma occupying one pole with surrounding parenchyma showing changes of colloid goiter. The aspiration from the surrounding parenchyma could have led to the wrong diagnosis of colloid goiter that could be avoided by USG-guided FNAC of the specific target site.

occasional macrophages favoring the diagnosis of nodular colloid goiter. Histology of this case showed the presence of microscopic focus of papillary carcinoma 8 mm in diameter. The cause of detection failure was possibly the presence of small minute focus of papillary carcinoma of thyroid that was missed during aspiration. Similar cases have been reported by others.[14,15]

Case 2: Cytological smears showed clusters of follicular cells arranged in clumps with scanty colloid favoring the diagnosis of a follicular neoplasm of thyroid. The histology though showed the features of a nodular colloid goiter. Aspiration was probably carried out from the hyper cellular areas of colloid nodules, which led to overdiagnosis. A possible remedy is multiple aspirations from different parts of the swelling that could demonstrate hypocellular, polymorphic, and colloid-rich areas. Demonstration of mono-layered sheets of epithelial cells representing macrofollicles and degenerative changes would suggest the possibility of nonneoplastic lesions.[14]

Case 3: Cytological smears showed numerous follicular cells arranged in clusters, often with syncytial cell aggregation. There was prominent nuclear crowding and overlapping without any colloid favoring the diagnosis of a follicular neoplasm [Figure 1]. The presence of follicular structure led to misinterpretation, as has been reported by others.[15] On histological examination, the case was diagnosed as follicular variant of papillary carcinoma (FVPTC) with typical nuclear features of a papillary carcinoma [Figure 2]. A possible remedial measure could be to repeat aspirations from different parts of gland, which could unravel the typical nuclear features of papillary carcinoma.

Case 4: Cytological smears were moderately cellular showing numerous macrophages, thick colloid, cohesive clumps, and sheets of follicular cells arranged in vague papillary patterns with nuclear crowding and overlapping. A few cells contained moderate amount of blue cytoplasm and round nucleus with pale open chromatin. Intranuclear inclusions were demonstrated in a few cells. The cytological features were thus suggestive of papillary thyroid carcinoma. The histology, however, showed features consistent with nodular colloid goiter. Misinterpretation of partly degenerated nonneoplastic follicular cells as cells of PTC, too much stress on papillary architecture and intranuclear inclusions were probably the causes of error in this case. Multiple samples collected from different parts of the lesion could help in proper diagnosis. For cytodiagnosis of PTC, the three most important features suggested are papillary structures with distinct anatomical border and without adherent blood vessels [Figure 3], intranuclear cytoplasmic inclusions and dense metaplastic cytoplasm of cells [Figure 4].[16] Attention to these features can lead to decrease in the wrong diagnosis of PTC.

Case 5: Cytological smears showed hypocellular smears with occasional thyroid follicular cells and moderate amount of thin colloid favoring the diagnosis of a colloid cyst. The gross as well as microscopic examination of the resected specimen showed cystic degeneration of one thyroid lobe obscuring the part of the gland harboring the papillary carcinoma [Figure 5]. Occurrence of cystic change in thyroid lesions is a common diagnostic pitfall in cytology. Ultrasonography (USG)-guided FNAC of the exact lesion could help in proper diagnosis in such cases.[17]

Case 6: Cytological smears showed moderate cellularity with small clumps of thyroid follicular cells arranged in poorly cohesive groups with a few colloid drops suggesting the diagnosis of nodular colloid goiter. Although histological features were consistent with papillary carcinoma, on gross examination, the lesion was occupying one of the poles of the thyroid lobe [Figure 6], which might have been missed by the needle at the time of aspiration. Again USG-guided FNAC of the specific target site could help in proper diagnosis.[17]

Case 7: Cytological smears showed abundant thyroid follicular cells arranged in small acini, clusters, and mono-layered sheets with nuclear crowding and overlapping. Occasional cells showed abundant blue cytoplasm with monomorphic round nucleus having pale, powdery chromatin, and nuclear grooves suggestive of FVPTC. Histology showed features of colloid goiter. The nuclear features in a few cells in this case were overinterpreted and the overall benign nature of the aspirate was overlooked. A detailed clinical examination and multiple aspirations from different sites would be the possible remedial measures.[18]

Conclusion

FNAC is an inexpensive and quick procedure that is also highly sensitive and specific in categorization of thyroid lesions. The positive influence of FNAC on the management of thyroid disease is perhaps best highlighted in the low rate of surgical intervention. Surgery was avoided mainly in colloid goiter and thyroiditis. We have also discussed the pitfalls encountered by us and possible inexpensive remedies for them in this report.

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