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Original Research Article

Oncocytic Lesions in Thyroid: A Prospective Cytomorphological Study in Uttar Pradesh, India

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Abstract

Background: Fine needle aspiration cytology (FNAC) is considered an essential step in the thyroid workup. Altered follicular cells are known as oncocytic cells, oxyphilic cells, Hurthle cells or Askanazy cells. Oncocytic cells may be encountered in a number of thyroid conditions.

Aims: To study the cytomorphological features of oncocytic lesions in thyroid aspirates.

Settings and Design: Hospital based and prospective study.

Methods and Material: The present study was a prospective study (June 2016 to November 2017) carried out in the Department of Pathology. Patients recommended for FNAC by the clinicians were incorporated into the study. Aspirated material was stained with Giemsa stain and Papanicolaou stain. Stained smears were subjected to microscopic examination.

Statistical Analysis: Chi square test was used.

Results: A total of 240 cases were included in present study. Oncocytic cells were seen in 154 cases. Oncocytic cells were seen in both neoplastic as well as non-neoplastic lesions of thyroid. In oncocytic cell positive cases, majority of cases were of Hashimoto's thyroiditis. Neoplastic lesions had cells in sheets without intra epithelial lymphocytes with no to scanty colloid.

Conclusions: Hashimoto's thyroiditis is most common thyroid lesion in this area. Oncocytic cells when present in follicles, large clusters or multilayered sheets & scanty colloid favor the diagnosis of neoplastic lesions. Abundant colloid favors the non neoplastic lesions.

Keywords: Cytology; FNAC; Hurthle Cells; Hashimoto's Thyroiditis; Oxyphilic Cells.

Introduction

Fine needle aspiration cytology (FNAC) of the normal thyroid tissue yields colloid and sheets of follicular cells together with similar dissociated cells [4,19]. Modified thyroid follicular cells with oxyphilic transformation are commonly known as oncocytic cells, oxyphilic cells, Hurthle cells or Askanazy cells. They have a characteristic granular eosinophilic cytoplasm. Mitochondrial proliferation is the reason of their granular and eosinophilic cytoplasm[2].

Variable number of oncocytic cells in thyroid aspirates is seen in various non-neoplastic and neoplastic lesions of thyroid [6, 11, 16, 17, 20, 23, 25]. Number and morphology of Oncocytic cells vary in thyroid aspirates [5].

The study was undertaken to study the cytomorphological features of oncocytic lesions in thyroid aspirates.

Methods

The present study was conducted in the department of Pathology, in a tertiary teaching hospital. This was a prospective type of study for duration of one and half year i.e. June 2016 to November 2017. Permission from the ethical committee of the college was taken. All the recommended patients underwent FNAC, wherever possible. The sample thus obtained was spread over a clean glass slide with minimum pressure to minimize cellular damage, to preserve cytologic details and the pattern of distribution. Smears were prepared and stained with Giemsa stain while alcohol fixed smears were stained with Papanicolaou stain.

Adequacy of sample was assessed as per the Bethesda system of reporting thyroid cytopathology, i.e. a minimum of six groups of follicular cells in that contain at least 10 cells each. Exceptions being, abundant colloid, lymphocytic abundance or any atypia [7].

All the cases advised for thyroid FNAC, falling in between the specified period of time interval were included while smears with marked crushing artefacts, acellular smears and massively hemorrhagic smears were excluded.

Results

In this study, recommended patients with enlargement of thyroid gland (both nodular and diffuse) were subjected to FNAC and their cytomorphology was studied in MGG and PAP stained smears. A total of 240 cases were found fit under inclusion criteria.

The patients studied were categorized into 2nd to 6th decade of life. The maximum number of cases belonged to 3rd decade accounting for 100/240 (41.67%). In all cases, male to female ratio was 1:1.58. Chi-Square test was applied to know the significance of age and sex in thyroid lesions and it was found statistically not significant (Table 1).

