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Hurthle cells in thyroid FNA: mimic or a dilemma? Is it possible to accurately differentiate non-neoplastic from neoplastic hurthle cell lesions?

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Abstract

Introduction: Hurthle cells (HC) are an enigma in thyroid lesions, from being a misnomer, their association with a variety of thyroid nodules and their unpredictable clinical behavior. These can be seen in many thyroid lesions ranging from inflammatory conditions, benign neoplasms and malignant lesions. This study was done to assess the spectrum of hurthle cell lesions of thyroid on cytology and try to establish features that can accurately differentiate between non-neoplastic and neoplastic thyroid lesions.

Materials and Methods: The thyroid FNA cases done during Jan 2015- Dec 2015 were collected from the archives of pathology department. Those cases were collected for study where the cytological diagnosis of hurthle cell lesions was made. The diagnosis was divided into follicular neoplasm, hurthle cell neoplasms and thyroid lesions with hurthle cell change. Cytohistological correlation was done wherever possible.

Observations & Results: 101 cases contained hurthle cells were identified and studied. The cytological diagnosis was 27 follicular neoplasms (FN) (26.7%), 04 hurthle cell neoplasms (HCN) (3.9%), 51 adenomatous goiter (50.5%) and 19 Hashimotos thyroiditis (HT) (18.8%). Of 27 FN, 22 were diagnosed as FA and 5 as FC. Of 4 HCN, 2 were diagnosed as HCA, 1 as HCC and 1 as PTC on histopathology.

Conclusion: Hurthle cells can be found in a large number of thyroid lesions both neoplastic and non-neoplastic. Although no particular finding can differentiate between non-neoplastic and neoplastic hurthle cell containing lesions but certain cytological features can help to diagnose the neoplastic nature of these lesions.

Keywords: Hurthle cells, Thyroid, Histopathology, Papillary

Introduction

Thyroid nodules are not uncommonly found in clinical settings and Fine needle aspiration cytology (FNAC) is an established tool in the diagnosis of these nodules. The nodules in thyroid can range from inflammatory conditions to benign thyroid neoplasms to malignant ones.[1,2] FNAC does a considerably good job in differentiating these conditions especially if done under ultrasound (USG) guidance but some lesions can pose considerable diagnostic challenges to the cytopathologist and dilemma to the clinician.[2]

Hurthle cells (HC) are an enigma in thyroid lesions, starting right from being a misnomer, their association with a variety of thyroid nodules and to add, their unpredictable clinical behavior. First coined way back in 1894 by a German pathologist Karl Hurthle from which it derives its name, those cells were actually parafollicular cells but the name remained associated. Max Askenazy made the actual discovery of hurthle cells 4 years later and thus these cells are also called as Askenazy cells although hurthle cell is still the more popular term used. Another synonym used for these cells is oncocytes/oxyphil cells, which have similar morphological appearance but are used more commonly in salivary gland lesions.[1,2,3,4]

Morphologically, hurthle cells are large polygonal cells with abundant finely granular cytoplasm, central nucleus and prominent nucleoli. The granularity is due to the presence of many large vacuolated mitochondria in the cytoplasm ultrastructurally along with paucity of other organelles.[1,3,4]

These cells can be seen in a variety of thyroid lesions ranging from inflammatory conditions i.e. Hashimotos thyroiditis (HD), benign neoplasms i.e. follicular adenoma (FA), hurthle cell adenoma (HCA) and malignant lesions i.e. follicular carcinomas (FC) and hurthle cell carcinomas (HCC) It can also be seen in variants of medullary (MTC) and papillary carcinoma (PTC).[2,3,4,5] No definite cytological criteria are presently used to differentiate between benign and malignant HC neoplasms and also because these are present in a wide number of thyroid nodules, the presence of HC can be a dilemma for the pathologist as well as the clinician. The WHO classifies HCA and HCC as oncocytic variants of FA and FTC respectively. Despite this, HCC is considered by many to be a distinctly separate entity by virtue of its distinct genetic profile and clinically more aggressive behavior when compared with PTC and FTC.[3,4,6,7]

This study was done to assess the spectrum of hurthle cell lesions of thyroid on cytology and try to establish features that can accurately differentiate between non-neoplastic and neoplastic thyroid lesions.

Materials and Methods

This was a retrospective study conducted in the department of pathology SGRDIMSR, Amritsar from January 2015 to December 2015 after taking the

necessary approval from the institution. The thyroid FNA cases done during this period were collected from the archives of pathology department. Those cases were collected for study where the cytological diagnosis of hurthle cell lesions was made. Further division was done on the basis whether histopathological examination for those hurthle cell lesions was done or not.

The cytological diagnosis was divided into follicular neoplasm, hurthle cell neoplasms and thyroid lesions with hurthle cell change (thyroiditis, adenomatous goiter) depending on the cytological features i.e. cellularity, presence or absence of colloid, lymphocytes, cellular dyscohesion and nuclear features. Those cases that underwent biopsy and underwent histopathological examination were also studied and cyto-histological correlation was done with regards to the presence of hurthle cells and final histopathological diagnosis. Sensitivity and specificity of FNAC in accurately diagnosing the hurthle cell lesions of thyroid was then calculated.

Observations and Results

A total of 623 thyroid FNAC were done in the above-mentioned period out of which 101 cases contained hurthle cells (16.2%) and were enrolled in the study. The age of these patients ranged from 21 to 83 years. The commonest age group was 21-40 years. M:F ratio was 3.6:1.

The cytological diagnosis was 27 follicular neoplasms (FN) (26.7%), 04 hurthle cell neoplasms (HCN) (3.9%), 51 adenomatous goiter (50.5%) and 19 Hashimotos thyroiditis (HT) (18.8%). (Table 1)

All of 27 FN and 4 HCN underwent surgical resection. Of 27 FN, 22 were diagnosed as FA and 5 as FC. Of 4 HCN, 2 were diagnosed as HCA, 1 as HCC and 1 as PTC. Of 51 cases of cytologically diagnosed adenomatous goiter, 39 underwent surgery and were diagnosed as multinodular goiter (MNG) (35 cases), FCA (3 cases), and PTC (1 case). 6/19 cases of HT were surgically excised and there was 100% cytohistological correlation among these lesions. (Table 1)

Table 1: Cyto-histological correlation of cases that underwent surgical excision

Diagnosis	**Follicular neoplasm**		**Hurthle cell neoplasm**			**Adenomatous goiter**			**Hashimotos thyroiditis**
FNAC	27		04			39			06
Histopathology	FA: 22	FC: 05	HCA 02	HCC 01	PTC 01	MNG 35	FCA 03	PTC 01	06

On basis of the above correlation certain parameters were enumerated that could possibly determine the neoplastic character of hurthle cell containing lesions.

Discussion

Thyroid FNAC is a routinely done, safe, rapid and an effective procedure for diagnosis of various thyroid lesions. Hurthle cells are a common presence in various thyroid lesions, which can range from non-neoplastic (HT, adenomatous goiter) to neoplastic lesions (FA, FCC, HCA, HCC, PTC and MTC).[1,2,3,4,6,7,8]

According to our study, 16,2% of total thyroid FNAC were comprised of hurthle cells in varying proportions which is in line with what various other studies have reported. Commonest age group affected was 21-40 years, which also corroborates well with what other authors have reported. Males outnumbered females in the ration of 3.6:1 that again correlates with other reported age groups.[1,2,4,5,7,8,9]

Cytologically, the diagnosis varied from FN (26.7%) to HCN (3.9%) to adenomatous goiter (50.5%) to HT (18.8%). Similar results have been quoted in other published studies by various authors.[2,4,5,9,10] Follicular neoplasm was diagnosed when there was predominantly micro follicular pattern on FNAC and scant colloid with presence of hurthle cells as a minor component. Hurthle cell neoplasm was diagnosed if the above features were present with >70% of the cells being hurthle cells. Definite evidence of malignancy could not be ascertained on cytology as evidence of capsular or vascular invasion could be identified only on histopathology. A diagnosis of adenomatous goiter was made in the presence of abundant colloid and presence of macro follicles. Cases of HT included intense lymphocytic infiltrate and formation of lymphoepithelial lesions.

On histopathology, 7/31 combined cases of FN and HCN were diagnosed as malignant (22.5%) which is in line with the reported malignancy rate of 20-30% in postoperative cases of cytologically diagnosed cases of FN and HCN.[1,2,3,4] Case of HCN was diagnosed as PTC on histopathology. This was due to the presence of large cells with abundant eosinophilic granular cytoplasm in majority of the slide that led to the mistaken diagnosis of HCN on FNAC (Fig. 1). Histopathology however showed typical features of papillary carcinoma with nuclear clearing, inclusions, overlapping along with presence of above-mentioned cells.

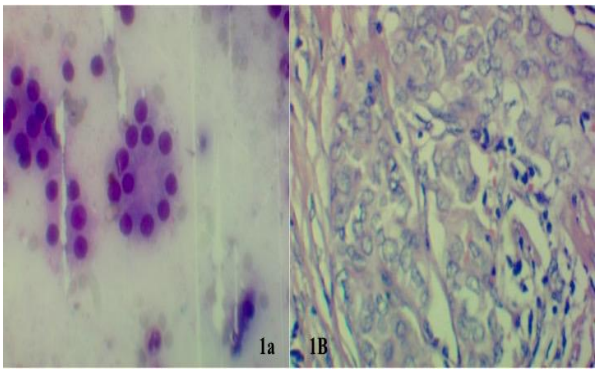

Fig. 1a: FNAC with cytological diagnosis of hurthle cell neoplasm showing follicular epithelial cells with hurthle cell change forming micro follicular pattern (MGG 400X). Fig 1b: Histopathology showing papillary carcinoma with nuclear features of papillary carcinoma with abundant eosinophilic cytoplasm