The various lesions in thyroid were distributed as per diagnosis. The maximum number of cases were of Hashimoto's thyroiditis i.e. 108/240 (45.00 %), followed by colloid goitre 85/240 (35.42%), follicular epithelial hyperplasia 21/240 (8.75%), follicular neoplasm 08/240 (3.33%), medullary carcinoma 04/240 (1.67%), papillary carcinoma 10/240 (4.17%) & oncocytic cell neoplasm 04/240 (1.66%). Follicular and Oncocytic cell neoplasms were confirmed on histopathology.

Out of 240 cases, Oncocytic cells were noted in 154 cases (64.17%). In oncocytic cell positive, majority of cases were of Hashimoto's thyroiditis (n=94 cases; 61.04%) followed by colloid goitre (n=43 cases, 27.92%), follicular epithelial hyperplasia with foci of oncocytic cells accounted for 10 cases (i.e. 6.49%), oncocytic variant of follicular neoplasm 02 cases (1.30%), oncocytic variant of papillary carcinoma 01 case (0.65%) and Oncocytic cell neoplasm were accounted for 04 case (2.60%) [Figure 1].

On the basis of arrangement of cells in various lesion containing oncocytic cells, out of 154 cases, 92 cases had monolayer sheets, 18 cases had single cells, 33 cases had small clusters (follicles) and 11 cases had large clusters. Out of 04 cases of oncocytic cell neoplasm, 03 cases had large loose clusters & 01 case had small cluster.

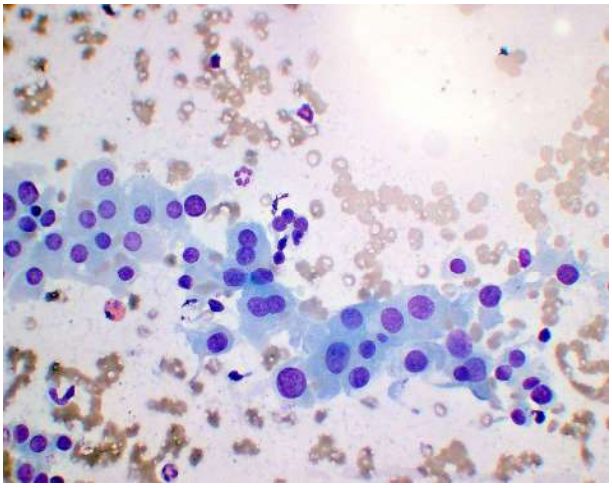

Fig. 1: Sheets of oncocytic cells with abundant finely granular cytoplasm. (MGG x 400)

Table 1: Age & sex distribution of patients in thyroid lesions and Oncocytic cell containing lesions

Age group (in yrs)	Total Thyroid Lesions Studied			Oncocytic Cell Containing Lesions		
	Cases distribution (Number with %)	Female	Male	Cases distribution (Number with %)	Female	Male
11-20	22 (9.17%)	15	07	12 (7.79%)	08	04
21-30	100 (41.67%)	65	35	72 (46.75%)	51	21
31-40	55 (22.91%)	32	23	33 (21.43%)	25	08
41-50	35 (14.58%)	20	15	22 (14.29%)	15	07
51-60	28 (11.7%)	15	13	15 (09.74%)	09	06
Total	240	147	93	154	108	46

Chi-Square test was applied to know the significance of arrangement of cells in oncocytic cell containing Hashimoto's thyroiditis and it was found statistically significant (p value<0.05).

In oncocytic cell positive cases cellular cohesion was seen in 136 cases. In oncocytic cells positive cases cellular cohesion was seen in 90 cases of Hashimoto's thyroiditis. Absence of cellular cohesion was seen in 03 cases of oncocytic cell neoplasms. Chi-Square test was applied to know the significance of cellular cohesion in oncocytic cell containing Hashimoto's thyroiditis & other thyroid lesion, & it was found statistically significant (p value <0.05) (Table 2).

Out of 154 cases, 101 cases had intra-epithelial lymphocytes & 53 cases had no intra-epithelial lymphocytes. In 94 cases of oncocytic cell containing Hashimoto's thyroiditis all the cases had intra-epithelial lymphocytes [Figure 2]. All cases of oncocytic cell containing oncocytic variant of follicular neoplasm, oncocytic variant of papillary carcinoma and oncocytic cell neoplasm showed absence of intra-epithelial

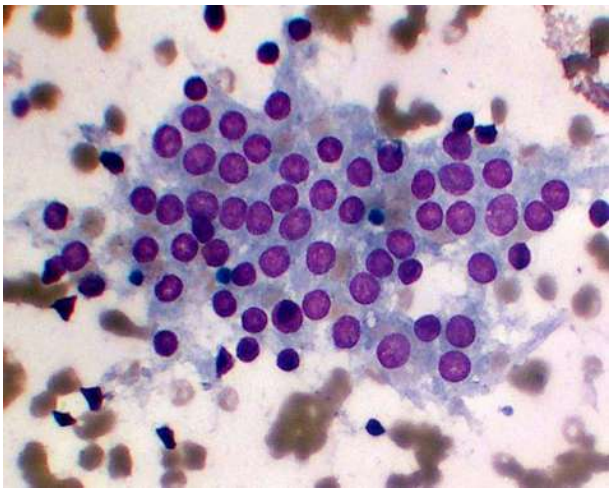

Fig. 2: Oncocytic cells with intra epithelial lymphocytes in Hashimoto's thyroiditis. (MGG x 200)

Table 2: Arrangement of cells and cellular cohesion in various Oncocytic cell containing lesions

Diagnosis	Number of cases	Arrangement of cells (Predominant pattern)				Cellular cohesion	
		Sheets (Mono-layer)	Small clusters (Follicles)	Large loose clusters (overlapping)	Single cell	+nt	—nt
Hashimoto's thyroiditis	94 (61.04%)	67	18	04	05	90	04
Colloid goitre	43 (27.92%)	21	09	01	12	35	08
Follicular epithelial hyperplasia with foci of oncocytic cells	10 (06.49%)	04	05	00	01	09	01
Oncocytic variant of Follicular neoplasm	02 (91.30%)	00	00	02 (loose arrangement)	00	01	01
Oncocytic variant papillary carcinoma	01 (0. 65%)	00	00	01 (loose arrangement)	00	00	01
Hurthle Cell Neoplasm	04 (02. 60%)	00	01	03(loose arrangement)	00	01	03
Total	154	92	33	11	18	136	18

Table 3: Evaluation of intra%epithelial lymphocytes and plasma cells in various Oncocytic cell containing lesions

Diagnosis	No. with %	Percentage of Oncocytic cells as compared to Follicular cells			Intra -epithelial Lymphocytes		Plasma cells	
		<10%	10—50%	>50%	+nt	None	None	—nt
Hashimoto's thyroiditis	94 (61.04%)	29	55	10	94	00	94	00
Colloid goitre	43 (27.92%)	35	08	00	05	38	05	38
Follicular epithelial hyperplasia with foci of oncocytic cells	10 (06.49%)	08	02	00	01	09	01	09
Oncocytic variant of Follicular neoplasm	02(91.30%)	00	02	00	00	02	00	02
Oncocytic variant papillary carcinoma	01(0.65%)	00	01	00	00	01	00	01
Hurthle Cell Neoplasm	04 (02.60%)	00	00	04	01	03	00	04
Total	154	72	68	14	101	53	100	54

lymphocytes. Chi-Square test was applied to know the significance of intra-epithelial lymphocytes in oncocytic cell containing Hashimoto's thyroiditis & other thyroid lesions, & it was found statistically significant (p value<0.05). (Table 3).

Out of 154 cases of oncocytic cell containing lesions of thyroid, 124 cases had no fire flares & 30 cases had fire flares [Figure 3]. Out of 94 cases of oncocytic cell containing Hashimoto's thyroiditis, 76 cases had no fire flares & 18 cases had fire flares.