Of 39 cases that underwent surgical resection for adenomatous goiter, it correlated with histopathology in 35 cases (89.7%) whereas 3 cases were diagnosed as FCA (Fig. 2) and 1 case as PTC (Fig. 3). Various studies have reported the incidence of malignancy in reported cases of adenomatous goiter between 9-30%.[1,2,3,4,11,12,13] In our study however, the rate was much lower (2.5%). The false diagnosis of adenomatous goiter in 3 cases of FCN was due to the presence of predominant macrofollicular pattern on FNAC with presence of colloid (Fig. 2). False diagnosis in case of PTC was due to the presence of follicular pattern on FNAC and presence of cystic change in an adenomatous goiter in which papillary carcinoma developed which was evident on histopathology (Fig. 3). Therefore PTC can be called a great gimmick, as it can be included in the differential diagnosis of non-neoplastic, benign neoplasms as well as malignant neoplasms due to its varied presentations. Other cases of hurthle cell neoplasms correlated well with histopathology. (Fig. 4)

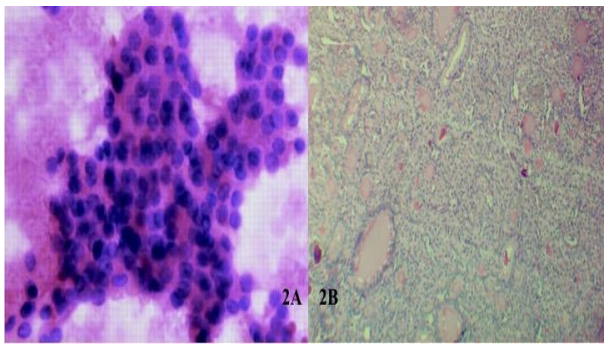

Fig. 2 a: FNAC showing follicular epithelial cells with colloid in the background (MGG 400X), b: Histopathology of same case exhibiting follicular neoplasm with presence of macro follicles in between filled with colloid (H&E 100X)

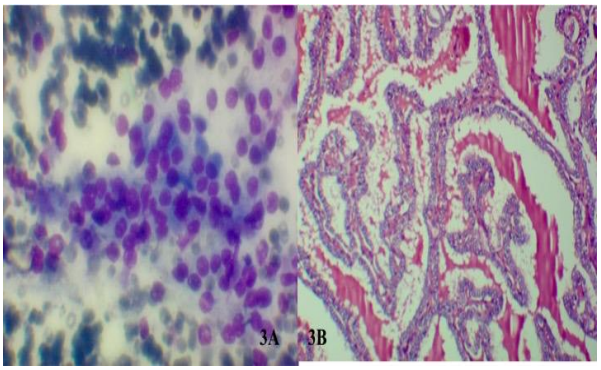

Fig. 3a: FNAC of cytological diagnosis of adenomatous goiter showing follicular epithelial cells with colloid in the background (MGG 400X), b: Histopathology of same case exhibiting features of papillary carcinoma arising in a cystic change in adenomatous goiter. (H&E 100X)

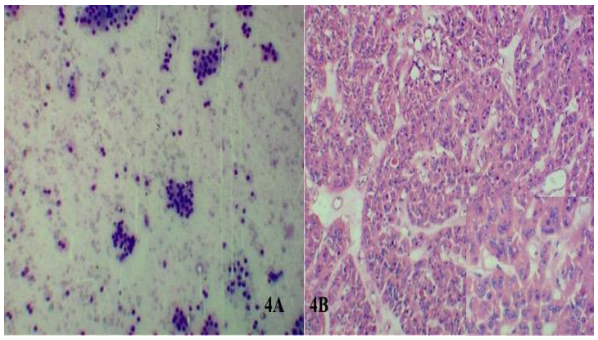

Fig. 4a: FNAC of cytological diagnosis of hurthle cell neoplasm showing hurthle cells in predominant micro follicular pattern (MGG 100X), b: Histopathology of same case confirming hurthle cell adenoma. (H&E 100X) Inset showing abundant eosinophilic cytoplasm of hurthle cells (H&E 400X)

All cases of HT were proven on histopathology and thus there was 100% concordance in theses lesions, which were diagnosed by the presence of abundant lymphocytic infiltrate, presence of lymphoid follicles in some cases and evidence of lymphoepithelial lesions.

Conclusion

Hurthle cells can be found a large number of thyroid lesions both neoplastic and non-neoplastic. Although no particular finding can differentiate between non neoplastic and neoplastic hurthle cell containing lesions but it can be safely stated that high cellularity, monomorphism (absence/paucity of non hurthle cells, microfollicular pattern, prominent nucleoli, nuclear enlargement and atypia, intranuclear inclusions, scant colloid and absence of lymphocytes point towards a possible diagnosis of a neoplastic lesion whereas polymorphism, honeycombing/ macrofollicular pattern, absence of nucleoli/ nuclear enlargement/ atypia, abundant colloid and presence of lymphocytic

infiltrate favor a diagnosis of non-neoplastic thyroid lesion.

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