Out of 94 cases of oncocytic cell containing Hashimoto's thyroiditis, 90 cases had none to scanty colloid, 04 cases had moderate amount of colloid. None to scanty colloid was seen in 02 cases of oncocytic variant of follicular neoplasm, one case of oncocytic variant of papillary carcinoma and 03 cases of oncocytic cell neoplasm [Figure 4].

Table 4: Evaluation of macrophages, colloid and fire flares in various Oncocytic cell containing lesions

Diagnosis	No. with %	Macrophages			Colloid			Fire Flares	
		None	Few	Many	Scanty/absent	Moderate	Abundant	+nt	—nt
Hashimoto's thyroiditis	94 (61.04%)	46	29	19	90	04	00	18	76
Colloid goitre	43 (27.92%)	04	18	21	10	25	08	10	33
Follicular epithelial hyperplasia with foci of oncocytic cells	10 (06.49%)	09	01	00	08	02	00	01	08
Oncocytic variant of Follicular neoplasm	02 (91.30%)	01	01	00	02	00	00	01	02
Oncocytic variant papillary carcinoma	01 (0.65%)	01	00	00	01	01	01	00	01
Hurthle Cell Neoplasm	04 (02.60%)	04	00	00	03	01	00	00	04
Total	154	65	49	40	114	32	08	30	124

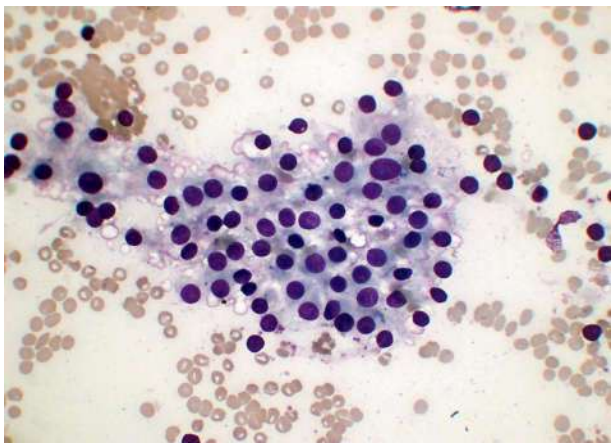

Fig. 3: Follicular epithelial hyperplasia with fire flares. (MGGx400)

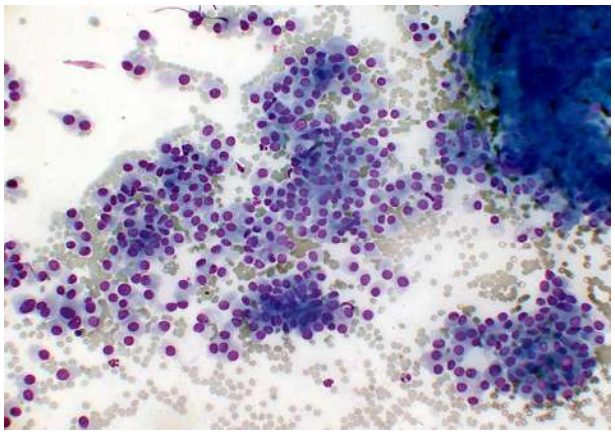

Fig. 4: Dispersed oncocytic cells with abundant granular cytoplasm and mild anisokaryosis in oncocytic cell neoplasm (MGGx200)

Chi-Square test was applied to know the significance of colloid in oncocytic cell containing Hashimoto's thyroiditis & other thyroid lesions, & it was found statistically significant (p value <0.05). Correlation of macrophages, colloid and fire flares is depicted in Table 4.

Discussion

Fine needle aspiration cytology (FNAC) plays a pivotal role in thyroid workup. Oncocytic cells represent an adaptive mechanism of thyroid follicular cells characterized by cytoplasmic accumulation of mitochondria with some morphologic, genetic, and functional abnormalities [1,10,26]. Non neoplastic conditions with oncocytic cell changes are -Hashimoto's thyroiditis, long standing Graves's disease, multi nodular goitre, and thyroid gland with previous history of local radiotherapy or systemic chemotherapy [22]. Neoplastic lesions with oncocytic cell change are oncocytic cell adenoma, Variants of Papillary Thyroid Carcinoma (oncocytic, Tall cell, & Warthin like variant), oncocytic variant of medullary carcinoma and oncocytic variant of follicular carcinoma [11]. Hashimoto's thyroiditis is characterized by oncocytic cell change and increase in number of mature and transformed immature lymphocytes impinging on follicular cell clusters [3].

A total of 240 cases were included in the present study. Out of 240 thyroid aspirates, 214 (89.17%) were non neoplastic lesions & 26 (10.83%) were neoplastic lesions.

This was in accordance with study of Sharma et al. [27]. In non neoplastic lesions, maximum cases were of autoimmune thyroiditis (108 cases, 45%) followed by colloid goitre (85 cases, 35.42%) and follicular epithelial hyperplasia (21 cases, 8.75%) which was at variance with study of Sharma et al, which showed colloid goitre was most common non-neoplastic lesion.

In neoplastic lesions, maximum numbers of cases (10 cases) were of papillary carcinoma, followed by 08 cases of follicular neoplasms and 04 cases each of medullary carcinoma and Oncocytic cell neoplasm. This was in accordance with study of Sharma et al. [27].

In the study of Handa U et al., the most frequently encountered lesion was the colloid goiter in 250 (57.60%) cases followed by thyroiditis in 119 (27.41%) cases, ten (2.30%) adenomatous goiters and two (0.004%) thyroglossal cysts. In the neoplastic group, 14 (1.38%) cases were reported as follicular/Oncocytic cell neoplasms and 17 (3.91%) as malignant tumors. These findings were at variance with present study, it may be because of small sample size in present study [14].

Oncocytic cells were seen in 154 cases (64.17%). Out of 154 cases, 147 cases (95.45%) were non-neoplastic & 07 cases (4.55%) were neoplastic. In non-neoplastic cases, maximum cases were of Hashimoto's thyroiditis (94 cases, 61.04%) followed by colloid goitre (43 cases, 27.92%) and follicular epithelial hyperplasia (10 cases, 6.49%). In neoplastic lesions, maximum number of cases were of Oncocytic cell neoplasm (04 cases, 2.60%) followed by 02 cases (1.30%) of oncocytic variant of follicular neoplasm and 01 case (0.65%) of oncocytic variant of papillary neoplasm. This was in accordance with study of Turanli et al. [29].

In present study, patients belonged to 2nd to 6th decade of life. Maximum number of cases belonged to 3rd decade accounting for 100/240 (41.67%). A minimum no. of patients 22/240(9.17%) were seen in 2nd decade. Male to female ratio was 1:1.58 in the present study. This was in accordance with the other studies [13,28].

Oncocytic cell containing lesions were mostly in 3rd decade accounting for 46.75% and minimum in 2nd decade (7.79%). A female predominance was observed in all decades of life. In this study, male to female ratio for all Oncocytic cell containing lesions was 1:2.38. This was in accordance to a study conducted by Yazgan et al. [31].

Vodanovic et al .observed that in their study of 12051 FNA's of the thyroid, 40 were cytologically diagnosed as Oncocytic cell tumors (0.33%) [30]. In present study, Oncocytic cell neoplasms were seen in 2.60% cases. Reason of this difference may be due to small sample size in present study. In present study, out of 154 cases, 92 cases (59.74%) had monolayered sheets, 33 cases (21.43%) had small clusters/ follicles cases (9.74%), 11 cases (7.14%) had large clusters and 18 cases (11.69%) had single cells. In non-neoplastic lesions, majority of cases showed monolayered sheets whereas multilayered sheets were more commonly seen in neoplastic lesions. This was in accordance with the other studies [8,24,30].

In present study, out of 154 cases of Oncocytic cell containing lesion of thyroid, 72 cases (46.75%) had less than 10% Oncocytic cell, 68 cases (44.16%) had 10-50% Oncocytic cells, and 14 cases (09.09%) had 50-90% Oncocytic cells. The results were found to be statistically significant ($p<0.005$). The presence of more than 90% of Oncocytic cells as compared to follicular cells favoured a diagnosis of neoplastic lesions (100%) over non-neoplastic lesions. Gonzalez et al. also found a statistically significant cytologic difference between Oncocytic cell tumours and non-neoplastic Oncocytic cell lesions [12].

In Oncocytic cell containing lesions, cellular cohesion was seen in 136 cases (88.31%) while it was absent in 18 cases (11.69%). The results were found to be statistically significant ($p<0.005$). Majority of cases in non-neoplastic lesions showed nuclear cohesion whereas 71.42% cases of neoplastic lesions showed nuclear dyscohesion. This was in accordance with Yazgan et al. [31]. The presence of lymphoid cells virtually excluded the presence of neoplastic lesions in the current study. Lymphocytic infiltration was exclusively associated with Hashimoto's thyroiditis (100%), extensively in chronic lymphocytic phase. This was in accordance with the other studies [13,18].

In present study presence of lymphocytes in Hashimoto's thyroiditis was found to statistically significant (p value <0.05) over other oncocytic cell containing lesions. Ravinsky et al found lymphoid cells in all 6 oncocytic cell tumors diagnosed [30]. The population was sparse in 5 cases and abundant in the solitary case of papillary carcinoma associated with Hashimoto's thyroiditis. This was at variance with present study. Kini et al. could not detect any lymphocytes in their cases of Oncocytic cell neoplasms [18]. One case of Oncocytic cell neoplasm in the current study showed lymphocytes because there is a possibility of developing Oncocytic cell neoplasm in a pre-existing Hashimoto's thyroiditis. However, Gonzalez et al. could detect more than a few lymphocytes in 11% of Oncocytic cell tumours and 37% of non neoplastic lesions [11]. This was also in accordance with studies of Jayaram et al. [15].

In present study, out of 154 cases, 114 cases (74.03%) had none to scanty amount of colloid, 32 cases (20.78%) had moderate amount & 8 cases (5.19%) had abundant colloid of colloid. Majority of cases of colloid goitre had moderate to abundant colloid. Scanty colloid was seen in majority of cases of Hashimoto's thyroiditis (95.74%). Almost similar findings were observed in study of Misiakos et al. [21]. Presence of abundant colloid favors

the presence of non-neoplastic lesions. Kini et al commented on presence of scanty colloid in Oncocytic cell tumours, which was at variance with present study [18].

Out of 154 cases of Oncocytic cell containing lesions of thyroid, 124 cases (80.52%) had no fire flares & 30 cases (19.48%) had fire flares. These findings are in agreement with other studies [8, 18, 30]. Marginal vacuoles were seen only in non-neoplastic conditions i.e. in 23.26% cases of colloid goitre and 19.15% cases of Hashimoto's thyroiditis. One case of oncocytic variant of follicular neoplasm showed fire flares. Dhimes et al. reported the presence of 'Fire-flare' in 1/4th of the cases of follicular carcinoma [8].

Majority of cases showed no macrophages i.e. 65/154 (42.21%). Gonazalez et al. found absence of macrophages in 68% cases of Oncocytic cell tumors and 53% in non%neoplastic Oncocytic cell lesions. Out of 154 cases, 100 cases had plasma cells. Absence of plasma cells in neoplastic lesions is correlated with the same study [12].

Some problem areas could be identified in cytologic interpretation of FNAs containing Oncocytic cells [8,18,30]. The first one related to the overlap between Hashimoto's thyroiditis and oncocytic cell neoplasm/ follicular neoplasm with oncocytic cell change. Helpful features favouring a diagnosis of Hashimoto's thyroiditis were the presence of sheets of oncocytic cells (as opposed to follicular arrangement), paucity of singly dispersed oncocytic cells, presence of lymphoid follicles replete with germinal centre and presence of intraepithelial lymphocytes.

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